THE NEUROPSYCHOLOGY OF SELF-CONTROL AND RISK-TAKING: A FOCUS ON IMPULSIVE BEHAVIOUR

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Abstract

Impulsivity is a behaviour that has received several definitions. The most recent and widely accepted definition hypothesises that it is influenced by several separate behaviours including self-control, risk-taking and inhibitory control. Drug abusers and pathological gamblers have been found to exhibit less self-control than healthy controls which may be linked to their focus on short term, potentially damaging rewards, (e.g. positive effects of drug taking) rather than longer term rewards (e.g. better health) thus exacerbating their addiction. The links between risk-taking and addiction are not well understood as the few studies in this area have found contrasting results.

This project was designed to explore self-control and risk-taking in pathological gamblers and substance abusers. Non-pathological gamblers were also recruited to investigate behaviour in a non-addicted sample. Novel delay discounting and probability discounting tasks were created which directly measured choice behaviour requiring self-control (or tolerance of delay) or assessment of risk. The tasks were designed to provide realistic consequences for every choice thus aiming to mimic real-world decision-making situations. These tasks also explored discounting behaviour when given real versus hypothetical monetary reward. Previous research has found contrasting results as to whether giving real reward in a delay discounting task significantly alters choice behaviour.

In addition to analysis of discounting behaviour, imaging tasks were also created to explore brain areas involved in self-control, risk-taking, inhibitory control, and gambling urges. Differences in activity between the groups were assessed in order to discover any abnormalities.

The results from this project have uncovered new information concerning everyday decision-making, the behaviour and neurology of behaviours affecting impulsivity and addiction. The results from the project also have wide ramifications for the validity of methodologies utilised in decision-making research.

Contents

Declaration

No portion of the work referred to in this thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

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Copyright

Abbreviations

5-HIAA	5-hydroxyindoleacetic acid
5-HT	Serotonin
5,7-DHT	5,7-dihydroxytryptamine
ACC	Anterior cingulate cortex
ADHD	Attention-Deficit/Hyperactivity Disorder
AISS	Arnett Inventory of Sensation Seeking
ANX	Participant diagnosed with an anxiety disorder
ASPD	Anti-Social Personality Disorder
AUC	Area Under Curve
AUDIT	Alcohol Use Disorder Identification Test
BA	Brodmann Area
BIS	Barratt Impulsivity Scale
Ca^{2+}	Calcium
CGT	Cambridge Gambling Task
CO	Control
CS	Conditioned stimulus
d	Delay
DA	Dopamine
DLPFC	Dorsolateral prefrontal cortex
DSM-IV	Diagnostic and Statistical Manual (version IV)
EDT	Experiential Discounting Task
EIS	Empathy Impulsivity Sensation seeking questionnaire
EPQ	Eysenck Personality Questionnaire
*f*MRI	Functional Magnetic Resonance Imaging
GABA	Gamma-aminobutyric acid
GAD	Generalized Anxiety Disorder
H	Parameter from the Multiplicative Hyperbolic Model of Choice denoting how risk affects reinforcer value
IP	Indifference point

IQ	Intelligence Quotient
IVE	Impulsivity Venturesomeness Empathy questionnaire
k	Parameter from Mazur's (1987) equation denoting how delay affects reinforcer value
K	Parameter from the Multiplicative Hyperbolic Model of Choice denoting how delay affects reinforcer value
MA	Methamphetamine
MHMC	Multiplicative Hyperbolic Model of Choice
MINI	Miniature International Neuropsychiatric Interview
MPQ	Multi-dimensional Personality Questionnaire
NE	Norepinephrine (noradrenalin)
NAC	Nucleus accumbens
NPG	Non-pathological gambler
OFC	Orbitofrontal cortex
PG	Pathological gambler
q	Quantity (or magnitude)
Q	Parameter from the Multiplicative Hyperbolic Model of Choice denoting reward sensitivity
QT	Quick Test (measurement of IQ)
RAVLT	Rey Auditory Verbal Learning Test
SA	Substance abuser
SCR	Skin conductance response
SN	Subthalamic nucleus
STAI	State Trait Anxiety Inventory
SOGS	South Oaks Gambling Screen
SSRI	Selective Serotonin Reuptake Inhibitor
SSS	Sensation Seeking Scale
TCI	Temperament and Character Inventory
TPQ	Tri-dimensional Personality Questionnaire
US	Unconditioned stimulus
V	Value

VMPFC	Ventromedial prefrontal cortex
VTA	Ventral tegmental area
θ	Odds against winning (defined as [(1/probability)-1])

The Author

The author of this work obtained a BSc(HONS) in Psychology at the University of Essex in 2002. The dissertation for this degree focused upon the use of information in decision-making with an emphasis on heuristics utilised to rapidly make valid and useful decisions.

This was followed by attainment of an MSc in Psychological Research Methods at the University of Wales, Bangor. The thesis focused upon a brain area that was hypothesised to respond selectively to body posture, which was implicated in social cognition. *f*MRI was utilised to explore the possible functions of this area.

The work for this Ph.D. began in September 2003.

Introduction

1. Overview of this chapter

This chapter will provide the reader with an introduction to the research that has investigated self-control and risk-taking. Firstly, self-control and risk-taking will be defined and their relationships to impulsivity, a behaviour inherent within many psychiatric disorders, will be explained. The different methods of measuring self-control, risk-taking and impulsivity will be outlined including the validity of such measures. At this stage there will be a focus upon discounting tasks including their ability to directly measure self-control and risk-taking tendency within humans and non-humans. The Multiplicative Hyperbolic Model of Choice will then be introduced as a method of modelling and quantifying self-control and risk-taking tendency. We will highlight research that has used the Multiplicative Hyperbolic Model of Choice and discounting tasks to investigate altered levels of self-control and risk-taking in psychiatric populations focusing upon substance abusers and problem gamblers. Theories as to how these possible differences in self-control and risk-taking may underlie their disorder are then introduced. The later sections will explore brain areas that are involved in self-control and risk-taking and introduce research that suggests that substance abusers and pathological gamblers have altered levels of brain function compared to 'healthy' individuals and whether these underlie their behavioural abnormalities in self-control and risk-taking.

2. Self-control, risk-taking, and their relationships to impulsivity

Everyday, we make decisions that involve us evaluating risks or acting in a self-controlled (or not) manner. For example, we can wait until we have earned enough money to purchase an item or borrow the money or buy a cheaper item that we may not want as much but can afford. In another example, we can buy a cheaper item that may have an increased chance of breaking or buy a more expensive item that

will probably be hardier. These examples involve elements of delay and risk. A self-controlled individual would be more able to wait until they have enough money for the item that they want. A risk-taker may choose the cheaper item that may possibly have an increased chance of breaking down because they are more tolerant of the inherent risk and will have to spend less money. Self-control is defined as the ability to tolerate delay in order to maximise outcome. Risk-taking tendency is defined as the propensity to dismiss, or accept, high risk when making decisions which leads to the preference of risky outcomes over safer alternatives. It has been hypothesised that these two behaviours are involved in impulsive behaviour.

Within the last 5-7 years there has been increased attention given to research into impulsivity. One of the reasons for this increased attention is because altered levels of impulsivity have been recorded in many psychiatric disorders. It is hypothesised to be a highly important factor in these disorders. However, before we probe further into the research investigating impulsivity, it is important to understand what is meant by the term 'impulsivity'. Impulsivity has received a number of separate definitions. Some researchers use a specific definition, i.e. that impulsivity refers to the inability to tolerate delay and instead a preference to obtain immediate or relatively short-term gains, also known as inter-temporal choice (Ho et al, 1999). These researchers state that the opposite of 'impulsivity', i.e. the ability to tolerate delay to maximise reward, is self-control. More recently, the definition has altered to a more general status. This general definition has viewed impulsivity as a behaviour that is made up of sub-factors such as inability to tolerate delay (the opposite of self-control), increased risk-taking, propensity to act before fully realising the consequences of said act, increased reaction time and lack of regard for long-term consequences (Mobini et al, 2002; Moeller et al, 2001). Within the last few years, more researchers have begun to believe that these behaviours are not sub-factors within the behaviour known as 'impulsivity' but are instead separate behaviours in their own right that influence 'impulsivity' (Cardinal, 2006; Enticott and Ogloff, 2006; Grant, 2004).

The previous definitions have highlighted the negative aspects of impulsivity. However, in some cases and increase in impulsivity can be advantageous. Impulsivity has been split into functional and dysfunctional effects (Dickman, 1990). The dysfunctional effects involve the tendency to act without forethought in a situation where all alternatives must be fully evaluated. Functional impulsivity appears when one must make rapid decisions, probably within a situation where stopping to evaluate the alternatives would construe negative consequences. In these situations, an ability to rapidly make choices or judgements would be advantageous. Previous research has nearly always focused upon the dysfunctional aspects of impulsivity.

For this research, the author uses the definition that states that impulsivity is a general concept that is influenced by separate and identifiable behaviours. Self-control and tendency to take risks are two of a number of behaviours that make up impulsivity.

As mentioned at the start of this chapter, it has been discovered that altered levels of impulsivity have been found to be a factor in many psychiatric disorders defined by the DSM-IV. Elevated levels of impulsivity have been found in cases of personality disorder (Peluso et al, 2006), affective disorder, schizophrenia, and substance (alcohol or other drugs) use disorders (Chambers and Potenza, 2003). Furthermore, DSM-IV has defined a number of disorders as “Impulse-control disorders”, hypothesising that a critical factor in these disorders is a significant elevation of levels of impulsivity. Disorders within this section include pathological gambling (a disorder that is gaining increasing attention in research), kleptomania, pyromania, and Intermittent-Explosive Disorder (APA, 1994). Impulsivity has also been associated with conscious execution of risky behaviours (Ryb et al., 2006). Elevated levels of impulsivity and low risk perception have been measured in individuals who intentionally commit risky behaviours when driving (e.g. speeding for the thrill, low seatbelt use and driving while under the influence of alcohol).

3. Measures of impulsivity

3.1 What measures are available?

There are many tasks and questionnaires available that measure aspects of the concept impulsivity. The measurements can be split into two main types; self-report questionnaires and neuropsychological tasks. There are advantages and disadvantages to using each. These will be discussed later in this section. Firstly, the individual questionnaires and tasks will be highlighted. Due to the high number and variability of questionnaires and tasks that have been used to measure individual behaviours of impulsivity or the concept as a whole, only the most commonly used will be described.

There are a number of self-report questionnaires that are commonly used in research investigating impulsivity. Some split impulsivity into sub-factors whilst others try to measure impulsivity as a whole. The Barratt Impulsiveness Scale (BIS) is perhaps the most widely used (Barratt, 1994). The BIS is currently in its 11^{th} version (BIS-11). The BIS-11 splits impulsivity into three sub-factors. These are cognitive (ability to plan ahead), motor (physically acting without thinking) and non-planning (future time orientation) impulsivity. Another common impulsivity questionnaire is the Impulsivity Venturesomness Empathy questionnaire. This questionnaire does not split impulsivity onto separate factors. There are a number of variants of the IVE. These variants measure the three factors mentioned above but have different numbers of items due to continual upgrading of the questionnaire. Variants include the Empathy Impulsivity Sensation seeking questionnaire (EIS) (Eysenck et al., 1985) and the Impulsiveness questionnaire or I_7 (Eysenck et al, 1990). The Temperament and Character Inventory (TCI) is another common personality questionnaire. The TCI contains four sub-scales of temperament that manifest in early life. These are novelty-seeking, harm avoidance, reward dependence and persistence. The remaining three sub-scales are

measures of personality, which occur in mature development and influence personal and social effectiveness. These are self-directedness, co-operativeness and self-transendence. Impulsivity is a sub-factor within the novelty-seeking sub-scale. However, harm avoidance (which measures elements of risk-taking) and persistence (somewhat similar to self-control) could also be construed as factors affecting impulsivity.

There are a number of questionnaires (that have not been specifically designed to measure impulsivity) that include an impulsivity sub-scale, however, many of these rate impulsivity as a whole. The scales that measure impulsivity as a whole must be viewed with some caution, especially in light of contemporary research considering the fractionated nature of impulsivity.

The behavioural tasks that can be used are numerous. Delay discounting tasks measure the ability to tolerate delay. Some researchers define this behaviour as 'impulsivity' or use its antithesis, 'self-control'. Probability discounting tasks measure propensity to take risks. These two tasks will be described in more detail later in this chapter. Another commonly used task is the stop task. The stop task measures an individual's ability to inhibit an unwanted response that they are already preparing to produce. The common version of the stop task repeatedly provides a cue to which the participant must respond. Following some of these cues, another cue is quickly presented which indicates to the participant that he/she must withhold their normal response. For example, the cue 'X' is repeated to the participant and the participant must respond to this cue by making a key-press. However, after some of the 'X' cues, the letter 'A' is shown. When the letter 'A' is shown the participant must inhibit the key-press they were preparing to make and instead make no response. Research has shown that individuals who have high ratings of impulsivity have an increased inability to withhold their responses (Avila and Parcet, 2001; Leonard et al, 2004).

Another common neuropsychological task is the Iowa task. This task measures the ability of an individual to learn from past outcomes and incorporate this knowledge into a decision-making framework that will lead to higher overall gain (Bechara et al., 1994; Bechara et al., 1999). This type of learning is known as reversal learning. The participant is presented with four decks of cards that are face down. Each card contains a hypothetical monetary gain. Some cards contain hypothetical monetary losses. The aim of the participant is to make as much money as possible (all rewards are hypothetical). Two decks (decks A and B) have high rewards but also carry periodic high losses. The other two decks (decks C and D) have relatively low gains but small periodic losses. The decks are constructed in such a way that repeated choices of decks A or B will lead to a negative outcome, whereas choosing from decks C and D will lead to monetary gain. Impulsive individuals tend to consistently choose from decks A and B (Zermatten et al., 2005). Contrary to this, controls learn the contingencies of the decks and shift their choices to decks C and D as the task progresses. This shift is hypothesised to reflect their ability to look back and learn from past choices, tendency to execute actions with more forethought and shifting focus from the immediate higher gains offered from the risky decks and instead concentrating on long term gains.

The Iowa task is a decision-making task that provides a situation where the risk associated with each choice is unknown and ambiguous. Other tasks, such as the probability discounting task and Cambridge Gambling Task (CGT), present choices where the risks are explicitly defined.

3.2 Comparison between questionnaire methods and neuropsychological tasks

Impulsivity, as has been outlined earlier, is a seemingly complex process made up from many separate behaviours. As researchers, we have many tasks at our disposal to explore impulsivity. As has been outlined in the previous section, there are several self-report questionnaires that purport to measure impulsivity. In addition to

these questionnaires, there are behavioural tasks that are defined as measuring impulsivity, but to what extent do these questionnaires and behavioural tasks measure the same thing? The answer to this question is important. As researchers we must utilise measurement techniques that are well-defined and if we are comparing behaviour on a number of different measures, then must know how the relationship between these measures. We must also take care with definitions. Two tasks may purport to measure impulsivity; however, if they do not correlate then we must create separate terms to describe the differences.

Each type of measurement technique has its advantages and disadvantages. Self-report questionnaires can obtain data from a large number of people relatively quickly and inexpensively. If the questionnaires contain close-ended questions then rating scales can be utilised to quickly gain data. Questionnaires can also obtain data on a wide variety of topics. In contrast to this, behavioural tasks typically take longer to administer and usually only to one individual at a time. In addition, behavioural tasks usually only measure one aspect of behaviour. However, behavioural tasks are much less open to problematic biases such as demand characteristics, therefore providing higher validity of results.

Recently, there has been increased interest in whether self-report measures of impulsivity correlate with behavioural measures. This interest has coincided with the proposal that impulsivity is a multi-faceted concept. Therefore, there is a need to address specifically what aspects of impulsivity each test measures and to separately label each term, which has not occurred in impulsivity research so far.

A handful of studies have compared behavioural tasks measuring aspects of impulsivity to the Barratt Impulsiveness Scale (BIS). This is due to the questionaire's design of fractionating impulsivity into several sub-factors, thus allowing researchers to investigate relationships between differently defined aspects of impulsivity. Some correlation has been found between tests of behavioural inhibition and self-reported levels of impulsivity in healthy normals

screened for medical and psychiatric issues. In a study of 58 adults, performance on a go/no-go task was found to be positively correlated to motor (r = 0.34) and cognitive (r = 0.28) impulsivity from the BIS-10 (Keilp et al., 2005). Response errors on a stop task have been found to be positively correlated with levels of non-planning in 31 adults (r = .40) (Enticott et al., 2006) and, in a separate study recruiting 60 adults, positively correlated with motor impulsivity (r = 0.34) (Gorlyn et al., 2004). Both these studies utilised the BIS-11. Although it appears that tasks measuring levels of behavioural inhibition (which are linked to impulsivity) are correlated to subscales of the BIS measuring specific behaviours involved in impulsivity, care must be taken when drawing conclusions from these studies and two main points must be considered. Firstly, only two out of the four correlations taken from the three studies described match (i.e. behavioural inhibition positively correlating with motor impulsivity). Secondly, two of the three studies performed a high number of correlation analyses in addition to using an alpha level of 0.05. Gorlyn et al. performed 36 correlations and Keilp et al. performed 80. Therefore, a portion of these results could have occurred by chance alone.

Many studies that have used behavioural and questionnaire procedures have tested groups that express pathological or problem behaviour. Many of these studies have utilised a delay and probability discounting task. Some groups that have shown low self-control on a delay discounting task, such as smokers and individual with ASPD, also show high scores on self-report measures of impulsivity (Madden et al., 1997; Petry, 2002), although these studies did not test for any correlation between different measures. In a study that recruited 19 active, 12 abstinent alcoholics (lifetime history of alcohol dependence but who had not drunk in the 30 days prior to testing) and 15 non-substance using controls, scores on the Eysenck Impulsivity Questionnaire were significantly correlated to levels of impulsivity measured by a delay discounting task providing hypothetical monetary rewards (r = 0.35 when the delayed reward was $100 and r = 0.48 when the delayed reward was $1000). However, no correlation was found if the discounting task rewarded participants with hypothetical amounts of alcohol instead of money (Petry, 2001).

In another study, 20 regular smokers (who smoked more than 15 cigarettes per day) and 20 non-smoking controls performed a delay discounting task and probability discounting task in addition to completing several questionnaires measuring aspects of impulsivity. Impulsivity measured by the delay discounting was correlated to the attention subscale of the BIS-11 ($r = 0.32$) and disinhibition on the Sensation-Seeking Scale ($r = 0.35$). High risk-taking measured by the probability discounting rates was correlated with impulsivity on the Eysenck Personality Inventory ($r = 0.36$). However, taking into account that there were 84 correlations and there were, in total, 8 correlations (there were other correlations with non-impulsivity related measures) that met statistical significance ($p < .05$), strong conclusions cannot be inferred from these results as we would expect approximately this number of significant correlations by chance alone (Mitchell, 1999). The results from these studies suggest that data from both the delay and probability discounting tasks are not well correlated with data from impulsivity questionnaires. In addition, any correlations found depend on the type of reward offered in the discounting task.

One study compared scores on a wide range of behavioural tasks and self-report questionnaires (Reynolds et al., 2006). The participants were 99 university students screened for Axis I psychiatric disorders. The questionnaires used were the BIS-11, I_7 and the constraint (impulsivity) factor from the Multidimensional Personality Questionnaire (MPQ). The behavioural tasks employed were a stop task, go/no-go task, delay discounting task and the Balloon analogue risk task (a measure of risk-taking). Separate factors from the different questionnaires correlated highly; out of 45 correlations, 31 were significant. However, out of 40 correlations performed between the behavioural tasks and questionnaires, only 1 was significant (go/no-go score and cognitive impulsivity from the BIS-11) which, again, could have occurred by chance alone. This study indicates a poor correlation between behavioural and self-report measures of impulsivity.

The most compelling evidence for a link between the delay discounting task and a self-report measure of impulsivity is from a larger scale study of 606 healthy

individuals aged 30-54 years. In this study, non-planning on the BIS-10R was correlated to a measure of delay discounting (de Wit et al., 2007). It would make sense that non-planning, which is related to planning for future events and consequences would be, at least partly, related to ability to tolerate delay. None of the other scales from the BIS-10R correlated with rates of delay discounting.

This research has highlighted somewhat of a lack of correlation between behavioural discounting tasks and questionnaire methods. However, the de Wit et al. (2007) study does provide powerful evidence for some link between delay discounting and non-planning impulsiveness. However, in general, these studies have indicated that behavioural tasks and questionnaires that both reportedly measure impulsivity may, in fact, be measuring separate concepts. This leads to the conclusion that multiple techniques must be used in research exploring impulsivity. In addition, great care must be taken when considering the relationship between these techniques. For example, it is not safe to assume that if someone scores highly on a subscale of the BIS-11, they will show greater delay discounting. These studies also provide more evidence for the fractionated nature of impulsivity.

4. The use of discounting tasks in impulsivity research

4.1 Introduction to discounting tasks

The discounting tasks are used to measure specific and separate behaviours that are thought to influence impulsivity. Discounting tasks present participants with a choice between two alternatives which provides a trade-off situation where one can typically have a certain immediate reward or a larger reward that is delayed or uncertain. During the course of the task, one characteristic of the choice (e.g. the chances of receiving the reward) is systematically altered. The tasks measure how the subjective value given to a reward alters as a function of its characteristics, e.g. delay). The behaviours investigated by these tasks represent decision-making

processes that are used in day-to-day situations including financial and consumer behaviour. For example, consider the individual deciding whether to purchase a cheaper washing machine that has a higher risk of breaking down or paying more for a machine that carries less risk of breakdown. Reaction to delayed outcomes has also been use do explain 'deadline rush', where one places less emphasis on a deadline that is situated in the future, however, when that deadline approaches it becomes more salient (Konig and Kleinman, 2005). These tasks also have important applications in psychiatric populations, which will be described in a later section.

4.2 Assignment of values to rewards

The discounting tasks present the participant with choices between reinforcers with different characteristics. Several theories of decision making state that when facing a choice scenario, the decision maker will assign a personal value to each alternative. Subjective expected utility theory is perhaps the most widely used model to describe human economic choice behaviour. The theory puts forward a set of axioms which, if followed, leads to the caluculation of a numerical value describing the "utility" of stimulus or event to an agent (Hastie and Dawes, 2001; von Neumann & Morgenstern, 1947). Frequently, human decision-makers do not follow these axioms. Instead, decision-makers commonly incorporate personal judgements and biases into their choices. However, this can still lead to the creation of personal utilities (although currently not quantifiable utilities), which are affected by subjective constraints and biases. Prospect theory states that when faced with a potential gain or loss an individual will assign a personal value which defines how much the loss or gain means to the individual (Kahneman and Tversky, 1979). This personal value will alter dependent on a reference level, which will represent the individual's status quo. Value alters dependent on the nature of the outcome (e.g. is it a potential gain or loss?) and also on the risk involved. In the discounting tasks, an assumption is made that the participant will

assign a personal value to each alternative and that the alternative with the highest value will be chosen.

Rewarding stimuli frequently occur concurrently, rather than singularly at specific points in time. How does the receipt of concurrent rewards affect the values assigned individually to each stimulus? One theory suggested to describe how delayed rewards are valued over time, termed 'parallel discounting', states that the values of rewarding stimuli are created in parallel and are additive (Ainslie, 1975). This view suggests that each reward in a sequence is discounted by its delay and magnitude as normal and then the discounted values are summed to create a value relating to the entire sequence of rewards. Experimental evidence has been found to support the existence of parallel discounting in humans (Kirby, 2006). However, within this study, there was a small subset of participants who discounted rewards in a way not predicted by parallel discounting. Instead this group valued the sequences less than the sums of their individual rewards.

4.3 Discounting tasks: What do they measure?

The most commonly used discounting task is the delay discounting task. The delay discounting task measures the ability to be self-controlled, i.e. ability to tolerate delay to maximise gain. The task presents the participant with 2 alternatives (called alternatives A and B). Each alternative carries a monetary reward and an amount of time that the participant must wait in order to receive that reward. In most research, the delays and rewards are hypothetical. This allows experimenters to test decision making behaviour with high monetary rewards and extremely long delays, e.g. $200 after 1 month vs. $40,000 after 12 years (Myerson et al, 2003). In a typical delay discounting task, A will have a smaller reward than B, but will also have a shorter delay period. The delay of B is then systematically altered in subsequent choices. This creates a trade-off situation where one must make the decision to gain a sooner small reward or larger reward that is delayed. Participants indicate their

preference by choosing one of the alternatives. In this way, we can measure where the participant's preference lies.

The probability discounting task measures propensity to take risk. This is another behaviour thought to be involved in impulsivity. The nature of the probability discounting task is similar to the delay discounting task, except that all rewards are given immediately. Instead, each of the two alternatives carries a probability of receiving that reinforcer (Estle et al, 2006; Rachlin et al., 1991; Reynolds et al, 2003). In this task, alternative A (the smaller reward) has a relatively larger probability of winning whereas B has a lower probability. This creates the trade-off situation.

There are some variants of discounting tasks. Some researchers have utilised a procedure that presents participants with a sequence of choices in which a characteristic (e.g. amount attached to one alternative) is increased linearly, followed by a linear decrease (e.g. Green et al, 1999). This procedure is the same as the 'method of limits' used in psychophysical research. Another procedure presents the participant with a fixed number of choices that are randomly or pseudo-randomly given. More data is collected on the participant's choice behaviour in this procedure compared to the linear procedure. However, it may also take longer. A development of this procedure has led to the adjusting procedure (Green et al., 2005). This utilises a staircase method in which the variable (e.g. delay) is altered one step at a time (e.g. in 1 second intervals). When the participant expresses a preference switch the variable swaps its direction of change (i.e. now decreasing in 1 seconds intervals). When the participant expresses another preference switch the variable alters direction again, and so on. In this way, the task focuses on the area around the participant's indifference point. This has the advantage of having choices that concentrated on the area of the preference switch.

The critical measurement of these tasks is the 'indifference point' or IP. The IP is defined as the point at which the participant assigns the same value to each

alternative (i.e. is indifferent to either alternative). For example, if the delay attached to A is 5 seconds, a participant may prefer A when B equals 10 or more seconds and prefer B when the delay of B is less than 10 seconds. Therefore, the indifference point is 10 seconds. In the delay discounting task, an individual who has low levels of self-control would tend to choose the sooner reward more often and therefore have a lower IP compared to someone who exhibits high self-control. In the probability discounting task, an individual who was a high risk taker would have a lower IP because they would prefer to take the higher risk for the possibility of larger gains. It is important to note that there are several terms used to describe behaviour on the delay discounting task. These are dependent on the researcher(s). If an individual has low IPs, this individual can be called 'impulsive' or can be said to exhibit high levels of '*impulsive choice'*. An individual with high IPs can be said to be relatively self-controlled.

When the indifference points are plotted, it is possible to show how much an individual devalues, or discounts the value of, a reinforcer as a function of its delay or risk; hence the name 'discounting' task.

Another analytical method for utilisation with discounting tasks is Area Under Curve (AUC) analysis (Myerson et al, 2001). This method calculates the trapezoidal area under each participant's plot of their indifference points. For example, in a delay discounting task an individual who showed high tolerance for delay would have higher IPs and, as a result, a larger AUC compared to a less self-controlled individual. This method is deemed to have some advantages over other methodologies of analysis. This method creates normally distributed data. Other methodologies, which will be discussed in the following section, use equational methods of analysis that can lead to highly skewed data. A limitation of AUC is that it does not take into account the shape of the curve while other methods do so. Different plot shapes could lead to the same AUC value. Taking the advantages and disadvantages, it can be considered a powerful tool when used in addition to other methods.

4.4 Hyperbolic vs. exponential discounting

The discounting tasks measure the subjective value that an individual assigns to a reinforcer when it carries a delay or risk of non-occurrence. It is, therefore, possible to create a graph that shows how the personal value assigned to a reward devalues as a function of its delay or risk. There have been two main theories regarding how individuals discount reward value as a function of its delay or risk. Some theorists hypothesised that individuals discounted reinforcers in an exponential manner. This method of discounting was considered 'rational' and aberrations of exponential discounting were thought to be indicative of irrational decision-making. More modern researchers have suggested that reinforcers are discounted in a hyperbolic fashion. Mostly, these theories have focused upon delay discounting although some studies have applied these theories to probability discounting (e.g. Green and Myerson, 2004).

The exponential discounting theory states that the subjective value assigned to a reward decreases exponentially with increases in delay or risk (Myerson and Green, 1995). The equation for this theory is thus:

$$V = Ae^{-kD}$$

Where V is the value assigned to the reinforcer, and A is the amount of reward delivered after delay D. k is the discounting parameter that describes how the individual discounts the value, V, of the delayed reward.

Another theory states that the form of the discount function is hyperbolic. Hyperbolic discounting states that, as delay increases, the reward is discounted steeply. However, the curve then starts to flatten so that increases in delay will lead to progressively smaller increases in discounting (Mazur, 1987). The equation for the hyperbolic discounting of delayed rewards is shown below:

$V = A/(1 + kD)$

The parameters in this equation are the same as for the equation describing the exponential theory.

The vast majority of studies investigating reward discounting behaviour which have compared the exponential and hyperbolic theories have found that hyperbolic model accounted for a significantly greater proportion of variance in discounting behaviour compared to the exponential theory (Hayden et al., 2007; Rachlin et al., 1991; Yi et al., 2006).

Some researchers have added a power function to Mazur's equation (Green and Myerson, 2004; Green, Fry & Myerson, 1994) to give the equation below:

$V = A/(1 + kD)^s$

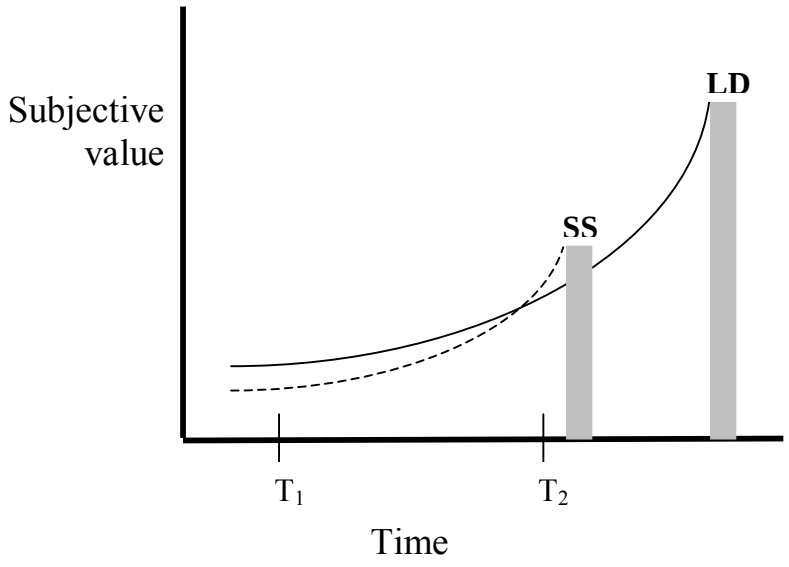
This provides an extra dimension that represents the nonlinear scaling of amount or time. When compared to the traditional hyperbolic model using statistical techniques, the addition of the exponent causes the model to account for a significantly greater amount of variance in human delay discounting behaviour (Green et al., 1999; Ostazewski et al., 1998). However, the addition of a power function would be expected to account for more variance in behaviour.

4.5 Preference reversals

Preference reversals are a decision-making bias that occurs when preference switches from one reward to the other after an equal delay being added to each alternative. For example, if you are given the choice between £100 now and £120 in a month, you may choose £100 now. However, if a year delay is added to each alternative so that the choice is now £100 in a year and £120 in a year and one

month, then your choice may now be to take the £120. This is due to the steep discounting of outcomes that have short-term delays but relatively shallower discounting of outcomes that are situated further into the future. Figure 1 below shows how preference reversal may occur.

Figure 1: graphical display of a preference reversal



Considering the graph above, at time point T_1 the individual prefers the larger delayed (LD) reward. However, at T_2 the individual now places more value on the smaller sooner (SS) reward. Preference reversals occur because the hyperbolic law of discounting states that as the delay associated with a reward decreases, the subjective value given to that reward will increase in a hyperbolic manner. When the smaller reward becomes closer in time, the reward will become more salient and appealing and its subjective value will increase more than that of the larger, delayed, reward (Green and Myerson, 2004). This leads to the value of the smaller reward overtaking that given to the larger reward.

This theory can be readily accounted for by the hyperbolic theory of discounting. However, it violates the assumption of the exponential theory which states that if alternative A is preferred over alternative B, then A will always be preferred over B. However, it has been suggested that instead of one *k* value that describes the discounting rates of all rewards, there may be one *k* for the small reward and one *k* for the large reward (Green and Myerson, 2004). This would lead to two lines being plotted on our graphs describing subjective value. These lines would then be free to cross, indicating preference reversal.

Before we take sides as to which theory is better we must inquire as to how common preference reversals are in discounting research. A low number of preference reversals may make this argument moot as it could be argued that they are biases shown only by a minority of individuals. When we check how common this effect is, we actually find that preference reversals have been reliably observed in human (Green, Fristoe, and Myerson, 1994) and non-human (Green et al., 1981) studies. One study has argued that hyperbolic discounting is a bias shown by a minority of participants and that not enough participants have shown preference reversals for hyperbolic discounting to be taken as the correct model to use (Sopher and Sheth, 2005). These researchers state that the exponential theory provides a better fit for the model and preference reversals reflect a decision making bias exhibited by a minority of participants. However, these researchers did not provide an improved exponential model that could explain preference reversals and fit participants discounting rates more than the hyperbolic model. Currently, most researchers agree that, so far, the hyperbolic theory has provided the best explanation of reward discounting behaviour.

4.6 The relationship of discounting behaviour to personality and social factors

In addition to levels of impulsivity, are there any other personality factors that influence discounting behaviour? Valid hypotheses could, certainly, be drawn up

regarding factors such as IQ, socio-economic status, age etc. But is there evidence that such factors play a role in discounting?

Kirby and Petry (2004) presented a delay discounting task to current or previous heroin abusers, cocaine abusers, alcohol abusers and healthy controls. The Shipley Institute of Living Scale was used to measure IQ. Heroin abusers scored significantly lower that alcoholics and controls and showed significantly faster discounting of delayed rewards. Cocaine abusers scored lower on IQ (but not significantly so, p=.09) and discounted delayed rewards at a faster rate compared to controls. However, when the scores from all four groups were taken, IQ was not correlated to delay discounting rates (Kirby and Petry, 2004). Other studies have also found no evidence for links between IQ and discounting behaviour. Compared to controls, faster discounting of delayed rewards but no difference in IQ scores were found in opioid-dependent patients (Madden et al, 1997), alcoholics (Petry et al, 2001) and substance abusers with and without ASPD (Petry, 2002). However, a recent study found a negative correlation between IQ (as measured by the Wechsler Abbreviated Scale of Quotient) and a measure of delay discounting (de Wit et al., 2007). This study had advantages over the previous research due to the sample size (303 men and 303 women) and health of the participants (no previous history of severe illness, neurological disorder, or psychosis plus no use of medications that may have altered their responses). This study provides powerful evidence for a relationship between IQ and delay discounting behaviour. This disagreement in findings may be due to the samples recruited. In the studies that found no correlation, substance misusing individuals were recruited whilst the de Wit et al. study recruited only healthy individuals screened for medical and psychiatric issues. In the substance abusing samples, IQ may have a lesser role in influencing delay discounting behaviour compared to variables related to substance abuse.

Age appears to have a significant role in discounting rate. Young children and adolescents commonly appear to act in a more impulsive fashion and engage in more risky acts compared to adults. Most research has recruited groups with

matched ages, therefore avoiding this possible confounding effect. One study gave a delay discounting task to groups of individuals of different ages (Green et al, 1994). The groups were younger children (mean age of 12.1 years), university students (mean age of 20.3 years) and older adults (mean age of 67.9 years). *k* was found to lowest in older adults, followed by students with younger children having the highest rates. The equation describing hyperbolic discounting, [$V = A/(1 + kD)^s$], was found to accurately describe the discounting of delayed rewards in all samples. Increasing age was found to be linked to decreases in the discount parameter *k*. Notably, in 12 year-old children, the discount curve "bottomed out" when the delay was higher than 5 years, whereas in the young and older adults decreases in value of the delayed rewards extended to 10 years and beyond. This may be due to lack of experience of extensive delays in young children, manifesting itself as an increase in the discounting of delayed rewards.

Learning and memory may affect discounting behaviour. Methamphetamine (MA) abusers showed lower scores on learning ability in the Rey Auditory Verbal Learning Test (RAVLT)[1] and increased delay discounting. However, learning ability was not associated with delay discounting rates once the correlation controlled for years in education (Hoffman et al, 2005). Some researchers have suggested that increased working memory load leads to greater delay discounting (Hinson et al., 2003). Taking this hypothesis, it would follow that individuals who show a high degree of delay discounting may have decreased working memory power. This low power would lead to decreased cognitive ability to deal with current problems and situations and impaired learning ability. However, low working memory function would, arguably, also affect short term memory. In the Hoffman et al. study, the MA-dependent group showed no memory impairments. Therefore, working memory capacity cannot wholly explain these findings. In addition, the theory by Hinson et al. has been criticised (Franco-Watkins et al., 2006). Franco-Watkins et al. suggested that, in a subset of participants, increased

[1] The RAVLT presents a list of 15 words to learn. Following the learning phase a memory test is given five times to assess learning. A distracter list is also given to test for interference on learning and memory (Rey, 1964).

working memory load did not cause a bias in delay discounting behaviour leading to an increase in impulsivity but rather that increased working memory load caused a more severe decision-making impairment in which responses were random, i.e. no decision-making heuristic was utilised (other than random choice). The effect from this subset of participants was powerful enough to lead to the original conclusions by Hinson et al.

Socio-economic factors may also have effects on discounting. Delay discounting rates have been found to be inversely related to level of education in smokers (Jaroni et al, 2004). However, despite differences in delay discounting, no differences have been found in educational level between healthy controls and alcoholics (Petry, 2001), opioid-dependent individuals (Madden et al, 1997), methamphetamine-dependent individuals (Hoffman et al, 2005), heroin or cocaine or alcohol abusers (Kirby and Petry, 2004) individuals with ASPD (Petry, 2002) and substance abusers with or without pathological gambling (Petry and Casarella, 1999) despite the increased delay discounting rates measured in these groups.

4.7 Effect of real versus hypothetical rewards on discounting

Nearly all previous research into discounting has focused on the use of hypothetical rewards. These types of rewards have been used due to methodological constraints and ethical reasons. For example, it is common in delay discounting tasks to be presented with large scale monetary rewards given after large scale delays (e.g. $50,000 after a delay of 25 years). Some other studies have investigated the discounting of drug rewards by offering hypothetical monetary rewards and equivalent hypothetical magnitudes of a drug of abuse such as heroin (Madden et al., 1997). The use of hypothetical monetary rewards has attracted criticism concerning its real world validity. It has been argued that individuals would respond in a different way when faced with hypothetical reinforcers compared to reinforcers that are actually received. This may be especially true when testing

psychiatric populations (e.g. pathological gamblers) who may be hyper-sensitive to rewards.

Research that has compared discounting of real vs. hypothetical rewards has found mixed results. Studies that have found no performance differences when individuals are given delay discounting tasks that carry real vs. hypothetical rewards (Madden et al, 2003; Madden et al, 2004; Lagorio and Madden, 2005) have contained methodological flaws. In many tasks each outcome did not provide a reward but instead employed a lottery where only the outcome of one choice was given, thus not presenting a true real reward task where every outcome was rewarded. Another study gave real outcomes on every trial but participants had to spend their rewards in a 'store' run by the experimenters that contained sweet foods and soft drinks. Therefore, this task compared hypothetical monetary rewards with real consumable rewards which cannot be directly compared.

One study provided smokers and non-smokers with the "Experiential Discounting Task" (EDT) which provided real rewards (Reynolds, 2006). One alternative gave a reward of $0.30 with a delay of 0, 15, 30 or 60 seconds and a 35% chance of receiving the reward. The second alternative had an adjusting amount of money that was certain and given immediately. This was done in order to measure the subjective value of the $0.30 alternative. Money was provided after each trial using a coin dispenser. Paper versions of hypothetical delay and probability discounting tasks were also given. Responses from the EDT and delay discounting task were correlated. Reponses from the the EDT and probability discounting task were not correlated. Due to the authors not reporting the data from these correlations, the strength of the correlation between the EDT and delay discounting task cannot be provided. In addition, no statistical procedure was used to report the scale of any differences between the tasks. Significant correlation between the EDT and delay task denotes that the directions of the results are similar, however, it may have been the case that indifference points were statistically different. Although this study

does provide some evidence that real and hypothetical delay discounting tasks give similar results, there is a lack of statistical evidence.

One study compared behaviour on three different types of delay discounting tasks (Lane et al., 2003). A "contingent" task was used that gave small real rewards ($0.01-0$0.15) and relatively smaller delays (5-90 seconds) which were experienced. In this task the smaller alternative was given immediately. Participants were significantly more self-controlled on this task compared to a "compressed hypothetical" task which was similar to the contingent task but did not gave real rewards, and a standard hypothetical delay discounting task. However, the compressed hypothetical task did not utilise real delays. Therefore, behaviour may have altered due to the withdrawal of real rewards and real delays.

These few studies suggest that the relationship between the discounting of delayed rewards remains unclear. Although evidence does suggest that discounting behaviour when faced with real and hypothetical monetary rewards may be similar, when individuals are continually rewarded it appears that behaviour changes. It is also unknown as to the possible differences between discounting of real and hypothetical probabilistic rewards. If we consider theories describing the attribution of subjective values to probabilistic reward (e.g. Kahneman and Tversky, 1979) the hypothesis could be generated that the presentation of probabilistic real rewards would promote risk-averse decision making compared to probabilistic hypothetical rewards.

4.8 The relationship between delay and probability discounting

In more recent discounting literature the question has been asked as to whether delay and probability discounting are driven by a singular behaviour. Fairly early in the research on discounting it was found that a hyperbolic function accounted for the highest amount of variance in both delay and probability discounting behaviour

(Rachlin et al., 1991). This was not evidence for a singular process involved in reward discounting behaviour but it did provide a chance for the question to be asked.

There are two views on the singular process account of delay and probability discounting behaviour (Green and Myerson, 2004). One side argues that probabilistic rewards are actually viewed by an organism as delayed rewards (Rachlin et al., 1991). For example, consider a reward that has a 50% chance of delivery. If this reward is repeatedly chosen by an organism, it has a virtually guaranteed payoff, albeit delayed. Therefore, this organism views probabilistic rewards as certain rewards, but delayed over a certain period of time. Probabilistic rewards will, therefore, be discounted in the same way as delayed rewards. This viewpoint has recently received support from a study of risk behaviour in two rhesus macaques (Hayden and Platt, 2007). The rhesus macaques were given a probability discounting task in which one alternative gave a certain 150 millisecond access to water via a solenoid valve. The second, risky, option had a 50% chance of giving 250 ms access to water and a 50% chance of giving only 50 ms access. When the inter-trial interval was 0 seconds, macaques preferred the risky option approximately 70% of the time. As the inter-trial interval increased, preference for the risky option decreased significantly despite the risk being held constant. If we consider that the delay was unavoidable and that the macaques were not waiting for any reward, inter-trial intervals added to the decrease in value of the risky alternative despite the risk being kept constant. This suggests that the delay is the major factor in reward discounting. A hyperbolic model fit the discounting behaviour very well ($r^2 = 0.86$) and better than an exponential model ($r^2 = 0.73$).

The second viewpoint argues that individuals see probability discounting as the central process. In the real world, the further a reward is delayed in time until it is received, the higher the risk that it will never be received (Myerson et al, 1995). Patak and Reynolds (2006) recruited 24 adolescent individuals aged 14-16 years and gave them a paper delay discounting task. Participants were asked to rate their

certainty of receiving any delayed rewards they had chosen. As the delay until the reward was available increased, so did the uncertainty of participants that they would receive the reward. In addition, individuals who discounted delayed rewards at a higher rate also reported greater uncertainty of receiving the reward (Patak and Reynolds, 2006). This indicates that delayed rewards may involve elements of probability discounting.

Other studies have found no similarities between probability and delay discounting behaviour. If there was a singular process underlying both discounting behaviours, we would expect these behaviours to be correlated to some degree. However, no correlation between delay and probability discounting has been found in normal samples (Adriani and Laviola, 2006; Green et al., 1999; Myerson et al., 2003) in addition to smoking and non-smoking samples (Reynolds et al, 2004). Delay and probability also seem to be correlated with different behaviours. Delay discounting has been linked to impulsivity while probability discounting has been associated with sensation seeking (Ostaszewski, 1997). If a single process was responsible for these behaviours then they would both correlate with the same behaviours (barring any confounding effects). Finally, neurobiological studies in rats have found dissociable circuits within the brain appear to underlie delay and probability discounting (Acheson et al., 2006; Mobini et al, 2000). A single process account would advocate that neurobiological alterations would probably affect both delay and probability discounting.

Although some evidence suggests that a single process accounts for both delay and probability discounting behaviour the majority of studies have found no direct links. Although further research is needed to settle this debate, after reviewing the literature, we must steer more towards the view that delay and probability discounting are separate behaviours.

5. The Multiplicative Hyperbolic Model of Choice

5.1 Introduction to the model

As has been previously outlined, impulsivity is a highly important factor in many psychiatric disorders. We have also outlined the definitions of impulsivity, with a focus on the hypothesis that impulsivity is a concept that is made up of separate behaviours. The Multiplicative Hyperbolic Model of Choice (hereafter named the MHMC) was originally designed to explore 'impulsive choice' (Ho et al, 1999). Ho et al. defined impulsive choice as the selection of short-term small gains over larger gains that are delayed, or selection of larger, delayed, losses over smaller, but immediate, losses. The model also brought together other separate mathematical principals theorised to be involved in the creation of subjective reinforcer value. The model assumed that reinforcer value is calculated by the association of these principles. The MHMC stated that the value ascribed to a reinforcer by an individual depends on three characteristics of the reinforcer. Each characteristic was independently discounted in a hyperbolic fashion. The rate of discounting altered between individuals depending on each person's reaction to the characteristics. For example, one person may place a higher value on risky, high paying alternatives compared to another person who may prefer the smaller, but ultimately safer alternative. For each alternative, the reinforcer characteristics were combined multiplicatively to create a value. In a choice situation involving more than one alternative, the alternative with the highest value is chosen. This chapter will explain the individual parts of the MHMC and will then describe how these parts are combined in order to calculate a subjective value for a reinforcer.

5.2 Reinforcer value is dependent on its delay until receipt

Within the framework of the MHMC, there are three characteristics that affect the reinforcer value. Firstly, the effect of delay upon the reinforcer will be described. The value of a reinforcer decreases in a negative hyperbolic trend as delay is

introduced. Equation (1) describes how the value of a reinforcer is altered as a function of delay when the reinforcer has a unit probability of being given.

$$V = 1/(1+K.d) \quad (1)$$

Where V is the value given to the reinforcer, d is the delay until receipt of the reinforcer, and K is a behavioural parameter that describes how an individual reacts to delay. In other words, it describes the individual's self control (the opposite of which is impulsiveness). The equation was proposed by Mazur (1987).

This equation states that if an individual has a high value of K, then the resulting overall reinforcer value of a delayed reinforcer would be less than the value calculated by someone who had a low value of K. Please note that K in this equation is the same as the lower-case k, used in the equations in the previous chapter describing exponential and hyperbolic discounting.

5.3 Reinforcer value is dependent upon its odds against receipt

The discounting of probabilistic rewards follows a negative hyperbolic trend. Equation (2) describes how the value of a reinforcer is altered as a function of the odds against winning. Odds against values are calculated using the equation $[(1/p)-1]$ where p is the probability of receiving the reinforcer. In this situation the reinforcer involves no delay until receipt.

$$V = 1/(1+H.\theta) \quad (2)$$

Where V is the value given to the reinforcer, θ is the odds against winning the reinforcer, and H is a behavioural parameter that describes how an individual reacts to the odds against winning. In other words, it describes the individual's propensity for risk-taking. Rachlin et al. (Rachlin et al, 1986, 1991) provided experimental evidence for this principle.

If an individual exhibits a high *H* then the overall value given to a probabilistic reinforcer will be lower than the value calculated by an individual with a low *H*. This principle can, therefore, be used to measure an individual's propensity to choose risky outcomes.

5.4 Reinforcer value is dependent upon its magnitude

The magnitude of a reward is discounted according to a positive hyperbolic form. Equation (3) describes the value given to a reinforcer as a function of its magnitude. The reinforcer has unit probability of being given and involves no delay until receipt.

$$V = 1/(1+Q/q) \quad (3)$$

Where V is the value given to a reinforcer, q is the quantity or magnitude of the reinforcer, and Q is a behavioural parameter that describes how an individual reacts to reinforcer magnitude. This principle was first proposed by Hernstein (1970) and has received experimental verification from human (Bradshaw and Szabadi, 1988; Kollins et al, 1997) and animal (Bradshaw and Szabadi, 1989; Heyman and Monaghan, 1987) studies.

An increase in Q^+ would lead to the decrease in the rewarding effect of a reinforcer. Individuals with frontal lobe damage (Bechara et al., 1999, 2001) and certain psychiatric disorders (Chambers and Potenza, 2003) have shown an increase in impulsive behaviour. According to this model, this could be due to an increase in K^+ (a decrease in delay tolerance) or an increase in Q^+ (an increase in the sensitivity between the reinforcer magnitudes). A decrease in Q^+ would lead to the decrease in the subjective value of the difference between the two reward magnitudes, therefore leading the individual to prefer not to wait long delays to

obtain rewards. However, for reasons that will be explained in the next section, it is possible to separate K^+ and Q^+.

5.5 How these three principles are conjoined to calculate reinforcer value

The MHMC proposes that the overall value given to a positive reinforcer is jointly determined by combining the three hyperbolic equations multiplicatively. This equation can be shown thus,

$$(4) \qquad V^+ = \frac{1}{(1+Q^+/q)} \cdot \frac{1}{(1+K^+.d)} \cdot \frac{1}{(1+H^+.\theta)}$$

Therefore, the parameter values that describe behavioural processes will significantly affect the final value that is calculated. For example, if we imagine an individual who has a Q^+ of 1, an H^+ of 1, and has a K^+ of 5 (so could be described as delay aversive but low risk-taking), K^+ will have more of an effect on the creation of a subjective value compared to the other parameters.

An equivalent equation is used to calculate value for a reinforcer with aversive outcomes. This equation is the same as equation (4) but all values are substituted for their negative counterparts. For example, V^+ and K^+ are now written as V^- and K^- respectively. If a choice entails both positive and aversive events then the total value is calculated by $V^{total} = V^+ - V^-$.

5.6 Calculation of parameter values

In a discounting task, the participant is typically presented with a series of choices between two alternatives with fixed salient features. One feature is then altered. For example, in a delay discounting task, the magnitude of alternative A, magnitude of

alternative B, and the delay until receipt of alternative A may be fixed while the delay of alternative B is varied. In this way, the preferences of the participant can be investigated. The participant is repeatedly given these types of choices (with differing delays of alternative B) until he/she regards the two alternatives as equal in value (i.e. when $V_A = V_B$). This is termed "the indifference point" or IP. These IPs can be used to define the value the individual places on the delayed reward, and can thus probe their tolerance of delay. For example, an individual who has high impulsiveness will be intolerant to delay and so will have lower IPs in a delay discounting task compared to someone who has higher IPs and shows higher levels of self-control. In a delay discounting task where the magnitudes of alternative A and alternative B, and the delay until receipt of alternative A are fixed, at indifference, the equation can be expanded thus,

$$(5) \qquad 1/(1+Q/q_A) \,.\, 1/(1+K.d_A) \;=\; 1/(1+Q/q_B) \,.\, 1/(1+K.d_B)$$

Where q_A and q_B are the magnitudes of alternative A and B respectively and d_A and d_B are the delays of alternative A and B respectively. This equation can be solved for d_B thus,

$$(6) \qquad d_B = \frac{1}{K^+}\left[\frac{\frac{1}{1+Q^+/q_B} - \frac{1}{1+Q^+/q_A}}{\frac{1}{1+Q^+/q_A}}\right] + d_A\left[\frac{1+Q^+/q_A}{1+Q^+/q_B}\right]$$

Equation (6) shows that there is a linear relationship between d_B (which is equal to the indifference point) and d_A. If a participant's IPs are plotted over a range of d_A values then a linear regression can be calculated. Equation (6) states that Q^+ features in both the slope and the intercept whilst K^+ features only in the intercept of the linear regression. This means that a change in the slope is tantamount to a

change in Q^+. K^+ can be calculated from the linear regression using the following equation [slope-1/intercept]. Calculating Q^+ is not as simple due to the cumbersome slope and intercept terms. In a probability discounting task, where had a similar methodology to the delay task described above was used, where the odds against receipt of alternative B were altered, the linear equation derived from the MHMC would appear the same as equation (6) but H^+ would be substituted for all instance of K^+. The equation for the calculation of H^+ would be [slope-1/intercept]. This follows from the previous section where it was mentioned that K^+ and Q^+ could be separated.

5.7 How useful are the parameter values laid out by this model?

The parameter values represent individual behaviours inherent within the individual. When we consider investigating the concept of impulsivity, we have here a model that can describe two important behaviours thought to influence that concept, namely self-control (delay discounting) and risk-taking (probability discounting). Therefore, this model may be of high value if we want to explore these two behaviours that are involved in impulsivity.

The parameter values laid out by the MHMC are hypothesized to be fairly stable properties of an individual. Parameter values will alter somewhat dependent on such factors as mood. For example, if we are late for an appointment and are stressed, our tolerance to delay would probably decrease therefore K^+ would increase. Ho et al. suggests that the parameter values could be altered due to pharmacological intervention. This would allow research to explore how such intervention would alter the behaviours set out by this model.

As described in section 4.6, the MHMC allows experimenters to calculate numerical values of K^+ and H^+, and obtain an estimation of Q^+. This allows researchers to compare levels of self-control and risk-taking between and within groups. This would allow the comparison of different samples (e.g. a typically

impulsive, substance addicted sample versus a non-addicted sample). The model could also be utilized to compare the before and after effects of a pharmacological or psychological intervention.

In summary, this model is useful to researchers wanting to explore impulsivity because it provides a method of describing and calculating values of self-control and risk-taking tendency, two behaviours thought to strongly influence impulsiveness.

5.8 How does the use of discounting tasks tie in with the MHMC

The discounting tasks that were described in chapter 3 can be used in conjunction with the MHMC. The discounting tasks use a methodology that allows the calculation of indifference points. The MHMC then uses indifference point methodology in order to calculate the parameter values. Therefore, by using the direct measure of the discounting tasks (the IPs), we can indirectly calculate numerical values of self-control and risk-taking tendency.

5.9 Research that has utilized the MHMC

The MHMC has been used to reliably compare delay and probabilistic discounting rates in rats receiving lesions to specific brain areas. These studies have compared the slopes and intercepts plotted from averaged IPs. If a lesioned rat shows a difference in the slope then this shows that Q^+, or sensitivity to reward magnitude has been affected. K^+ can then be compared by using the appropriate equation. Rats who received injections of 5,7-dihydroxytryptamine in order to destroy their ascending 5-HT pathways showed decreased tolerance to delayed rewards compared to sham lesioned rats (Mobini et al, 2000[a]). This suggests that the 5-HT system may play an important role in rates of delay discounting. Destruction of the ascending 5-HT system did not affect sensitivity to probabilistic rewards compared to sensitivity to delayed rewards (Mobini et al, 2000[b]). Lesioning of the

orbitofrontal cortex (OFC) in rats increased rates of delay and probability discounting (Kheramin et al, 2003) suggesting that the OFC plays a critical role in an individual's sensitivity to delayed and probabilistic rewards.

6. Impulsivity and reinforcer discounting in clinical populations

6.1 Impulsivity in psychiatric disorders

Previous research has provided a large body of evidence for increased levels of impulsivity in many psychiatric disorders (Evenden, 1999; Moeller et al., 2001) including bipolar disorder (Bornovalova et al., 2005; Peluso et al., 2006; Swann et al, 2001; Wilson et al., 2006), suicide and para-suicide (Blaszczynski et al, 1997; Roy, 2006; Wilson et al., 2006), Attention-Deficit Hyperactivity disorder (Cardinal et al, 2004), drug abuse (Allen et al., 1998; Kirby and Petry, 2004; Madden et al, 1997; Reynolds, 2006), alcohol abuse (Grano et al., 2004; Petry, 2001), pathological gambling (Reynolds, 2006), and Anti-Social Personality Disorder (Petry, 2002) in addition to potentially problematic non-psychiatric behaviours such as smoking (Grano et al., 2004; Mitchell et al., 2004; Reynolds, 2006; Reynolds et al., 2004).This increased level of impulsivity is hypothesised to be a major characteristic within these conditions. However, it is unknown as to whether elevated levels of impulsivity, perhaps amongst other symptoms, lead to the onset of the disorder or whether this relationship is, in fact, the reverse. This chapter will focus on impulsivity in two commonly reported addictive disorders; substance abuse and pathological gambling. Impulsivity and reinforcer discounting in anxiety disorders will also be outlined. Anxiety disorders may also be influenced by abnormal levels of self-control and risk-taking. For example, extreme levels of risk-aversion may cause hyper-sensitivity to potential risks causing high anxiety in response to stimuli which carry low threats (e.g. social situations).

6.2 Impulsivity and reinforcer discounting in substance users

Substance abuse can lead to many problematic outcomes including addiction in addition to financial and social problems. Prevalence of the substance abuse (other than alcohol) by adults (in the U.S.) has been estimated to be approximately 5.8% and prevalence of alcohol abuse has been estimated to be slightly higher at approximately 7% (Young et al., 2002). It has also been described as a problem in adolescent samples with some studies finding that 42.8% of 15-24 year olds (in a U.S. survey) having used illicit drugs at least once (Warner et al., 2001).

Many studies have investigated impulsivity and reinforcer discounting behaviour in individuals with substance abuse disorders. On self-report questionnaires, substance abusing groups frequently report higher levels of impulsivity compared to non-drug taking controls (Allen et al, 1998; Chambers and Potenza, 2003; Dawe and Loxton, 2004; Moeller et al, 2001; Wagner, 2005). Dawe and Loxton (2004) suggested that there were two behaviours involved in substance abuse; a motivational state that involves planning in order to obtain the drug and a rash, impulsiveness, when supplied with the drug. It was hypothesized that these two behaviours may have separate biological bases (Dawe and Loxton, 2004).

There is a large amount of evidence that substance abusers exhibit elevated levels of delay discounting behaviour compared to non-drug users which would be indicative of a lack of self-control (Allen et al, 1998; Bornovalova et al, 2005). There have been very few studies investigating probability discounting in individuals showing addictive behaviour. Heroin and cocaine abusers have reported significantly higher rates of delay discounting compared to non-drug using controls (Kirby et al, 1999; Kirby & Petry, 2004). Indeed, delay discounting rates in the heroin abusers were almost twice as high as those reported by the controls. In another study, opioid-dependent individuals reported higher rates of delay discounting compared to non-drug users (Madden et al, 1997). Furthermore, the

discounting rate of the opioid-dependent sample was higher than that of children aged 10-12 years.

Alcohol abusers also tend to show higher rates of impulsivity (Grano et al, 2004) and delay discounting compared to healthy controls (Petry, 2001). In one study, participants reported how many 'substance use variables' they met. These variables included such factors as earliest age of 1st alcohol/drug use, number of times passed out from alcohol, amount of drug taken in a certain time period, etc. Delay discounting rates were positively correlated with the number of a subset of variables that participants reported had occured to them within their lifetime (Kollins, 2003). Individuals showing other types of addiction, such as cigarette addiction, have also shown increased delay discounting and probability discounting rates compared to healthy controls (Bickel et al, 1999; Reynolds et al, 2003; Reynolds et al, 2004; Reynolds, 2006). However, another study found smokers exhibit higher levels of delay discounting but similar rates of probability discounting compared to non-smokers (Mitchell, 1999). Therefore, although the evidence for a lack of self-control in addiction appears to be clear, the role of risk-taking in addiction, especially smoking addiction, is not be as clear-cut.

There is some evidence to suggest that increased rates of delay discounting in addicted individuals may be reversible. In one study, ex-smokers reported comparable rates of delay discounting to healthy controls whereas current smokers exhibited higher rates than both groups (Bickel et al, 1999). However, it could be argued that delay discounting rates were initially lower in the ex-smokers, which would provide some explanation for their ability to quit smoking compared to the more impulsive current smokers. One currently outstanding question is whether the increased rates of impulsive choice, and possibly increased tendency to take risks, pre-disposes individuals to abuse drugs or whether it is a results of drug taking.

As has been outlined in a previous chapter, the term impulsivity can be viewed as a concept constructed by several separate behaviours. One behaviour that may be

related to impulsivity is 'sensation seeking', or the need for new and varied experiences. These experiences are often coupled with a relatively high incidence of risk (Zuckerman, 1979). In one study, the Tridimensional Personality Questionnaire (TPQ) was given to 457 adolescents. The TPQ was adapted for use in adolescents; the researchers excluded any questions they deemed would have little applicability to adolescents. The TPQ is divided into three sub-scales; novelty seeking, harm avoidance and reward dependence. Adolescent substance abusers appeared to exhibit elevated levels of novelty seeking, in addition to low levels of harm avoidance and reward dependence (Wills et al., 1994). High novelty seeking may be associated with the urge to experiment with drugs.

High levels of delay discounting have been reliably measured in individuals who use addictive substances including drugs of abuse, alcohol and cigarettes. There is also evidence that these groups tend to be higher risk-takers, however, this may differ between groups. For example, individuals who abuse drugs that are classified as highly addicitive and dangerous to health (e.g. heroin) may have significantly different rates of risk-taking compared to those who abuse more socially acceptable drugs such as cigarettes.

6.3 Impulsivity and reinforcer discounting in pathological gamblers

Pathological gambling is a highly problematic disorder. Its prevalence within society is estimated to be from 1-3.4% of the population (Black et al., 2006; Del'Osso et al., 2006). It has been classified as an impulse control disorder in the Diagnostic and Statistical Manual (DSM-IV). Pathological gambling can lead to loss of family and peer contact, severe debt problems or bankruptcy, and illegal behaviour to fund the addiction. It is important that this behaviour is researched to find its causal and contributory factors in order to decrease the frequency and severity of these problematic events.

When we consider the literature concerning impulsivity and pathological gambling we must remember that we should not consider all pathological gamblers to be part of one homogenous group. Environmental, psychological and biological factors determine our behaviours and pathological gambling is no different (Blaszczynski and Nower, 2002). It is true that some individuals may have a genetic or biological predisposition to develop addictive traits that could lead to pathological gambling (Bergh et al.,1997; Hollander and Rosen, 2000; Potenza, 2001). However, certain environmental factors have been found to significantly increase pathological gambling behaviour including availability of gambling outlets, acceptance of gambling by peers and family and even religion (Welte et al., 2006). Taking this into account, we still see much research that has found that groups of pathological gamblers, regardless of possible environmental factors, reliably show different personality characteristics compared to healthy controls. This research focuses mainly on the biological and psychological factors involved. The following section will discuss mainly these areas.

The research investigating links between impulsivity and delay discounting within substance abuse is extensive. Unfortunately, this is not the case in pathological gambling, although there has been some comparable research. One problem with the research into pathological gambling is the criteria and definitions used by researchers to define gambling samples. For example, the term ‘pathological gambling’ is most often used to describe those individuals meeting relevant DSM criteria. However, several different terms have been used such as disordered gambler, addictive gambler, and problem gambler. Usually the term ‘problem gambler’ refers to an individual or group that exhibits some behaviours associated with pathological gambling but, at the stage of diagnosis, does not meet enough criteria to be defined as a pathological gambler. Where the term ‘pathological gambler’ is used in the following text, the researchers have used DSM-IV criteria. Where other terms are used, appropriate definitions have been included.

Early research has indicated that pathological gambling, in a similar fashion to substance abuse, is characterized by increased impulsivity (Sinha, 2004). Pathological gamblers have reported higher scores on the impulsivity subscale of the IVE (Steel & Blaszczynski, 1998) and EIS (Blaszczynski et al, 1997). Furthermore, IVE-I scores were correlated with scores on the South Oaks Gambling Screen (SOGS), a measure of gambling severity (Lesieur and Blume, 1987) and indicators of possible pathological gambling behaviour. When discussing the characteristics of impulse-control disorders, such as pathological gambling, Del'Osso et al. (2006) suggested that there were three main characteristics; failure to resist an impulse that is harmful to the individual or others, increased arousal prior to the act and gratification, or release of tension, following the act (Del'Osso et al., 2006).

There have been some studies that have investigated delay discounting in gamblers, but far fewer than in the field of substance abuse. These studies have found that, similar to the drug abusers, pathological gambling is characterised by a loss in self-control (Goudriaan et al, 2004; Raylu and Oei, 2002; Reynolds, 2006). Dixon et al. (2003) found that pathological gamblers discounted delayed rewards at a faster rate compared to non-gambling controls (Dixon et al., 2003). One study gave a delay discounting procedure to two groups of gamblers defined as 'severe' or 'less'severe' gamblers dependent on SOGS scores. Severe gamblers (SOGS score of over 13) discounted delayed rewards significantly more rapidly than less severe gamblers. In a regression analysis, SOGS scores and levels of impulsivity (as measured by the IVE) were found to be significant predictors of the value of *k* obtained form the delay discounting task. Petry and Casarella (1999), in a study that will be described in section 5.5, found that substance abusing pathological gamblers had higher *k* values than non-substance abusing pathological gamblers who in turn had higher *k* values than healthy controls (Petry and Casarella, 1999). These studies highlight the role of self-control in gambling. However, there have been only a handful of studies investigating self-control (using a delay discounting procedure) in gamblers.

In a review of pathological gambling, Raylu and Oei (2002) highlighted evidence for the presence of high levels of impulsivity and sensation-seeking in pathological gamblers (Raylu and Oei, 2002). Although the evidence for increased levels of impulsivity in pathological gambling is fairly clear, the magnitude of sensation-seeking within pathological gamblers is somewhat open to interpretation. It could be hypothesized that pathological gamblers would exhibit high levels of sensation seeking, which would be related to a heightened tendency for risk-taking. One study compared impulsivity and sensation seeking between female and male non-gamblers, social gamblers, problem gamblers and disordered gamblers (Nower et al., 2004). The diagnostic criteria used to define gambling severity were from the pathological gambling scale from the DSM-IV-J. This was based upon pathological gambling criteria from DSM-IV and is created for use in individuals under 21 years. Out of nine criteria, a social gambler was defined by meeting 0-2 criteria, a problem gambler met 3 criteria, and a disordered gambler met 4 or more criteria. Impulsivity was measured by the EIS and sensation seeking was measured by the Arnett Inventory of Senation Seeking (AISS) (Arnett, 1994). The AISS was a 20-item self report measure split into two sub-scales; Intensity Seeking (the need for intense sensory experiences) and Novelty Seeking (the need for new and different experiences). In males, impulsivity (measured by the EIS) and substance abuse were the most predictive factors for disordered gambling. In females, impulsivity and sensation seeking were the most predictive factors. Another study recruited probable/pathological gambling and non-gambling male and female university students. Probable/pathological gamblers scored higher on several measures of sensation seeking including the AISS and SSS (described below) compared to non-gamblers (Powell et al, 1999). In another study, probable pathological gamblers, potential pathological gamblers and non-problem gamblers (defined by their scores on the SOGS) did not exhibit different scores in the venturesomeness scale on the IVE (MacKillop et al., 2006). Venturesomeness is defined as the tendency to take risky decisions or engage in risky activities. These studies indicate a possible role for sensation seeking in some groups of problem gamblers but the evidence is

mixed. It is important to note that these studies did not recruit pathological gamblers, as defined by DSM-IV, but used other measures such as the SOGS. Therefore, there may be differences in the characteristics of the different samples.

However, the evidence for the role of sensation seeking in gambling behaviour is not clear. In a sample of female fruit-machine players, sensation-seeking was inversely correlated with frequency of gambling (Coventry & Constable, 1999). However, in this study there was no attempt to classify the gamblers. Fruit-machine players were recruited from Bingo Halls and local leisure halls. Therefore, the history and severity of gambling behaviour in these individuals was unknown. It could have been the case that pathological fruit-machine players have altered levels of sensation seeking compared to non-pathological players. In this study, sensation seeking was measured by the Sensation Seeking Scale (SSS). The SSS is comprised of four sub-scales; thrill and adventure seeking, disinhibition, experience-seeking and boredom susceptibility (Zuckerman, 1979). The results of this study have been used to suggest that different personality types gamble in different ways (Coventry & Constable, 1999). For example, low sensation-seekers may be attracted to fruit-machines whereas high-sensation seekers are attracted to other forms of gambling. In a comparison of French non-gamblers and French gamblers who play games in cafes, levels of sensation seeking were comparable (Bonnaire et al., 2004). It was suggested that these games are more passive and, therefore, attract a gambler with relatively low levels of sensation seeking.

One could hypothesise that increased levels of sensation seeking would imply a higher tendency to take risks due to the need to obtain more exciting and arousing sensory stimuli. This would predict an increase in probability discounting. The evidence for increased levels of probability discounting in pathological gamblers is unclear. There have been few studies investigating probability discounting in gamblers. In one study, pathological gamblers have reported lower rates of probability discounting compared to non-gambling controls (Holt et al, 2003) suggesting a tendency within pathological gamblers to be more accepting of risks.

However, the classification of pathological gamblers was performed using ths SOGS, and not DSM criteria. Therefore, the pathological gambling sample here could only be defined as *probable* pathological gamblers. In a study comparing the SOGS and the DSM-IV criteria, out of 93 individuals classified as probably pathological gamblers by the SOGS, only 7 individuals met DSM-IV criteria for pathological gambling (Ladouceur et al., 2005). Therefore, the degree to which the SOGS and DSM-IV criteria are in accordance is small.

There are some possible confounds that indicate caution when interpreting the results of many of the studies described in this chapter. It can be common for individuals who abuse drugs, and especially those who gamble pathologically, to be in financial difficulties. This may lead to a change in behaviour when faced with monetary reinforcers (Goudriaan et al, 2004). For example, for a pathological gambler a small amount of money may obtain increased value compared to a non-gambler. However, there is evidence for a lack of self-control in pathological gambling. The role of sensation-seeking and risk-taking is much less clear due to mixed, or lack of, research.

6.4 Impulsivity and reinforcer discounting in anxiety disorders

Substance abuse and pathological gambling populations appear to be characterised by a decrease in self-control. There is also some evidence for increased levels of novelty seeking. It could be hypothesised that characteristics of anxiety disorders would be high risk-aversion and extremely low novelty-seeking. These extremely low characteristics may exacerbate the levels of anxiety. The role of self-control would be open to debate. Anxious individuals may have low-levels of delay tolerance if delay is associated with uncertainty. There has been extremely little published research investigating impulsivity and anxiety disorders. In one study of healthy individuals, participants who were induced into an anxious mood by reading an anxiety-provoking scenario, made less risky decisions compared to those who read a neutral or sad scenario. It was also found that this effect only

occurred if the consequences of the choice had consequences for themselves. If they were informed that the consequences would only affect a third party, there was no effect of mood on risk-taking (Ragunthan and Pharm, 1999). This suggests that anxious individuals may be highly risk-averse compared to non-anxious individuals but only in situations where they evaluate possible consequences for themselves.

There has been one study investigating delay discounting in anxiety (Rounds et al., 2006). In this study, participants were divided into low and high anxiety groups. Participants were then given a hypothetical scenario to read that either involved connotations of social threat or no threat. Anxious individuals discounted reward at a faster rate but only in the non-threat condition. This suggests that anxious individuals may actually discount delayed rewards at a faster rate to low-anxious individuals. Perhaps anxious individuals evaluate the delayed rewards as more uncertain compared to low-anxious individuals so therefore choose the immediate reward. However, because anxious participants did not discount more highly in the threat condition, which was designed to increase their anxiety, this idea must be viewed with caution. In addition, the studies above investigated healthy individuals using mood induction techniques so the applicability of the results when discussing anxiety disorders is questionable.

The role of impulsivity in anxious disorders is currently unknown. However, it may have an important role to play. Further investigation is warranted to explore whether extreme levels of impulsive behaviours are associated with anxiety disorders.

6.5 The effects of comorbid psychiatric disorders on delay discounting

Some studies have found that the presence of comorbid psychiatric disorders has an additive effect on delay discounting rates within an individual. Petry and Casarella (1999) recruited substance abusing pathological gamblers, non-substance abusing

pathological gamblers and healthy controls. Rates of delay discounting (*k*) were found to be highest in the substance abusing pathological gamblers, followed by the non-substance abusing pathological gamblers, with the healthy controls having the lowest values of *k* (Petry and Casarella, 1999). Another study recruited substance abusers with ASPD, substance abusers without ASPD, and healthy controls and found similar results. Substance abusers with ASPD reported higher values of *k* than substance abusers with no history of ASPD, and healthy controls produced the lowest *k* values. These studies suggest that values of *k* are elevated in these disorders and the presence of each disorder has an additive effect on final values of *k*.

7. Neurobiological function in pathological gamblers, substance abusers, and anxiety-disordered groups: a focus on impulsivity, self-control and risk-taking

7.1 Areas of the brain involved in impulsivity, self-control and risk-taking

Research investigating neurological regions involved in impulsivity, self-control and risk-taking has repeatedly found a wide number of brain areas involved in these processes. New procedures such as *f*MRI have proved extremely valuable in rapidly extending our knowledge. This section will describe brain areas individually although it must be borne in mind that they all form an interconnected network and some structures will affect, and will be affected, by others. In this chapter, brain areas are introduced individually to aid the reader; however, interconnections will be highlighted. Later sections will introduce the topic of neurological function in pathological gamblers and substance abusers and what information we have obtained from this research.

7.1.1 Orbitofrontal cortex

The prefrontal cortex plays a major role in the processing of stimuli. More specifically, it is involved in attention, decision-making and planning. Damage to the prefrontal cortex can lead to severe cognitive impairments. Individuals with lesions to the prefrontal region show deficits in decision making and planning (Clark et al., 2003; Goel et al., 1997) compared to non-lesioned individuals. In addition, damage to the prefrontal cortex in pigeons has been found to cause impairments in the judgement of delays (Kalensher et al., 2006). The prefrontal cortex has been split by researchers to order to describe different topological areas. Firstly, we will focus upon the orbitofrontal cortex.

The orbitofrontal cortex (OFC) has been a central focus for researchers wishing to investigate systems involved in reward, decision-making, impulsivity and emotion. The OFC is located on the orbital area of the prefrontal cortex. Its location remains under some debate. Some researchers define more ventral and dorsal areas as belonging to the OFC. Additionally, it cannot be simply defined using Brodmann areas. The OFC spans several Brodmann areas including areas 10, 11, 47 and 25, although it does not span the whole of some of these areas. The OFC densely connects with several other regions. Input is received from all sensory modalities (visual, auditory, olfactory, somatosensory and gustatory). The OFC has dense reciprocal connections to several structures including the anterior cingulate cortex, inferior temporal cortex, inferior parietal cortex, entorhinal cortex, ventral tegmental area, insula, amygdala, caudate nucleus, thalamus and hypothalamus (Elliott and Deakin, 2005; Kringelback and Rolls, 2004).

The OFC is thought to have a wide variety of roles. It is a critical area for determining and updating the *subjective* (rather than absolute) reward value of a stimulus (Cardinal et al., 2004; Montague and Berns, 2002). Its activity correlates with the relative value of primary and secondary reinforcers. For example, as one eats to satiety the activity of the OFC in relation to food decreases. In addition, when one is repeatedly presented with a food, OFC activity decreases in response

to that food. This is due to habituation and an increasing boredom response (negative emotional state) to the item of food. However, if a new food is presented, OFC activity increases significantly due to the high novelty and higher value placed upon the new food. The OFC also responds to preferred foods (such as sugary foods) with increased activity (Kringelbach and Rolls, 2004).

In the mid-1930s the newly discovered role of the OFC in emotion led to the prevalence of prefrontal lobotomies in order to eradicate unwanted pathological emotional reactions. These procedures primarily severed connections between the OFC and other areas of the brain. The procedures were dubbed a success due to their effects of diminishing pathological emotional reactions but causing no apparent changes in intellectual ability. However, they also conveyed problematic changes in personality such as increased irresponsibility, immaturity and the inability to carry out plans (Carlson, 2001). The results from these procedures display the role of the OFC in emotion and personality but not in intelligence.

The OFC plays a critical role in decision-making. Damage to this area can cause severely altered decision-making strategies. When given the Iowa task individuals with lesions to the OFC and ventromedial prefrontal cortex reliably chose from the risky decks rather than the safer decks. This was contrary to the behaviour of controls who learnt the contingencies of the decks and shifted preference to the safer choices (Bechara et al., 1994; Clark et al., 2003). However, some care must be taken when drawing conclusions from these studies as the lesions sometimes included prefrontal areas other than the OFC.

In rats, excitotoxic lesions in the OFC caused them to develop a strong preference for the smaller immediate reward in a delay discounting task (Kheramin et al., 2003; Mobini et al., 2002). This effect also occurred if 5-hydroxydopamine was injected into the OFC of rats causing an average 80% decrease in the amount of dopamine within the OFC (Kheramin et al., 2004). OFC lesions were, therefore, altering the delay discounting parameter K, the magnitude discounting parameter

Q, or both. The answer could be found by exploring the slope and intercepts calculated by plotting individual indifference points. The MHMC states that if the slope alters then this shows a change in *Q*. The delay discounting parameter *K* was numerically calculated so this could be easily compared between groups. Investigation of these values led to the conclusion that disruption of the OFC altered both *K* and *Q*. *K* was altered so that preference shifted to the impulsive, immediately rewarding, alternative. However, in parallel with this effect, *Q* was being altered so that the sensitivity to the difference between the rewards was increased. The effect on Q^+ alone would have led to a preference for the higher rewarding, delayed, alternative. However, these effects occurring together masked each other. In the experiments above OFC damage caused a larger alteration in *K* compared to *Q* so the rats exhibited more impulsive behaviour. These studies suggested that OFC lesions, or the reduction of dopamine within the OFC, caused significant increases in impulsivity alongside weaker yet significant increases in reward magnitude sensitivity. However, the picture was not so clear. In a separate study, OFC lesions in rats were found to decrease impulsive behaviour on a delay discounting task (Winstanley et al., 2004). Differences may have been attributable to task design. Mobini et al. (2002) and Kheramin et al. (2003) trained their rats post-operatively whilst Winstanley et al. trained their rats pre-operatively. In addition, in the Mobini and Kheramin studies the highest number of pellets given was two whilst Winstanley et al. gave four pellets as a reward for choosing the delayed alternative. The OFC has been found to play a role in learning (Elliott and Deakin, 2005; Kringelbach and Rolls, 2004; Rolls et al., 2006; Rushworth et al., 2007) so post-operative training may have led to an inability to learn the contingencies of each choice, leading to the preference for the easier, immediately rewarding, choice. The presence of higher differences between rewards could have also led to changes in *Q* overcoming the effects of changes in *K*, leading to an increase in self-controlled behaviour. The OFC has also been linked to response inhibition. When given a go/no-go task the right anterior lateral region of the OFC shows high activity (Horn et al., 2003). Damage to this area in the rats in the above studies may have caused an inability to inhibit preference for the impulsive choice

or ability. Indeed, it may be a culmination of several impaired behaviours that contributes to disruption in self-control following damage to the OFC.

In human imaging studies, the OFC has been found to be active in decision-making tasks involving risk. In a risk-taking task where participants could play safe for a small amount of money or take a risk for a larger amount, the OFC showed high activity during both the selection phase and during anticipation of the reward (Ernst et al., 2004). This provides support for the role of the OFC in both the analysis of preference and keeping the reward value in memory whilst waiting for it. In a meta-analysis of *f*MRI experiments using tasks judged to involve risky decisions (mostly using the Iowa task or Cambridge Risk Task), the most significant clusters were found in the orbitofrontal cortex, especially the more ventro-medial region (Krain et al., 2006). A functional dissociation has been found within the OFC with ventro-medial regions being primarily activated by monetary gain and lateral areas being primarily activated by monetary loss (Kringelbach and Rolls, 2007).

There is evidence to suggest that different neural systems are involved in the valuation of immediate and delayed monetary rewards. This may provide an account of the preference reversal effect because there would be two parallel neurological systems underpinning the valuation of sooner and delayed alternatives. The OFC was part of a circuit that was disproportionately activated by immediate, as opposed to delayed, rewards (Bickel et al., 2006; McClure et al., 2004). However, the areas active when presented with delayed rewards were not specified. This provides some evidence for two separate neural systems perhaps jointly responsible for the preference reversal effect and again gives evidence for the OFC having a role in decision-making and reward.

When considering the role of the OFC in decision-making and impulsivity it is important to note the density of connections between this area and others. Due to the presence of connections to all sensory modalities the OFC has been considered to be important in providing a "sensory-visceral link" for consummatory

behaviours (Kringelbach & Rolls, 2004). In the second paragraph of this section the number of connections was outlined. For this research, perhaps the most important system including the OFC to consider is the limbic system. This is a circuit of areas involved in emotional processing. In addition to the OFC it contains areas such as the amygdala, thalamus, hypothalamus, anterior cingulate cortex and nucleus accumbens, each of which has a role in decision-making (which will be described later in this chapter). This system is critically innervated by dopaminergic neurons which have been found to play an important role in decision-making (van Gaalen et al., 2006; Winstanley et al. 2005[b]) (the role of dopamine in decision-making and impulsivity will also be described later in this chapter). Areas within this circuit have been posited to have different, but interconnected roles in decision-making. Medial prefrontal regions, including the OFC, and the nucleus accumbens have been posited to play connected roles when valuing delayed and probabilistic rewards (Kable & Glimscher, 2007; Rolls et al., 2007). Interactions between the OFC, amygdala and nucleus accumbens have been suggested to underlie differences in impulsivity. The effects of damage to these areas have been linked to animal models of attention-deficit hyperactivity disorder (ADHD) (Cardinal et al., 2004). The OFC and amygdala have been identified as two areas critically involved in impulsivity. These areas have been linked in emotional processing with the amygdala thought to process bottom-up (inflexive) aspects of emotional evaluation while the OFC processes top-down (context-dependent) aspects (Wright et al., 2007). OFC lesions in rats have been found to lead to alterations in delay discounting behaviour. This research led to the supposition that the OFC was involved in coding for subjective reward valuation while the amygdala was involved in creating and/or maintaining the representation of a delayed reward on-line (Winstanley et al., 2004). It is important to note that these areas do not operate by themselves by influence one another through associated systems; the output of which then leads to behaviour expression.

The OFC is an area that appears to have many functions. Critical functions include the assignment of subjective values to stimuli and impulsive decision-making. The

OFC is active during situations where a reward is being chosen and when a reward is being anticipated. This may be due to the OFC creating a value for the alternatives and keeping the value of the chosen alternative on-line in working memory whilst waiting for its receipt. Disruption of the OFC significantly alters self-control, although the type of disruption seems to be dependent on certain aspects such as the magnitude of rewards or learning involved in the decision-making scenario. Different areas of the OFC may have different roles, perhaps explaining why the OFC as a whole has many different functions. Although previous research has uncovered many possible functions of the OFC many questions still remain such as; what, specifically, is the role of the OFC as regards self-control; how does OFC damage affect other interconnected areas; can the OFC be further split into regions with separate functions? The OFC is a critical area involved in decision-making and impulsivity and is, therefore, a structure that must be focused upon in research such as this.

7.1.2 Ventromedial prefrontal cortex

The ventromedial prefrontal cortex (VMPFC) encompasses some medial areas of the OFC but also extends medially and dorsally through to the superior frontal gyrus. This area is thought to be involved in conscious decision-making and emotion. Damage to this area can lead to decision-making biases and altered personality.

Perhaps one of the most well-known and classic cases in neuropsychological literature is that of Phineas Gage. Phineas Gage was a railroad construction worker, who had an iron bar blasted through his skull after a demolition accident. Mr Gage survived the accident retaining his intelligence, speech, memory, and mobility. However, following the accident his personality appeared to alter. He was described as irresponsible, untrustworthy, and unable to acknowledge other people's desires or advice if they conflicted with his own. It could be argued that some of these traits are similar to behaviours shown by some pathological

gamblers, e.g. irresponsibility with money, not acknowledging the advice of others, etc. Damasio and colleagues (Damasio et al, 1994) used contemporary neuroimaging techniques to conclude that the most likely point of damage included the VMPFC. However, other brain areas were damaged such as the OFC, so the changes in behaviour cannot be solely blamed on VMPFC damage. However, the change to a more impulsive behaviour state following the damage is intriguing.

In a reward task, Petersen et al. (2005) found that the medial prefrontal cortex became highly active when presented with a stimulus that an individual preferred over another (e.g. coke vs. pepsi) and when receiving the preferred item (Petersen et al., 2005). This provides evidence for the role of the medial prefrontal cortex in emotion and the valuation of rewards. However, in this study, the area of interest included the VMPFC and certain areas of the OFC.

In studies recruiting patients with specific VMPFC lesions, altered decision-making has been found. On the Iowa task, VMPFC-lesioned patients prefer the riskier decks, which ultimately lead to overall loss, compared to non-lesioned controls that learn the contingencies of the decks and, after a learning phase, prefer the safer decks. Three possible reasons were given for this. The first is that lesions to the VMPFC cause hypersensitivity to rewarding stimuli. The risky decks do contain larger rewards than the safer decks that, perhaps, the patients with VMPFC lesions assign a much higher value compared to controls. The second possible reason was insensitivity to punishment. The risky decks contain far higher punishers than the safer decks. If the patients with VMPFC lesions were ‘blind’ to these punishments and selectively responded to the rewards they would prefer the risky decks. The third reason was an insensitivity to future outcomes, i.e. a bias to select immediately rewarding alternatives (Bechara et al., 1994).

To discover which of these possible factors could apply, other researchers repeated the use of the Iowa task on VMPFC-lesioned individuals. They found the same bias for the risky decks compared to controls. They then provided a shuffled version of

the task where all the same outcomes were used but the loss trials were given first (Fellows and Farah, 2005). In the normal task, the first few choices contain wins only. When the losses begin one must use take into account past choices and consider whether it is worth continuing to choose from decks A and B considering the losses that are now being faced. This was termed 'reversal learning' as one must take account of past outcomes to make a decision in the present. The shuffled version eliminated the need for reversal learning because participants did not need to take account of past outcomes as the losses were experienced first. If the lesions caused impairments in reversal learning then the shuffled task should have aided individuals into preferring the safer decks. When given the shuffled Iowa task, VMPFC-lesioned individuals did switch preference to the safer decks. This provided evidence that VMPFC lesions impaired reversal learning ability. This finding was also supported by researchers who conducted a meta-analysis of 10 studies using the Iowa task (Yechiam et al., 2005). These researchers concluded that VMPFC damage did lead to impairments in learning ability.

Another study presented a decision making task where the participant could choose a smaller, safer, alternative or a larger, risky, alternative (the same task as in Ernst et al., 2004). Adults and adolescents were recruited. The researchers hypothesised that the increased risky behaviour viewed in adolescents was due to the delayed maturation of the cingulate cortex and ventral prefrontal regions. They found that, when making risky decisions, the VMPFC and OFC of adults exhibited higher activity than those of the adolescents. In addition, increased risk-taking behaviour was associated with reduced activity in these areas (Eshel et al., 2007). This study provides further evidence that decreases in VMPFC and OFC activity lead to increased risk-taking behaviour.

To explain the effects of VMPFC lesions on risk-taking behaviour, Bechara and colleagues theorised that the VMPFC had a role in the integration of information about a stimulus from structures such as the amygdala (which evaluated emotional valence of the stimulus) and the hypothalamus and brainstem nuclei (which sends

somatosensory information). This hypothesis was based upon physiological evidence from lesioned and non-lesioned individuals. Healthy individuals, when choosing a card from the risky decks, showed a skin conductance response (SCR) which is hypothesised to indicate an increased anxious response to high risk. Individuals with VMPFC lesions did not show a SCR when choosing from the risky decks. This was interpreted as being due to the effects of the lesions on the role of the VMPFC in integrating emotional and somatosensory information. Individuals with VMPFC lesions repeatedly chose from the risky deck as the 'normal' aversive emotional reaction that was associated with those decks was not present (Bechara et al., 1999). This was termed the "somatic marker hypothesis" (Bechara & Damasio, 2005; Damasio, 1996, Suzuki et al., 2003). However, VMPFC-lesioned individuals and healthy controls do show SCR responses when a slide is paired with a loud, aversive, noise. This suggested that the ability to emit emotional responses to stimulus-reinforcer learning situations was not impaired.

VMPFC lesions were also found to impair level of foresight (Fellows and Farah, 2005). Individuals with VMPFC lesions and non-prefrontal lesions were given a task in which they were asked to come up with any five events that will happen to them in the future and when they would happen. There were two dependent variables; the mean future time for all five events and the maximum time generated by one event (or "future extension"). VMPFC-lesioned patients had significantly shorter mean future times and mean future extensions compared to patients with lesions to non-prefrontal areas and controls. This suggests that VMPFC have a decreased ability to predict events that will happen in the future. It could be hypothesised from these results that lesions to this area would increase impulsive choice on a delay discounting task. However, in the same study, when given a hypothetical delay discounting task, there was no difference in behaviour between these groups. It is possible that the discounting of delayed outcomes is a separate process to future orientation.

The VMPFC appears to have several roles in decision-making and cognition. It may play a role in planning for future outcomes. Damage to the VMPFC seems to cause focus to shift on sooner, rather than later, events. The VMPFC also may play a role in learning. Damage may cause severe impairments in the ability to take account of past outcomes and integrate them into the current decision making strategy. Finally, the VMPFC may integrate signals from several areas of the brain responsible for evaluating emotional and somatosensory information. Damage may lead to this information not being included in current decision-making strategies.

7.1.3 Dorsolateral prefrontal cortex

The dorsolateral prefrontal cortex (DLPFC) extends laterally through the prefrontal cortex on the lateral gyri. This area is thought to be used in learning, memory and integrating sensory information (Rorie and Newsome, 2005). It is also active when selecting a reward during a risk task (Ernst et al., 2004). However, unlike the OFC, it is not active during anticipation of reward.

Lesions to the DLPFC, like the VMPFC, cause biased preference towards the risky decks on the Iowa task (Fellows and Farah, 2005). However, unlike VMPFC-lesioned individuals, when a shuffled version was given to erase the need for reversal learning, individuals with DLPFC lesions still preferred the risky decks. This suggests that the DLPFC is not utilised in reversal learning. Instead, risky decision-making may occur as a result of impairments to working memory or deficit in the integration of sensory information. There has been no research investigating the somatic responses of patients with DLPFC lesions so the applicability of the somatic marker hypothesis is, as yet, unknown.

The DLPFC also does not seem to play a role in future orientation. In the Fellows and Farah (2005) study, when thinking of five events that would happen to them in the future, DLPFC-lesioned individuals did not differ from controls in their mean

future times and mean future extensions. DLPFC lesions also did not affect delay discounting behaviour (Fellows and Farah, 2005).

In a meta-analysis of *f*MRI studies investigating risky decision making, the DLPFC was found to be predominantly an area used in decision making situations where risks and reward magnitudes for different alternatives were similar in probability, and therefore do not include a marked degree of affect (termed "cool" executive function). Examples of these types of tasks include the Rock, Paper, Scissors task where each outcome has an equal chance of occurring. In contrast, the OFC was active during decisions that included risky gambles and, therefore, involve a high degree of emotional attachment (termed "hot" executive function) such as the Iowa task or Cambridge Risk Task (Krain et al., 2006).

Although research has shed light on some of the functions of the DLPFC, relatively little appears to be known about this area. From what research we do have, we believe the DLPFC has several functions. Compared to the OFC which plays a role in affective, "hot", decision making, the DLPFC role is in decision-making situations that involve more purely cognitive, rather than emotional, processing. Unlike the OFC, it does not play a role in valuation of anticipated rewards suggesting that it is not involved in keeping a representation of the reward on-line during a delay to its receipt. The DLPFC does not appear to be involved in reversal learning, although its role in other forms of learning (e.g. conditional learning) cannot be dismissed. The DLPFC also does not seem to have a role in self-control as tested by a delay discounting task. Damage may lead to the impairment in integration of sensory information when making decisions.

7.1.4 Anterior cingulate cortex

The anterior cingulate cortex (ACC) is involved in decision-making. However, it appears to have different roles compared to other decision-making structures such as the OFC. The ACC has connections with frontal areas including the OFC, in addition to parietal areas.

The ACC may be important when the decision-making situation involves the expenditure of effort in order to obtain a reward. ACC lesions do not induce increased delay discounting. However, in a task where rats must choose whether to choose an alternative that involves little effort to obtain a small reward, or a higher amount of effort in order to obtain a larger reward, rats who usually chose the larger reward tended to switch their preference to the easier option when they received lesions to the ACC (Rushworth et al., 2007). This suggests that the ACC, although not having a role in self-control behaviour, does process the amount of effort that is needed to obtain rewards.

The ACC also seems to be important in situations that involve exploration and action monitoring. In one task, participants had to find their way around a virtual maze. Their starting place within the maze changed in each trial. Participants worked out, using trial and error, where they were in the maze and the best way to get to a point within the maze. Compared to when simply following instructions, when the participants were allowed to freely explore the maze the ACC was active. Sometimes participants realised they had to revise their beliefs about their position within the maze and then had to back-track to a previous position. The ACC was highly active during these back-track movements (Rushworth et al., 2007; Yoshida and Ishii, 2006) implicating a role in action monitoring.

There is evidence that there are functional segregations of the ACC. Evidence suggests there is an occipito-parietal-prefrontal pathway moving through the caudal section of the ACC that is involved in “cool”, cognitive, decision-making and a rostral-ventral pathway implication in “hot”, emotional, processing (Krain et al., 2006). In addition, the more dorsal region of the ACC has been implicated in processing reward magnitude, error detection, and monitoring the behaviour of competitors (Ernst et al., 2004) while the more ventral region is associated with the processing of reward amount (Marsh et al., 2007). Furthermore, areas of the posterior cingulate gyrus that interconnect to the ACC appear to be involved in the

processing of the variance in probabilities of receiving rewards (Rushworth et al., 2007).

As mentioned earlier, the ACC does not seem to have a role in delay discounting behaviour. Lesions to the ACC do not significantly affect impulsive choice (Cardinal, 2004; Cardinal et al., 2004). However, ACC lesions do increase motor impulsivity. Lesions in rats tend to induce premature responding in tasks where they are required to wait (Muir et al., 1996). Although this sounds like a possible deficit in self-control, it is more likely to be due to impairment in the inhibitory control of motor responses. Less is known about the role of the ACC in risk-taking and probability discounting. Deactivation of the ACC in primates leads to impairment in decision-making when faced with probabilistic rewards, however, it is unknown whether this is due to an effect on magnitude processing or processing of probability (Cardinal, 2006). In the Eshel et al. (2007) study (which compared frontal and anterior cingulate activity in adults and adolescents) decreased activity was measured in the dorsal ACC (BA32) in addition to reduced activity in the VMPFC and OFC. This is suggestive that the ACC processes some elements of risky decisions.

The ACC, although it plays a role in decision-making, appears to have dissociable functions to the OFC. The ACC seems to be involved in the processing of choices in which obtaining a reward involves the expenditure of effort. It has also been found to be active in situations where exploration and the monitoring of one's own, or another individual's, behaviour is necessary. It seems not to be a structure that has a role in delay discounting; however, it may be important in the processing of probabilistic rewards. It is also important to note that the ACC can be segregated into a more rostral area that is involved in affective decision-making and a more caudal area that is involved in more purely cognitive decision-making.

7.1.5 Nucleus accumbens

The nucleus accumbens (NAC) has been repeatedly implicated in mediating the reinforcing aspects of stimuli. It shares many connections with other areas involved in reward and emotion including the orbitofrontal cortex, medial prefrontal cortex, anterior cingulate cortex, limbic system, and ventral tegmental area. It is a major site of dopamine innervation and also receives glutaminergic and 5-HT input. The roles of dopamine and 5-HT are discussed in later sections.

In humans, NAC activity precedes reward anticipation and the amount of activity measured has been found to be positively correlated with reward magnitude (Peterson, 2005). Excitotoxic lesions of the NAC in rats causes them to alter preference to smaller or less-valued rewards over, pre-operatively preferred, larger or more-valued rewards if they require effort to obtain them such as a button press or wall climb (Cousins et al., 1996; Salamone et al, 1991). It is a region that has been associated with the reinforcing hedonic characteristics of drugs of abuse and drug craving (Koob et al., 1998), primarily due to its high number of dopamine receptors. Cocaine and amphetamine administration has been found to increase dopamine concentrations within the NAC (Petit & Justice, 1989; Di Ciano et al., 1995; Wise et al., 1995). Drugs that inhibit dopamine activity in the NAC cause drugs of abuse to lose much of their effects (Caine & Koob, 1994; McGregor and Roberts, 1993).

NAC lesions lead to increased motor impulsivity in rats (Cardinal & Cheung, 2005; Cardinal et al, 2001). Lesions to the core region of the NAC increased impulsive choice on a delay discounting task in rats (Cardinal et al, 2001). This effect does not seem to occur due to changes in *Q* because the rats with NAC lesions were still able to discriminate between rewards of different magnitudes (Cardinal et al., 2004). Other studies have also found that NAC lesions did not affect the ability of rats to discriminate large from small reinforcers (Salamone et al., 1994; Salamone et al., 2001). Increased delay discounting in rats with NAC lesions was also not due to inflexible response bias towards the alternative providing the immediate reward because preference switched to the larger reward when both rewards had no delays

(Cardinal et al., 2004). One interesting finding was that lesions of the NAC core in rats impaired stimulus-outcome learning when the outcome was delayed by 10 or 20 seconds but not when the outcome was presented immediately after the stimulus (Cardinal and Cheung, 2005). From this research it appears that the NAC core promotes the selection of delayed rewards and is involved in learning the association between stimuli and their delayed outcomes. However, the story concerning of the NAC and delay discounting is not so clear. In a later study, it was found that NAC lesions caused rats to behave in a less impulsive way on a delay discounting task (Acheson et al., 2006). There were several possible reasons for the discrepancy between the studies. In the Cardinal et al., (2001) study the delay was varied within a single session whereas within the Acheson et al. study, delay was kept constant over several sessions. It was suggested that NAC lesions impair delayed outcome learning or ability to adapt to changes in delay rather than affecting toleration of delay. Secondly, the Cardinal et al. study utilised longer delays (up to 60 seconds) compared to Acheson et al. (up to 8 seconds). If, as Cardinal et al. discovered, delayed outcome learning is impaired if the delays exceed 10 seconds, then the delays utilised by Acheson et al. may not have been long enough for this impairment to have an effect. Finally, the rats in the Acheson et al. study received excitotoxic lesions to the NAC core and shell. In the Cardinal et al. study, the rats received excitotoxic lesions only to the NAC core. However, this is likely not to have had a significant effect as lesions to the NAC shell only have previously been found to have no effect on choices between certain, delayed, rewards and uncertain, immediate, rewards (Pothuizen et al., 2005).

The NAC has also been implicated in risky decisions. In a financial decision task, which is designed to simulate real-word decisions regarding the purchase of stocks and bonds, NAC activity preceded the choices that involved risk. The NAC was also active preceding where a risk was taken that was unnecessary (compared to a risk-neutral agent that made decisions that maximised expected utility) (Kuhnen & Knutson, 2005). Studies using probability discounting tasks have found mixed results. Excitotoxic lesions of the NAC in rats have been found to increase risk-

averse choice (Cardinal & Howes, 2005) and not significantly affect choice behaviour (Acheson et al., 2006) on probability discounting tasks.

The role of the NAC in delay and probability discounting is still under debate. NAC lesions appear to affect impulsive choice behaviour in a delay discounting task, possibly due to impaired ability to learn stimulus-outcomes rules when the outcome is delayed by 10 seconds or more. The NAC in humans has been found to be involved in risky decisions. However, the animal research has found mixed results as to whether NAC damage actually affects behaviour on a probability discounting task. Research investigating the NAC and utilising delay and probability discounting tasks are few and more research is needed, especially concerning the NAC and its role in risky decision-making.

7.1.6 Limbic system

The limbic system is traditionally associated with motivation and emotion (Carlson, 2001). The main structures within the limbic system that have been repeatedly implicated in these roles are the amygdala and hippocampus.

The amygdala is a structure primarily involved in affective processing. In primates, it shows increased activity when a pleasant or aversive stimulus is presented. Damage to the amygdala in primates can lead to a loss of fear and decreased stress response. In contrast, when electrically stimulated, primates show an increase in physiological signs of fear and agitation. The amygdala has also been associated with the creation of conditioned emotional responses. Finally, elevated activity of the amygdala has been associated with anxiety disorders and the anxiolytic effects of some drugs are though to be due to their effects on the neurotransmitter systems within the amygdala (Carlson, 2001).

The amygdala has afferent connections with the hippocampal formation and receives sensory information from the thalamus and sensory cortex. It projects to

the hypothalamus, midbrain, pons and medulla oblongata. The amygdala also projects to the nucleus accumbens and has reciprocal connections with the OFC. This circuit is thought to have a major role in impulsivity, decision-making and reward processing (Cardinal et al., 2004).

In rats, amygdala lesions lead to increased impulsive behaviour on a delay discounting task (Winstanley et al., 2004). This was hypothesised to be due to impairment in the ability to hold a representation of the value of the reward during the delay. Decreased self-control could also be due to an increase in *K* without disruption of *Q*. This is the only task that has investigated the role of the amygdala in delay discounting.

It is also possible that the effect found by Winstanley et al. (2004) was due to impairments in learning. In a separate study, lesions to the amygdala in rats did not lead to deficits in reversal learning, whereas lesions to the OFC did (Stalnaker et al., 2007). Interestingly, lesions to the amygdala reversed the deficits in reversal learning caused by lesions to the OFC. The researchers hypothesised that reversal learning deficits after OFC lesions occur due to abnormally persistent representations of the choice situation in "downstream" regions, such as the amygdala. Destruction of the amygdala did not, by themselves, cause deficits in reversal learning. Therefore, they caused these persistent representations not to be formed and sent to the OFC.

Damage to the amygdala also leads to increased risk-taking. When presented with the Iowa task, patients with amygdala lesions prefer the risky decks (Bechara et al., 1999) in a similar way to individuals with VMPFC lesions. Physiological studies have found that patients with amygdala lesions, unlike healthy controls, do not express a skin conductance response when choosing a card from one of the risky decks. Bechara and colleagues hypothesised that damage to the amygdala impaired the processing of affective aspects of a reinforcer. In healthy individuals the amygdala processes the emotional aspects of a choice and aids in the decision-

making process. However, patients with amygdala lesions have to use a simpler, non-emotional, cost-benefit decision-making strategy that takes into account the positive and negative aspects of each choice regarding immediate and future benefit (Bechara and Damasio, 2005). The somatic marker hypothesis was again used to explain the effects of amygdala lesions on behaviour on the Iowa task. It was hypothesised that processing of affective stimuli preceded the expression of the somatic state associated with picking one of the risky decks. Therefore, in patients with amygdala lesions, the somatic expression – i.e. the SCR – did not occur. Unlike patients with VMPFC lesions, those with amygdala lesions did not produce an SCR response when a visual cue was paired with a loud aversive noise. This showed evidence of impairment in affective conditional learning. However, one must be careful when drawing conclusions from this research as the number of patients with amygdala lesion that were recruited was low (N=5).

In a previous section, the functions of the VMPFC were described. One function involved the integration of somatosensory information. One may then question how damage to the VMPFC does not mirror damage to the amygdala as regards physiological deficits. Bechara and colleagues hypothesised that the amygdala was involved in the processing of "primary" inducers of emotion. These included affect induced from salient, real, stimuli in addition to more basic, primal, emotional reactions, such as a fear of snakes. The VMPFC was involved in the processing of "secondary" inducers of emotion, which were artificial affective stimuli such as memories or hypothetical situations (Bechara and Damasio, 2005). Reaction to the Iowa task would principally employ the "primary" emotional area.

The hippocampus has been linked to learning and memory. Although not thought to be involved in the storage or retrieval of memories, it is suspected to be involved in memory consolidation, i.e. the transference of a memory into a long-term memory, of episodic (but not declarative) memories. Damage to the hippocampus has been found to cause anterograde amnesia. The hippocampus has also been linked to Pavlovian conditioning to contextual conditioned stimuli (Carlson, 2001).

To highlight the effects of hippocampal damage on memory and learning we can take the example of patient W.C., who sustained bilateral damage to the hippocampus (Bechara et al., 1995). When given a task that paired a visual cue with a loud aversive noise, W.C. exhibited a skin conductance response, which is indicative of an emotional response and learning of the attributes of the conditioned stimulus. However, when quizzed afterwards, W.C. could recall no information as to what had occurred during the task. Many other studies have found that hippocampus lesions lead to the impairment of Pavlovian conditioning in rats (Chen et al., 1996; Honey & Good, 1993; Jarrard, 1993; Phillips & LeDoux, 1992).

Lesions to the hippocampus have been associated to delay aversion. In a Y-maze task that gave a choice between certain but delayed (by 10 seconds) access to water and immediate but 25% chance of access to water, rats with excitotoxic hippocampal lesions switched preference to the immediate uncertain reward compared to sham-lesioned controls who favoured the delayed certain reward (Rawlings et al., 1985). When the certain reward had no delay all rats preferred the immediate certain reward over the immediate probabilistic alternative. By itself this study does not distinguish whether damage to the hippocampus alters Q^+, K^+, or H^+. In separate research, hippocampus lesions in rats have found not to affect memory of reinforcer magnitudes (Kesner & Williams, 1995). This implies that hippocampus lesions do not affect Q^+. In another study that presented a delay discounting task to rats with sham lesions and hippocampus lesions, lesions to the hippocampus caused an increase in impulsive choice (Cheung & Cardinal, 2005). This research suggests that damage to the hippocampus affects K^+. Its role in probabilistic choice is still under question.

The amygdala and hippocampus are areas that have been implicated in impulsive choice and risk-taking. The amygdala has a critical role in emotional decision-making. Damage to the amygdala can cause significant decreases in self-control and increases in risk-taking. Damage to the amygdala may mean that affective

information concerning stimuli is not taken into account, which is represented by absence of somatic markers that represent affective response. The hippocampus appears not to have any affect on *Q*. Damage to the hippocampus can cause decreased self-control. Damage may also lead to increased tolerance of uncertainty.

7.1.7 Basal Ganglia

The basal ganglia are a sub-cortical collection of structures which are situated under the anterior area of the lateral ventricles. The structures of the basal ganglia that are of interest in this research are the caudate nucleus, putamen, globus pallidus and subthalamic nuclei. One of the main functions of the basal ganglia is in the control of movement. The basal ganglia monitor somatosensory information and movements being carried out by the motor cortex. Damage to the basal ganglia can lead to impairments in movement and has been associated with motor deficits in Parkinson's disease. The basal ganglia have also been implicated in instrumental conditioning. (Carlson, 2001).

Some structures of the basal ganglia have been associated with impulsive choice. Activation of the caudate nucleus and putamen preceded the choice of the immediate reward over a delayed reward in a delay discounting task (Wittman et al., 2007). In addition, asymmetry of the left and right caudate nucleus has been associated with symptoms of Attention-Deficit/Hyperactivity Disorder (Schrimsher et al., 2002), a disorder characterised by high levels of impulsivity, hyperactivity and impairments in attention. Caudate nuclei asymmetry significantly predicted inattentive behaviours but did not significantly predict hyperactive/impulsive symptoms. In a rat model of ADHD, cerebral blood flow in the caudate nucleus and globus pallidus were found not to differ between a control group and a group of rats whose behaviour mimicked the symptoms of ADHD (Danker & Duong, 2007).

The subthalamic nuclei (SN) have been associated with motor movements. Motor deficits inherent in Parkinson's disease have been linked to possible abnormal function in the SN (Baunez et al., 1995). The SN has connections with other regions of the basal ganglia including the globus pallidus in addition to limbic and prefrontal areas (Carlson, 2001: Nakano, 2000). Lesions to the SN have been found to cause motoric impulsivity in rats (Baunez et al., 1995; Baunez et al., 2001; Baunez & Robbins, 1997).

Lesions to the SN in rats has also been found to lead to decreased impulsive choice (i.e. increased self-control) in a delay discounting task (Winstanley et al., 2005). This research also found that SN lesions impaired the Pavlovian learning of conditioned stimulus (CS)-unconditioned stimulus (US) associations (otherwise known as 'autoshaping'). However, if the rats were given training on the autoshaping task, and therefore given the chance to learn the CS-US associations, before surgery then behaviour on the task was not significantly affected post-surgery. This leads to the conclusion that lesions to the SN cause deficits in Pavlovian CS-US learning. Autoshaping has been previously linked to impulsive choice behaviour (Chudasama & Robbins, 2003). Due to the immediate delivery of the small reward in rat discounting tasks, Pavlovian associations will be created between the choice of the small reward and its delivery. The larger reward, however, is always delayed which will impair the creation of Pavlovian associations between the choice and delivery of this reward. If autoshaping is impaired, then associations created for the small immediate reward will not conflict with choices for the larger reward. Instead, preference will be biased more by reward-delay trade-offs. This may lead to increased choice of the larger reward.

The similarity in impulsive choice behaviour following OFC and SN lesions has lead to a hypothesis that these systems function jointly in determining levels of self-control. Lesions to areas that connect the OFC and SN, therefore causing disconnection of these areas, mimic damage to the SN by itself (Chudasama et al, 2003).

The role of the SN in relation to risk-taking is currently unknown.

These results suggest that regions of the basal ganglia are involved in self-controlled behaviour. The caudate nucleus and putamen may be part of a structure that promotes the selection of immediate over delayed rewards (evidence is suggestive that there are separate circuits involved in promoting choice for immediate and delayed rewards). The subthalamic nuclei also appear to be involved in self-control, possibly in collaboration with the OFC. It is interesting to note the opposite effect of lesions to the subthalamic nuclei and lesions to the caudate nucleus and putamen. This is suggestive of different local circuits in the selection of immediate and delayed rewards.

7.1.8 Ventral tegmental area

The ventral tegmental (VTA) area forms part of the midbrain, adjacent to the substantia nigra. It contains ascending projections of serotonergic, noradrenergic and dopaminergic axons. The dopaminergic projections play an important role in the process of reinforcement and reward behaviour. The mesolimbic dopaminergic system projects to a number of systems including the amygdala, hippocampus and nucleus accumbens. This system also projects to a diffuse number of regions including the prefrontal cortex, hippocampus, and the limbic cortex including the anterior cingulate cortex. As we know, the nucleus accumbens has an important role in reward and reinforcement. Stimulation of the VTA causes increased dopaminergic innervation within the NAC. This increase in dopaminergic innervation within the NAC has been linked to the reinforcing properties of rewarding stimuli (Schultz et al., 1997).

In addition to connections with the NAC, another important connection of dopaminergic neurons is between the VTA and orbitofrontal cortex. This pathway

is thought to be responsible for coding reward expectation (Martin and Potts, 2004). In a primate *f*MRI study, higher medial OFC and NAC activity was associated with the presentation of an unexpected reward of juice compared to activity when a reward was expected. This increase in activation was thought to be due to the projection of dopamine to the OFC and NAC (Berns et al., 2001).

No studies have asserted that the function of the VTA directly affects impulsive behaviour. However, considering its role as a mediator of dopaminergic activity within structures such as the NAC, OFC and hippocampus, it would seem that it would play a supporting role in reward and reinforcement behaviour.

7.1.9 Insula

The insula (or insular cortex) is an area that has been linked to decision-making under uncertainty and with delayed outcomes. The anterior and posterior regions of the insula have been linked to different types of decision-making.

In a delay discounting task, selection of a delayed outcome rather than an immediate outcome has been found to activate the bilateral posterior insula in humans (Wittman et al., 2007). Selection of immediate alternatives activated other cortical regions. This is suggestive that decisions with immediate or delayed outcomes employ separate neurological circuits. The posterior insula may also be a site that is involved in the selection of delayed alternatives. Possible roles of the posterior insula could be its role in self-control or learning of associations between stimuli and their delayed outcomes.

In choices that involve risk, anterior insula activity has been found to precede risk-averse choice in humans (Kuhnen and Knutson, 2005). In this study, the insula was found to play an opposite role to that of the nucleus accumbens, whose activity preceded risk-taking decisions. These authors have suggested that, whereas the NAC represents predictions of gain, the insula represents predictions of loss.

The role of the insula in delay and probability discounting is little understood, although a few studies have shed some light on its possible roles. It appears that the posterior insula is involved in the selection of delayed over immediate reinforcers while the anterior insula represents decisions that involve loss, a dissociable role to that of the nucleus accumbens.

7.1.10 Parietal cortex

Activity of the parietal cortex has been linked to cognitive numeric reasoning (Culham & Kanwisher, 2001). A delay discounting task, in humans, has been found to engage the posterior parietal cortex irrespective of delay (McClure et al., 2004). This is possibly due to the use of mathematical rules created to compare the trade-off between the reward and delay of the two alternatives.

Decision-making under situations of risk have been found to engage the left inferior parietal cortex. In contrast to this, when a decision must be made between two alternatives that have equal magnitudes and an equal chance of occurring, the right parietal cortex is active (Krain et al., 2006). This suggests that the left parietal cortex is involved in numerical reasoning and judgement, a view that has received experimental support (Ernst et al., 2004; Pesenti et al., 2000; Sandrini et al., 2004). The ambiguous tasks do not involve explicit numerical computation so do not activate the left parietal cortex.

7.3 The role of neurotransmitter systems in decision-making, reward and impulsivity

7.3.1 Serotonin (5-HT)

Serotonin (or 5-hydroxytryptamine, shortened to 5-HT) is a neurotransmitter that has important roles in the generation and regulation of emotion (Mattay & Goldberg, 2004). Most cell bodies of 5-HT neurons are found in the dorsal and medial raphe nuclei. They project to a number of structures including the basal ganglia, limbic system, and prefrontal cortex.

5-HT has been closely linked to impulsivity. Dysfunction of serotonergic transmission has been found to correlate with a wide range of impulsive behaviours including suicidality and impulsive aggression (Carver et al., 2006; Heinz et al., 1998). High levels of raphe 5-HT transporters in addition to a low 5-HT turnover rate in non-human primates have been found to positively correlate with aggression (Wrase et al., 2006). Primates with low concentrations of the 5-HT metabolite, 5-HIAA, in the cerebrospinal fluid show an increased number of behaviours indicative of impaired impulse control such as unrestrained aggression (Higley & Linnoila, 1997). In a study of 26 of 4,500 free-roaming rhesus macaques, relatively lower concentrations of 5-HIAA within the cerebrospinal fluid was inversely related to aggression (measured by the number of aggressive chases and acts of physical violence in addition to the number of physical wounds exhibited) and risk-taking (measured by the number of 'long leaps', i.e. leaps that traversed the most distance from tree to tree and at dangerous heights) (Mehlman et al., 1994). In addition to direct markers of 5-HT, other biological processes within the body affected by 5-HT have been linked to impulsivity. 5-HT stimulated calcium (Ca^{2+}) release from platelets has also been found to be significantly lower in impulsive individuals compared to controls suggesting that impulsivity may also be linked to impairments in 5-HT second messenger systems (Reist et al., 2000). Impulsivity has also been liked to gene expression of the 5-HT system. In a study investigating the 5-HT_{2A} receptor gene, which has three polymorphisms, a group of individuals who had the A-1438A allele made more commission errors on a go/no-go task compared to the group who had the G-1438G allele (Nomura et al., 2006).

5-HT function has been linked to performance of a delay discounting task. Using in-vivo microdialysis in rats, 5-HT levels in the medial prefrontal cortex increased during task performance. 5-HT levels did not alter when the rats simply had to press a button to obtain a reward. Therefore, the change in function was thought to be specifically due to performance on the delay discounting task. No change in 5-HT levels was found in the OFC (Winstanley et al., 2005). Global destruction of ascending 5-HT pathways in rats, caused by injection of 5,7-dihydroxytryptamine (5,7-DHT), has been found to cause significant increases in impulsive choice in a delay discounting task (Bizot et al., 1999) due to increases in K^+ (Mobini et al., 2000[a]; Mobini et al., 2000[b]). However, sometimes no effect of global ascending 5-HT function has been found on choices in a delay discounting task (Winstanley et al., 2005). This is possibly due to the different effects of separate receptor subtypes (Cardinal et al., 2004). The 5-HT_{2C} and 5-HT_{2A} receptor subtypes have shown contrasting effects on performance of a delay discounting task. In rats, the administration of SB242084, a 5-HT_{2C} receptor antagonist lead to increased premature responding (mimicking effects of 5-HT depletion using 5,7-DHT). However, administration of M100907, a 5-HT_{2A} receptor antagonist led to decreased premature responding in sham-operated rats but not in 5-HT depleted rats (Winstanley et al., 2005). These two receptor subtypes appear to have contrasting roles as regard one type of impulsive behaviour (premature responding). In this study, global 5-HT depletion appeared to mask the effects of the 5-HT_{2A} receptor.

Some drugs that elevate serotonergic function have been found to decrease impulsive behaviour. The injection of fluoxetine or fluvoxamine, which are Selective Serotonin Reuptake Inhibitors (SSRI), have been found to increase self-controlled behaviour on a delay discounting task (Bizot et al., 1999). However, the administration of other SSRIs such as citalopram has been found to have no significant effect on choice behaviour (Evenden & Ryan, 1996).

Studies linking 5-HT function and performance on probability discounting tasks have been few. Global destruction of ascending 5-HT pathways in rats has been found not to affect behaviour on a probability discounting task (Mobini et al., 2000). Studies in humans using trytophan depletion, a dietary method of temporarily depleting 5-HT levels, has also been found not to affect performance on a probability discounting task (Anderson et al., 2003).

The 5-HT system has an important role in the regulation of some impulsive behaviours. Decreased 5-HT function has been found to increase premature responding and decrease self-control in rats in addition to increasing impulsivity, aggression and risk-taking in primates. Sometimes, depletion of 5-HT has led to different effects. This may be due to pharmacological effects on different 5-HT receptor subtypes. When altered by pharmacological mechanisms, different receptor subtypes have appeared to have possible dissociable roles in impulsivity. Regarding risk-taking in rats and humans, 5-HT function has been found to have no effect. This is suggestive of different neural mechanisms and neurotransmitter systems involved in self-control and risk-taking.

7.3.2 Dopamine

Dopamine (DA) has been implicated in several functions including movement, learning, attention and reinforcement. There are a number of dopamine pathways within the brain. The nigrostriatal system projects from the substantia nigra to the basal ganglia and is involved in movement. The second system is the mesocortical system which projects from the ventral tegmental area to the prefrontal cortex and is involved in learning and attention. The third system is the mesolimbic system which projects from the ventral tegmental area to the nucleus accumbens (which then connects to other limbic regions). This pathway is involved in reinforcement.

DA has been linked to impulsivity through studies of ADHD. It has been proposed that many behaviours of ADHD, namely lack of self-control and hyperactivity, are

due to abnormally steep discounting of delayed outcomes (Johansen et al., 2002; Sagvolden et al., 1998). Psychostimulants that affect DA, such as amphetamine and methylphenidate, have been found to be effective therapies for ADHD. However, it is not known exactly how these therapies work, whether ADHD reflects a hyperactivity or hypoactivity of DA, or what roles other neurotransmitters have in the disorder (Fone & Nutt, 2005; Russell et al., 2005; Solanto, 2002).

Regarding the role of DA in self-control, many researchers have found that alteration of DA function affects levels of self-control. Using in-vivo microdialysis on rats, it has been found that performance of a delay discounting task, compared to a simple response-reward task, leads to increased dopaminergic activity in the medial prefrontal cortex and OFC (Winstanley et al., 2005). Many studies have utilised pharmacological interventions to alter DA and measure responses on a delay discounting task. *d*-amphetamine, which blocks reuptake of DA and noradrenalin has been found to decrease impulsive responding in rats on a delay discounting task and similar results have been found with methylphenidate, which also blocks reuptake of DA (Pietras et al., 2003; van Gaalen et al., 2006). However, administration of methylphenidate to bipolar patients has been found to produce mania (Oswald et al., 2007). This suggests that it is not solely this drug's effects on DA that produce increased self-control.

As with 5-HT, dissociable roles between DA receptor subtypes have been found. In one study, injection of the D1 receptor antagonist SCH-23390 led to increased impulsive choice in rats whereas administration of the D2 receptor antagonist eticlopride did not affect choice behaviour. D1 and D2 receptors may, therefore, have dissociable roles regarding self-control. In addition to these findings, in rats that were pre-treated with SCH-23390, administration of *d*-amphetamine caused a transient decrease in impulsive choice, therefore, cancelling out the effects of SCH-23390 (van Gaalen et al., 2006). This could be due to the general DA-innervating effects of amphetamine (amphetamine principally activates D2 receptors although effects on D1 receptors cannot be ruled out). This research leaves us with an

unclear picture of the precise role of the D1 and D2 receptors in impulsivity, however, a dissociable role in impulsive choice is evident.

As has been mentioned in an earlier section, the nucleus accumbens appears to play an important role in self-control with damage leading to decreased self-control. In an effort to understand the role of dopamine innervation within the NAC in impulsive choice, the NAC of rats was infused with 6-hydroxydopamine (6-OHDA), a neurotoxin that decreased levels of DA within the NAC by 65-70% (Winstanley et al., 2005). When given a delay discounting task, lesioned rats did not behave differently from sham-lesioned rats. Post-operative administration of *d*-amphetamine led to decreases in impulsive choice suggesting that the effects of the drug are not dependent on mesolimbic DA activity within the NAC. This may lead to the conclusion that DA activity within the NAC has no role in self-control, however, previous research has found that NAC lesions significantly increased impulsive choice. Is this a discrepancy in the research? It is possible that lesions to the NAC caused widespread damage to more than just the DA pathway. 5-HT neurons are also found within the NAC so lesions could have caused increases in impulsive choice due to decreased 5-HT function. NAC lesions could also have lead to information concerning the reinforcing properties of the choice not being sent to other regions of the brain causing biases in decision-making.

The role of DA in probabilistic discounting is uncertain. While individuals addicted to opiates and amphetamines, which increase DA activity, exhibit biases in decision-making under situations of risk (Kirby et al., 1999; Kirby and Petry, 2004; Madden et al., 1997), it is unknown whether these biases are present before the taking of drugs or are a product of drug abuse.

General increases in DA innervation have been shown to increase self-control. This is a fact that has been exploited to provide treatment for ADHD, a psychiatric disorder characterised by a lack of self-control and hyperactivity. It appears that

separate DA receptor subtypes have dissociable roles in impulsivity. However, it is still unknown as to what their exact roles are.

7.3.3 Noradrenalin

Noradrenalin (also known as norepinephrine) pathways connect to almost every structure within the brain. Its primary function is to increased vigilance and attention to salient stimuli. It also has roles in the mediation of sexual behaviour and appetite (Carlson, 2001).

Little is known about the role of norepinephrine (NE) in self-control and risk-taking. *d*-amphetamine has been shown to lead to decreases in impulsive choice (van Gaalen et al., 2006). Although these effects may have been attributed primarily to the drug's effects on dopamine innervation, the drug also blocks reuptake of NE so a possible role cannot be ruled out. One study has provided evidence for a role of NE in impulsive choice. Levels of salivary alpha-amylase (SAA) in humans, a marker of noradrenergic function, was found to be associated with performance on a delay discounting task. Individuals who had low levels of SAA, inferring low noradrenergic function, tended to make more impulsive choices.

NE may not have any role in risk-taking. Inhibition of NE reuptake has been found not to affect behaviour on the Iowa task (O'Carroll & Papps, 2003). It could, however, be hypothesised that individuals who are risk-averse would exhibit negative emotional reactions to risky situations which may lead to an increasingly vigilant state caused by NE activity.

The role of NE in self-control and risk-taking is unknown. Some drugs that increase self-control increase levels of NE in addition to levels of other neurotransmitters. A link has been found between a measure of NE function and

self-control. More research is needed to understand the role of NE in self-control and risk-taking tendency.

7.4 Altered neurological function in addiction disorders and anxiety disorders that may underlie abnormalities in self-control and risk-taking

In chapter five, the existence of abnormalities in self-control and risk-taking in drug abusers, pathological gamblers and anxiety-disordered individuals was highlighted. In this section, possible differences in neurological function that have been measured in these groups and their effects on behaviour will be introduced.

As has been introduced earlier, patients with lesions to orbitofrontal, ventromedial and dorsolateral pre-frontal areas show impairments on the standard Iowa task. These patients appear to continually select from the risky decks, thus utilising a decision-making strategy that does not maximise gains and, indeed, lead to an increase chance of completing the task with a negative total. Healthy, non-lesioned, controls learn from previous choices and, over the course of the task, shift their choices to the safe decks (with smaller rewards) that give maximal outcome in terms of winnings (Bechara et al., 1994; Clark et al., 2003; Manes et al., 2002). It has also been shown that pathological gamblers show similar decision-making impairments as the lesioned patients (Orford, 2005; Petry, 2001). This is suggestive that pathological gamblers may have abnormal function in pre-frontal areas that may lead them to persevere with the impaired strategy. In addition to this indirect evidence, pathological gamblers also have been found to show similar impairments in physiological response on this task. The lesioned participants did not show a skin-conductance response when choosing risky decks. Healthy controls show this response as a somatic marker of anxiety in response to the risky choice. Pathological gamblers also show a blunted SCR in response to the selection of a risky card (Goudriaan et al., 2006). This suggests that pathological gamblers have

impairments in brain regions that integrate and process the emotional valence of alternatives in a choice situation similar to those impairments shown by lesioned patients. Direct evidence has shown that alcohol and stimulant (methamphetamine or cocaine) abusers, when performing the Iowa task, tend to shift their choices to the advantageous decks but at a much slower rate compared to controls. In a comparison between alcohol/stimulant abusers and VMPFC-lesioned patients, it appeared that some alcohol/stimulant abusers behaved similar to VMPFC-lesioned patients while some behaved in a similar manner to controls (Bechara et al., 2001). However, other studies that utilised the Iowa task (Dom et al., 2005) found that substance abusers did show performance differences in addition to differences in neurological activation. In these studies, substance abusers showed impairments in OFC activity compared to healthy controls.

There is a large body of research showing that chronic drug abuse leads to significant changes in the neurobiology of the brain (Kieres et al., 2004). The reinforcing effects of drugs of abuse stem primarily from their innervating effects of intra-accumbal dopamine (Carlson, 2001). The reason why individuals take drugs of abuse may be attributable to the decreased dopaminergic neurotransmission that has been reliably measured within chronic drug abusers (Baker & Volkow, 2006). Research introduced in section 6.2.2 describes how decreased dopaminergic activity has been associated with increased levels of impulsivity. Therefore, the decreased self-control inherent within an individual would work in conjunction with the strong innervating effects of the drug. The use of the drug would, through Pavlovian learning, become a powerful positive reinforcer (Volkow et al., 2006) which would be highly salient to the drug user (Wang et al., 2004) as it would mimic increases caused by the provision of natural reinforcers (Volkow et al., 2004; Wise, 2002) but to a much higher level. Pathological gamblers also exhibit relatively low dopaminergic activity (Bergh et al., 1997). It is interesting to note that, although co-morbidity between pathological gambling and substance abuse has been reported to be as high as 50%, many

pathological gamblers that are non-drug abusers show similar decreases in DA levels compared to substance abusers but are not addicted to a tangible 'drug'.

Decreased serotonergic transmission has also been measured in some drug abusers and pathological gamblers. The action of tryptophan hydroxylase, the rate-limiting enzyme in the synthesis of 5-HT has been associated with impaired impulse control. Several impulsive behaviours, including parasuicide and alcoholism have been associated with a low turnover rate of this enzyme (Nielsen et al., 1998). Levels of CSF 5-HIAA has also been found to be inversely correlated with voluntary alcohol consumption in rhesus macaques (Barr et al., 2004). Artificial disruption of serotonergic function has been found to influence behaviour towards drugs. 5-HT_{2c} receptor knock-out mice have been found to be more likely to self-administer intravenous cocaine compared to healthy controls (for a review see Higgins & Fletcher, 2003). The use of 5-HT agonists such as fenfluramine (a SSRI) and $_{L}$-tyrptophan also reduce self-administration of both amphetamine (Fletcher et al., 1999; Smith et al., 1986) and cocaine (McGregor et al., 1993) in rats. In contrast to these findings, cerebrospinal fluid levels of 5-hydroxyindoleacetic acid (5-HIAA), the serotonin metabolite, were found not to differ between alcoholics, alcoholics who have attempted suicide and healthy controls (Roy et al., 1990). In addition, tryptophan depletion caused no difference in performance on a delay discounting task between individuals with or without a paternal history of alcoholism (Crean et al., 2002).

Decreased serotonergic activity has been associated with pathological gambling. Pathological gamblers have been found to show a blunted prolactin response (static measure of 5-HT activity) compared to controls (Moreno et al., 1991). In this study prolactin was measured from two blood samples taken 30 minutes apart via an intravenous catheter. One study measured lower concentrations of 5-HT and tryptophan but higher concentrations of 5-HIAA in cerebrospinal fluid in pathological gamblers compared to healthy controls (Nordin & Sjödin, 2006). This was suggestive of increased metabolic consumption of tryptophan and high

turnover of 5-HT in pathological gamblers. Artificial excitation of 5-HT neurotransmission using sertraline (a SSRI) has been found not to alter self-reported levels of gambling in a pilot study used to test the efficacy of this drug as a treatment for pathological gambling (Saiz-Ruiz et al., 2005).

It is well documented that many drugs of abuse exhibit their reinforcing effects by significantly increasing dopamine innervation within the nucleus accumbens (Melis et al., 2005; Wise & Rompre, 1989). However, it cannot be true that this effect is solely responsible for the reinforcing properties of drugs because non-dependent individuals also show similar activity in response to other reinforcers (Lingford-Hughes, 2005; Lubman et al., 2004). There are four main neurological circuits that are hypothesised to underlie drug addiction. These four systems have roles in reward (nucleus accumbens and ventral striatum), motivation (orbitofrontal cortex), memory and learning (amygdala and hippocampus) and inhibitory control (anterior cingulate cortex and prefrontal cortex including the OFC). These four neurobiological circuits are all sub-served by dopamine systems. Disruption of these four systems is thought to lead to higher subjective value being given to drug-related stimuli and, in turn, decreasing the subjective value of natural reinforcers in addition to biasing Pavlovian learning and inhibitory control (Baler & Volkow, 2006).

Areas involved in inhibitory control have been found to function abnormally in drug abusers. Areas of specific interest have been the orbitofrontal cortex and anterior cingulate cortex, two key areas thought to mediate reward value and behavioural inhibition. Research has commonly found that substance abusers show different ACC and OFC function on a variety of tasks compared to non-drug using controls. OFC lesions are also associated with compulsive behaviours (Rolls, 2000). Therefore, this area is very likely to have a major role in the mediation of motivation to obtain drugs. As described above, substance abusers choose more frequently from the disadvantageous decks on the Iowa task compared to controls. This impairment in decision-making, possibly due to increased risk-taking,

impaired reversal learning and/or impaired inhibition appears related to function within the OFC (Best et al., 2002), with substance abusers showing hypoactivity of the OFC when performing this task compared to controls (Bolla et al., 2005). Substance abusers also show impaired performance on tasks that demand a degree of behavioural inhibition. On a go/no-go task, substance abusers showed impaired performance compared to controls (Franken, 2003; Goldstein et al., 2001). During this task, substance abusers also showed hypoactivity in the ACC and OFC compared to controls (Hester & Garavan, 2004; Volkow et al., 1992). On a Stroop task (a task that also demands inhibition of learned responses) substance abusers show altered responses in the ACC and DLPFC compared to controls (Gruber & Yurgelun-Todd, 2005). The OFC and ACC have also been implicated in drug craving. Injection of methylphenidate into cocaine abusers causes increases in OFC and ACC activity, which was associated with reports of increased cocaine craving (Breiter et al., 1997). There is strong evidence to suggest the presence of neurological impairments in the OFC and ACC in drug abusers. This would lead to abnormal valuation of drug-related stimuli and impair inhibitory control to not take drugs. One difficulty with this research is assessing if the measured abnormalities in brain function are caused by chronic use of the drug or pre-existing trait.

Pathological gambling has also been linked to impairments in the same systems as those mentioned above for substance abusers, i.e. systems involved in reward, motivation and learning (Chambers & Potenza, 2003). Research using pathological gamblers does have the advantage that many of these individuals do not take drugs of abuse but show similar behavioural responses to gambling as drug abusers show to drug stimuli including euphoria, craving and tolerance (Reuter et al., 2005). However, the co-morbidity between pathological gamblers and drug use can be as high as 50% (Hollander & Rosen, 2000) so the sample used must be selected with care. In a task involving ambiguous risk in order to obtain rewards, pathological gamblers exhibited hypoactivity of the ventral striatum and ventromedial prefrontal cortex, two areas implicated in reward and impulsivity. Pathological gamblers also show hypo-activation in certain brain areas in response to gambling cues. When

viewing videos of individuals in gambling experiences accompanied by audio commentary of the actor's experiences and feelings, pathological gamblers report higher excitement or urge to gamble compared to controls but show decreased activity in the frontal and orbitofrontal cortex, basal ganglia and thalamus (Potenza et al., 2003). However, in a separate experiment in which pathological gamblers were showed videos of gambling situations, pathological gamblers exhibited hyperactivity in the DLPFC, right VMPFC, right parahippocampal gyrus, left fusiform gyrus and visual cortex (Crockford et al., 2005). Pathological gamblers also show heightened activation in the prefrontal cortex, cingulate cortex, ventral striatum and visual cortex when playing blackjack for money instead of points (Hollander et al., 2005) suggesting that areas of the brain involved in reward, motivation and inhibition are hyperactive when faced with real reinforcers. This research suggests that pathological gamblers exhibit abnormal activity in areas responsible for inhibition and reinforcer value. Abnormalities in gamblers may mirror those found in substance abusers with only the outcome, i.e. 'drug' of use, being different. One interesting question concerns the level of similarity of neurological abnormalities between drug use and pathological gambling as, if the neural abnormalities were found to be very similar, then research into pathological gambling may uncover which abnormalities in drug abusers were caused by the chronic use of a tangible drug.

When reading this introduction, a valid question that can be asked is, "How similar are substance abusers and pathological gamblers and, if they are similar, what makes one person abuse drugs and another, gambling?" Samples taken from these two populations have shown fairly similar patterns in impulsivity-related behaviour compared to controls. Both show heightened levels of impulsivity and more rapid delay discounting of rewards. Both show evidence of impaired behavioural inhibition compared to controls. One very interesting factor to take into account is the additive factors upon *k* of pathological gambling and substance abuse (Petry & Casarella, 1999). This suggests that, regarding levels of delay discounting, these two pathologies have definite and similar effects on *k* and that they interact with

one another to exacerbate levels of this behaviour. One difference may lie in the level of risk-taking or sensation seeking. Increased levels of novelty-seeking have been measured in substance abusers (Wills et al., 1994), however, mixed results have been found in gamblers (note that this may be because of the increased number of studies measuring risk-taking in gamblers compared to substance abusers). One study found that sensation seeking was a predictive factor of problem gambling in women (but not men) (Nower et al., 2004). Another study found no differences in levels of venturesomeness between probable pathological gamblers, potential pathological gamblers and non-gambling controls (MacKillop et al., 2006). Other studies have found that problem gamblers show decreased levels of sensation seeking and risk-taking compared to non-gamblers (Coventry & Constable, 1999; Holt et al., 2003). Regarding neural function in these groups, both show evidence of impaired decision-making on the Iowa task at a level similar to VMPFC-lesioned patients (Bechara et al., 2001; Orford, 2005; Petry, 2001). However, it is important to note that there are subsets of substance abusers who show similar performance to controls, suggesting that some substance abusers show unimpaired behaviour, contrary to that of the pathological gamblers (Bechara et al., 2001). Hypoactive dopaminergic (Baker & Volkow, 2006; Bergh et al., 1997) and serotonergic (Moreno et al., 1991; Nielsen et al., 1998) activity has been measured in both groups. Both groups also show hypoactivity in certain neural regions. Hypoactivity in regions associated with behavioural inhibition, i.e. OFC & ACC, has been measured in substance abusers (Gruber & Yurgelen-Todd, 2005; Hester & Garavan, 2004; Volkow et al., 1992). In pathological gamblers, hypoactivity of regions associated with reward, i.e. nucleus accumbens and VMPFC, has been measured. These groups do show many similarities in both behaviour and neural function. However, some important points come to light when answering the question posed in the first line of this paragraph. Firstly, there is some evidence that suggests that pathological gamblers may exhibit differences in risk-taking/sensation-seeking/venturesomness to substance abusers. Secondly, although both groups show hypoactivation of areas involved in reward and decision-making these areas are not in similar systems (e.g. the ‘reward’ or ‘motivation’ systems),

therefore, the hypotheses that can be made from previous research are tenuous. Thirdly, to my knowledge, no study has directly compared substance abusers and pathological gamblers on the same task. Further research comparing the neural function of these two groups is therefore needed. However, we can currently hypothesise as to what possible differences may exist between these groups. Both groups show comparable levels of heightened delay discounting; however, they may differ in levels of risk-taking. The research posits that substance abusers do show increased risk-taking tendencies compared to controls while in pathological gamblers levels of risk-taking are more variable. Both show performance deficits on the Iowa task indicative of dysfunction in frontal circuitry; however, the performance, and thus the indication of dysfunction, of the substance abusers is more variable than that shown by the pathological gamblers. Concerning neural function, substance abusers have repeatedly exhibited dysfunction of prefrontal areas and the ACC in tasks measuring behavioural inhibition. Pathological gamblers have exhibited similar dysfunction of prefrontal areas but also within the nucleus accumbens. These findings may be indicative of altered dysfunctional systems within limbic circuitry between these two groups. Alternatively, it may be the case that these two groups are extrememly similar as regards behavioural and neural abnormalities, but environmental and social factors (e.g. access to gambling venues, peer participation in gambling) provide the final effect in creating the preference for either drugs or gambling. In this project, the performance of these two groups will be directly compared to ascertain whether these hypotheses hold ground.

Anxiety disorders have also been linked to abnormalities in the functioning of the 5-HT system. SSRIs, such as fluoxetine (Coplan et al., 1992), sertraline (van Ameringen et al., 2001) and paroxetine (Stein et al., 1998) have been found to alleviate symptoms of anxiety disorders although it takes about six weeks for the therapeutic effects to appear, therefore, the mechanism by which the drug alters the biochemistry of the brain involves adaptation of one, or a number, of neurological systems. Nefazodone, a 5-HT_2 agnonist, has been found not to alleviate symptoms

of social phobia suggesting that other systems need to be considered in treatment of anxiety disorders (van Ameringen et al., 2007). The amygdala has been focused upon in research investigating anxiety disorder due to its core role within emotional processing and learning. Physical volumetric analysis of amygdala volume has found that children and adolescents with Generalized Anxiety disorder have enlarge amygdala volumes compared to healthy children and adolescents (de Bellis et al., 2000) suggesting that abnormal development of the amygdala may be associated with anxiety disorders. The amygdala contains a high density of benzodiazepine receptors. Admistration of benzodiazepines has been found to be an effective treatment for anxiety disorders (Pinel, 2003). However, administration of benzodiazepines into rats with amygdala lesions also causes anxiolytic effects suggesting that other structures are involved (Yadin et al., 1991). Injection of benzodiazepines, 5-HT receptor antagonists and $GABA_A$ receptor agonists into the amygdala has been found to decrease conditioned fear in rats (Graeff et al., 1993). Injection of $GABA_A$ receptor agonists and benzodiazepines into the periaqueductal gray produced similar outcomes. However, innervation of the 5-HT system in this area led to anxiogenic effects, suggesting that abnormal activity of the 5-HT system has dissociable roles in the amygdala and periaqueductal gray concerning anxiety. Furthermore, increase in DA activity in humans by administration of metoclopromide has been linked to increased levels of anxiety (Kluge et al., 2007). However, care must be taken with this result as it was a single-case study. In addition to this finding, Generalised Social Phobia has been linked with hypofunction of the striatum (Sareen et al., 2007) possibly suggesting dysfunction of neurotransmitter systems including 5-HT and DA.

This chapter has introduced a large body of evidence that supports the view that drug abuse and pathological gambling are linked to abnormal function in certain areas of the brain. Most research has found that areas innervated by dopamine and 5-HT and that are implicated in subjective valuation and inhibitory control function abnormally compared to healthy controls. Special focus has been placed upon the orbito-frontal cortex and the anterior cingulate cortex. Abnormalities in these areas

in drug abuser and pathological gamblers, in addition to abnormal function in the mesolimbic reward circuit, have been linked to significant decreases in inhibitory control and reinforcer strength, leading to the increases valuation of drug and gambling-related cues and the inability to inhibit the motivation to take drugs/gamble.

8. Key gaps in the research and how this project aims to explore them

This introduction was written with the express aim of introducing the reader to the psychology and neurology of self-control and risk-taking. To this end, key areas within these areas of research have been discussed and a number of questions have subsequently arisen. In this section, these questions will be outlined and explanations will be given as to how these questions will be investigated.

One of the primary aims of the project is to design new delay and probability discounting tasks that will build upon the knowledge obtained from previous studies. These new tasks will be utilised to measure self-control and risk-taking with increased validity. These tasks will assess more realistic decision-making behaviour by making the participant experience the consequences of their choice after every trial, i.e. by experiencing the delay or probability of their preferred alternative. It is hoped that these tasks will then be used by subsequent researchers interested in self-control and risk-taking behaviour because, currently, there are no standard discounting tasks which raises some concerns when comparing performance across studies. Another reason for creating new discounting tasks is to investigate claims that performance on a delay discounting task alters as real, rather than hypothetical, monetary rewards are introduced[2]. If this claim is substantiated then this would provoke a discussion concerning the results of previous studies utilising hypothetical rewards. We may find that the hypothetical tasks are not as valid a measure as previously thought or, alternatively, that tasks providing

[2] See section 4.7 for more details

hypothetical rewards measure a different behaviour compared to those giving real rewards. This project will utilise delay and probability discounting tasks that provide real and hypothetical rewards to order to compare choice behaviour and interpret any differences. In addition to healthy controls, the tasks will also be provided to so-called 'impulsive' samples that have been commonly recruited in delay discounting experiments, i.e. substance abusers and pathological gamblers in order to test choice behaviour in non-control samples.

The new delay and probability discounting tasks will also be utilised to test the applicability of the Multiplicative Hyperbolic Model of Choice in describing choice behaviour in humans. The model has been previously used to evaluate behaviour in rats[3] but has never been used to describe choice behaviour in humans. If this model can be successfully used in humans then it will provide high quality information as to how humans make everyday decisions and how delay and probability affect the choices that we make. The model will also be applied to explain decision-making biases exhibited by substance abusers and pathological gamblers that have been suggested to underlie their addictive behaviour. Previous research has found that these populations show significantly decreased self-control on a delay discounting task. The new tasks, providing real consequences, will be used to assess their choice behaviour in a more realistic environment. The extent of risk-taking behaviour exhibited by these groups is currently unknown. To assess risk-taking behaviour, the probability discounting task will be utilised.

Currently, there are numerous hypotheses concerning the relationship between behaviour on the delay and probability discounting tasks and other personality and social factors[4]. One study has suggested that delay discounting behaviour is correlated with IQ (de Wit et al., 2007). There are also questions regarding the relationship between working memory capacity and delay discounting (Hinson et al., 2003). However, this study was later criticised for methodological problems

[3] See section 5 for an introduction to the model and section 7.1.1 for details of its research findings
[4] See section 4.6 for details

(Franco-watkins et al., 2006). Another study has linked years of education and delay discounting (Jaroni et al, 2004). In addition to these possibly studies, there may also be other relationships that have not been discovered. An investigation utilising a delay discounting task in addition to numerous other measures would provide useful information as to any possible relationships. Furthermore, no research has investigated the relationships between the probability discounting task and other behavioural or social factors. This project will provide a battery of tasks which will measure a wide range of behaviours including a demographic questionnaire which will provide information about socioeconomic status, educational status etc. The conclusions from this investigation will produce useful information into the nature of self-control and risk-taking. It will also provide information as to how alterations in social or behavioural factors may affect self-control and risk-taking.

The final part of the project will utilise *f*MRI to answer a number of questions regarding impulsive behaviour. Only two studies have previously used an imaging version of a delay discounting task in humans. Although there have been many studies in rats, more research is needed in humans to discover the brain areas involved in self-control. Previous studies have identified some areas involved in delay discounting including the orbitofrontal cortex, nucleus accumbens, hippocampus, amygdala, substantia nigra and insula. No study has previously used an imaging version of a probability discounting task so the brain areas involved in this task are unknown. Conclusions from this section of the project will provide extremely useful information as to the neurobiology of self-control and risk-taking behaviours that are used in everyday life. This project will analyse brain areas involved in choice behaviour in delay and probability discounting tasks.

Following on from this area of research, the discounting tasks will be used (in conjunction with more established tasks) to explore self-control, risk-taking and inhibitory control in populations that have previously been labelled as ‘impulsive’, i.e. substance abusers and pathological gamblers. This will be done to assess

whether these groups show abnormalities in brain activity compared to controls that would underlie their biases in decision-making (which may lead to their addictive behaviours), especially those measured by the delay discounting task. Studies recruiting patients with brain lesions have found that damage to the orbitofrontal cortex, ventromedial prefrontal cortex or dorsolateral prefrontal cortex has impaired behaviour in a range of tasks including the delay discounting tasks and Iowa task. Further studies have discovered that substance abusers and pathological gamblers behave in similar ways to the lesioned patients suggesting that they may exhibit abnormalities in these brain areas. These findings can be assessed alongside findings from non-human studies that have found that artificially damaging certain brain structures can cause increased impulsive behaviour. No previous study has provided imaging versions of a delay or probability discounting task to substance abusers and pathological gamblers.

Although previous studies have concluded that pathological gamblers and substance abusers show both behavioural and neurological abnormalities compared to controls, no study has assessed the differences or similarities between the two addicted groups. It could be argued that, although there are similarities, there must also be differences that may cause an individual to prefer the use of drugs or acts of gambling. Although co-morbidity between these two disorders has been reported to be as high as 50%, there must still be some differences explaining differences in preferred addictive stimulus. It may be the case that drug abusers are more risk-taking because they prefer a stimulus which has potential serious short-term and long-term negative impacts on health whereas the pathological gambler chooses a stimulus which does not. One could also argue that substance abusers would show decreased self-control and inhibitory control for the same reason. Therefore, this project will assess the similarities and differences, both behavioural and neurological, between these two groups as regards impulsivity.

In addition to the tasks outlined above, another novel task will be provided that will assess the brain areas involved in the urge to gamble. The results from this task will

produce highly useful information into the neurobiology of the precursor behaviour to gambling itself, thus providing information concerning the primary stages of the expression of the addictive behaviour. Information concerning this stage is important as treatments that can be produced that will attenuate this precursor behaviour will, in turn, decrease the addiction. There have been two previous studies that have aimed to assess the brain areas involved in gambling urges which have found contrasting results. One study found decreased activity in the OFC, basal ganglia and thalamus in response to gambling cues while the other found increased activity in the prefrontal cortex, parahippocampal gyrus, fusiform gyrus and visual cortex. Further investigation is needed to resolve this issue.

Finally, at all stages of the research a group of non-pathological gamblers will be recruited in order to investigate a group that expresses the same behaviour as in the addicted population but to a non-addicted level. No previous study has investigated impulsivity in non-pathological gamblers. They will be recruited to test the hypothesis that pathological gambling occurs through accruement of a progression of behavioural changes caused by progressive abnormal function of areas of the brain. In addition, brain abnormalities or behaviours that predispose individuals to become gamblers can be discovered. If predispositional factors were present they would be expected to occur in the pathological and non-pathological gamblers but not in the non-gambling controls and substance abusers.

9. Hypotheses

1. Real rewards will evoke higher self-control compared to hypothetical rewards on the delay discounting task and evoke lower risk-taking behaviour compared to hypothetical rewards on the probability discounting task
2. Substance abusers and pathological gamblers will show higher levels of impulsivity compared to controls. More specifically, these will be reflected by:

   a. Substance abusers and pathological gamblers showing lower self-control in the delay discounting task compared to controls and higher risk-taking on the probability discounting task compared to controls
   b. In addition, substance abusers will show increased risk-taking on the probability discounting task and decreased self-control on the delay discounting task compared to pathological gamblers.
3. Anxiety-disordered individuals will show higher self-control in the delay discounting task compared to controls and decreased risk-taking on the probability discounting task compared to controls
4. Pathological gamblers and substance abusers will show abnormal levels of activity in brain areas involved in impulsivity compared to controls. More specifically:
   a. Pathological gamblers and substance abusers will show impaired activity in the prefrontal cortex on the go/no-go task, Iowa task and delay and probability discounting tasks compared to controls.
   b. The pattern of prefrontal function will differ between pathological gamblers and substance abusers thus:
      i. Pathological gamblers will exhibit impaired function within ventromedial prefrontal areas compared to substance abusers
      ii. Substance abusers will exhibit impaired function within the orbitofrontal cortex and anterior cingulate cortex compared to pathological gamblers.
   c. Pathological gamblers and non-pathological gamblers will show higher prefrontal activity compared to controls and substance abusers on the urge to gamble task.
5. Non-pathological gamblers will mirror the behavioural and neurological abnormalities measured in pathological gamblers but to a lesser degree

General Methods

Participants

Participant details

Participants were recruited from the student body at the University of Manchester and from the community. A previous study (Green et al., 1994) found that there are effects of age on delay discounting rates, therefore, participants were excluded if they were younger than 18 years or older than 60 years. Due to the high volume of textual instructions, participants were required to have a very good understanding of the English language.

The details of the participant groups were different in each experiment. Although there was some overlap, extra participants were recruited as some participants did not return for the later stages of testing. Details of the participant groups are shown in the "Participants" section within the description of methods for each experiment.

Recruitment advertisements were sent to all university students within the University of Manchester. Advertisements were also located on the GamCare website[5].

Participants who were recruited for the *f*MRI study were given a list of criteria that they had to fulfil to be eligible for the study. These criteria mainly focused on health and safety aspects, e.g. metal in the body, previous head surgery, possible pregnancy etc. Corrective lenses in the form of glasses were unable to be worn. Participants were excluded if they were unable to see clearly at a distance of four metres without corrective lenses. Participants were allowed to wear contact lenses.

[5] GamCare is a registered charity providing information regarding support, advice and counselling for people affected by gambling problems. For further details see the website www.gamcare.org.uk.

Due to the position of the body within the scanner, participants were also questioned on possible claustrophobia or disinclination to somewhat confined spaces. If potential participants answered positively then they were advised not to take part. All participants were right-handed.

Four samples were recruited, pathological gamblers, non-pathological gamblers, individuals with Generalized Anxiety Disorder and healthy controls. Samples were matched for age and ratio of males to females. Unfortunately, this proved to be difficult due to the majority of male compared to female gamblers who responded to recruitment and the majority of females who volunteered for the anxious group.

Criteria for diagnostic groups

The screening procedure utilised was the Miniature International Neuropsychiatric Interview or MINI (Amorim et al., 1998; Lecrubier et al., 1997; Sheehan et al., 1997; Sheehan et al., 1998). The MINI contains diagnostic criteria for all major axis I disorders as defined by the DSM-IV and ICD. The MINI is designed to be brief, lasting approximately 10-30 minutes. The South Oaks Gambling Screen (SOGS) was also utilised when screening pathological and non-pathological gamblers. There are three outcomes of the SOGS dependent on score. A score of 5 or more indicates probable pathological gambling, a score of 1-4 indicates some problems with gambling and a score of 0 indicates no gambling problems

When a potential participant first expressed interest they were screened by telephone using the DSM-IV criteria for the disorder corresponding to the group they thought they fit into (taken from the MINI). Pathological gamblers and non-pathological gamblers were given DSM-IV criteria for pathological gambling. They were also asked questions from the SOGS. Pathological gamblers were deemed eligible once they met 5 or more criteria from the DSM-IV and scored over 5 on the SOGS. Non-pathological gamblers were considered eligible if they gambled weekly, met 0-4 criteria on the DSM-IV and scored 0-4 on the SOGS.

Non-pathological gamblers were also explicitly asked if they had any problems controlling their gambling. A positive answer to this question would have warranted exclusion from the non-pathological group and testing for eligibility in the pathological group. Depending on their drugs of abuse, substance abusers were given DSM-IV criteria for alcohol abuse or dependence, or non-alcohol psychoactive substance use disorders. All substance abusing volunteers used psychoactive drugs in addition to drinking alcohol, therefore, both criteria were given to each participant. Potential participants for the anxious groups were given DSM-IV criteria for Generalized Anxiety Disorder (GAD).

At the time of testing subjects it was checked that they still met criteria for the specific disorders as outlined above. Substance abusers, pathological and non-pathological gamblers still met criteria. Three participants that were tested for GAD no longer met criteria. This was related to the time of screening, which was during examination time, and subsequent decreasing anxiety following this period. However, each of these cases did meet criteria for social phobia. Consequently, the criteria for inclusion into the anxious groups were widened to include DSM-IV criteria for GAD or Social Phobia. Healthy controls were not screened using the MINI until they came in for testing but were instructed to inform the researcher at telephone screening if they felt they had any personality or behaviour disorders/difficulties. None of the controls met any DSM-IV criteria contained within the MINI.

Materials

Self-report measures and neuropsychological tasks that were commonly used in this research

Several self-report questionnaires and neuropsychological tasks were utilised in several different experiments in this research. There were a number of measures

available for use. Participation time was a critical factor in determining which measures to use. Therefore, the measures chosen were felt to be able to obtain the most amount of useful information with the most efficient utilisation of time. The measures chosen are described below.

Self-report measures

Barratt Impulsiveness Scale (BIS-11)

The BIS-11 is a 30-item questionnaire (Barratt, 1994). The BIS has three sub-scales. A total score can be calculated from summing the scores from all three sub-factors. These sub-factors are cognitive (or attentional), motor, and non-planning impulsivity. The cognitive impulsivity sub-factor measures an individual's tendency to make rapid decisions and judgements, (e.g. "I am a careful thinker"). The motor sub-scale measures the individual's propensity to physically act without thinking (e.g. "I do things without thinking"). The non-planning sub-scales rates an individual's present orientation or ability to plan for the future (e.g. "I am more interested in the present that the future").

Impulsivity Venturesomeness Empathy questionnaire (IVE)

The IVE is a 54-item questionnaire (Eysenck et al, 1985,1990). The IVE is split into three factors. The impulsivity sub-scale measures the tendency to act without forethought. The venturesomeness sub-scale measures an individuals tendency to take risk and take part in risky activities (e.g. "I enjoy sky-diving). Impulsiveness and venturesomeness, as defined by the IVE, can be viewed as somewhat opposite tendencies. High impulsivity is the tendency to act without considering risks and consequences. High venturesomeness is the tendency to consider the risks and consequences but engage in a risk act regardless of these. The empathy sub-factor measures an individual's social cognition, or ability to understand the emotional states of others.

Temperament and Character Inventory (TCI)

The TCI is a 255-item questionnaire. The TCI is based upon Cloninger et al.'s psychobiological model of personality (Cloninger et al., 1993). The TCI is split into seven sub-scales. Four are measures of temperament that manifest in early life and are heritable. These are novelty-seeking, harm-avoidance, reward dependence and persistence. The remaining three sub-scales are measures of personality, which occur in mature development and influence personal and social effectiveness. These are self-directedness, co-operativeness and self-transendence.

Big-5 personality questionnaire

The Big-5 has 44 items (John et al, 1991). The Big-5 is based upon the Five-Factor theory of personality (John et al, 1990; McCrae and Costa, 1996). The Big-5 measures these five personality factors; extraversion, agreeableness, conscientiousness, neuroticism and openness to experience.

Quick test for IQ (QT)

The QT presents individuals with three sets of four pictures. Individuals are presented with words shown individually. Each word ranges in complexity from very easy to relatively hard. IQ is calculated dependent on how many correct responses given. Participants must indicate which picture that word best describes. Individuals who have high IQ would have a larger vocabulary and respond to more items correctly and vice versa for individuals with a low IQ.

Alcohol Use Disorder Identification Test (AUDIT)

The AUDIT is a 10-item questionnaire designed to assess severity of problem drinking. Scores range from 0-40. A score of 8 or more is associated with

hazardous drinking. A score of 13 or more in women or 15 or more in men indicates probable alcohol dependence (Saunders et al, 1993).

South Oaks Gambling Screen (SOGS)

The SOGS is a 16-item questionnaire that assesses severity of gambling. A score of 5 or more indicates probable pathological gambling. A score of 1-4 indicates some problems with gambling and a score of 0 indicates no gambling problems (Lesieur and Bloom, 1987).

State-Trait Anxiety Inventory (STAI)

The STAI is a 40-item questionnaire (Spielberger et al, 1983). The STAI measures two levels of anxiety. These are state anxiety (transitory anxiety felt at the moment of taking the test) and trait anxiety (general levels of anxiety).

Demographics questionnaire

This was a 22-item questionnaire that obtained personal information on age, gender, ethnicity, family status, previous psychiatric and medical history, socioeconomic status and educational status.

Neuropsychological tasks

Nback Task

This task was designed to measure working memory. The task presents a series of numbers presented sequentially. After the series of numbers is given the participant is instructed to recall the number currently presented or the one that was 1, 2 or 3 back in the sequence. There were six trials in each condition (0, 1, 2 or 3back). Each number is presented for 500 milliseconds followed by a blank screen for 500

milliseconds. 2-16 numbers are presented in a series. The last number of the series remains on the screen whilst the participant was asked to recall the correct number.

Stop Task

The stop task was designed to measure an individual's ability to withhold unwanted prepotent motor responses. The task repeatedly presented the participant with a cartoon of a plane. The participant was asked to make a key press when the plane was seen. This was termed a go trial. However, sometimes the plane was quickly followed by a cartoon of a bomb. When this occurred the participant was required to make no response. This was termed a stop trial. There were 73 go trials and 27 stop trials. In a go trial the plane was shown for 1000 milliseconds followed by a blank screen for 1666 milliseconds. In a stop trial the plane was presented for 250 milliseconds followed by the immediate presentation of the bomb for 550 milliseconds. A blank screen was then shown for 1666 milliseconds. Stop errors occur when the participant made a response on a stop trial and is a measurement of ability to inhibit unwanted responses. Go reaction time indicates the time an individual took to make a response on a go trial and is thought to be an indicator of one factor of impulsivity (increased reaction time).

Delay and probability discounting tasks

These tasks were designed to assess how individuals valued reinforcers that carried delays or probabilities of not being given. These tasks are described in detail in the following chapters

Experiment 1: A pilot study to develop the discounting tasks

Introduction

Delay and probability discounting tasks provide direct measures of self-control and risk-taking tendency. They can also provide estimates of the sensitivity to the magnitudes of delayed and probabilistic rewards. Research using these tasks has provided important information concerning these behaviours that are used in everyday decision-making situations. These tasks can also be utilised to explore behavioural biases that underlie many psychiatric disorders.

One consideration concerning early research using delay and probability discounting tasks is that they mostly provided hypothetical outcomes. Debatably, hypothetical outcomes do not mimic real-life decision-making environments. A small number of studies have utilised tasks that provide some types of real outcome (Lane et al., 2003; Madden et al, 2003; Madden et al, 2004; Lagorio and Madden, 2005). However, these studies have included methodological considerations which may have affected the results[6]. Further studies need to be performed that compare discounting behaviour on tasks that have real consequences. Currently, there are no standard discounting tasks in use. Therefore, new tasks would have to be constructed.

The aims of this experiment were to create a set of novel discounting tasks that would cause the participant to experience real consequences that are associated with their decisions. The tasks would be constructed so that, at a later stage in this project, real and hypothetical monetary rewards could be easily incorporated within the framework of the task. A delay discounting task that has employed real

[6] See section 4.7 of the introduction for more details

consequences and that gave real monetary rewards for every choice has only been previously used in one study (Lane et al., 2003). Therefore, the construction of the tasks, especially the probability discounting task needed pilot testing. In this experiment, a sample of individuals was recruited in order to measure performance on new versions of a delay and probability discounting task in order to check the validity of the tasks and to obtain feedback from these participants.

Method

Participants

Eight participants were selected using opportunity sampling. Participants were colleagues or acquaintances of the researcher. No personal data was collected from any participant.

Apparatus

The delay discounting task consisted of 86 choices between two alternatives. Alternative A had a hypothetical reward of £0.10 and carried a delay of 1, 2, 4, 6, 8, 10, or 12 seconds. Alternative B had a hypothetical reward of £0.20 and carried a delay ranging from 1-28 seconds in two second intervals. The delay of alternative B was either equal or more than the delay associated with alternative A. The delay of alternative B was systematically altered in order to calculate indifference points. There were two presentations of the task (43 choices in each) in order to increase the reliability of sampling. Rewards of £0.10 and £0.20 were used because the provision of real rewards had to be affordable to the researchers.

Each choice was presented on two A4 cards. Each card held the details for one alternative. Each card had the name of the alternative at the top and the delay in seconds written in the centre of the page at a height of 65mm and a width of at least 35mm (width was dependant on the number presented).

There were two versions of the probability discounting task that were tested. The first contained 65 binary choices. Alternative A had a hypothetical reward of £0.10 and carried a win probability of 1.00, .75, .67, .5, .33, .25, .20 or .165. Alternative B had a hypothetical reward of £0.20 and had a win probability equal or less than that of alternative A. The win probability of alternative B was systematically altered in order to calculate indifference points. The second probability task trialled contained 28 binary choices. Alternative A and B gave the same reward amounts. Alternative A now only had four permutations, .75, .50, .25, and .165 (which will henceforth be known as *p*A values). This task was tested in order to see if the task could retain validity having been significantly shortened. Each choice was presented on A4 cards similar to the delay discounting task. However, instead of delays, a 'wheel of fortune' was shown in the centre of the card (similar to Rachlin et al., 1991, 1994) measuring 193mm in diameter. A cardboard spinner was used to ensure that the outcome in the probability task was random. The tasks were each tested on four participants.

All participants also completed the BIS-11 and Stop Task[7].

Procedure

Participants were sat at a table facing the researcher. The nature of the task was explained to them using a set of standardized instructions (shown in appendix 1).

Participants were first given the delay discounting task. Participants were presented with each choice sequentially. To make a response, participants stated out loud "A" or "B" depending on which alternative they preferred. When the participant had made a response, the researcher used a stopwatch to measure the delay associated with the alternative the participant had chosen. During this time, the researcher and

[7] See "General Methods" section for descriptions of these measures.

participant sat in silence. When the delay had ended, the next choice was given to the participant.

The procedure for the probability discounting task was similar, except that when the participant had stated a choice they placed a spinner onto the wheel of fortune associated with the alternative they had chosen. They then spun the arrow upon the spinner to see if they had won. The arrow had to travel around the spinner three times in order to ensure that the outcome was random. If the arrow landed in a white segment then the participant won. If it landed in a black segment then the participant did not win. All rewards were hypothetical.

After the discounting tasks had been completed, participants were given the BIS-11 and Stop Task.

Data Analysis

Responses on the discounting tasks were used to calculate indifference points. To find the indifference point, the area at which preference for one alternative changed to the other was found and an average of these two points was calculated. For example, in a situation where dA = 4 seconds, the participant may prefer alternative B if the dB was 8 seconds or less but prefer alternative A if the delay was 10 seconds or more. This would mean that the preference switch was between 8 and 10 seconds. The indifference point was then calculated to be 9 seconds. An algorithm was used to calculate IPs (shown in appendix 2). For each individual, the IPs were plotted for each task. A linear regression was calculated for each plot. The slope and intercept were obtained from the linear regression. Using the slope and intercept, discounting parameters were calculated. K^+ and H^+ were calculated by the equation [(slope-1)/intercept] from the plots of the delay and probability task respectively.

K^+, H^+, slope, and intercept values from their respective tasks were correlated using Spearman's rank-order correlation. This was done to assess the relationship between these calculated indirect measures. K^+ and H^+ values were also correlated to each other to assess any possible relationship.

K^+ and H^+ values were correlated with scores on the BIS-11 and Stop Task using Spearman's rank-order correlation coefficient. Spearman's was used due to a high positive skew in parameter values.

Results

From the participants' responses on the delay and probability discounting tasks, indifference points were measured and used to plot the linear regression and calculate parameter values. Individual measured data and calculated values for each participant are shown below in table 1.

Table 1: Individual data and calculated values taken from the neuropsychological tasks and the pilot delay and probability discounting tasks.

Participant number	Delay Discounting Task			Probability Discounting Task			Barratt Impulsivity Scale				Stop Task	
	K^+	slope	int	H^+	slope	int	Tot	Att	Mot	NP	SE	RT
1	0.11	1.29	2.57	-4.45	2.50	-.34	49	16	20	13	4	675.48
2	0.02	1.09	5.75	6.35	2.78	.28	47	14	22	11	0	772.06
3	1.33	2.00	0.75	-68.10	2.43	-.02	21	8	9	4	15	414.62
4	0.49	1.62	1.27	-68.10	2.43	-.02	48	19	17	12	15	480.23
5	0.07	1.39	5.29	1.83	1.94	.51	41	15	16	10	6	587.48
6	0.10	1.33	3.18	-2.42	8.66	-3.16	50	12	22	16	5	637.62
7	2.33	2.05	0.45	1.17	1.45	.38	29	11	14	4	2	702.02
8	0.27	1.70	2.55	-8.60	2.37	-.16	34	11	13	10	7	660.33

In the delay discounting task, K^+ was correlated with the slope, $r_s = 0.88$, $p = .004$, and intercept, $r_s = -1.0$, $p < .001$. Slope and intercept were negatively correlated, $r_s = -0.88$, $p = .004$.

In the probability discounting task, H^+ values were not correlated with the slope, r_s = 0.1, p = .99, and intercept values, r_s = 0.47, p = .24. Slope and intercept were not significantly correlated but there was a trend, r_s = -0.66, p = .07.

There was a trend for K^+ and H^+ values to be negatively correlated, r_s = -0.64, p = .09.

Slope from the delay discounting task was highly negatively correlated with the motor subscale, r_s = -0.86, p = .006, non-planning, r_s = -0.76, p = .03, and total score, r_s = -0.76, p = .03, on the BIS-11. Slope from the probability discounting task was positively correlated to the motor subscale, r_s = 0.76, p = .04, and non-planning, r_s = 0.77, p = .03, on the BIS-11. There was a trend for H^+ to be correlated with reaction time on the Stop Task, r_s = 0.68, p = .06.

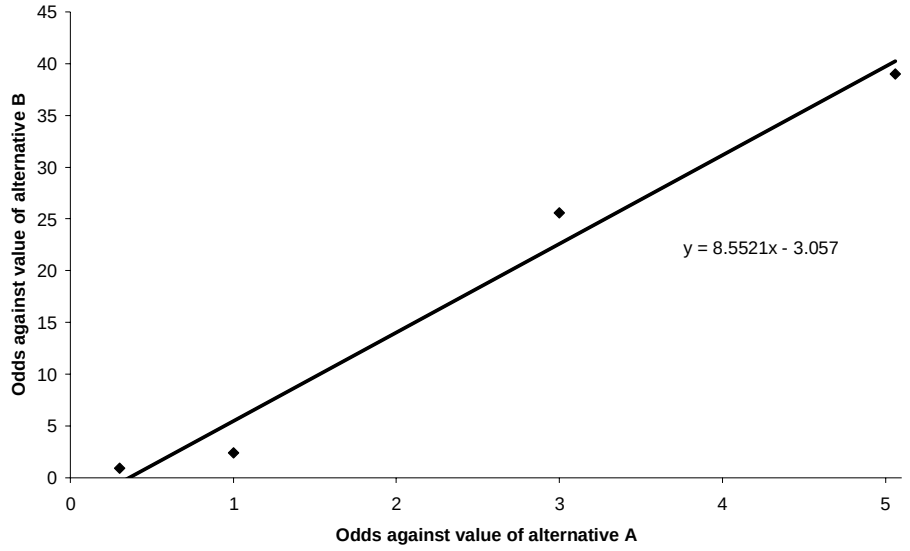
Discussion

The pilot study was designed in order to test the performance of novel delay and probability discounting tasks. Only one previous study has incorporated a delay discounting task providing real outcomes for every choice and compared performance to a hypothetical task (Lane et al., 2003). To our knowledge, this is the first probability discounting task providing real vs. hypothetical rewards. It must be noted that this experiment included a pilot task and that the sample size was low (N = 8). Therefore, any conclusions drawn from this study are investigatory and are not used to answer hypotheses. Hypotheses will be addressed by testing in later experiments. The pilot study was performed to test the discounting tasks and to investigate whether reliable measurements could be obtained and, if issues where raised, if these issues could be addressed by alteration of the tasks.

Using the tasks, the indifference points measured from each participant could be efficiently plotted. The calculation of parameter values could also easily be performed from the linear regressions.

In the delay discounting task, all IPs were within our expected range. However, in the probability discounting task there were problems with the calculation of H^+ from five participants. In these cases, H^+ was calculated as a negative value. In two cases the value was extreme (-68.1). In terms of the Multiplicative Hyperbolic Model of Choice, a negative intercept would reflect highly irrational behaviour. Consider figure 2 below that shows the plotted indifference points from a hypothetical participant.

Figure 2: Indifference points from a hypothetical participant taken from the probability discounting task



The graph states that if the participant is given a choice where alternative A has an odds against value of 0.3 (p = .75) then the indifference point exhibited by the participant would be zero. In other words, if there was a probability of winning on alternative A equivalent to .75, this participant would not take any risk to gain the larger reward. They would prefer the smaller risky alternative compared to

alternative B that would have twice as much reward but significantly less risk. This behaviour is clearly irrational and would probably not reflect the true behaviour shown by the participant at the time of testing. The problem may be related to the power that low *p* values have on the placement of the linear regression. The probability scale is a ratio scale so equally spaced values would have equal power on the linear regression. However, because the calculation of θ involves [*(1/p)-1*] the intervals between integers becomes non-linear. To clarify, if we have four *p* values that have equal intervals; 1.0, .75, .5, and .25, when calculated into θ these measurements become 0, 0.3, 1, and 3 respectively. The biasing effect of θ may invalidate this measure as it places more emphasis on certain choices (i.e. those that involve more risk compared to less risky choice). However, it may be the case that the measurements taken by the pilot task (rather than task invalidity) are exacerbating the problem and by adapting the task, this issue can be resolved. The problem could be overcome in two ways, inclusion of only one high risk *p*A and inclusion of a *p*A of 1.0. The latter may aid in anchoring the linear regression in the positive area of the *y* axis. These methods will be incorporated into further tasks to investigate whether the potentially biasing effect of θ can be addressed.

Slope from the delay discounting and probability discounting tasks were correlated to several sub-scales of the BIS-11 suggesting that Q^+ may be linked to motor impulsivity and non-planning. It was interesting to note that Q^+ from the delay discounting task was negatively correlated with these sub-scales and Q^+ from the probability discounting task was positively correlated with the same subscales suggesting that sensitivity to delayed and probabilistic rewards may have opposite relationships with impulsivity. Testing in later experiments will further probe this relationship.

The new tasks aimed to obtain valid and reliable tests of self-control and risk-taking with the participant expending the minimum of effort. The tasks had contained a large range of delays and probabilities in order to test which combination gave the best results. Linear plots were created in order to calculate K^+

and H^{+}, therefore, it was vital that the tasks retained at least three delays or probabilities of alternative A and that these alternatives were spaced out upon the graph so that each had an approximately equal effect on the regression line. Taking an example, if we had three delays of A which were 2, 4 and 10 seconds then, when plotted upon the graph, the location of the indifference point when the delay of A was 10 seconds would have a much larger effect on the placing of the regression line compared to the location of the IP at 2 and 4 seconds. In order to test which delays and probabilities were to be retained, a number of linear plots and regression lines were calculated for each participant using different permutations of delays and probabilities. Regarding the delay discounting task, the delays of A that appeared to give the best results were 2, 4, 8 and 10 seconds. It was decided that a 0 seconds delay would be introduced because all discounting tasks in previous research had utilised immediately rewarding alternatives. It was also suspected that behaviour might be different when faced with an immediate vs. a delayed reward compared to when both rewards are delayed. This decision was fortuitous as a later study by other researchers supported this hypothesis (Estle et al., 2006). For the probability discounting task, probabilities of 1.0, .75, .5 and .25 were chosen. This corresponded to odds against values of 0, 0.3, 1 and 3 respectively. One concern with this distribution of probabilities was that the odds against value of 3 could have a heavily biasing effect on the regression line. The responses when the probability of A was .33 and .16 were very similar to those calculated when the probability was .25. It was felt that a low probability choice had to be included within the tasks as this would give important information as to how individuals reacted to situations of high risk. Therefore, it was decided that a probability of .25 would be included by itself as other probabilities around this mark did not give additional information. It was also felt that the addition of a probability of 1 ($\theta = 0$) would anchor the regression line should the lower probabilities have too much bias on the regression. In addition, when viewing the wheels of fortune the probabilities of 1.0, .75 and .5 created wheels in which the probability was easy to estimate as the green section filled the whole, three-quarters, or half the wheel respectively. The visual representation of a probability of .25 was of a wheel that was a quarter

full so this kept to the convention of presenting a representation of alternative A that was easy to distinguish.

This experiment presented new discounting tasks to participants in order to pilot test them. The results have provided useful information that will be utilised in order to create further new, more efficient, tasks to test the hypotheses stated at the beginning of this project.

Experiment 2: Delay and probability discounting in healthy controls

Introduction

As has been outlined previously, impulsivity is a multi-factorial concept (Evenden, 1999) constructed from several separate and identifiable behaviours. Self-control and risk-taking are posited to be two behaviours that influence impulsivity and it is these behaviours that the project aims to explore. The Multiplicative Hyperbolic Model of Choice (Ho et al., 1999) is an equational model that attempts to describe decision-making under situations requiring self-control or assessment of risk[8]. This model has been successfully utilised to explain decision-making behaviour (in certain environments) in rats.

Previous research has questioned as to whether the behavioural parameters from the MHMC, *K* and *H*, reflect the same process. One viewpoint argues that delayed rewards are viewed as probabilistic. These researchers have suggested that uncertainty of receiving a reward increases as that reward is more delayed in time (Myerson et al., 1995; Patak and Reynolds, 2006). The other viewpoint is that probabilistic rewards are seen as delayed rewards. According to this view, an organism that chooses a probabilistic reward sees it as a certain outcome but that may incur a delay to receive (Hayden & Platt, 2007; Rachlin et al., 1991). Some studies have reported that they found no associations between performance on a delay and probability discounting task (Adriani and Laviola, 2006; Green et al., 1999; Myerson et al., 2003; Reynolds et al., 2004) with other studies finding that behaviour on the two tasks correlated with separate personality characteristics (Ostazewski, 1997).

[8] See section 5 of the introduction for more details.

One question that must be asked concerning the research that has utilised delay and probability discounting tasks regards the validity of using tasks that employ hypothetical outcomes. Nearly all experiments using discounting tasks have provided choices with hypothetical rewards, delays and probabilities of winning. It has been debated whether these tasks simulate real-world environment. A small number of studies have aimed to compare behaviour on discounting tasks providing real vs. hypothetical outcomes[9]. These studies found no difference between delay discounting behaviour on a real vs. hypothetical task (Madden et al, 2003; Madden et al, 2004; Lagorio and Madden, 2005). One problem concerning the results from these studies is that they all, arguably, had methodological flaws. In addition, only delay discounting behaviour was measured (probability discounting was not investigated). One study found that participants were more self-controlled on a task giving real, small, rewards (and real, short, delays) compared to a tasks giving comparable hypothetical rewards and delays (Lane et al., 2003). However, there were two variables that had been changed between the tasks (reward and delay) so the results found may have been due to the effects of either of these variables. In addition, only delay discounting behaviour was assessed. More research is needed to discover whether provision of real rewards would significantly affect behaviour on a delay or probability discounting task.

This experiment aimed to explore decision-making in healthy controls that required assessment of delay or risk and in which every choice carried real consequences. Arguably, these tasks would mimic real-world behaviour more than pure hypothetical discounting tasks. The discounting tasks would also be used to test the applicability of the Multiplicative Hyperbolic Model of Choice in humans. Tasks that had been piloted in experiment 1 were adapted for use in experiment 2. In the delay discounting task, participants would have to wait through the delay associated with their choice. On the probability discounting task the alternatives would have a probability of being won and thus the participant would have a chance of receiving nothing with the results being due to luck. In addition, each

[9] See section 4.7 of the introduction for more detail

task would be split into two versions. One version would give real monetary rewards while the other would give hypothetical monetary rewards. This would be the only variable that would change between the tasks. Therefore, these tasks could be used to explore the effect of rewarding outcomes on discounting behaviour. As these types of tasks had not been utilised before in any population, it was important to first examine performance in control subjects, therefore healthy 'normal' participants were recruited. In addition to measuring delay and probability discounting behaviour, participants also completed a battery of neuropsychological tests and self-report questionnaires. Previous research has found little correlation between behavioural and self-report measures of impulsivity so it was felt to be important that correlations between our tasks and others was to be explored.

Method

Participants

Thirty eight healthy normal participants (21 female) were recruited using advertisements at the University of Manchester, UK. Participants ranged in age from 19-30 years (M = 22.3 years, SD = 3.05).

All participants were screened for personality disorders using the Miniature International Neuropsychiatric Interview (MINI)[10]. Participants did not meet any criteria for any disorder identified by the MINI.

Materials

Discounting tasks

Based on the results from experiment 1, computerized versions of the discounting tasks were created. They were adapted from tasks designed by Rachlin et al (1991,

[10] See the section "General Methods"

1996). The tasks were programmed using Cogent 2000 and Cogent Graphics developed by researchers at the FIL and the ICN and John Romaya at the LON at the Wellcome Department of Imaging Neuroscience.

Each delay and probability discounting task contained four blocks. In the delay discounting task, each block contained 30 choices. In the probability discounting task, each block contained 42 choices. In each type of task (delay or probabilistic), each block contained the same choices but in different orders that were chosen in a pseudorandom order before testing took place. Four blocks were used in order to obtain several measures of indifference points, thus increasing the validity of the measurements. The hypothetical rewards tasks contained the same blocks as the real rewards tasks but were presented in a different, pseudorandom, order.

The discounting tasks presented a number of choices between two alternatives. The reward amount for alternatives A and B were £0.10 and £0.20 respectively. Alternative A carried a delay that was 0, 2, 4, 8, or 10 seconds or a win probability of 1.0, .75, .5, or .25. The delay/probability of alternative B was systematically altered so that it was either the same or a longer delay/lower probability to alternative A.

The tasks were presented on a laptop (Ergo Ensis Pentium IV, 15" TFT). On the screen, a large 'A' was shown in the top left of the screen and a large 'B' was shown in the top right. The reward for each alternative was shown under their respective letter. Underneath this, the delay/probability associated with each alternative was shown. In the delay discounting task the associated delay was written in the format "X seconds", where X was the delay written in numerical format. In the probability discounting task the associated probability was shown in a "wheel of fortune" format similar to Rachlin et al (1991). The wheel of fortune had green and red segments indicating the chances of winning and losing respectively. For example, if there was a .75 chance of winning a whole segment comprising ¾ of the wheel would have been green and a whole ¼ segment would

have been red. Examples of these screens are shown in appendix 3. This screen was shown for 5 seconds. If a choice had not been made by this time a screen appeared warning the participant "You did not make a choice. Please make a choice next time". If participants had made a choice, they were presented with a screen showing the outcome of their choice. In the delay discounting task the outcome screen was shown for a period of time equal to the delay associated to the alternative they had chosen. This screen stated "You chose ["A" or "B" was written here dependent on the alternative chosen]. Please wait". When the associated delay had finished the next trial was immediately presented. In the probability discounting task the wheel of fortune associated with the alternative they had chosen was shown by itself in the centre of the screen with an arrow centred on the wheel indicating if they had won or lost. The outcome was shown for two seconds. If the arrow pointed to the green segment it was deemed a win and another screen was shown for two seconds stating "Well done. You have gained 10p/20p". If the arrow pointed to the red segment, the participants did not win any money and a screen was shown for two seconds that stated "Sorry, the arrow was in the red. This means that you will not get any money this time". Then the next trial was immediately presented. The positions of the arrows were decided in a pseudorandom order before testing began.

In the real rewards condition participants received the money associated with each alternative that they chose in the delay discounting task and each alternative they won in the probability discounting task. This money was given to them after their participation in the study was complete. In the tasks with hypothetical rewards, participants received none of the rewards that they chose. However, it was stressed to participants that they should try to make decisions as if the rewards were real.

A battery of behavioural tasks and self-report questionnaires were given to all participants. These have been listed in the "General Methods" section.

Procedure

Each participant sat by themselves within a quiet testing room. The self-report questionnaires and behavioural tasks were given first followed by the discounting tasks. Participants were given the delay discounting task first, followed by the probability discounting task. These tasks carried either real or hypothetical rewards. Participants then performed the delay discounting task followed by the probability discounting task once again. These tasks gave the type of reward that was not given in the first two tasks. Reward type order was counterbalanced.

When the delay and probability discounting tasks were given for the first time, each was preceded by a set of instructions (shown in appendix 4) and five practice trials. After participants had completed the practice trials they were asked if they understood the task. Before each task began, the participants were verbally instructed as to whether the task would give real or hypothetical rewards.

Each task was also preceded by a screen reminding participants to be sure if the task involved real or hypothetical rewards and to ask the researcher any questions that they had concerning the task.

Data analysis

Indifference points were calculated for each of the five delays of alternative A in the delay task and each of the four probabilities of alternative A in the probability task (probabilities were converted to odds against values, which were calculated using the equation $[1/p]$-1). Each task contained four blocks. This gave four measurements per delay/probability of A for each reward type. The median indifference points were calculated for each task (delay/probability) for each reward type. The median was used to avoid bias from outliers. A linear regression was applied to each participant's median IPs. From the linear regressions the

discounting parameters (K^+/H^+), slope, and intercept values were calculated. The parameters were calculated using the equations K^+ = slope-1/intercept (for the delay discounting parameter) and H^+ = slope-1/intercept (for the probability discounting parameter). Changes in Q^+ could be estimated by calculating changes in the slope of the linear regressions.

To be included within the analysis, each participant's raw data had to contain an acceptable amount of information, which was defined by the number of indifference points that were calculated over the four blocks. In the delay discounting task, alternative A had five possible delays. Combined with the four blocks, this meant that there were a maximum of 20 points that could be plotted in order to create a linear regression. To be included within the analysis each participant had to have at least 15 points that could be plotted. In the probability discounting task, alternative A had four odds against values. This meant that there were 16 points that could be plotted. To be included within the analysis, each participant had to have at least 11 points that could be plotted.

Individual K^+, H^+, slope and intercept values were plotted. Any participant who had a score more than two standard deviations from the mean was excluded.

For analysis of the delay discounting task a 2x5 repeated measures ANOVA was performed. Reward type was one factor and average IPs for the delays of alternative A was the second factor.

In the probability discounting task a 2x4 repeated measures ANOVA was calculated. Reward type was one factor and average IPs for each probability of alternative A was another factor. A second 2x4 ANOVA was constructed that used probabilities instead of odds against values.

Area under Curve (AUC) analysis was also employed to investigate further the difference between reward types. AUC was utilised as an additional measure to the

repeated measures ANOVA and not as a replacement. Previous studies have utilised AUC as a measure of discounting behaviour. In this research, the ANOVAs were favoured as they were direct measures of indifference points and not based upon derived values. It was decided that, if the AUC provided information above that of the ANOVA, then its use would be continued. If it provided no further information then it would be cut from following experiments. To calculate area under curve, participants mean indifference points over the four blocks were plotted and the trapezoidal area under the plot line was calculated. If an individual was more impulsive (i.e. had lower indifference points) then a lower AUC value would be calculated. Previous researchers (e.g. Myerson et al., 2001; Holt et al., 2003) have calculated AUC using a graph plotting subjective value on the abscissa against the proportion of maximum delay (or odds against winning) on the ordinate. Considering the data from this study, subjective value cannot be calculated. Taking a delay discounting task as an example, previous studies have altered the magnitude of the immediate and delayed reward and can, at indifference, calculate an estimate of the magnitude of the immediate amount that is equal to the larger delayed amount. In this study, the two amounts were fixed as the focus was specifically placed upon K^+ and H^+ and not the magnitude discounting parameter Q^+. However, AUC methodology can still be used to create values in order to compare discounting rates between reward types.

Parameter values, slopes and intercepts were compared between reward types for each task to provide a separate method of comparing performance between reward types. Comparisons were calculated using paired sample *t*-tests.

To assess reliability of participant responses on the real and hypothetical tasks the indifference points, parameter, slope, and intercept values were correlated between reward types. If the correlations were significant then this implies that participant responses are reliable over the different reward types and, although indifference points may be different between reward types, the trends of participant responses would be similar.

Correlations were performed between the values calculated from the delay and probability discounting tasks and the self-report and neuropsychological tasks.

Correlation analyses were also performed between K^+, slope and intercept from the delay discounting task and H^+, slope and intercept calculated from the probability discounting task. These correlations were performed to explore any relationship between values calculated from these two tasks.

Results

Table 2 (on page 150) shows the main characteristics for the control group. Figures 3a and 3b below shows the mean K^+ and slope calculated from the delay discounting task. Error bars indicate standard deviations (+/- 2 SD).

Figure 3a: Mean K^+ from the real and hypothetical reward versions of the delay discounting task

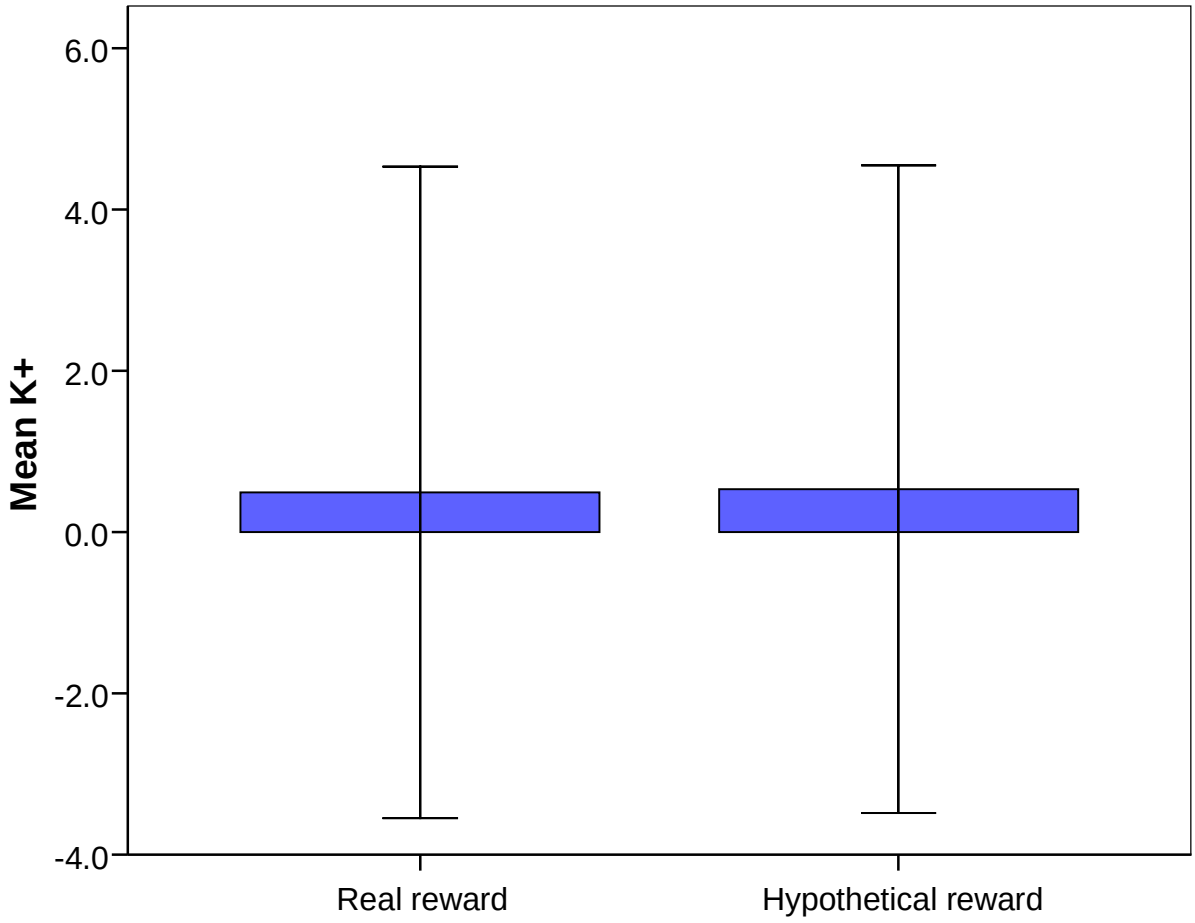
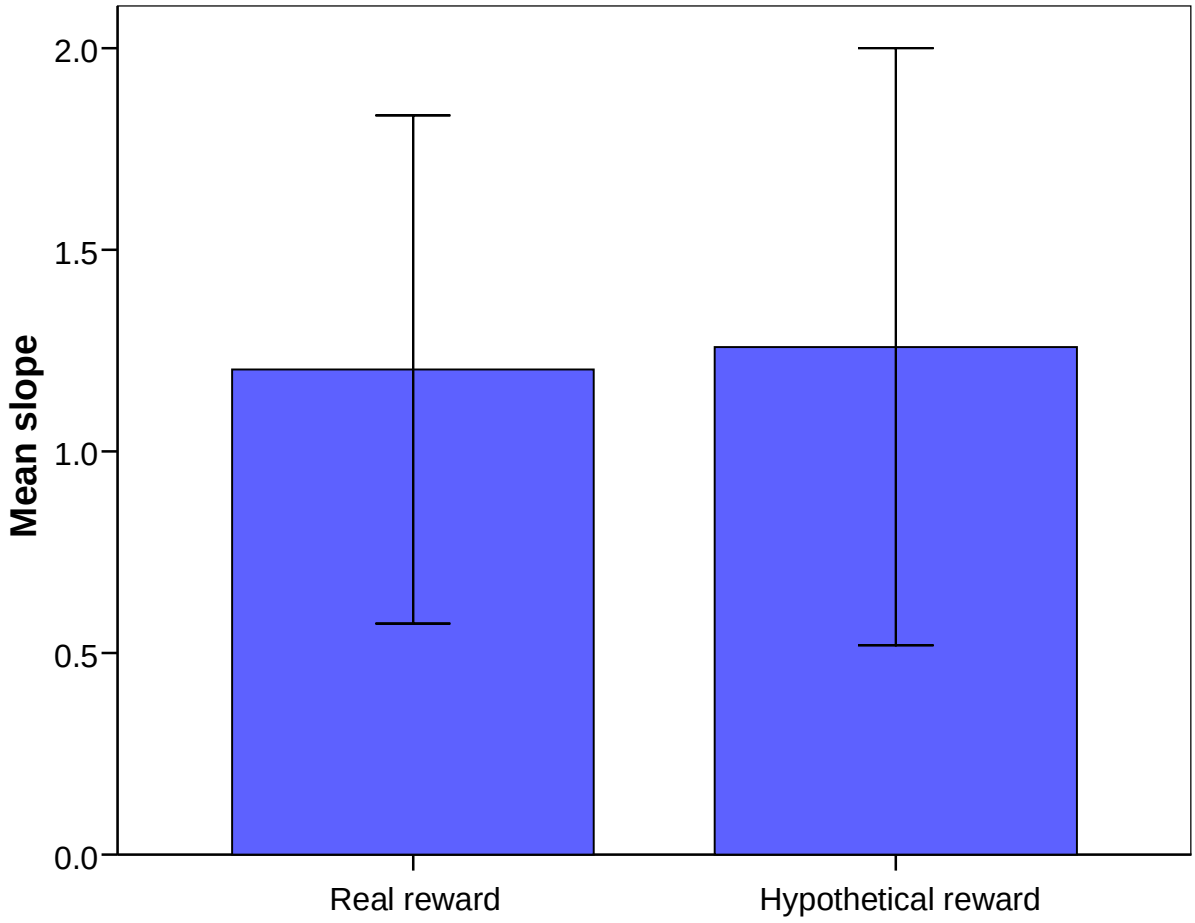


Figure 3b: Mean slope from the real and hypothetical reward versions of the delay discounting task.



Figures 4a and 4b below shows the mean H^+ and slope calculated from the probability discounting task. Error bars indicate standard deviations (+/- 2 SD).

Figure 4a: Mean H^+ from the real and hypothetical reward versions of the probability discounting task

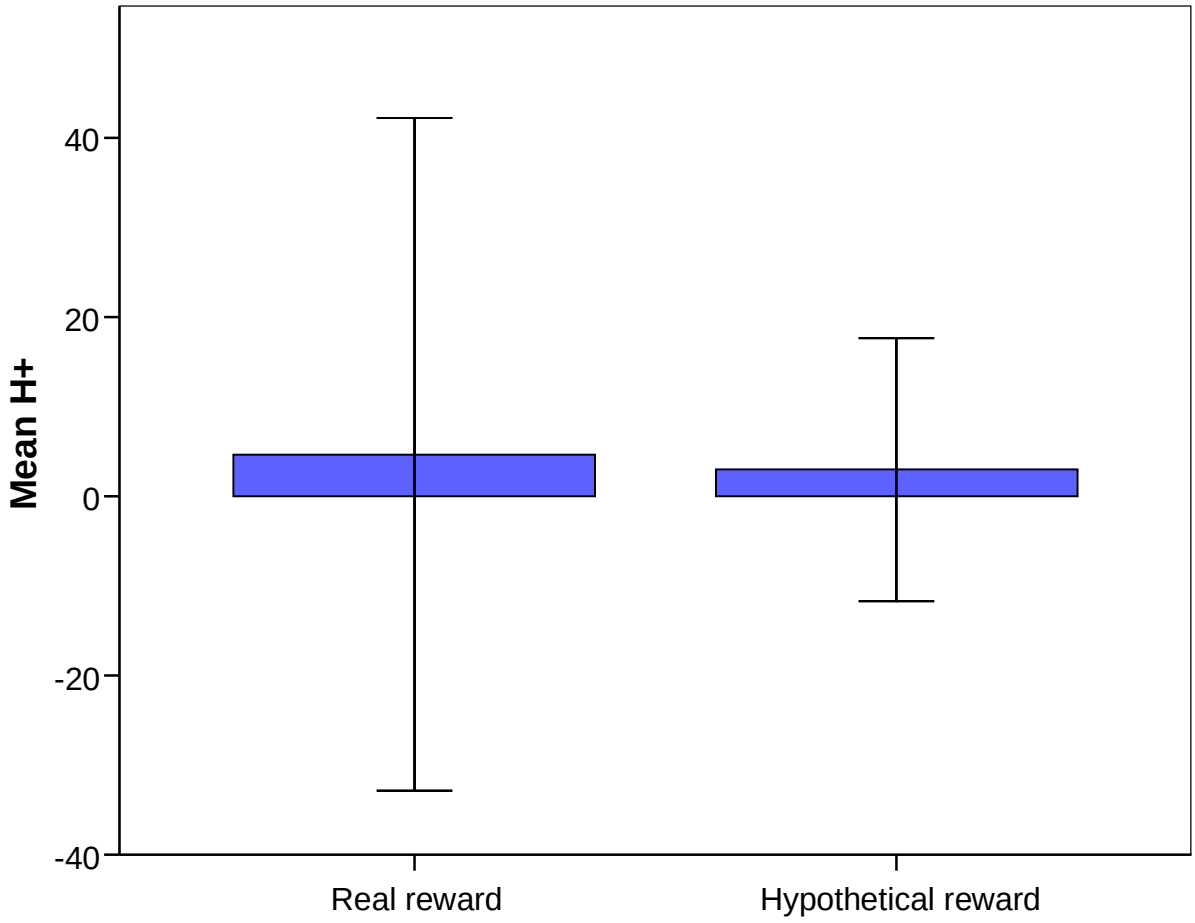
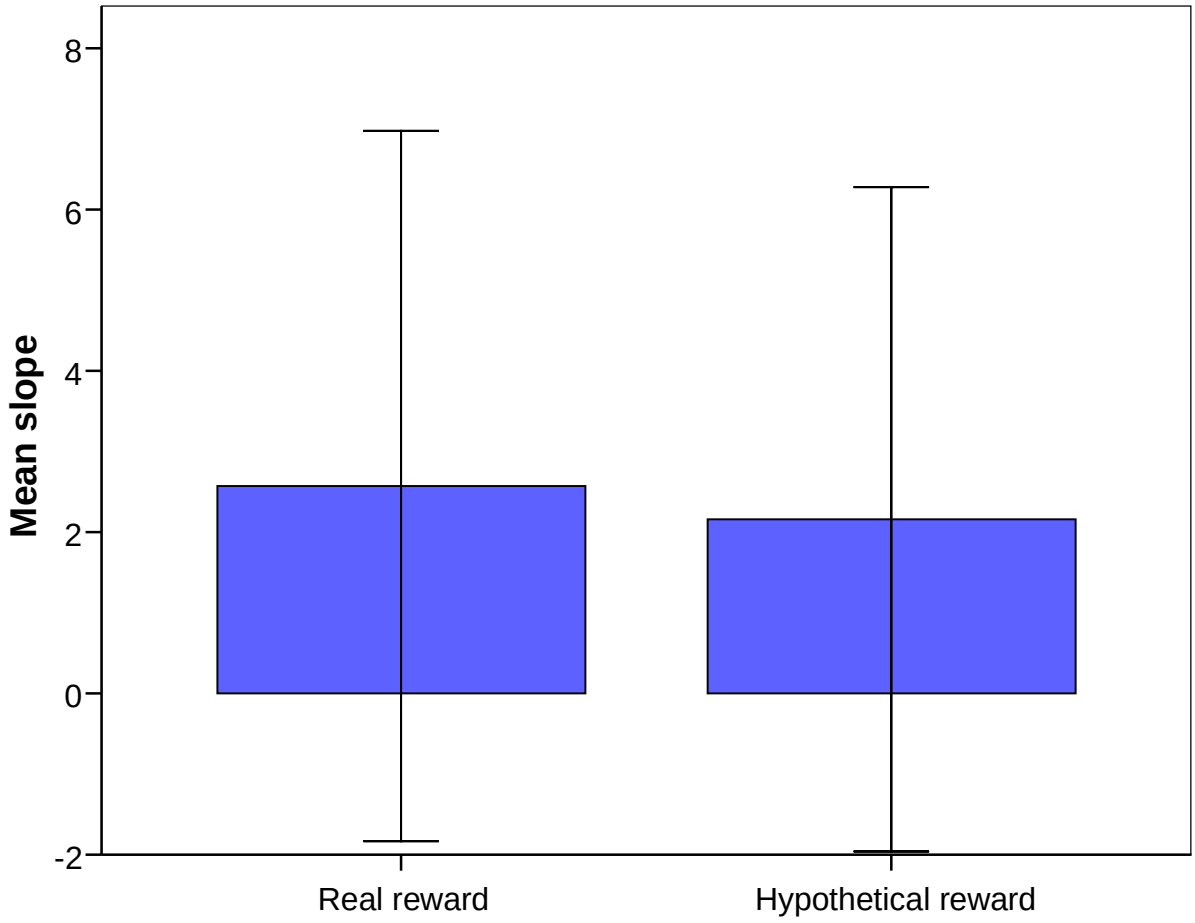


Figure 4b: Mean slope from the real and hypothetical reward versions of the probability discounting task.



Delay discounting task: Real vs. hypothetical rewards

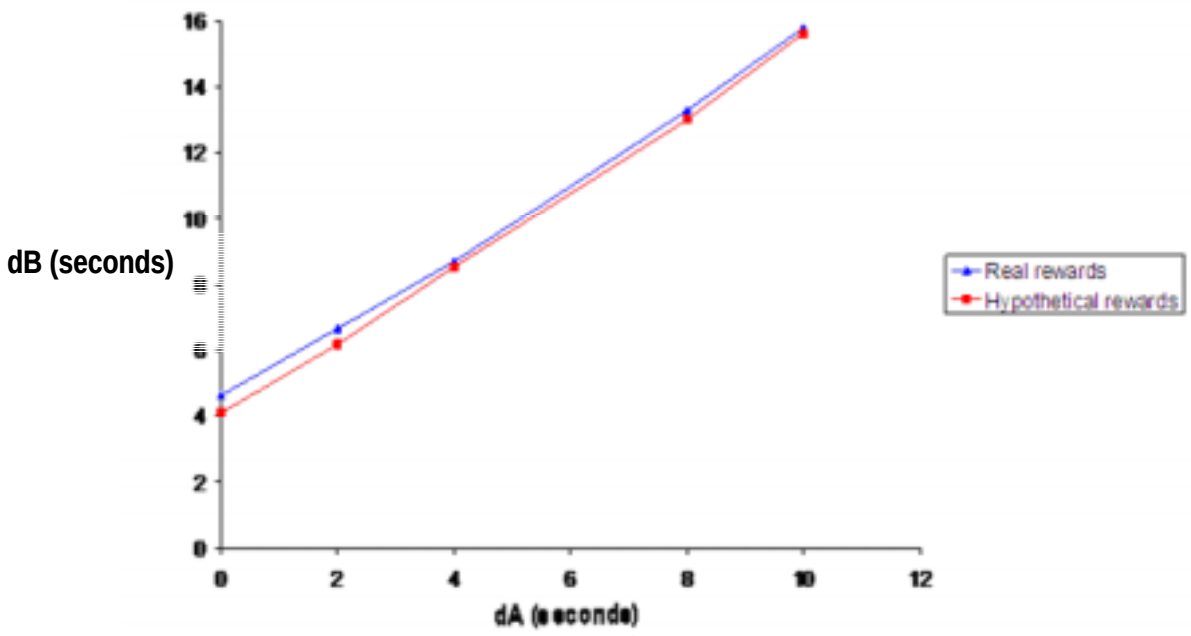
Six participants had to be discarded from the analysis of the delay discounting task as they did not meet the inclusion criterion stated previously in the methods section.

Median participants IPs were found for each reward type and plotted in order to investigate how much they conformed to a linear function, and therefore to the

principles stated by the Multiplicative Hyperbolic Model of Choice. Participants IPs conformed highly to a linear function (mean r^2 = .97).

There was a significant main effect of reward type, $F(1,31) = 7.64$, $p = .01$. There was a significant main effect between indifference points between different delays of alternative A, $F(4,124) = 495.78$, $p < .001$. This effect was expected to be significant as an increase in d_A would significantly alter decision making behaviour. There was no interaction between reward type and delay, $F(4,124) = 0.38$, $p = .82$.

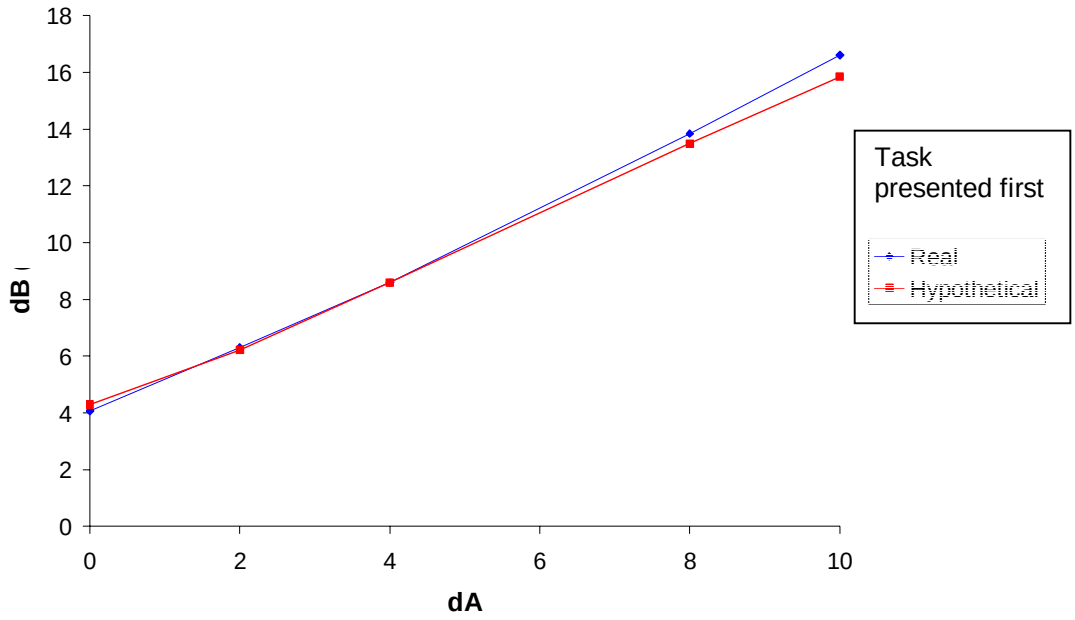
Figure 5: Mean indifference points in response to each reward in the delay discounting task



There was a significant effect of the order in which the rewards were given (either real or hypothetical rewards first), $F(1,30) = 20.48$, $p < .001$. There was a significant interaction between reward, delay and order, $F(4,120) = 8.20$, $p < .001$. Figure 5 shows the mean indifference points given by participants in the real and hypothetical reward conditions of the delay discounting task. Figure 6 below shows the effect of order on choice behaviour. When dA = 8/10, participants who were

given the real reward version of the task tended to have higher indifference points delays compared to those who were given the hypothetical reward version first. Conversely, when dA = 0, participants who were given the real reward task first tended to be more risk-averse compared to participants who were given the hypothetical reward task first.

Figure 6: Effect of task order on choice behaviour in the delay discounting task



Area under curve was calculated from the mean indifference points given from each participant in the two reward conditions. The mean AUC value calculated for the real rewards condition was 101.27. The mean AUC in the hypothetical rewards condition was 98.92. A paired t-test was used to compare mean AUC values between reward types. There was a significant difference in the mean AUC values between reward types, $t(31) = 2.39$, $p = .02$.

Paired *t*-tests were utilised to compare K^+, slope and intercept between reward type. There were no differences of K^+, $t(31) = -0.21$, $p = .83$, or slope, $t(31) = -0.72$, $p =$

.48 between reward type. There was a trend for intercepts to be different between reward type, $t(31) = 1.98$, $p = .06$.

Spearman's rank-order correlation coefficients were performed on K^+, slope, and intercept values between reward types. Spearman's was used due to the positive skew of K^+ values. K^+ were significantly correlated, $r_s = 0.60$, $p < .001$. Slope values were highly correlated, $r_s = 0.63$, $p < .001$, in addition to intercept values, $r_s = 0.58$, $p < .001$.

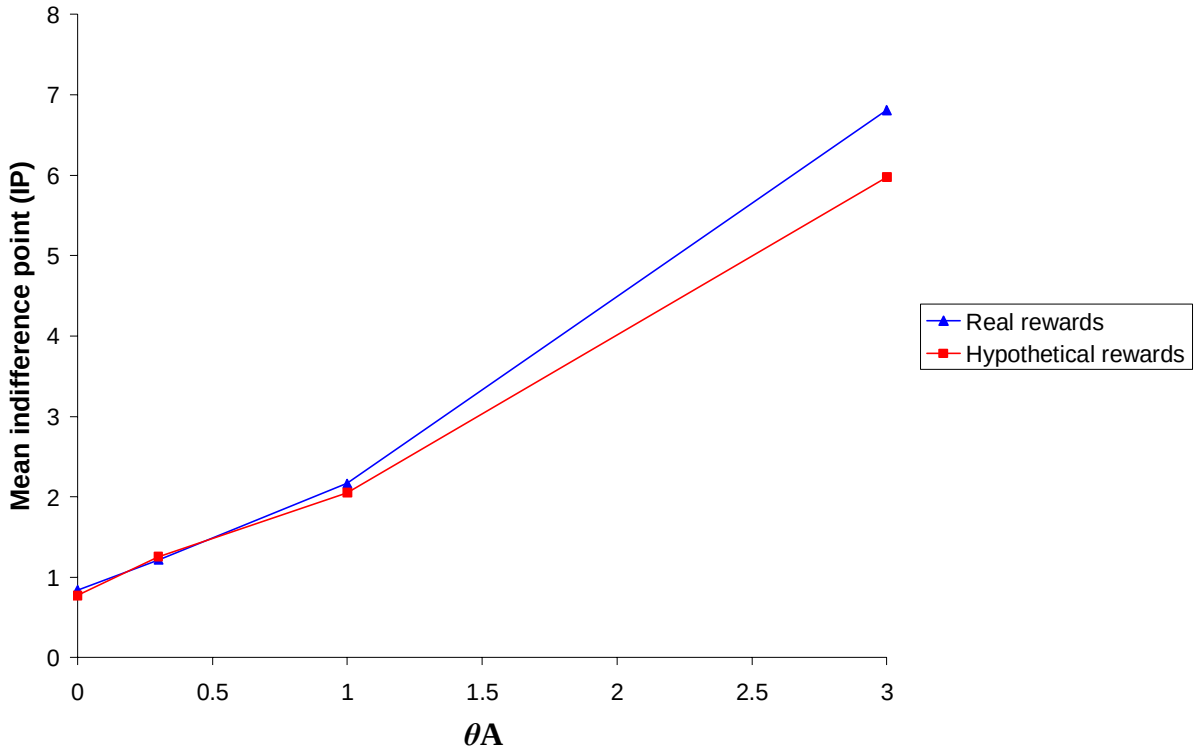
Probability discounting task: Real vs. hypothetical rewards

Data from seven participants had to be discarded from the analysis of this task because they did not meet the inclusion criterion for the minimum amount of indifference points calculated from their responses.

Graphs were plotted with the median IPs from each reward type. Participants IPs conformed very highly, $r^2 = .97$.

There was a significant effect of reward type, $F(1,30) = 9.94$, $p = .004$ and of odds against value, $F(3,90) = 197.03$, $p < .001$. This effect was expected as a change in θ_A would alter participant indifference points. There was an interaction between reward type and odds against values, $F(3,90) = 7.98$, $p < .001$. There was no effect of task order on choice behaviour, $F(1,30) = 0.06$, $p = .80$. Figure 7 shows the indifference points obtained in the real and hypothetical reward conditions.

Figure 7: Mean indifference points in response to each reward in the probability discounting task (odds against values are plotted on the y-axis)



There was no reward effect if probabilities were used instead of odds against values in the ANOVA, $F(1,30) = 1.01$, $p = .32$. There was an effect of indifference points calculated from the probabilities of alternative A, $F(3,90) = 430.87$, $p < .001$, which was expected.

Mean area under the curve was calculated from each participant's mean indifference points on the hypothetical and real rewarding probability discounting tasks. The mean AUC value calculated from the real rewards and hypothetical rewards condition was 12.46 and 10.73 respectively. A paired sample t-test was used to compare AUC between reward types. There was no significant difference in mean AUC between reward types, $t(30) = 0.96$, $p = .33$.

Paired *t*-tests were utilised to compare H^+, slope and intercept between reward type. There were no differences of H^+, $t(30) = -0.92$, $p = .37$, or intercept, $t(30) = -1.03$, $p = .31$ between reward type. There was a trend for slope to be different between reward type, $t(30) = 1.94$, $p = .06$.

H^+, slope and intercept values were correlated between reward types. Spearman's rank-order correlation coefficient was used due to the positive skew of H^+ values. H^+ values were not significantly correlated, $r_s = 0.07$, $p = .641$. However, slopes, $r_s = 0.37$, $p = .007$, and intercepts, $r_s = 0.43$, $p = .002$, were significantly correlated.

Correlations between the values calculated from the delay discounting task and other neuropsychological/self-report measures

Median K^+, slope, and intercept values were calculated and correlated with scores from the other personality measurements used (see "General Methods" section). Correlations were performed separately for the real and hypothetical rewards tasks. TCI scores were missing from one participant. K^+ scores were highly positively skewed therefore Spearman's rank-order correlation coefficient was used for all correlations.

Real reward condition

K^+ scores were positively correlated with stop errors in the stop task, $r_s = 0.27$, $p = .04$. Intercept was negatively correlated with stop errors, $r_s = -0.35$, $p = .03$. Intercept was positively correlated with Go RT on the stop task, $r_s = 0.27$, $p = .04$. K^+ was negatively correlated with the persistence sub-scale on the TCI, $r_s = -0.27$, $p = .03$. Slope was negatively correlated with persistence, $r_s = -0.26$, $p = .05$. Intercept was positively correlated with persistence, $r_s = 0.33$, $p = .01$.

Hypothetical reward condition

Slope was positively correlated with scores on the novelty seeking sub-scale of the Temperament and Character Inventory, $r_s = 0.27$, $p = .05$. K^+ was positively correlated with disorderliness, a factor of novelty seeking, $r_s = 0.26$, $p = .05$. Slope was also positively correlated with disorderliness, $r_s = 0.27$, $p = .04$. K^+ was correlated with openness, a sub-scale of the Big 5, $r_s = 0.46$, $p = .003$. Slope was also positively correlated with openness, $r_s = 0.44$, $p = .005$.

Correlations between the values calculated from the probability discounting task and other neuropsychological/self-report measures

Median H^+, slope, and intercept values were calculated and correlated with scores from personality measurements. Correlations were performed separately for the real and hypothetical rewards tasks. TCI scores were missing from one participant. Spearman's rank order correlations were used because H^+ scores were positively skewed.

Real reward condition

Slope values were negatively correlated with trait anxiety on the STAI, $r_s = -0.36$, $p = .04$. Slope was negatively correlated with state anxiety on the STAI, $r_s = -0.37$, $p = .03$. H^+ was negatively correlated with conscientiousness as measured by the Big-5 personality questionnaire, $r_s = -0.46$, $p = .1$.

Hypothetical reward condition

Intercept values were negatively correlated with stop errors on the stop task, r_s = -0.37, p = .007. Intercept was positively correlated with Go RT, r_s = 0.32, p = .02. Intercept was negatively correlated with extravagance, a factor of novelty-seeking on the TCI, r_s = -0.33, p = .02. Slope was negatively correlated with reward dependence, a sub-scale from the TCI, r_s = -0.42, p = .003. H^+ was positively correlated with extraversion as measured by the Big 5, r_s = 0.37, p = .04.

Correlations between parameter values, slope and intercept calculated from the delay and the probability discounting task

K^+, slope and intercept from each reward version of the delay discounting task were correlated with H^+, slope and intercept (calculated from theta values), and slope and intercept (calculated from probabilities). This led to a total of 60 correlations. Four of the correlations were significant. Intercept from the real reward condition of the delay discounting task was correlated with slope (calculated from theta) from the real reward condition of the probability discounting task, r_s = 0.26, p = .05; slope (calculated from theta) from the hypothetical reward condition of the probability task, r_s = 0.29, p = .03; and intercept (calculated from probabilities) from the real reward condition of the probability task, r_s = -.029, p = .03. Finally, H^+ from the hypothetical reward condition was correlated with intercept from the real reward condition of the delay task, r_s = 0.29, p = .03. However, if alpha was decreased to .01 then no correlations were found to be significant.

Grand means of K^+, H^+, slope and intercept were calculated by taking the mean of the real and hypothetical medians. K^+, H^+, slope and intercept from the delay and probability discounting tasks were correlated. This gave a total of nine correlations. Only one correlation was significant; the grand mean of the slope from the

probability discounting task correlated with the grand mean of the intercept from the delay discounting task, $r_s = 0.36$, $p = .005$.

Discussion

In the delay discounting task, participants were found to be more self-controlled when given the opportunity to gain real monetary rewards compared to when hypothetical monetary rewards were given. In addition, participants tended to be more risk-taking when given real rewards compared to hypothetical rewards in the probability discounting task. Area-under-curve (AUC) analysis, a method of directly comparing behaviour on the delay and probability discounting tasks, supported these result for the delay discounting task but not for the probability discounting task. Differences in behaviour may be attributable to advantages that alterations in choice behaviour between reward type would confer. Being self-controlled on the real rewarding version of the delay discounting task would lead to a definite increase in monetary gain. Being self-controlled on the hypothetical rewards delay task would not affect monetary gain but would increase task time. These results suggest that hypothetical delay discounting tasks do cause individuals to act in a more impulsive manner compared to tasks giving real rewards. However, the difference in behaviour was small. In the probability discounting task, individuals may take more risks in order to increase their potential winnings. This result is contrary the model designed by Kahneman & Tversky (1979) which states that individuals tend to be risk-averse when given the chance of winning positive rewards. In this task, the difference in behaviour between reward types may have been affected by the small rewards that were given. Each alternative gave a possible reward of £0.10 or £0.20. The subjective value of a negative outcome (i.e. not winning) may have so small that the participant may have become somewhat insensitive to this outcome. This effect may have been exacerbated by the presentation of the delay task first. Participants may have realised that they have gained a large amount of money from playing the delay discounting task (average winnings were £15.00). Therefore, participants may have felt that they were able to

take more risks on the probability discounting tasks as they knew that the money that they had gained from the delay task would not be taken from them. Even though the difference in behaviour was quite small, there is a significant difference in behaviour on a probability discounting task when given real vs. hypothetical rewards.

One concern regarding the Multiplicative Hyperbolic Model of Choice is the lack of effects between the parameter values, slopes and intercepts between reward types. It may be that because the parameter values, slopes and intercepts are indirect measures of performance they do not measure behaviour as accurately as indifference points. There was a trend for slopes to be significantly different between the two reward versions of the probability discounting task. This would suggest that the difference in behaviour noted between these two tasks was due to alterations in reward sensitivity between the real and hypothetical rewards and not due to changes in assessment of risk. More research is needed to investigate the applicability of the MHMC in humans. Further parameters may need to be inserted into the model or, alternatively, the model may not accurately reflect human behaviour, which could be argued to be more complex than animal behaviour (in which the model has been previously tested). Researchers have questioned whether human behaviour can be modelled in a highly accurate, mathematical, way (Glimcher et al., 2003). Instead, they suggest that human behaviour is biased by significantly more factors compared to animals, which tend to focus on a more limited number of reinforcers. This is the first study that has utilised the MHMC in humans. The researchers who designed the MHMC admit that further parameters may be needed to create a more accurate model (Ho et al., 1999). At present, care must be taken when using these derived values as indicators of human behaviour.

The order in which the different reward versions of the delay discounting task were given was found to affect choice behaviour. As outlined before, the delay discounting task was always presented before the probability task. When dA = 8/10, participants tended to be more tolerant of delays associated with alternative B

when performing the real reward task first compared to the hypothetical reward task. Conversely, when dA = 0, participants tended to be risk-averse when performing the real reward task first compared to the hypothetical reward task. This may be due to the length of participation. The discounting tasks were presented after approximately 1 hour 45 minutes (after all other tasks and questionnaires were completed). Completing all four versions of the delay and probability discounting tasks took a further 1 hour 15 minutes approximately. By the time that the delay discounting task was given for the second time participants may have become increasingly delay averse, especially if participants had already completed the task in which they were gaining money. At debriefing, the delay task was described by a minority of participants as monotonous. The tasks were given at the end because the amount of reimbursement the participant took away from the study equalled their winnings in the real reward versions of the discounting tasks. It was felt that if the tasks came first and participants knew approximately how much they had won, they might quickly lose interest in the remainder of the study and their responses on the following tasks would be less valid. Conversely, the probability discounting task may have provided an element of excitement due to emotional reactions associated with risk so interest may have been higher during this task.

Area-under-curve (AUC) analyses were utilised to investigate the use of these measures in addition to the ANOVAs. Some previous researchers have utilised AUC as their primary measure of discounting behaviour (Holt et al., 2003; Myerson et al., 2001). After use in this research, it was decided not to utilise AUC in subsequent analysis for four reasons. Firstly, it supported the results from the ANOVA but did not provide extra information, therefore, its use may be deemed unnecessary. Secondly, the ANOVAs provided direct analysis of IPs, whereas AUC was calculated using indirect, derived, values. Thus, the ANOVA would appear to be the most valid and efficient measure. Thirdly, AUC does not provide information about the linear plot of the participant's choices. For example, if we calculate a participant's AUC, then take his plot and rotate the linear regression line around its midpoint, the same AUC value will be derived. Fourthly, due to

differences in methodology in this research compared to previous studies using AUC (i.e. we altered *d* instead of *q*), subjective value could not be calculated, thus, our AUC values were not comparable with previous research.

In the delay discounting task, K^+, slope and intercept were highly correlated between the tasks giving real or hypothetical rewards. This suggests that choice behaviour patterns were somewhat similar between the two versions of the task. In the probability discounting task, slope and intercept were correlated between the versions of the tasks giving real or hypothetical rewards. However, H^+ values were not correlated suggesting that choice behaviour patterns were similar but not to the degree as measured in the delay discounting task. This may have been due to the rules participants utilised to make decisions. Participants were given feedback sheets after the experiment to provide information concerning their experience of the study. One question asked participants if they used any decision-making rules in the two tasks. A large number of participants reported that they employed a mathematical decision-making rule in the delay discounting task. The most popular rule was:

IF [delay of alternative B] < (2[Delay of alternative A])+2 THEN choose B, IF NOT THEN choose A.

However, very few participants constructed a similar rule to guide choice behaviour in the probability discounting task. Instead, choice seemed to depend more on transient emotional factors. Reliance on more emotional decision-making strategies may be due to the visual differences between the tasks. In the delay discounting task, the delays were expressed explicitly in numerals that could be easily and rapidly compared. In the probability discounting task, the probabilities were shown as wheel of fortunes so comparison would have relied more upon spatial, rather than mathematical, processes that may have employed emotional judgements. In addition, participants knew that each choice in the delay discounting tasks would provide a monetary reward but not every choice in the probability

discounting task provided a reward as the outcome was dependent on chance. Therefore, an outcome in one trial may have affected emotional judgement and altered behaviour in subsequent trials even though each trial was independent. For example, a string of losses may induce transient risk-averse behaviour and vice-versa.

When comparing choice behaviour between the delay and probability discounting task, there was very little correlation. This result supports claims that delay discounting and probability discounting behaviour are not factors of a singular behaviour but are separate. It is possible that they are closely connected and work in conjunction to influence impulsivity, albeit in separate ways. This may account for previous findings that have found that altering delay affects probability discounting or that delayed rewards are inherently seen as uncertain. In the real world, it would certainly be true that delayed rewards are always associated with uncertainty as one can never be sure what events will occur on the future. In addition, increasing delays between the choices we make may lead us to decrease our risk-taking behaviour as we would realise that we have to maximise gain in a shorter timeframe. This may lead to risk-averse behaviour as taking risks and loosing would decrease our chances of maximising reward in this limited time-period. Therefore, delay discounting and probability discounting behaviour may work in close partnership but are separate and independently functioning behaviours.

On the plots that contained participants' indifference points, a linear regression line fit choice behaviour extremely well (a mean R^2 of 0.97 in both tasks). This supports the assumption of the Multiplicative Hyperbolic Model of Choice that states that a linear regression can be utilised to examine decision-making behaviour in choice situations involving delay or risk. This also means that decision-making behaviour, when in an environment with low reward magnitudes and relatively low delays, is highly predictable. Theoretically, it would be possible to extend the linear regression in order to predict choice behaviour if delay were to increase. However,

care must be taken as some research has suggested that a magnitude effects occurs in delay and probability discounting, in which small rewards are discounted differently to large rewards (Estle et al., 2006).

Considering the correlations between the parameters calculated from the discounting tasks and the other measures from behavioural and self-report questionnaires, there are some interesting results. From the real reward version to the delay discounting task, K^+ was positively correlated with the number of stop errors made on the stop task. This means that low self-control (as indicated by a high value of K^+) would be positively correlated to inhibitory control. Although self-control is defined as the ability to tolerate delay to maximise gain, it could be expected that the ability to be able to tolerate delay would be related to the ability to control one's own behaviour. Intercept was inversely correlated to stop errors, probably due to the high correlation between K^+ and stop errors. The problem concerning any correlation between the intercept and another measure is that the measure could be related to Q^+, K^+ or both. If the measure is also correlated to the slope or behavioural parameter then this provides us with information as to the direction of correlation. However, if no such correlations exist, then it must be assumed that both Q^+ and K^+ are having a, less powerful, additive effect. Slope was also positively correlated with the persistence subscale from the TCI. This suggests that sensitivity to reward magnitude is related to the ability to persevere and tendency to be hard-working and ambitious. If an individual is hard-working and ambitious then it would make sense that the individual must do so because they expect to be rewarded either by oneself or a third party for achieving effortful goals.

In the hypothetical rewards version of the delay discounting task, K^+ and the slope were correlated with disorderliness, a sub-factor of novelty-seeking from the TCI. High levels of disorderliness refer to the tendency to not plan one's actions and to be untidy in thought and action. It might be expected that low self-control would be related to these behaviours. Q^+ was also positively related to disorderliness. This

may be due to the type of reward that individuals with high reward sensitivity seek. These individuals may leave their home environment to gain external rewards that carry higher subjective value while their home environment becomes neglected and more disordered (possibly because keeping their immediate environment ordered carries lower subjective value). Slope was also correlated with the novelty-seeking subscale of the TCI, most likely due to the correlation with disorderliness. K^+ and slope were correlated with openness on the Big 5 questionnaire. Openness measures the individual's tendency to be open to new experiences and enjoy 'sophisticated' pursuits such as art, music and theatre. Reward sensitivity may be related to openness as those who seek out rewards may enjoy these pursuits possibly for their personal and socially rewarding nature. The correlation between K^+ and openness appears contradictory. It could be expected that individuals with low self-control would not generally seek out such pursuits. It may the case that individuals with low self-control may need to seek out a wide variety of stimuli to provide enough sensory stimulation. Individuals with high self-control may be more content to have a lifestyle that contains a more sedate rate of stimulation.

In the real rewards version of the probability discounting task, slope was inversely related to trait and state anxiety measured by the STAI. One reason for this is that highly anxious individuals may incline to attenuate reward-seeking behaviour, due to the tendency to withhold their participation in activities that would provoke anxiety. H^+ was inversely correlated with conscientiousness as measured by the Big 5. Conscientiousness measures an individual's propensity to work diligently and be empathic. It could be argued that conscientious individuals would be highly aware of any risks involved in a choice situation. They may also be low risk-takers as taking risks could lead to negative consequences, a situation that a conscientious individual may strive to avoid.

In the hypothetical rewards version of the probability discounting task, H^+ was correlated with extraversion. Extraversion has been linked to impulsivity. It could be suggested that extraverted individuals are more prone to risk-taking as they may

be more adventurous. Slope was inversely correlated with reward dependence, a sub-scale of the TCI. Reward dependence measures the tendency of an individual to be sentimental, honest and dependent. It is perhaps the case that individuals who have low sensitivity to reward magnitude are more dependable as they will not have the urge to seek out novel stimuli (and novel, perhaps transient, relationships with other individuals).

One problem that must be confronted when all these correlations are considered is the tendency for the measures of behaviour from the different versions of the same discounting task to show different correlations. This may be due to the reward itself, i.e. perhaps performance in the real rewards version of the delay discounting task takes a more valid measure of self-control. It is interesting to note that if grand means of the parameter values, slopes and intercept between reward types for each task are calculated, then these grand means correlate to a very small number of other measures. Previous research has reported low correlation between self-report measures and behavioural measures[11]. Taking into consideration previous research that has compared behavioural and self-report measures of impulsivity, a high number of correlations between the discounting tasks and self-report measures was not expected.

One problem with the tasks utilised in experiment one was the number of negative H^+ values that were calculated. In the tasks used in experiment two, there were only 5 out of 31 participants for whom a negative value of H^+ was calculated. The use of an anchor point on the graph (when pA = 1.0), as discussed in experiment 1, and distribution of probabilities attached to alternative A appeared to be a solution to the problematic biases inherent within the pilot task.

Conclusions

[11] See section 3.2 of the introduction for more detail

Choice behaviour on a delay and probability discounting task has been found to alter in normal, healthy, participants dependent on whether real or hypothetical monetary outcomes were given. These changes in behaviour may be due to intolerance of delays associated with hypothetical rewards and increased risk-taking when given the chance to win small probabilistic rewards. This finding has important applications for all studies utilising discounting tasks with hypothetical outcomes. In these studies, it may be advantageous to utilise, where permissible, tasks that contain real consequences.

Experiment 3: Delay and probability discounting in individuals with impulse-control or anxiety disorders

Introduction

Altered levels of impulsivity appear to have a major role in several psychiatric disorders. Research has shown that individuals with addictive disorders such as alcoholics, substance abusers and pathological gamblers report increased levels of general impulsivity compared to non-addicted controls (Allen et al, 1998; Blaszczynski et al., 1997; Chambers and Potenza, 2003; Dawe and Loxton, 2004; Moeller et al, 2001; Steel & Blaszczynski et al., 1998; Wagner, 2005). Individuals with addictive disorders also tend to show decreased levels of inhibitory control compared to controls (Franken, 2003; Goldstein et al., 2001).

Delay discounting tasks measure self-control (defined as the ability to tolerate delay in order to maximise gain). Pathological gamblers and substance abusers reliably show a decreased ability to make self-controlled choices in delay discounting tasks compared to controls (Allen et al, 1998; Bornovalova et al, 2005; Kirby et al, 1999; Kirby & Petry, 2004). It has been suggested that individuals exhibiting problematic addictive behaviours discount future rewards (e.g. better health) more than non-addicts and instead focus on sooner or immediate rewards (e.g. positive effects from drug etc.). This behaviour may pre-dispose an individual to act in an addictive manner or it may develop as a consequence of the addiction.

There have been relatively fewer studies investigating levels of risk-taking in individuals with addictive disorders and those that have been performed have found mixed results. Problem gamblers, who would have been hypothesised to have increased levels of risk-taking, have been found to express lower risk-taking behaviour on a probability discounting task compared to controls (Holt et al, 2003).

Altered levels of risk-taking may be a characteristic that has a powerful effect on impulsivity and therefore on addiction. One may hypothesise that substance abusers may be high risk-takers due to the potential adverse effects of drug use. More research is needed to uncover information concerning the role of risk-taking in addictive disorders.

There may be some links between altered levels of impulsivity and anxiety disorders. Altered levels of self-control and risk-taking may lead to decision-making biases that exacerbate levels of anxiety. One study has found that healthy participants who have higher levels of anxiety discount delayed rewards at a higher rate to healthy low-anxiety individuals (Rounds et al., 2006). In another study, healthy individuals inducted into a high anxiety state were more risk-averse than healthy individuals inducted into a low-anxiety state (Ragunthan & Pharm, 1999) but only if their choices contained personal consequences as opposed to choices only affecting a third party. These studies suggest that individuals with high anxiety levels may have altered levels of impulsivity. Studies are needed that focus on self-control and risk-taking in individuals with anxiety disorders in order to uncover biases in these individuals that may underlie their disorder.

This experiment was designed to assess self-control and risk-taking in individuals showing addictive behaviours and those with anxiety disorders. Participants were recruited from four populations; pathological gamblers, non-pathological gamblers, substance abusers and individuals with anxiety disorders. Non-pathological gamblers were recruited to examine any possible abnormalities in behaviour that may have manifested at a non-pathological gambling stage and which, when exacerbated, may have led to the onset of pathological gambling. It was hypothesised that there was a continuum between non-gambler and pathological gambler with behavioural changes occurring along this continuum that led to pathological gambling. Participants were given the same tasks given in experiment 2. Previous studies using delay discounting tasks have found that there may be significant differences in choice behaviour in healthy normal individuals when

given real rather than hypothetical rewards. In experiment 2, it was found that providing real, rather than hypothetical monetary rewards significantly altered choice behaviour on delay and probability discounting tasks in healthy normal participants. Arguably, individuals with addictive disorders may be more sensitive to the difference between real and hypothetical rewards. The discounting tasks that were used provided real consequences for each choice made and, as such, are hypothesised to provide more valid measures of self-control and risk-taking. We are not aware of any other study that has utilised delay and probability discounting tasks such as these in these populations. Data from the sample recruited in experiment 2 will be used as a comparative, control, group.

Methods

Participants

17 pathological gamblers, 15 non-pathological gamblers, 15 substance abusers and 16 individuals diagnosed with an anxiety disorder were recruited from a community sample. All participants met DSM-IV criteria for their respective disorders[12]. Mean ages (and minimum/maximum age) were 29.7 years (20-49 years) for the pathological gamblers, 20.0 years (18-22 years) for the non-pathological gamblers, 20.62 years (18-26 years) for the substance abusers and 26.14 years (19-54 years) for the anxious individuals. The data from the control sample was derived from experiment 2. Table 2 shows the main characteristics of each participants group.

[12] Refer to "General Methods" section for details of screening

Table 2: Characteristics of each group (standard deviations are shown in brackets)

	N	Sex (no. of female participants)	Age	IQ
Controls	38	21	22.31 (3.05)	95.17 (9.77)
Pathological gamblers	17	1	29.7 (9.42)	91.36 (8.08)
Non-pathological gamblers	15	2	20.55 (2.65)	90.87 (10.23)
Substance abusers	15	6	21.68 (3.06)	97.55 (8.79)
Anxiety-disordered	16	7	26.14 (10.09)	99.00 (9.59)

Two participants from the substance abusers group were excluded as they did not meet DSM-IV criteria for substance abuse or dependence. One individual from the ANX group was excluded as they did not meet DSM-IV criteria for an anxiety disorder.

Group differences on measures assessing differences key to the definition of each group, i.e. gambling tendencies, drug and alcohol abusage and levels of anxiety, were investigated. There was a significant group effect on scores from the SOGS, $F(4,58) = 41.21$, $p < .001$. Pathological gamblers had significantly higher scores compared to the non-pathological gamblers, $p < .001$, substance abusers, $p < .001$, ANXs, $p < .001$, and controls, $p < .001$. There was also a significant group effect on scores from the AUDIT, $F(4,58) = 5.77$, $p = .001$. Substance abusers reported significantly higher scores compared to pathological gamblers, $p = .05$, ANXs, $p = .02$, and controls, $p < .001$. There was also a trend for substance abusers to have higher scores compared to non-pathological gamblers, $p = .08$. Finally, there were

significant group effects on trait anxiety, $F(4,56) = 8.92$, $p < .001$, and state anxiety, $F(4,56) = 6.52$, $p < .001$, scores from the STAI. On the trait subscale, the ANXs reported significantly higher scores compared to substance abusers, $p = .02$, non-pathological gamblers, $p < .001$, and controls, $p < .001$. Pathological gamblers also had significantly higher scores compared to the non-pathological gamblers, $p = .009$, and controls, $p = .005$. On the state subscale, ANXs reported significantly higher scores compared to the substance abusers, $p = .04$, non-pathological gamblers, $p = .004$, and controls, $p < .001$. In addition, pathological gamblers had higher scores compared to controls, $p = .04$.

Materials

The materials used were the same as in experiment 2[13].

Procedure

The procedure used was the same as in experiment 2.

Data analysis

Indifference points were measured and behavioural parameters were calculated using the same methods as in experiment 2. Inclusion criteria were also the same as in experiment 2.

For analysis of the delay discounting task a 2x5 repeated measures ANOVA was performed. The dependent variable was delay tolerance. Reward type was one factor and average IPs for the delays of alternative A was the second factor. Group

[13] Refer to the "General Methods" section for all other tasks used (except the discounting tasks which are decribed in experiment 2)

was included as a between subjects factor. If a reward effect was found then four further 2x5 repeated measures ANOVAs would be performed, each comparing performance within each group (except for the controls as their performance had already been assessed).

In the probability discounting task a 2x4 repeated measures ANOVA was calculated. The dependent variable was risk-aversion. Reward type was one factor and average IPs for each probability of alternative A was another factor. Group was included as a between subjects factor. There were two ANOVAS performed, one using theta values and one using probabilities. If a reward effect was found then further 2x4 repeated measures ANOVAs would be performed, each comparing performance within each group (except for the controls as their performance had already been assessed). Four ANOVAs incorporated theta values and four incorporated probabilities.

Area under Curve (AUC) analysis was not utilised in this experiment. For reasons, refer to the discussion of experiment 2.

To assess reliability of participant responses on the real and hypothetical tasks the indifference points, parameter, slope, and intercept values were correlated between reward types.

To further examine possible differences in choice behaviour between each reward type and between each group, six one-way ANOVAs were performed which included the parameter values, slopes and intercepts from each task. Reward was entered as a within-subjects factor and group was entered as a between-subjects factor.

In addition, the group differences between scores on the self-report and neuropsychological tasks (described in the section 'General Methods') needed to be

explored. One way ANOVAs were performed with the task measurement included as one factor, as group inputted as a between-groups factor.

Correlation analyses were also performed between K^+, slope and intercept from the delay discounting task and H^+, slope and intercept calculated from the probability discounting task.

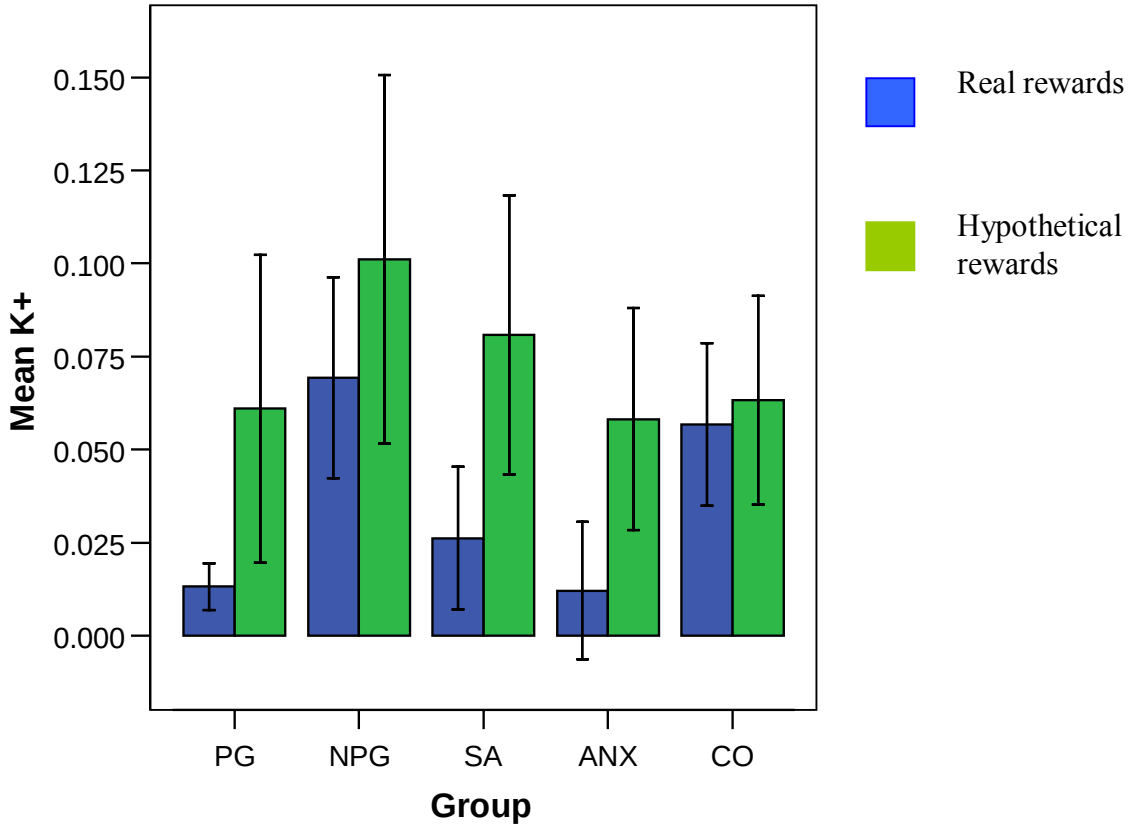
Results

Mean scores from all other behavioural tasks and self-report questionnaires are shown in appendix 4.

Three anxiety-disordered participants withdrew from the study before completion; therefore, their data was not included. Data regarding delay discounting task performance was lost for one substance abuser and one anxiety-disordered participant due to computer problems. Data from the probability discounting task was also lost for one pathological gambler. One substance abuser and one anxiety-disordered individual were excluded from the analysis of the delay discounting task because they did not meet criteria for the minimum acceptable number of indifference points. Data from two pathological gamblers, one substance abuser and two anxiety-disordered individuals were excluded from the probability discounting task for the same reason. Due to the calculation of parameter values or slope values that were more than two standard deviations from the mean, data from two pathological gamblers, four non-pathological gamblers and one anxiety-disordered participant were excluded from analysis of the delay discounting task. Data from three pathological gamblers, two non-pathological gamblers and three substance abusers were excluded from analysis of the probability discounting task for the same reason.

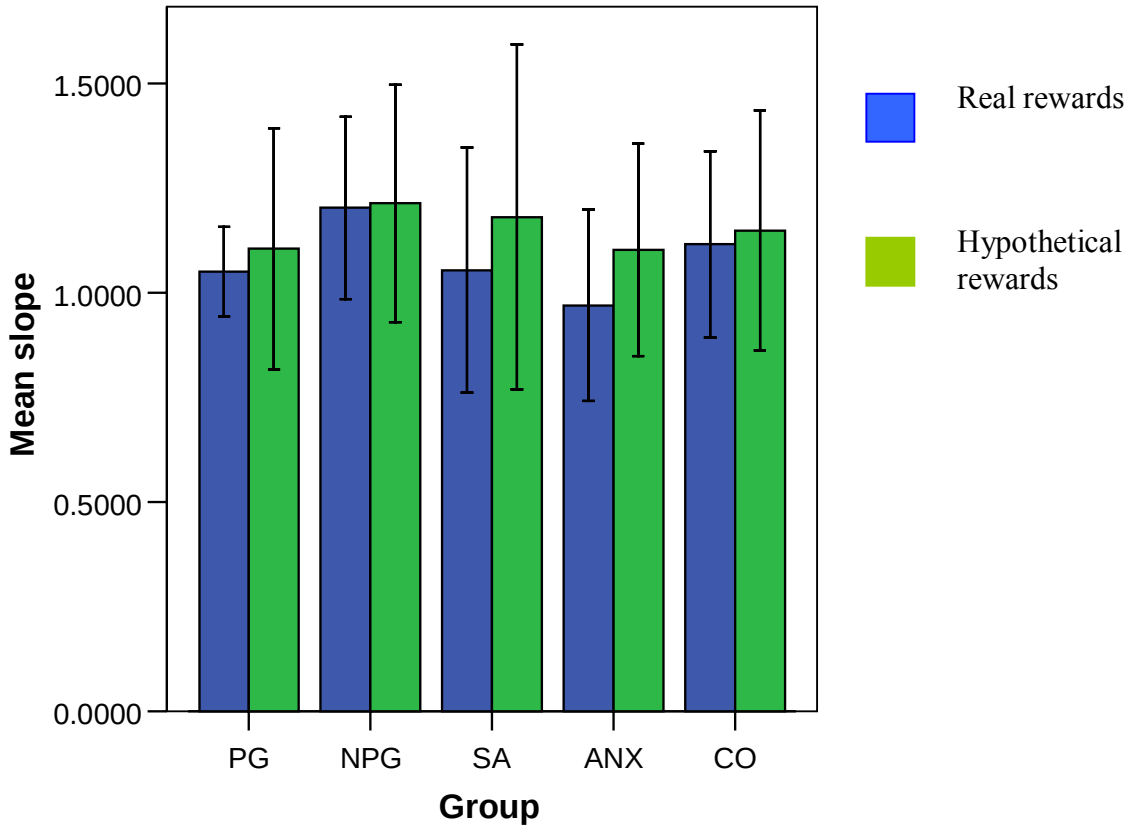
The figures below show the K^+ and slope values from the delay discounting task and the H^+ and slope values from the probability discounting task. Intercept values are not shown as they are a marker of both the value of the parameter value and the slope. Values are split into groups.

Figure 8: Mean K^+ values from each reward condition in the delay discounting task split into groups



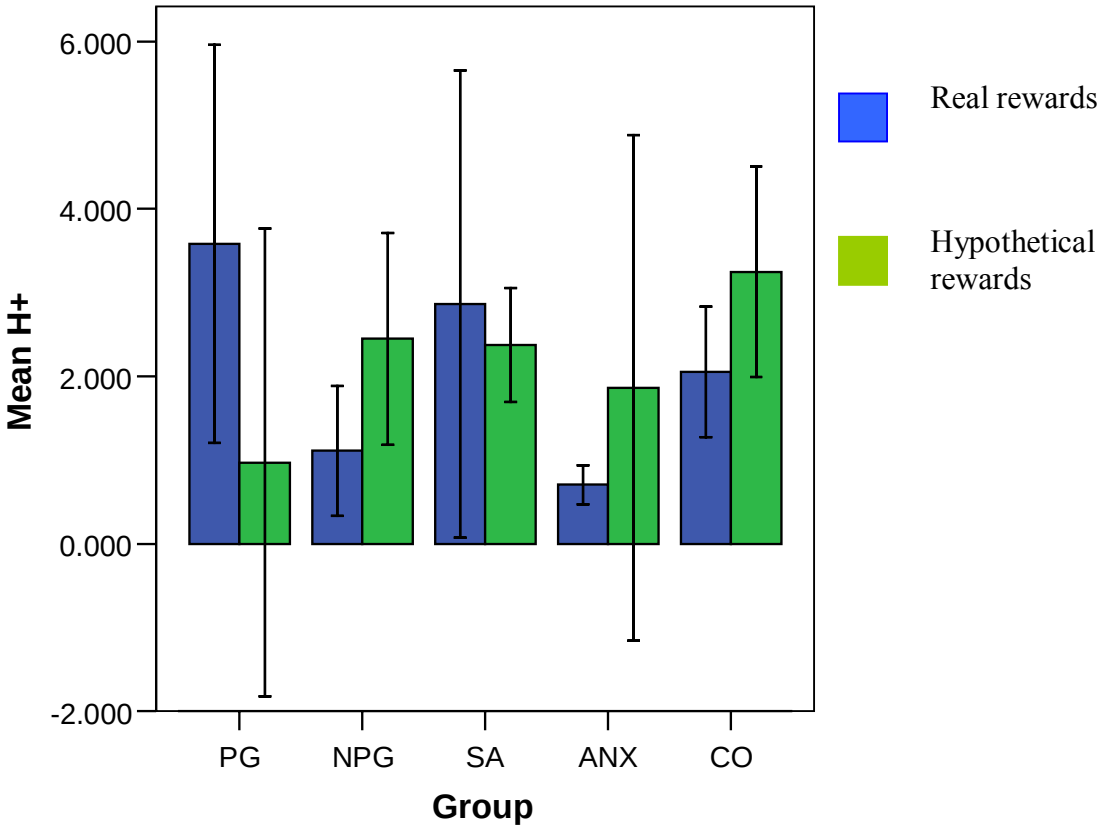
Error bars = +/- 2SD

Figure 9: Mean slope values from each reward condition in the delay discounting task split into groups



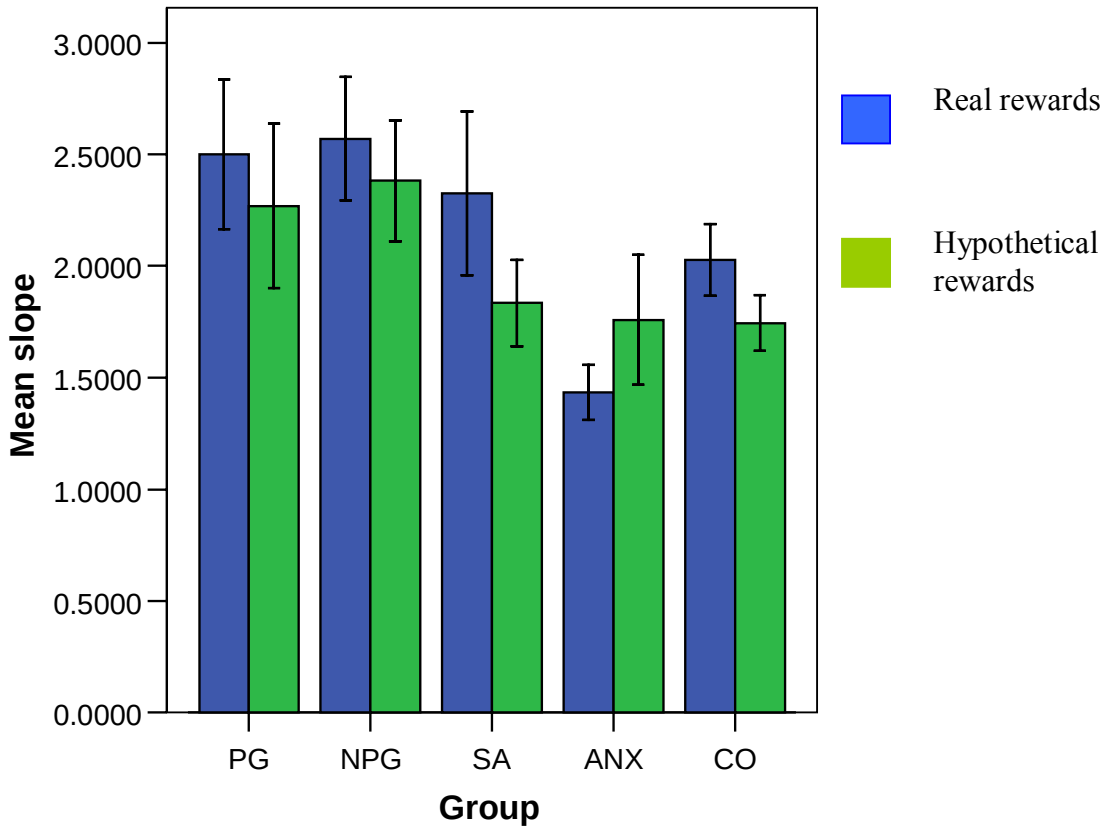
Error bars = +/- 2SD

Figure 10: Mean H^+ values from each reward condition in the probability discounting task split into groups



Error bars = +/- 2SD

Figure 11: Mean slope values from each reward condition in the probability discounting task split into groups



Error bars = +/- 2SD

Real vs. hypothetical rewards

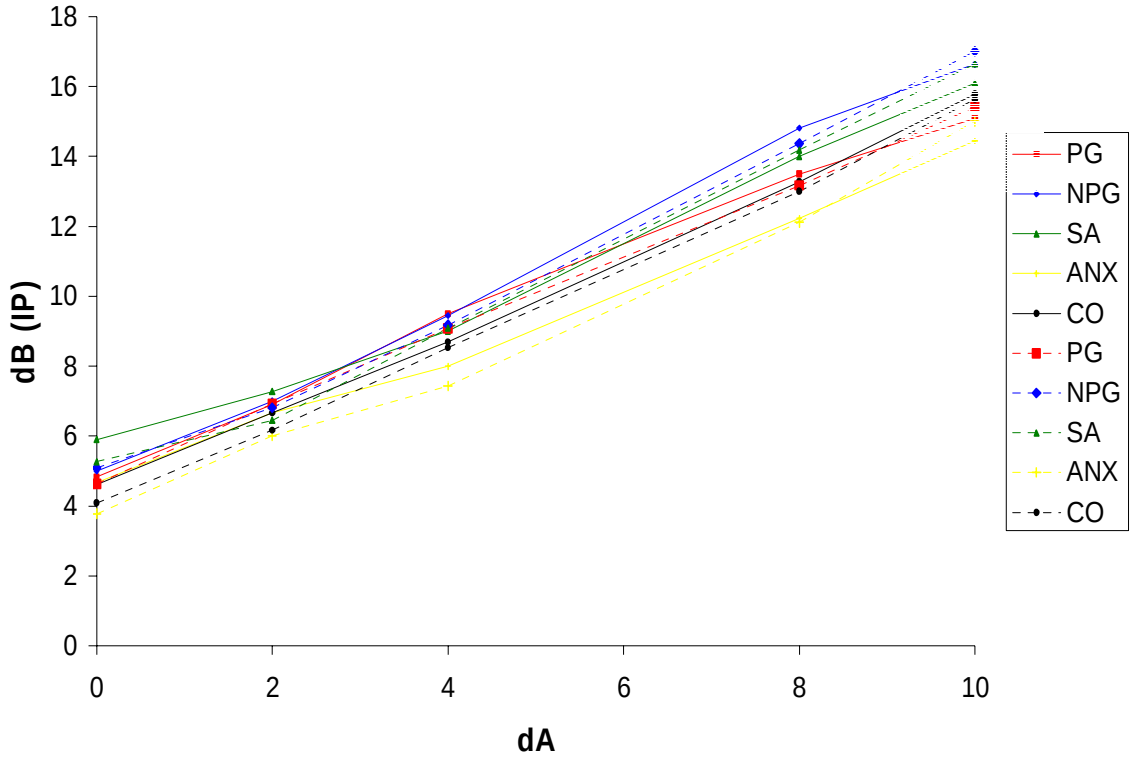
Delay discounting task

14 pathological gamblers, 11 non-pathological gamblers, 11 substance abusers, 9 anxiety-disordered individuals and the control sample were included in this analysis.

A linear function was fitted to each individual's indifference points and the mean R^2 was found from all participants, which was 0.97.

Figure 12 below shows the mean IPs calculated from each reward version for each group.

Figure 12: Group indifference points from both reward versions of the delay discounting task



NB: IPs from the real rewards task are shown by the unbroken lines. IPs from the hypothetical rewards task are shown by the dotted lines.

Figure 12 contains many data points so error bars are not included for the purpose of clarity. Table 3 below shows the indifference points for each group on each reward version of the delay discounting task. Standard deviations are shown in brackets.

Table 3: Group indifference points (with standard deviations) from each reward version of the task

Reward type and delay (seconds)	**Group**	PG	NPG	SA	ANX	CO
Real						
0		4.85 (1.46)	5.00 (2.05)	5.91 (1.76)	4.67 (2.35)	4.63 (2.15)
2		7.00 (1.08)	7.00 (1.48)	7.27 (1.49)	6.67 (2.12)	6.66 (1.66)
4		9.46 (1.05)	9.46 (1.36)	9.00 (0.89)	8.00 (1.12)	8.69 (1.26)
8		13.62 (1.33)	14.82 (1.33)	14.00 (1.61)	12.22 (0.97)	13.28 (1.28)
10		15.23 (1.24)	16.64 (1.63)	16.09 (1.53)	14.44 (1.42)	15.78 (1.74)
Hypothetical						
0		4.81 (1.89)	5.09 (2.43)	5.27 (2.24)	3.78 (2.22)	4.09 (1.84)
2		6.92 (0.95)	6.82 (1.47)	6.45 (1.44)	6.00 (1.58)	6.18 (1.46)
4		9.08 (1.04)	9.18 (1.47)	9.09 (0.54)	7.44 (1.24)	8.53 (1.05)
8		13.38 (1.71)	14.36 (1.12)	14.18 (1.94)	12.11 (1.83)	13.00 (1.95)
10		15.54 (1.94)	17.00 (1.10)	16.64 (2.34)	15.00 (1.12)	15.63 (2.07)

There was a trend for a main effect between reward type, $F(1,37) = 3.18$, $p = .08$. There was a significant main effect of delay, $F(4,16) = 993.81$, $p < .001$. There was a significant interaction between reward and delay, $F(4,268) = 2.52$, $p = .04$. There

was no effect of task order (real or hypothetical given first), $F(1,67) = 0.37$, $p = .55$. There was a significant main effect of group, $F(4,67) = 5.38$, $p = .001$.

Post-hoc tests, using Tukey's HSD test, were performed in order to discover how the groups differed in their responses. Non-pathological gamblers showed significantly higher mean IPs compared to controls, $p = .021$, and ANXs, $p = .001$. Substance abusers also showed higher IPs compared to ANXs, $p = .004$ and a trend for higher IPs than controls, $p = .079$. There was trend for pathological gamblers to have higher IPs than ANXs, $p = .074$.

There was no significant effect of reward type on indifference points obtained from the pathological gamblers, $F(1,12) = .08$, $p = .78$, non-pathological gamblers, $F(1,10) = .04$, $p = .85$, substance abusers, $F(1,10) = .55$, $p = .47$, or anxiety-disordered individuals, $F(1,8) = 2.50$, $p = .15$.

A further ANOVA was performed which included all individuals excluded due to a having parameter or slope values more than two standard deviations from the mean. There was still a trend for an effect of reward, $F(1,84) = 2.86$, $p = .09$, a significant effect of delay, $F(4,336) = 837.94$, $p < .001$, and a significant effect of group, $F(4,84) = 3.85$, $p = .01$. Tukey's HSD tests were used to explore group differences. Non-pathological gamblers, $p = .03$, and substance abusers, $p = .01$, had significantly higher IPs compared to the anxiety-disordered group.

Spearman's rank-order correlation coefficients were performed on K^+, slope, and intercept values between reward types. Spearman's was used due to the positive skew of K^+ values. K^+ values were highly correlated, $r_s = 0.29$, $p = .01$. In addition, slope values, $r_s = 0.32$, $p = .005$, and intercept values, $r_s = 0.38$, $p = .001$, were correlated

Probability discounting task

10 pathological gamblers, 13 non-pathological gamblers, 9 substance abusers, 7 anxiety-disordered individuals and the control sample were included in this analysis.

A linear function was fitted to each participant's plot of his or her IPs. The mean R^2 for the fit of the linear regression was 0.97.

Figure 14 below shows the IPs from both reward versions of the task measured from each group.

Figure 14: Group indifference points from both reward versions of the probability discounting task

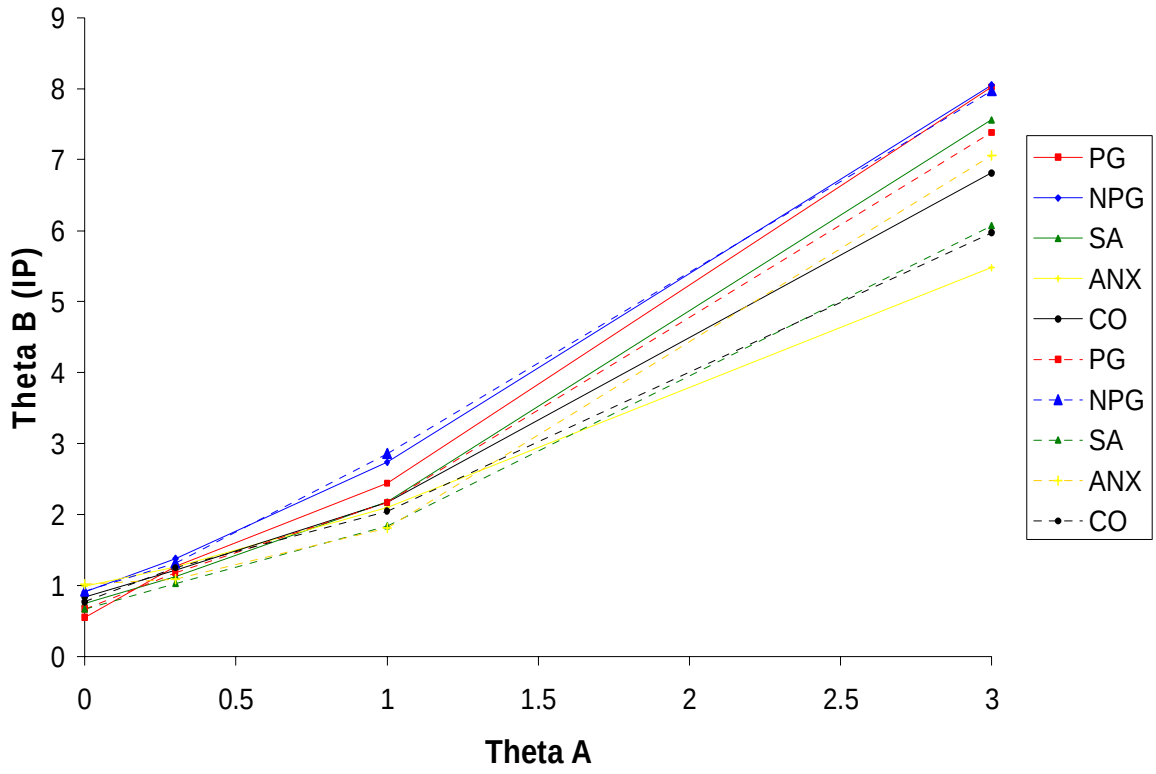


Figure 14 contains many data points so error bars are not included for the purpose of clarity. Table 4 below shows the indifference points for each group on each reward version of the probability discounting task. Standard deviations are shown in brackets.

Table 4: Group indifference points (with standard deviations) from each reward version of the task

Reward type and odds against (θ)	**Group**	PG	NPG	SA	ANX	CO
Real						
0		0.55 (0.32)	0.91 (0.32)	0.74 (0.49)	1.00 (0.58)	0.83 (0.47)
0.3		1.28 (0.34)	1.38 (0.29)	1.13 (0.30)	1.22 (0.35)	1.22 (0.32)
1		2.44 (0.44)	2.74 (0.69)	2.17 (0.72)	2.01 (0.38)	2.17 (0.53)
3		8.02 (2.93)	8.05 (2.42)	7.56 (3.31)	5.37 (0.90)	6.81 (2.61)
Hypothetical						
0		0.67 (0.29)	0.92 (0.39)	0.67 (0.34)	1.03 (0.63)	0.75 (0.46)
0.3		1.18 (0.35)	1.32 (0.34)	1.03 (0.39)	1.09 (0.29)	1.24 (0.44)
1		2.17 (0.80)	2.86 (0.74)	1.85 (0.46)	1.70 (0.30)	2.02 (0.66)
3		7.38 (3.31)	7.97 (3.02)	6.07 (1.88)	6.55 (1.98)	6.97 (6.09)

When calculating the ANOVA inputting theta values, there was no effect of reward, $F(1,60) = 2.47$, $p = .12$. There was a main effect of odds against, $F(3,180) = 368.32$, $p < .001$. There was no effect of task order, $F(1,60) = 0.25$, $p = .62$. There was a strong trend for a group effect, $F(4,60)$ 2.47, $p = .054$. Least significant difference tests were used to examine group differences as this test was less stringent. Non-pathological gamblers had significantly high IPs compared to controls, $p = .01$.

A further ANOVA was calculated that included data from participants who had H^+ or slope values more than two standard deviations from the mean. There was no effect of reward, $F(1,79) = 1.47$, $p = .23$. There was an effect of odds against, $F(3,237) = 278.46$, $p < .001$. There was no effect of group, $F(4,79) = 0.68$, $p = .61$.

When probabilities were used in the ANOVA there was no effect of reward, $F(1,59) = 1.37$, $p = .27$. There was a main effect of probability, $F(3,177) = 544.06$, $p < .001$. There was no effect of order, $F(1,59) = 0.45$, $p = .51$, or group, $F(1,59) = 1.31$, $p = .28$.

To further explore the effects of reward type on AUC values, four repeated-measures t-tests were used to assess which groups altered their choice behaviour between rewards. Substance abusers were significantly more risk-taking with real rewards compared to hypothetical rewards, $t(9) = 2.37$, $p = .04$. There was a trend for pathological gamblers to be more risk-taking with real compared to hypothetical rewards, $t(12) = 1.85$, $p = .09$. Reward type did not significantly affect choice behaviour in non-pathological gamblers, $t(8) = 0.35$, $p = .73$, and anxiety-disordered individuals, $t(6) = -0.82$, $p = .45$.

H^+, slope and intercept values were correlated between reward types. Spearman's rank-order correlation coefficient was used due to the positive skew of H^+ values. The correlation between H^+ values was high but not significant, $r_s = 0.21$, $p = .08$.

However, slopes, $r_s = 0.48$, $p < .001$, and intercepts, $r_s = 0.57$, $p < .001$, were significantly correlated.

Correlation analysis of parameter values, slopes and intercepts between the task types

Spearman's rank-order correlation coefficient was used to assess the relationships between calculated values from the delay and probability discounting tasks. K^+, slope and intercept from the delay discounting task (both reward types) was compared to H^+, slope and intercept from the probability discounting task (both reward types), which gave 36 possible correlations. Slope from the real reward version of the delay discounting task was correlated to intercept from the real reward version of the probability discounting task, $r_s = 0.38$, $p = .04$. Slope from the hypothetical reward version of the delay discounting task was correlated to intercept from the hypothetical reward version of the probability discounting task, $r_s = 0.36$, $p = .05$. No other correlations were significant.

Differences in group choice behaviour between the reward versions of the discounting tasks: Comparison of parameter values, slopes and intercepts between reward type

Firstly, calculated values from the delay discounting task were compared. There was a trend for K^+ values, $F(1,72) = 3.60$, $p = .06$, and slopes, $F(1,72) = 3.71$, $p = .06$, to differ between reward. There was a significant reward effect on intercepts, $F(1,72) = 5.10$, $p = .03$. There were no group effects in any of the ANOVAs.

In the probability discounting task, there was no effect of reward on H^+, slope or intercept. There was a trend for a group effect in the slopes, $F(4,66) = 2.44$, $p = .06$.

Group differences between scores on the self-report and neuropsychological tasks

Tables are shown in appendix 4 that contains all mean scores, split by group, from the neuropsychological tasks and questionnaires. One-way ANOVAs were performed on key measures from the self-report and neuropsychological tasks. Where significant group effects were found, Tukey's HSD tests were performed. There were group differences on scores from the impulsivity, $F(4,57) = 4.36$, $p = .004$, and venturesomeness, $F(4,57) = 4.44$, $p = .004$, scales of the IVE. On the impulsivity sub-scale both pathological gamblers, $p = .01$, and substance abusers, $p = .05$, had significantly higher scores than the controls. On the venturesomeness sub-scale, substance abusers had significantly higher scores compared to the pathological gamblers, $p = .03$, and the ANXs, $p = .01$. There was a trend for non-pathological gamblers to have higher scores than ANXs, $p = .06$. From the BIS-11, there was a significant group effect on total scores, $F(4,57) = 2.69$, $p = .04$. However, there were no group effects on any of the sub-scales. When Tukey's HSD test was used, there were no significant group effects on total BIS scores. There was a trend for substance abusers report higher scores compared to controls, $p = .06$. There was also a trend for pathological gamblers to have higher scores than controls, $p = .09$.

There were no group effects on stop errors or go reaction time from the stop task.

On the Big-5 questionnaire, there was a significant group effect on scores on the openness, $F(4,57) = 4.47$, $p = .003$, and neuroticism sub-scales, $F(4,57) = 3.28$, $p = 3.28$, $p = .02$. On the openness sub-scale, substance abusers, $p = .002$, and controls, $p = .024$, had significantly higher scores compared to the pathological gamblers. On the neuroticism subscale ANXs had significantly higher scores compared to the non-pathological gamblers, $p = .02$, and controls, $p = .02$. There was a trend for ANXs to have higher scores than the substance abusers, $p = .09$. There were trends

for groups effects on the agreeableness, $F(4,57) = 2.46$, $p = .06$, and the conscientiousness sub-scale, $F(4,57) = 2.21$, $p = .08$.

On the TCI, the sub-scales that were focused upon were novelty-seeking, harm avoidance, reward dependence and persistence as these can be argued to be associated with impulsivity and decision-making. There was a significant group effect on impulsiveness, $F(4,56) = 6.16$, $p < .001$, and disorderliness, $F(4,56) = 7.91$, $p < .001$, (which were subscales of novelty seeking). On the impulsiveness subscale, pathological gamblers, $p = .002$, and substance abusers, $p = .02$, reported higher scores compared to controls. On the disorderliness subscale, pathological gamblers, $p = .002$, non-pathological gamblers, $p = .008$, substance abusers, $p = .001$, reported higher scores compared to controls. There were no significant group differences on the subscales of harm avoidance, but there were trends for a group effect on anticipatory worry, $F(4,56) = 2.26$, $p = .08$, shyness, $F(4,56) = 2.24$, $p = .08$, and fatigability, $F(4,56) = 2.31$, $p = .07$. On the reward dependence scale, there was a group effect on sentimentality, $F(4,56) = 3.20$, $p = .02$. Controls showed higher scores compared to non-pathological gamblers, $p = .02$. There was a significant group effect on persistence scores, $F(4,56) = 3.59$, $p = .01$. Controls had higher scores compared to substance abusers, $p = .04$.

Discussion

There was no significant effect of reward type on choice behaviour in both the delay and probability discounting tasks. There was a trend suggesting that participants were more self-controlled when given real rewards in the delay discounting task. However, when the performance of each group was assessed (within groups) there was no significant difference in choice behaviour in the pathological gamblers, non-pathological gamblers, substance abusers and anxiety-disordered individuals between the different reward types. Therefore, although the data cumulated from all groups showed an increase in self-control when given real rewards, it was only the performance of the controls that caused this main effect.

There was no effect of reward type on choice behaviour in the probability discounting task when comparing indifference points. When the choice behaviour was assessed in each group it was found that substance abusers took more risks when offered real compared to hypothetical rewards. There was also a trend for pathological gamblers to act in a similar way. This gives some support to the theory that increased risk-taking in substance abusers and pathological gamblers may be linked to their addictive behaviour. This result is critically important when reviewing previous research measuring probability discounting behaviour in gamblers or substance abusers. In summary, it appears that providing real opposed to hypothetical rewards does affect behaviour in the delay discounting task but only in healthy 'normal' samples. This finding is important for studies recruiting addiction-disordered and healthy samples utilising delay or probability discounting tasks that provide real consequences (e.g. Reynolds, 2006). If the tasks provide small rewards and delays it is important to consider whether or not the task should provide real, rather than hypothetical, monetary rewards in order to obtain a more valid measure of self-control. Use of hypothetical outcomes would be permissible if there were important constraints against the provision of real rewards.

As in experiment 1, the choice behaviour of the participants fitted extremely well to a linear regression. This suggests that behaviour in these psychiatric samples, in addition to healthy controls, follows a strict pattern and rarely deviates from this. It also suggests that choice behaviour in these populations can be predicted at longer delays by extending the regression line. Again, caution must be taken as we must consider that studies recruiting healthy individuals have found that smaller rewards are discounted in a different way to larger rewards (Estle et al., 2006). Caution must also be taken when plotting IPs using odds against values. As can be seen in figure 14, the lines do not adhere to a linear function as well as the data from the delay discounting task. This is most likely due to the use of odds against values, which are a non-linear measurement. If a researcher aims to predict risk-taking behaviour, then it may be advantageous to plot probabilities.

There was a significant main effect of group in the delay discounting task. Perhaps surprisingly, non-pathological gamblers and substance abusers were the most self-controlled and individuals diagnosed with anxiety disorders were the least self-controlled. The healthy controls behaved in a slightly less self-controlled manner, similar to the ANXs, except when *d*A was at the higher delays (eight and ten seconds) when they exhibited slightly more self-control than the ANXs but less than other groups. The levels of self-control measured in the pathological gamblers were reliably located in the middle of the other groups. In terms of statistical significance, non-pathological gamblers showed significantly more self-control compared to ANXs and controls. Substance abusers also exhibited significantly more self control compared to the ANXs. This finding is, perhaps, contrary to what we would expect, especially in light of the number of studies concluding that pathological gamblers and substance abusers discount delayed rewards at significantly higher rates than controls. However, no study has utilised tasks such as these, which provide real consequences of choices, in these populations. One study (Reynolds, 2006) provided smokers and non-smokers with a delay discounting task that provided real consequences and found that smoking severity was not related to task performance but was correlated to performance on a pen-and-paper hypothetical delay discounting task. The study by Reynolds, when combined with the results from this study, suggests that the behaviour of an individual on a delay discounting task giving realistic outcomes may be very different compared to that in a pen-and-paper task giving hypothetical situations. Arguably, the real task would provide more of an accurate measure as we can be certain that individuals are taking account of the reward to delay trade-off because individuals are forced to experience the consequences of their choice. The real task has the disadvantage of only being able to test behaviour to small rewards and delays. It must be questioned as to whether participants can accurately estimate how they would feel in an imaginary situation where someone was offering them £200 immediately or £20,000 in 25 years time and whether this situation can be described as realistic. It may be the case that substance abusers and pathological gamblers who appear to focus on more immediate events compared to controls

(Petry et al., 1998) have more difficulty in envisaging consequences in a delay discounting task that will happen in the future. Tasks such as those used in this study may provide a more accurate measurement of delay discounting in these populations. It may also be questioned as to whether the psychiatric samples recruited for this experiment were consistent in their behaviour. It could be the case that participants from these groups showed increased variance in their choice behaviour, thus decreasing the validity of the measurement. However, this was found not to be the case with choice behaviour from all participants over the separate presentations being reliably similar. As in experiment 2, the participants were questioned afterwards as to any possible decision-making rules they followed. A number of participants reported using similar types of rules to those reported by the controls.

As far as we are aware, this is the first study that has provided delay and probability discounting tasks that give real outcomes to pathological gamblers, non-pathological gamblers, substance abusers and individuals with anxiety disorders. Their behaviour was, therefore, an unknown. Further studies could compare behaviour on the tasks used in this project with hypothetical discounting tasks that have been utilised in previous research in order to explore their relationship.

On the probability discounting task, there was no significant difference in choice behaviour between the groups but there was a trend. When $\theta A = 0$ then the ANX group was the most risk-taking, followed by the non-pathological gamblers. This suggests that the anxious participants were especially sensitive to the certain reward and were increasingly willing to take risks when a certain reward was offered. This seems counterintuitive as one might expect the anxious individuals to favour the certain reward in order to decrease risk and forego the possible negative emotions associated with making risky choices. It must be noted that there was only a trenbd for a group effect so no valid inferences can be derived from this data. However, there is some evidence to suggest that individuals with Generalized Anxiety

Disorder are more impulsive, as measured by the BIS-11 and IVE (Palm & Anderson, 1994).

In summary, non-pathological gamblers were more tolerant of delay and were more risk-taking compared to controls. The behaviour of pathological gamblers did not significantly differ from controls. It must be noted that many of the pathological gamblers had experienced negative life events due to their gambling problems such as job loss, counselling and divorce. It may be possible that these negative consequences of their gambling may have caused them to significantly change their behaviour and, perhaps, act in a more restrained manner. Another explanation concerns the learning of risky outcomes. Perhaps non-pathological gamblers, who possibly gamble more for fun than any other reason, are generally risk-taking as they do not evaluate the full characteristics of each risky choice. Conversely, pathological gamblers (particularly 'professional' gamblers for whom gambling is their only income) take more account of the mathematical characteristics of the risky choices. Indeed, some pathological gamblers mentioned to the researcher during the study that they only took 'calculated' risks and were not particularly risk-seeking (although these were subjective views and therefore open to bias). Substance abusers were more tolerant of delay compared to the anxious participants. One concern is that substance abusers did not differ in their behaviour compared to controls. However, as has already been mentioned this may be due to the nature of the task which has not been tested before in these populations.

There was a trend for K^+ values and slopes to differ between the reward versions of the delay discounting task. This may explain, to some degree, the weak effect of reward on indifference points. Indifference points may have altered between reward types because the participants were less impulsive (have a lower K^+) and had a increased sensitivity to the reward amounts between the two alternatives (higher Q^+) when given real rewards opposed to hypothetical rewards. However, it must be stressed that all these effects were not significant. It is interesting to note that the only group whose K^+ did not differ markedly between reward type was the

controls. When this group was removed from the ANOVA, a significant reward effect was found (p = .04). Therefore, although all the non-control samples were more impulsive when given hypothetical rewards compared to real rewards, this did not markedly alter their choice behaviour.

One interesting finding was that the ANX group showed an opposite slope function compared to the other groups. The ANXs had a higher slope when given the hypothetical rewards as opposed to the real rewards. This may be due to an attenuation of reward sensitivity in individuals with anxiety disorders.

In the delay discounting task, there were no group effects on parameter or slope values even though group effects were found when performing the ANOVA using indifference points. This suggests that the group differences were not due to K^+ or Q^+, suggesting that there were effects on behaviour in the delay discounting task other than those accounted for by K^+ and Q^+. This is an important consideration in terms of the MHMC as it suggests that other parameters may have to be included to provide a more accurate description of behaviour.

There were group differences in several of the self-report measures and behavioural tasks (other than the discounting tasks). On the impulsivity sub-scale of the IVE, pathological gamblers and substance abusers had higher scores compared to controls. The same pattern of results was also found on the impulsivity sub-scale of the TCI. Therefore, the pathological gamblers and substance abusers recruited in this study had higher levels of general impulsivity compared to controls, and this effect was reliable. There were no significant group effects on the BIS-11, possibly due to the different construction of the questionnaires, in which the IVE and TCI group impulsivity as one subscale while the BIS-11 attempts to fractionate the behaviour. Substance abusers reported higher levels of venturesomeness compared to controls and anxiety-disordered individuals. Higher venturesomeness in substance abusers may be linked to their acceptance of the risks associated with drug use (e.g. potentially negative health and social outcomes). Pathological

gamblers, non-pathological gamblers and substance abusers had higher scores on the disorderliness sub-scale of the TCI suggesting an increased lack of organisation exhibited by these groups compared to controls. These results fall in line with results from previous research concluding that psychiatric populations exhibiting addiction, such as pathological gamblers and substance abusers, are more impulsive than healthy controls. It is interesting to note that on nearly all of these measures, the non-pathological gamblers showed levels of behaviour that split the pathological gamblers and controls lending some support to the hypothesis there is a continuum between healthy normals and pathological gamblers as regards levels of impulsivity. If these elevated levels of impulsivity are further increased then this may significantly contribute to problem gambling behaviour. There were no group effects on the stop task, therefore, level of inhibitory control was fairly similar between the groups. To investigate the correlation between questionnaire measures and behavioural measures of impulsivity, the sub-factors of the stop task were correlated with all the self-report measures measuring elements of impulsivity. Out of 44 correlations, only 4 were significant. Reaction time on the GO trials was inversely correlated with total scores on the BIS-11 ($p = .01$), the motor sub-scale of the BIS-11 ($p = .02$), impulsivity on the IVE ($p = .03$) and impulsivity from the TCI ($p = .01$). This suggests that GO RT is correlated with these self-report measures that specifically rate levels of general impulsivity but that stop errors are not related to any measures relating to impulsivity, suggesting that the task, in general, is poorly correlated with self-report measures related to impulsivity.

Considering the STAI, participants from the anxiety-disordered group scored significantly higher than substance abusers, non-pathological gamblers and controls on both the measures of state and trait anxiety. Anxiety-disordered individuals also reported significantly higher scores on the neuroticism sub-scale of the Big 5 compared to non-pathological gamblers and controls. Interestingly, the pathological gamblers had significantly higher scores compared to the controls on both the measures of state and trait anxiety (and scored significantly higher than non-pathological gamblers on the trait measure). Increased levels of anxiety may have

been due to previous experience of negative life events linked to their gambling problems (as described above).

Pathological gamblers showed significantly higher scores on the South Oaks Gambling screen compared to all other groups. The mean score for pathological gamblers was 12.19 whilst controls reported a mean score of 0.89. Non-pathological gamblers had a mean score of 3.00 indicating that these participants had experienced some problems with their gambling behaviour but not at a scale comparable with the pathological gamblers.

On the AUDIT, which measures the severity of any alcohol abuse, the substance abusers had significantly higher scores compared to pathological gamblers, anxiety-disordered individuals and controls (there was also a trend for substance abusers to show higher scores than non-pathological gamblers). These results show that the substance abusers generally showed higher numbers of problematic alcohol-related behaviours compared to other groups. It may be questioned as to why the pathological gamblers did not show high alcohol intake. Many of the pathological gamblers reported that they had attenuated or halted their alcohol usage as they associated it with their addictive gambling, which some were trying to control.

There were no group differences of IQ. However, we must note that the Quick Test of IQ is not as sensitive as other, more comprehensive, tests and measures only verbal IQ. The Quick Test was chosen for its brevity as the majority of IQ tests take over 20 minutes to complete.

There were also no differences in the Nback task, which measures working memory. Working memory has been linked to delay discounting (Hinson et al., 2003) although this link has been debated (Franco-Watkins et al., 2006). It appears, in this study, that working memory capacity, as measured by the Nback task, did not differ between the groups.

One confound we must consider concerns the nature of each group. For example, it may be possible that pathological gamblers who gamble in casinos have different personality types to those who bet on horses. It would be beneficial if research were conducted that segregated gambling types. One problem with this approach is that many gamblers do not gamble on specific events. In this study, all of the pathological gamblers used on-line gambling websites. However, some of them also bet on horses, other sports, and in casinos. This suggests that it might be difficult to segregate gamblers into specific gambling subtypes.

Another potential criticism concerns the standard deviations from calculations of the parameter values, which were relatively high in a minority of groups. This is indicative of high intra-group variance. It may be the case that a population, such as pathological gamblers, cannot be labelled as 'impulsive' because there are many sub-sets within that population, which may have different behavioural profiles. A similar case may be put forward for individuals with anxiety disorders (these are the two groups that showed the highest intra-group variance). If the groups were split into those with high, medium and low parameter values then this would have decreased the power of any statistical test to unacceptable levels. Further studies could be performed which recruit a larger number of pathological gamblers and anxiety-disordered individuals. These larger groups could then be split into sub-groups showing different levels of IPs, H^+ or K^+ to investigate their properties.

Conclusions

Pathological gamblers reported higher levels of general impulsivity. However, their behaviour on the delay discounting and probability discounting task was no different to controls. This may be due to a number of factors including task design, low correlation between self-report and behavioural measures or a conscious alteration of behaviour after experiencing negative life events caused by addictive gambling. Substance abusers reported higher levels of risk-taking on questionnaire methods. This was not mirrored by their behaviour on the probability discounting task. This may be due to the low correlation between self-report and behavioural measures or to the nature of the risks contained within the probability discounting task. This task provides risks with immediate outcomes whereas the risks inherent in drug use are mostly delayed. Interestingly, the non-pathological gamblers had equal levels of risk-taking on the probability discounting task to the pathological gamblers. This suggests that slightly elevated levels of risk-taking may pre-dispose individuals to become gamblers. If risk-taking increased along a continuum from non-gambler to pathological gambler we would expect non-pathological gamblers to show levels of risk-taking in the middle of these two extremes, which is the pattern that was seen in most of the other measures. This suggests that there are behaviours inherent within non-pathological gamblers that increase in severity along the road to becoming a pathological gambler.

Reward type (either real or hypothetical) was found to, again, have an effect on choice behaviour, but only in controls. A reward effect was found on the probability discounting task but only on one of two measures. These findings have important contributions to the field of discounting, and more widely, to the any field where providing real rewards may increase the validity of any task utilised. Researchers utilising a delay discounting or probability discounting task must consider the ramifications of using hypothetical or real outcomes, especially if testing healthy control samples.

Experiment 4: Neurobiology of inter-temporal decision making, probabilistic decision making, behavioural inhibition and urge to gamble

Introduction

Impulsivity is a multi-factorial concept that is affected by a number of separate and identifiable behaviours (which have been introduced in previous sections). Altered levels of impulsivity have been hypothesised to have an important role in pathological gambling and substance abuse/dependence. Previous research has found that pathological gamblers (Blaszczynski et al, 1997; Steel & Blaszczynski, 1998) and substance abusers (Allen et al, 1998; Chambers and Potenza, 2003; Dawe and Loxton, 2004; Moeller et al, 2001; Wagner, 2005) report significantly higher levels of general impulsivity on self-report measures. Pathological gamblers and substance abuser also show significant impairments in inhibitory control compared to healthy controls (Franken, 2003; Goldstein et al., 2001). Furthermore, pathological gamblers (Dixon et al., 2003; Goudriaan et al, 2004; Raylu and Oei, 2002; Reynolds, 2006) and substance abusers (Allen et al, 1998; Bickel et al, 1999; Bornovalova et al, 2005; Kirby et al, 1999; Kirby & Petry, 2004; Kollins, 2003; Madden et al, 1997; Petry, 2001; Reynolds et al, 2003; Reynolds et al, 2004; Reynolds, 2006) show significantly lower levels of self-control (a factor of impulsivity) on a delay discounting task compared to healthy controls (self-control here is defined as the ability to tolerate delay in order to maximise gains). There is also some evidence that pathological gamblers (Powell et al, 1999) and substance abusers (Wills et al., 1994) may exhibit different levels of risk taking compared to healthy controls. On the Iowa task, pathological gamblers (Petry, 2001) and substance abusers (Bechara et al., 2001) tend to continually choose from the risky decks whilst controls shift their preference towards the safer decks. However, when other measures of risk-taking are utilised, the evidence for abnormal differences in

risk-taking is mixed with some studies finding no differences between pathological gamblers and controls (Bonnaire et al., 2004) and some finding that pathological gamblers are significantly risk-averse (Coventry and Constable, 1999; Holt et al., 2003).

The question that has been put forward by neuroscience researchers is whether these behavioural differences exhibited by pathological gamblers and substance abusers are caused by differing neurological function compared to non-addicted individuals? There is indirect evidence from studies investigating decision-making in individuals with lesions to parts of the brain. Patients with lesions to their ventromedial or dorsolateral prefrontal cortex prefer the risky decks on the Iowa task (Bechara et al., 1994; Clark et al., 2003; Manes et al., 2002). Pathological gamblers and substance abusers behave in similar ways to the lesioned participants. These results provide tentative indications that pathological gamblers and drug abusers may have impaired function within their VMPFC or DLPFC.

Several studies have shown that pathological gamblers and substance abusers do show altered neurological activity. A hypo-dopaminergic state has been reliably measured within these psychiatric groups (Bergh et al., 2007; Kieres et al., 2004), which could be due to the effects of drug use/gambling or be a pre-dispositional factor. This hypo-dopaminergic state affects functioning of the nucleus accumbens and related reward structures. Lower levels of 5-HT activity have also been measured in pathological gamblers (Moreno et al., 1991; Nordin & Sjordin, 2006) and substance abusers (Barr et al., 2004; Higgins & Fletcher, 2003; Nielsen et al., 1998) although 5-HT levels have found not to differ in alcoholics (Roy et al., 1990) or individuals with a paternal history of alcoholism (Crean et al., 2002). Some SSRIs have also been found not to decrease problematic gambling behaviour in pathological gamblers (Saiz-Ruiz et al., 2005).

Abnormal function in frontal areas, particularly the orbitofrontal cortex, has been reported in pathological gamblers and substance abusers. Substance abusers show

hypo-activation of the OFC and anterior cingulate cortex (Bolla et al., 2005; Hester & Garavan, 2004; Volkow et al., 1992). The OFC is involved in reward valuation and motivation while the OFC and ACC are involved in inhibitory control (Baler & Volkow, 2006; Best et al., 2002; Rolls, 2000).

Pathological gamblers show hypo-activation of the ventromedial prefrontal cortex, including the OFC, in decision-making tasks involving risk (Chambers & Potenza, 2003). Pathological gamblers also show abnormal activity in brain areas including the OFC and other ventromedial and dorsolateral prefrontal areas, basal ganglia, right parahippocampal gyrus and visual cortex in response to gambling cues (Crockford et al., 2005; Hollander et al., 2005).

This experiment was designed to investigate neural function within pathological gamblers, non-pathological gamblers, substance abusers and healthy controls in tasks that assess aspects of impulsivity and (gambling) cue-reactivity. Therefore, it is prudent to provide conjectures as to how these groups may differ in neural activity. The delay discounting, probability discounting and Iowa task are designed to measure neural activity during the selection/processing of delayed/probabilistic outcomes. Several areas have been linked to delay discounting behaviour including the nucleus accumbens, amygdala, hippocampus, basal ganglia and prefrontal cortex. Previous studies investigating substance abusers and pathological gamblers have found that these groups exhibit hypoactivity within the OFC, a key area in choice selection[14]. Lesioning of the OFC in rats has been found to significantly alter both K^+ and Q^+. Different methodologies (i.e. lesioning pre- or post-operatively) has led to opposite outcomes concerning levels of delay discounting. In humans, OFC activity has been associated with choice of the immediate outcome rather than the delayed outcome. OFC damage has also been linked to the presence of compulsive behaviours, which are present in addiction disorders (i.e. significantly heightened motivation to seek out drug/gambling stimuli at the cost of

[14] For a review of this research, see section 7 of the introduction (section 7.4 provides a review of this research area concentrating on substance users and problem gamblers)

one's own wellbeing). Reviewing this evidence, we are presented with somewhat of a paradox. OFC activity in impulsive substance abusers is decreased compared to controls while, in controls, heightened OFC activity is associated with selection of the more impulsive alternative. However, in healthy controls, one hypothesises that both immediate and delayed outcomes are processed in detail, whereas impulsive substance abusers simply focus on the immediate outcome at the expense (in terms of processing) of the delayed outcome. In this study, we would expect to see hypoactivation of the OFC in substance abusers and pathological gamblers (if these groups exhibit impulsive tendencies) compared to controls. The question as to whether activity within the OFC (or other areas) in non-pathological gamblers compared to controls is more difficult to answer. The non-pathological gamblers do exhibit gambling tendencies, and a possible increase in risk-taking (in certain gambling scenarios), however, this group does not show gambling addiction. It could be envisaged that, if the tendency to gamble is sub-served by a biological effect, OFC activity may be different in this group compared to controls.

Regarding the probability discounting task, again the OFC, in addition to the VMPFC, may play key roles. Increased activity within these areas has been associated with increased risk-aversion. Pathological gamblers and substance abuser show decreased levels of activity within these areas when performing the Iowa task. However, this effect is probably underlying impairments in reversal learning rather than an abnormality in risk processing. Combined with evidence from the delay discounting task, it could be concluded that pathological gamblers and substance abusers show a general deficit in OFC activity during decision-making tasks. This impairment may affect behaviour on the probability discounting and Iowa task. However, research has shown that not all substance abusers are homogenous in their behaviour on the Iowa task with a subset of this population performing in a similar way to controls. Therefore, the substance abusers, as a group, may not show as serious an abnormality in OFC function as the pathological gamblers. Lastly, activity within the nucleus accumbens has been found to precede risky choices on a simulated financial decision-making task. Therefore, there may

be group differences in the activity of this area, reflecting differences in risk processing.

OFC and ACC activity have been associated with response inhibition in the go/no-go task. Substance abusers have previously shown hypoactivation of the OFC and ACC during this task, linked to poor inhibitory control. We could hypothesise that the pathological gamblers (who also have shown poor response inhibition compared to controls) and substance abusers would show hypoactivation of the OFC and ACC in this task. However, previously in this project, we have found that our samples did not differ in inhibitory control (as measured by the stop task). Therefore, whether the addiction-disordered groups will show any differences in neural function is questionable.

Finally, considering in the urge-to-gamble task, we are faced with conflicting information. One study showed that the presentation of gambling cues was associated with hypoactivity of the OFC, basal ganglia and thalamus, suggesting possible decreases in inhibitory control and blunted emotional processing (possibly leading to a 'numbing' effect, allowing the gambler to gamble). Conversely, another study showed that presentation of gambling stimuli was associated with hyperactivation of the VMPFC, DLPFC and visual cortex, suggesting increased visual processing and increased emotional processing, possibly leading to an excitatory effect on the gambler.It is interesting to note that the same areas were not identified. It may be the case that gambling cues attenuate the activity of some areas involved in emotion processing and excite areas involved in reward. This may lead to emotional 'numbing' allowing the gambler to gamble without feeling the negative emotional states induced by its consequences, in addition to allowing heightened experience of the positive effects.

This experiment was designed to explore the possible differences in neurological function between pathological gamblers, substance abusers and controls. The focus of the experiment was on brain areas involved in decision-making involving delays

(delay discounting task) and involving risk. These decision-making tasks all involved real consequences so that participants experienced the delays and chances of winning inherent within each task. An *f*MRI delay discounting task involving real delays had not been performed before. Two tasks that analysed decision-making under risk were employed. One task explicitly stated the probabilities of winning associated with each choice (probability discounting task) whilst the other involved the learning of rules which defined whether the choice was risky or safe (Iowa task). An *f*MRI probability discounting task had not been utilised in any previous research. In addition to decision-making processes, brain areas involved in inhibitory control and gambling urges were focused upon. A group of non-pathological gamblers was also recruited. If, as was described in experiment 3, there was a continuum between non-gambler and pathological gambler with a steady change in behaviour, then it may be the case that non-pathological gamblers show minor differences in brain function that are pronounced, but not as much as in pathological gamblers. Possible differences in brain function in these tasks in non-pathological gamblers had not received any study before this experiment.

Methods

Participants

9 pathological gamblers, 10 non-pathological gamblers, 11 substance abusers and 12 controls were recruited from the groups in experiments 2 and 3 in addition to advertisements in the University of Manchester. Further participant were recruited due to a small number of participants not returning for experiment 4. Therefore, it is important to note that the descriptive statistics for this sample are not the same as those in previous experiments. Mean ages (and sex) were 28.2 years (range 21-42 years, SD = 7.95 years) for the pathological gamblers (4 female), 21.0 years (range 18-23 years, SD = 1.8) for the non-pathological gamblers (8 female), 22.9 years (range 18-30 years, SD = 4.27) for the substance abusers (7 female) and 22.6 years (range = 19-30, SD = 3.3 years) for the controls (6 female). Mean IQ scores for

each group were as follows; pathological gamblers, 93.13 (SD = 5.49); non-pathological gamblers, 96.78 (SD = 6.61); substance abusers, 96.25 (SD = 10.5); controls, 93 (SD = 12.7). There was no significant difference in IQ scores between groups, $F(3,39) = 0.42$, $p = 0.74$.

For details of the screening procedure see the "General Methods" section.

Experimental tasks

Delay discounting task

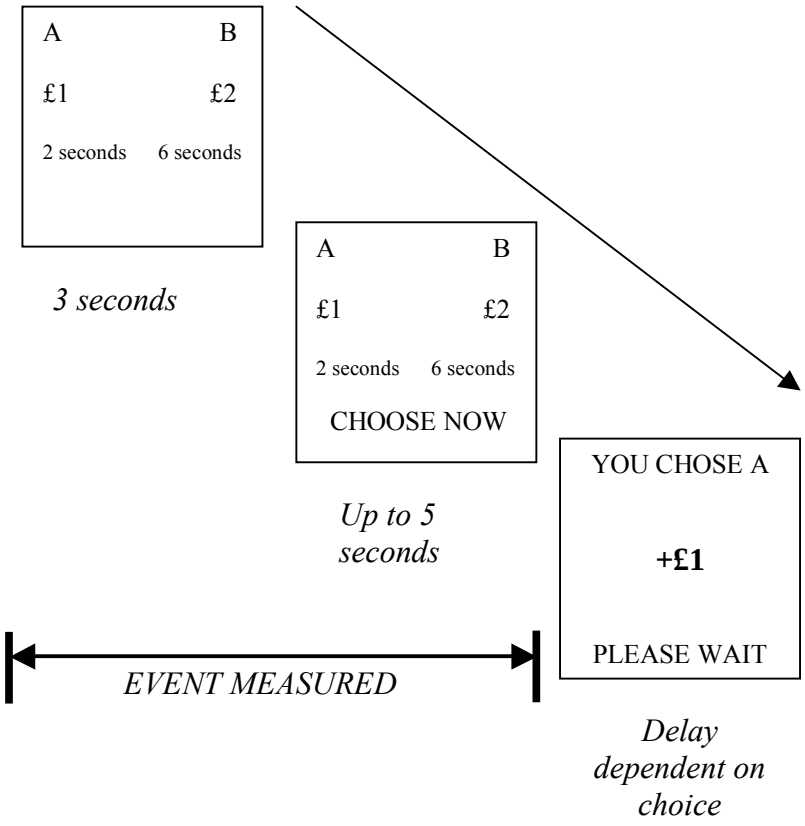
The delay discounting task was designed to explore neurological areas involved in decision making in choice environments involving delays that the participant had to wait through to obtain a delay (i.e. involved self-controlled/impulsive decision-making)

The delay discounting task presented the participant with 56 binary choices. There were 28 free choices and 28 forced choices. In the free choices, alternative A carried a reward of £1 and a delay of 2, 4, 6, 8 or 10 seconds. Alternative B gave a reward of £2. The delays for alternative B were systematically altered (such as in the behavioural version of this task described in experiment 2). Free choices were either 'hard' or 'easy'. There were 12 'hard' choices which were designed so that the delay of alternative B was situated around the mean IP (therefore it was hypothesised that a preference might be difficult to calculate). Mean IPs were calculated using the data from experiment 2. There were 16 'easy' choices which presented clear choices. For example, A might have had a delay of 2 seconds while B had a delay of 24 seconds. All rewards were hypothetical but participants were instructed to behave as if the rewards were real. When given a forced choice, both alternatives gave exactly the same reward with the same delays. In half the forced choice trials the reward amount was £1, in the other half £2 was given. The delays ranged from 2 – 15 seconds.

Participants were first presented with five screens of instructions. These instructions are shown in appendix 6. Following the instructions the choices were presented. The first screen showed the choice. On the screen the header "Alternative A" was shown on the top left of the screen while the header "Alternative B" was shown on the top right. Underneath each header was the reward amount for choosing that alternative (£1/£2). All rewards were hypothetical. Situated directly underneath the reward was the delay. The delay was shown in the format "X seconds" where X was the delay in seconds shown in numerical form. This screen was shown for three seconds. During this time, the participants could not make a choice. This was done in order to make sure that the participant had ample time to understand all aspects of the choice and to make sure that the event was long enough. After 3 seconds the participant was allowed to make a response. If the trial involved a free choice, "CHOOSE NOW" was written at the bottom of the screen. Otherwise, if the trial was a forced choice "CHOOSE ALTERNATIVE X" was written at the bottom of the screen where 'X' was the alternative they had to choose. Participants had 5 seconds in which to make a preference response. The event measured was from the moment the choice screen was presented until the participant made a response, i.e. the decision making process. If a participant did not make a response in time a cue that told them that they had not made a response and needed to make one on the next trial was shown. The participant also lost the chance to gain any winnings from that trial and the next choice was shown. No participant missed a trial due to not responding. The forced choice trials were designed to mimic the free choice in every way except that there was no choice presented. Participants were presented with the same visual stimuli and responded in the same way by making a button press. In the forced choice trials participants were told which button to press. This was done to ensure that participants could not express a preference for the buttons. In both the free and forced choice trials, after the choice screen another screen was presented which showed the alternative that they had chosen at the top. "+£1" or "+£2" was shown in the middle of the screen (in larger, bold, script) dependent on what reward had been given by the alternative

they had chosen. "Please wait" was written at the bottom of the screen. This screen was shown for a delay equal to the delay associated with the alternative they had chosen. Therefore, participants experienced the real consequences of the delay they had chosen. A diagrammatic representation of the task structure is shown in figure 16.

Figure 16: Task structure of the fMRI delay discounting task



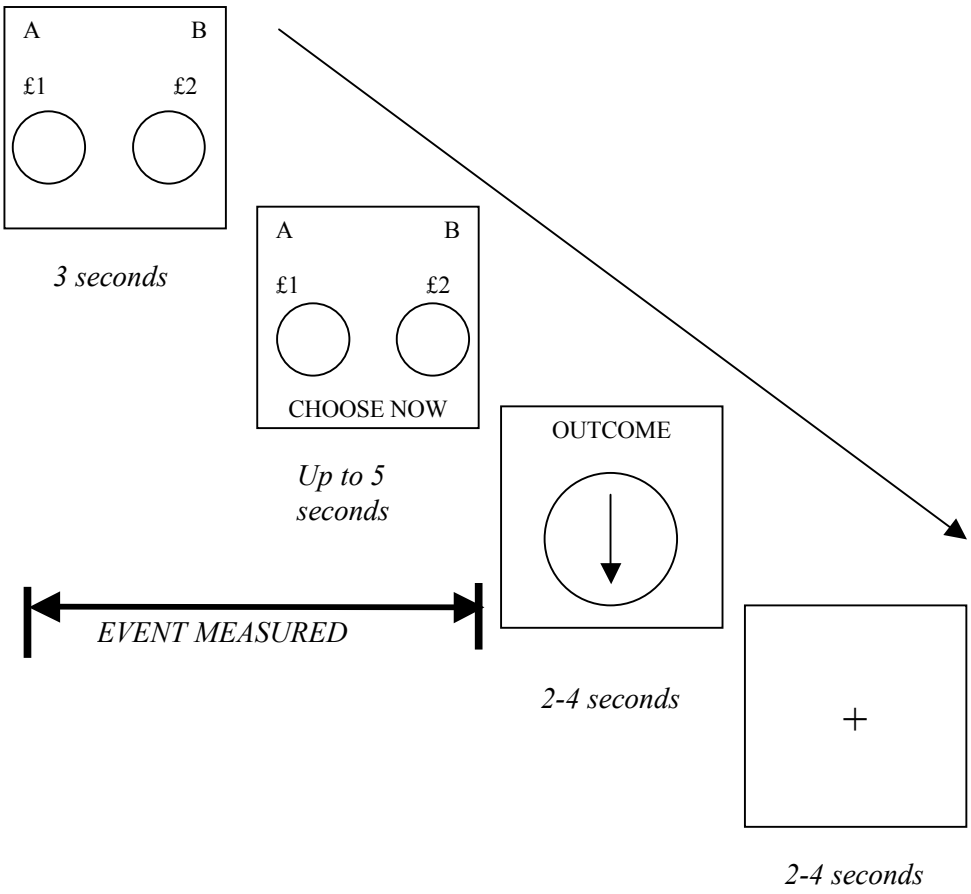
Due to the utilization of real delays, the total task length could not be of a fixed time limit. The scan length was limited to 12 minutes. A time limit was imposed in order to control the amount of time that the participant could spend performing the task.

Probability discounting task

The probability discounting task was designed to investigate neurological areas involved in decision making in situations involving the analysis of risk, where the risk associated with each choice is well defined.

The structure of the probability task was very similar to that of the delay discounting task. Instructions were presented first (shown in appendix 6). Participants were given 24 free and 24 forced choices. 10 of free choices were 'easy' and 14 were 'hard' (see the outline of the delay discounting task above for more details). Instead of delays, two 'wheels of fortune' were presented that described the probabilities of winning each reward. These were constructed in the same way as in the behavioural probability discounting task. When participants made a response the wheel associated with their chosen alternative was immediately shown in the centre of the screen with an arrow centred upon it. The arrow designated whether the outcome was a win or not a win dependent on whether it pointed to the green or red segment respectively. The header 'outcome' was situated above the wheel. This screen was shown for 2-4 seconds. A fixation point was then shown for 2-4 seconds. These two screens were shown for a variable amount of time in order to introduce 'dither'. Dither is used to overcome biological adaptation to the task structure, therefore, increasing task validity. The fixation point screen was used in order to minimise the haemodynamic response to the outcome affecting the response to the choice (which was the event that was measured). Following this, the next choice was presented. Figure 17 below shows the structure of one trial of the task.

Figure 17: Task structure of the fMRI probability discounting task



Iowa (Bechara) task

The Iowa task is designed to explore brain areas involved in decision-making when the risks involved are not explicitly known and must be learnt.

The aim of the Iowa task is to gain as much money as possible on a gambling task. Each participant was initially given a pot of £2000. The participant was presented with four decks of cards that were face down (called decks A, B, C and D from left to right). In each trial, the participant chose one deck from which a card was drawn. Each card had a monetary reward and some had monetary punishers. Cards from decks A and B had large rewards but large punishers and cards from decks C and D had smaller rewards but smaller punishers. The decks were set up so that a majority

of choices from decks A and B would eventually lead to overall loss while choosing more often from decks C and D would lead to overall gain.

The participant was given two screens of instructions (shown in appendix 7). These screens described the general contingencies of the decks. This was done so that the participant did not have to go through an extended period of learning. It was felt that, as the participants had previously completed the behavioural Iowa task, a significant amount of learning had already taken place before performing the fMRI task. This ensured that a large amount of learning was not necessary in the fMRI Iowa task, thus we could infer that the vast majority of events were focusing on the neural substrates underlying risk-taking rather than trial-and-error learning.

At the beginning of each trial the choice screen was presented for 1000 milliseconds. The four decks were presented, in a line, in the centre of the screen. 'Pick a card' was written at the top of the screen. Two of the four decks were crossed out, and could not be chosen. This left only two decks from which a choice could be made. 'Free' or 'forced' choices were given. In the free choices the participant was allowed to choose between a high risk (decks A or B) and a low risk (decks C or D) deck. Forced choices involved a choice between A and B or C and D (i.e. one is forced into choosing between two high risk or, alternatively, two low risk choices). There were two contrasts in this task; free-forced and high-low. The high-low contrast compared the two types of forced choice, i.e. those that presented a choice between the high risk decks and those that gave a choice between the two low risk decks. A response was made using one of the four buttons from the button box. If a choice was not made the decks were withdrawn and 'Too slow' was written across the middle of the screen. The next choice was then presented. If a response was made, the next screen presented the words, "You have gained £XX" written across the top of the screen, where £XX was the reward associated with that card. A yellow circle was shown below this with a smiley cartoon face. Below this the four decks were shown with the chosen card highlighted. This screen was shown for 1000 milliseconds. The next screen

described what punisher was associated with the chosen card. 'You have lost £XX' was written across the top of the screen, where £XX was the punisher associated with the card chosen. If no punisher was associated with the card 'You have lost nothing' was written. Below this header, there was a neutral cartoon face or sad cartoon face shown dependent on whether the participant did not lose or lost money respectively. This screen was shown for 1000ms. Following this, the next choice was presented. The Iowa task lasted for 9 minutes in total.

Before scanning, participants also completed a traditional behavioural version of the Iowa task. The behavioural version was the same as the *f*MRI version except for four differences. In every trial participants could choose any card from the four decks (thus, choice was not restricted in any way) and the instructions at the beginning did not confer any hints as to the contingencies of the decks. There was a time limit of 5000 milliseconds for each choice (not 1000 milliseconds). There was no time limit to the task. The task ended after 100 choices were made.

Go/no-go task

The Go/no-go task measured neurological activity associated with response inhibition. The task repeatedly presented participants with a letter from the English alphabet. The participant had to make a response to each letter except when the letter 'V' appeared, to which participants were required to make no response.

The participants were given simple instructions first. When they were ready the first letter was presented. Each letter appeared on the screen for 500 milliseconds regardless of participant response. A blank screen was then presented for 1731 milliseconds. When a letter (other than 'V') was presented, participant had to respond by pressing any button on the button box. If the letter 'V' was presented the participants had to make no response and were required to wait for the next letter to be presented. The task lasted for six minutes. The task was split into 8 blocks. Each block had 26 trials. Four blocks contained only go trials. The other

four blocks contained 13 go trials and 13 no-go trials. The contrast subtracted activity on the no go trials from the go trials (go – no-go).

Urge to Gamble Task

The Urge to Gamble task (UTG) was designed to investigate neurological regions involved in gambling craving and response to gambling cues. The task presented images of gambling and non-gambling scenarios.

The task was split into twelve blocks. Six blocks contained images of gambling stimuli and the other six contained matched non-gambling stimuli. There were three types of gambling and matched non-gambling stimuli. The stimuli used are shown below in table 3. There were two presentations of each block of stimuli. The block order was partially counterbalanced.

Table 5: Gambling stimuli and their associated matched non-gambling stimuli used in the UTG (reasons for employing the matched gambling stimuli are also shown). Abbreviations for each condition are shown in brackets.

Gambling stimuli	Matched non-gambling stimuli	Reasons for using non-gambling stimuli
Casino (CG)	Groups of people eating/having meetings (CN)	All the casino stimuli involved individuals gambling around tables, usually with food or drink present
Horse racing (HG)	Horses not racing (e.g. horse trekking) (HN)	The horses in the controls stimuli were approximately equal to race horses in size and fitness, however, each image showed no evidence of racing
Internet (IG)	Internet games (non-gambling) (IN)	Internet gambling stimuli were colourful and had many different button options depending on the game type. The control stimuli were used to mirror this but with no gambling or tangible reinforcers

Each block lasted 12 seconds. 5 images were presented in each block. Each image was shown for 2300 milliseconds. Following each image a blank screen with a fixation point was shown for 100 milliseconds. Following the presentation of the images, five questions were presented that asked the participant to rate certain aspects of their behaviour. Each screen explicitly stated that the participant should rate their behaviour for the set of pictures that were just shown. Participants were asked to rate their urge to gamble, excitableness, happiness, anxiety and sadness. Each rating used a four-point scale. When rating their urge to gamble, participants could respond with “no urge”, “weak”, “fairly strong” or “very strong”. For the other four ratings, participants could respond with “not at all”, “somewhat”,

"moderately" or "a lot". Two examples of a question screen are shown in appendix 8. Participants responded by using one of the four buttons on a button box. Each choice screen was presented for 1750 milliseconds. This time period was used because we wanted to capture the participant's first impression and control the amount of time the participant could spend on each rating. Following the five questions, the next block was shown. If a gambling block had just been shown the matched non-gambling block was shown.

Concerning the nature of the neutral stimuli, the researchers aimed to create images that replicated the gambling stimuli as much as possible. Therefore, for the casino condition in which groups of individuals were surrounding a table with a gambling activity upon it, the neutral stimuli were individuals surrounding a table to eat and individuals sat around a table having a business meeting. In the horse condition, neutral stimuli involved horses moving at a non-racing pace. The neutral internet stimuli were screenshots of non-gambling internet games which were colourful and involved different options for button presses. The neutral stimuli were rated previously by an opportunity sample of colleagues and were deemed to be acceptable as neutral images.

The UTG had four main subtractions, CG-CN, HG-HN, IG-IN, and GAMB-NEUT (in which data from all non-gambling blocks was subtracted from all the data from the gambling blocks). For each of these conditions the 8 individual group activation effects and 12 group subtractions were performed. The table below shows these contrasts.

Data acquisition

Functional Magnetic Resonance Imaging (*f*MRI) images were acquired using a 1.5T Philips Gyroscan ACS NT (Philips, Best, NL). 95 volumes were obtained each comprising of 40 T2-weighted contiguous axial slices with a slice thickness of 3.5 mm. The slices were acquired using a single-shot echo planar (EPI) pulse

sequence (in plane resolution = 3x3 mm, TE = 40 ms). The TR for the urge to gamble and go-no/go tasks was 5 seconds. The TR for the delay discounting, probability discounting and Iowa task was 3.142 seconds.

Scanning procedure

Stimuli were back-projected from a laptop onto a screen positioned at the foot of the scanner bed. A mirror was located above the participant's head and positioned so that the participant could view the whole of the screen.

Responses were made using a four-button box. Tasks required the participant to use either two or four buttons. The participant was told which buttons were to be used for each task prior to scanning and before each task.

Participants were presented the tasks in the following order; Urge to Gamble task, delay discounting task, probability discounting task, Iowa task, and then the Go/no-go task.

The total time that the participant was in the scanner was approximately 45 minutes.

Data analysis

FMRI data were analysed using Statistical Parametric Mapping (SPM5) (http://www.fil.ion.ucl.ac.uk/spm). Individual scans were realigned using the first scan as a reference and normalized into the Talairach and Tournoux stereotactic space (Talairach and Tournoux, 1998) using the Montreal Neuroscience Institute (MNI) templates. Spatial smoothing was applied with a 10 mm Gaussian kernel. All individual templates were then entered into a second level analysis. If an individual displayed movement artifacts larger than 3mm in the x, y or z axis or

over 3^{o} change in pitch, yaw, or rotation then they were excluded from the second level analysis.

For each contrast in each task, effects of the task were plotted for each participant group. In addition, for each task, 12 subtractions were applied that were designed to compare performance across all groups. The contrasts were as follows: pathological gamblers – controls (PG-CO), pathological gamblers – non-pathological gamblers (PG-NPG), pathological gamblers – substance abusers (PG-SA), non-pathological gamblers – controls (NPG-CO), non-pathological gamblers – substance abusers (NPG-SA), substance abusers – controls (SA-CO). The reverse subtractions were also performed.

Due to the nature of the statistical methodology used in subtraction analysis, it could be inferred whether the brain activations shown in one group were significantly different from those measured in a contrast group. However, the difference could occur due for one of two reasons. To outline these reasons we will take, as an example, the free-forced choice condition of the delay discounting task. If the group subtraction that is being calculated is pathological gamblers – controls, a significant difference in activity in a voxel can be calculated due to one of two reasons; either the pathological gamblers show more activity in the free choice condition or the controls show more activity in the forced choice condition. A mask can be used to infer direction of a statistical difference. In this example, we would use the activations calculated from the free – forced subtraction in pathological gamblers and forced – free subtraction in the controls.

Statistical analysis was carried out using the general linear model with a delayed boxcar waveform to model blood oxygenation level dependent (BOLD) signal changes in each condition. These conditions will be defined per task in the results chapter. The statistical parametric maps from each individual were entered into a second-level analysis. The group effects were assessed through applying a factorial design, where there were four factors corresponding to each group. A voxel was

deemed significant if its z score was higher that 3.09, corresponding to $p < .001$ (uncorrected). Due to the exploratory nature of these tasks and the smaller than planned final sample sizes, uncorrected thresholds were utilised. All voxels meeting threshold were presented, however, only areas about which hypotheses included (see introduction to this experiment) were discussed.

A high-pass filter was applied to all participants' data. The filter was calculated differently dependent on whether the task employed a block or event-related design. If a block design was employed, the filter was calculated by taking the delay between the start of one block and the start of the next. The largest delay between any two blocks was taken and multiplied by 1.5. If the design was event related, the individual delays between each different type of trial were taken. The longest delay was then multiplied by 1.5. This method was used because using the default value defined by SPM (128 seconds) may have led to under- or over-inclusion of data from the time-series.

Analysis of the data from the ratings in the UTG was performed using SPSS v11.5. For each stimulus type, two ratings of each behaviour were obtained (because each type of stimulus was shown in two separate blocks). The mean rating for each behaviour was calculated. For each stimulus type, five one-way ANOVAs were used to compare scores for each rating across groups. This led to a total of 30 one-way ANOVAs being used. To minimise the chance of a type I error occurring an alpha level of .0017 was used (calculated by [0.05/30]).

The behavioural Iowa task was split into 5 blocks, each comprising of 20 choices in order to measure changes in decision-making over the course of the task. For each block, the percentage number of choices from a risky deck (decks A or B) was calculated. Using a one-way ANOVA these percentages were compared across groups. Choice behaviour was entered as a within-subjects factor and group was entered as a between-subjects factor. Total winnings were also compared between groups using a one-way ANOVA. Finally, Iowa score was compared across groups

using a one-way ANOVA. Iowa score was calculated as (total choices from safer decks – total choices from risky decks).

In the fMRI Iowa task, one concern when evaluating this task was with the spread of choices across the decks in the free-forced comparison. If an individual did not make choices that were spread (to some degree) over the four decks then this would have meant that there would not be enough events to render the statistical tests valid. When the data was collected, it was determined that for each participant, out of the 30 choices in the free-forced comparison, at least 10 had to include their least preferred decks (either A/B or C/D).

The number of commission errors on the go/no-go task was compared using a one-way ANOVA. A commission error is committed when a button is incorrectly pressed on a no-go trial. Group was entered as a between-subjects variable.

Results

The following sections contain details and results reported from each task. The results from each task are shown separately, each followed by discussion of the findings. A general discussion is presented at the end of the experiment. Slice overlays are shown in appendix 9 which show the brain activity for most contrasts. For reasons of brevity, only overlays from the most critical comparisons tasks are included.

Delay discounting task

One participant did not finish the task within the time permitted. Their data was still included as only five events were missing.

The delay discounting task had two conditions, free-forced and easy-hard[15].

Free vs. forced choice

Table 6: Foci of significant brain activations in the free-forced condition in all groups.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free-forced							
Orbitofrontal gyrus	11	L	63	-45	40	-17	3.18
Middle frontal gyrus	46	R	3389	45	38	14	6.6
	9	L	285	-52	25	31	4.43
Medial frontal gyrus	47	R	21	24	16	-21	3.48
Precuneus extending to inferior parietal gyrus	19/7/40	L	534	-28	-69	39	5.08
Middle occipital gyrus extending to fusiform gyrus	19	L&R	2118	31	-91	8	5.61
Lingual gyrus	18	L	30	-3	-88	1	3.25
Thalamus extending into globus pallidus		L&R	509	-10	-17	7	4.47
Forced-free							
Middle frontal gyrus extending to precentral gyrus	6	R	41	24	-7	58	3.33
Anterior cingulate cortex	24	R	29	3	24	-4	3.76
Precentral gyrus extending through postcentral gyrus to inferior parietal gyrus	6/40	R	167	66	-5	26	4.04
Inferior parietal gyrus	40	L	28	-66	-26	24	3.58
Middle temporal gyrus	22/21	R	139	49	-41	-1	3.81
	21	L	39	-49	-4	-20	3.34
	22	L	31	-62	-30	5	3.30
Lingual gyrus	18	R	14	17	-78	1	3.36
Insula		L	20	-31	7	13	3.17

In the free-forced comparison, widespread activity was reported in the frontal cortex including the left lateral OFC, right VMPFC and bilateral DLPFC. High activity was also shown in the bilateral occipital gyrus, right fusiform gyrus, and

[15] For an explanation see the "Methods" section of experiment 4

left lingual gyrus. There were also high amounts of activity in the bilateral thalamus and right globus pallidus.

In the forced-free subtraction, activity was reported in dorsal areas of the frontal cortex and precentral gyrus through to the inferior parietal, bilateral temporal gyri and right lingual gyrus. The anterior cingulate cortex showed a marked increase in activity in addition to the left anterior insula.

Table 7: Foci of significant brain activations in the free-forced condition in pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free - forced							
Middle frontal gyrus extending to thalamus	46/9	R	307	49	47	17	4.25
Medial frontal gyrus extending to cingulate gyrus	8/32	R&L	115	3	46	40	3.32
Inferior parietal gyrus extending to angular gyrus	39/40	R	765	35	-63	39	4.72
Thalamus		R&L	43	3	-13	7	3.21
Forced - free							
Anterior cingulate cortex	24/25	R	73	3	24	-4	3.60
Postcentral gyrus	43	R	16	62	-6	16	3.16
Middle extending to superior temporal gyrus	21/22	R	112	59	-4	-6	3.52
Lingual gyrus	18	R	15	21	-75	4	3.82

In the free-forced condition, pathological gamblers showed increased activation in the bilateral OFC and right VMPFC in addition to the right DLPFC. There was also significant activity in the bilateral thalamus.

In the forced-free subtraction, activity was reported in the anterior cingulate gyrus, right postcentral gyrus, right temporal gyrus and right lingual gyrus.

Table 8: Foci of significant brain activations in the free-forced condition in non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free- forced							
Orbitofrontal gyrus	10/11/47	R	122	35	34	5	3.28
Superior frontal gyrus extending through caudate nucleus to thalamus	6	R	914	17	23	60	3.87
Medial frontal gyrus	25	R	32	14	13	-15	3.20
Precentral gyrus	6	L	26	-45	1	29	3.27
Inferior parietal gyrus	39/40	R	362	35	-63	39	4.00
Inferior parietal gyrus extending to precuneus	40/7/19	L	266	-42	-55	51	3.29
Precuneus	7	R	55	14	-66	42	3.91
Middle temporal gyrus	20	L	34	-59	-41	-10	3.94
Middle occipital gyrus extending through fusiform gyrus to inferior temporal gyrus	19/37/20	R	500	35	-91	8	3.90
Inferior extending to middle occipital gyrus	18/39/19	L	158	-42	-85	-2	4.27
Cerebellum		L	178	-31	-59	-21	3.89
		L	50	-38	-76	-26	3.36
		R	17	31	-83	-31	3.40
Forced - free							
Precentral gyrus	6	R	25	66	-2	26	3.75

There was widespread activity in non-pathological gamblers in the free-forced subtraction. Significant activity was reported in frontal areas including the right lateral OFC and right DLPFC. There was also increased activity in bilateral inferior parietal, bilateral temporal and bilateral occipital gyri in addition to bilateral cerebellum. Increased activity was only reported in the precentral gyrus (ventral BA6) in the forced-free condition.

Table 9: Foci of significant brain activations in the free-forced condition in substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free - forced							
Medial extending through superior frontal gyrus	6	R	407	10	26	34	4.12
Dorsolateral prefrontal cortex	46/9	R	472	49	45	17	4.20
Precentral gyrus extending to middle frontal gyrus	6/9	L	90	-42	2	32	3.39
Inferior parietal gyrus	40	R	363	42	-39	37	4.36
	40	L	147	-38	-36	34	3.69
Superior temporal gyrus	41	L	14	-42	-40	8	3.27
	38	L	42	-42	10	-9	3.25
Precuneus extending into superior occipital gyrus	19	L	92	-28	-69	39	3.96
Inferior occipital gyrus extending into fusiform gyrus	19/37	L	201	-38	-78	-2	4.92
Cingulate gyrus	24/23/31	L	98	-3	1	29	3.41
Globus pallidus extending into thalamus		L	60	-10	-3	3	3.27
Hypothalamus		R	45	3	-1	-15	4.45
Cerebellum		L	119	-42	-63	-32	3.80
		R	405	31	-92	2	4.61
Pons		R & L	48	7	-32	-31	3.86

In the free-forced subtraction, significant activity was measured in the right lateral OFC, right VMPFC and left DLPFC. There was also bilateral activity in the inferior parietal cortex in addition to the left superior temporal gyrus, left occipital gyrus and left fusiform gyrus. The left cingulate gyrus, globus pallidus, thalamus and right hypothalamus also showed increased activity in addition to the bilateral cerebellum and brainstem. No voxels crossed the threshold for statistical significance in the forced-free subtraction.

Table 10: Foci of significant brain activations in the free-forced condition in controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free - forced							
Middle extending to inferior frontal gyrus	46/9	R	224	49	35	21	3.95
Superior extending to middle frontal gyrus	6	R	34	21	23	60	3.57
Superior frontal gyrus	8	L	44	-24	36	47	3.20
Inferior parietal gyrus	40	L	25	-38	-42	34	3.38
Precuneus extending into inferior parietal gyrus	19/40	R	189	31	-66	39	4.36
Middle temporal gyrus extending into cerebellum	20	L	180	-59	-41	-13	3.55
Middle occipital gyrus	19	L	32	-35	-81	4	3.23
Inferior occipital gyrus extending into fusiform gyrus	19/37	R	312	38	-78	-2	3.62
Posterior cingulate gyrus	23/29	L	168	0	-26	30	3.52
Forced - free							
Inferior frontal gyrus	45	L	26	59	24	2	3.55
Medial frontal gyrus	9	L	40	-17	42	17	3.20
Superior frontal gyrus	6	R	45	10	10	54	3.45
Medial extending to superior frontal gyrus	6	L	42	-14	3	55	3.16
Precentral extending to postcentral gyrus	4/3	L	10	-38	-27	66	3.12
Precentral gyrus extending to cingulate gyrus	6/31	R	135	24	-11	49	3.80
Supramarginal gyrus extending to insula	40	R	85	66	-43	31	3.71
Postcentral gyrus	40	L	104	-66	-26	21	3.51
Postcentral gyrus extending to precuneus	5/7	L	126	-14	-41	57	3.19
Insula extending to precentral gyrus	6	L	43	-38	4	9	3.79
Middle temporal gyrus extending to fusiform gyrus	21/20	R	85	55	-27	-5	3.39
Middle temporal gyrus extending into uncus	21/20	L	123	-49	-4	-17	3.09
Insula extending to putamen		R	28	35	4	9	3.36
Caudate nucleus		R	95	17	21	15	3.53
		R	20	10	-6	23	3.24
		L	12	-10	21	15	3.13
Cerebellum		L	91	0	-39	25	4.10
		L	31	-24	-46	-33	3.55
		L	55	-14	-31	-13	3.52
Pons		R	31	10	-15	-23	3.24

In the free-forced subtraction, controls showed increased activity in the prefrontal cortex including the right DLPFC. Significant activation was also reported in the right precuneus, right parietal gyrus, left temporal gyrus, right fusiform gyrus, and bilateral occipital gyrus in addition to the posterior cingulate cortex.

In the forced-free subtraction, activity was shown in the left VMPFC and lateral inferior prefrontal cortex. Increased activity was also present in the bilateral precentral gyrus, left postcentral gyrus, right cingulate cortex, bilateral insula, bilateral temporal gyrus, bilateral caudate nucleus, left cerebellum and brainstem.

Table 11: Foci of significant brain activations in the free-forced condition: Comparison of pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-CO							
Orbitofrontal gyrus	47	R	22	59	24	-1	3.35
Inferior frontal gyrus	47	L	30	-49	21	2	3.14
Insula extending into inferior frontal gyrus	47	R	130	35	24	12	3.83
Medial frontal gyrus extending into anterior cingulate cortex	9/32	L	36	-14	42	20	3.75
Medial frontal gyrus	6	L	60	-7	6	51	3.46
Cingulate cortex	31	R	96	21	-53	28	3.15
Paracentral gyrus extending to precuneus	40/7	L	90	-21	-42	54	3.28
Midbrain		L	22	14	-18	-29	3.19
CO-PG							
Middle temporal gyrus extending to fusiform gyrus	20/37	L	20	-59	-41	-13	3.71

When given free opposed to forced choice trials, pathological gamblers showed higher activation in the right lateral OFC, left inferior frontal gyrus, anterior insula and cingulate cortex compared to controls. In the same comparison, higher activity was measured in the left temporal cortex and fusiform gyrus in controls compared to pathological gamblers.

In the forced – free comparison, controls showed significantly increased activity in the left VMPFC, right inferior frontal gyrus, dorso-medial frontal gyrus, paracentral gyrus, precuneus and midbrain.

Table 12: Foci of significant brain activations in the free-forced condition: Comparison of non-pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-CO							
Orbitofrontal cortex	10/47	R	370	31	34	5	3.79
Inferior frontal gyrus	45	R	20	62	21	9	3.29
Anterior cingulate extending to caudate nucleus	33	R	476	10	-9	20	4.56
Postcentral extending to precentral gyrus	3/4	L	65	-42	-21	62	3.68
Precuneus	7	R	73	21	-49	44	3.20
Middle temporal gyrus	39	L	14	-45	-57	9	3.69
Middle extending through superior temporal gyrus	21/22	R	29	55	-27	-5	3.10
Uncus	28/34	R	45	14	-18	-29	3.18
Uncus extending through amygdala to fusiform gyrus	20	L	147	-31	-15	-26	3.28
Cerebellum		L	78	-24	-56	-35	3.92
		L	58	0	-35	-25	3.26

Following the free-forced comparison, non-pathological gamblers reported higher activity in the right OFC, left temporal cortex, left uncus, left amygdala, fusiform gyrus and left cerebellum compared to controls.

In the forced-free comparison, controls showed significantly higher activation in the right OFC, anterior cingulate cortex, right caudate nucleus, right temporal cortex, right uncus and left cerebellum.

The CO-NPG subtraction did not yield any voxels that exceeded the threshold for statistical significance.

Table 13: Foci of significant brain activations in the free-forced condition: Comparison of substance abusers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
SA-CO							
Orbitofrontal cortex	47	R	222	42	27	-7	3.77
Anterior cingulate cortex extending to medial frontal gyrus	9	L	27	-17	35	18	3.30
Superior frontal gyrus	6	R	116	7	13	48	3.19
Postcentral gyrus	2	R	31	35	-29	37	3.64
Inferior parietal gyrus	40	L	16	-38	-51	61	3.26
Superior temporal gyrus	41	L	37	-42	-40	8	3.14
Insula		L	161	-42	0	-6	3.22
		R	27	45	-33	21	3.53
Thalamus extending to caudate nucleus		R	43	10	-9	20	3.37
Cerebellum		L & R	339	0	-39	-27	4.06
		R	32	24	-42	-27	3.18

Following the free – forced comparison, substance abusers (compared to controls) showed significantly higher activity in the right lateral OFC, left parietal cortex and right cerebellum. In the forced – free comparison, controls showed significantly higher activation in the left VMPFC, anterior cingulate cortex, dorso-medial frontal cortex (BA 6), left temporal cortex, left anterior and right posterior insula, right thalamus, right caudate nucleus and bilateral cerebellum.

Table 14: Foci of significant brain activations in the free-forced condition: Comparison of pathological and non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-NPG							
Superior frontal gyrus	9	R	13	14	52	20	3.10
NPG-PG							
Orbitofrontal gyrus	11	R	14	21	47	-11	3.54
Anterior cingulate extending into inferior frontal gyrus	25/47	R	88	3	6	-6	3.13
Postcentral gyrus	43	L	11	-59	-9	20	3.28
Middle temporal gyrus	20	L	38	-59	-41	-10	3.85
	39	L	10	-45	-57	9	3.41
Superior temporal gyrus	38	R	27	38	9	-27	3.38
Parahippocampal gyrus extending to hippocampus	30/36	L	62	-28	-51	3	3.34
Thalamus extending to caudate nucleus		R	56	10	-13	20	3.18
Cerebellum		R	42	28	-39	-25	3.48
		L	17	-24	-53	-33	3.13

When performing free compared to forced choice trials, pathological gamblers showed increased activity in the right VMPFC compared to non-pathological gamblers. In the same comparison, non-pathological gamblers showed significantly higher activity in the right medial OFC, left temporal gyrus, left parahippocampal gyrus including hippocampus, thalamus, caudate nucleus and bilateral cerebellum.

In the forced-free comparison, pathological gamblers showed higher activity in the right inferior frontal gyrus and anterior cingulate cortex compared to non-pathological gamblers.

Table 15: Foci of significant brain activations in the free-forced condition: Comparison of pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
SA-PG							
Orbitofrontal cortex	11	R	10	21	47	-11	3.52
Superior temporal gyrus	38	L	61	-45	6	-6	3.10
Inferior occipital gyrus	19	L	26	-35	-78	-2	4.06
Thalamus		R	19	17	-13	4	3.16
Hypothalamus		R	65	3	-1	-15	4.04
Cerebellum		R	49	28	-42	-21	3.91

In the free – forced comparison, substance abusers showed increased activation of the left temporal gyrus, left occipital gyrus, right thalamus and hypothalamus and right cerebellum. There was also a significant difference in the level of right medial OFC activation. The PG-SA subtraction yielded no voxels that were above the threshold for statistical significance.

Table 16: Foci of significant brain activations in the free-forced condition: Comparison of non-pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-SA							
Medial temporal gyrus	39	L	15	-45	-57	9	3.39

In the free – forced choice comparison, non-pathological gamblers showed higher activation of the left temporal gyrus compared to substance abusers. The SA-NPG subtraction yielded no voxels that exceeded statistical significance.

Easy vs. hard choices

Table 17: Foci of significant brain activations in the easy-hard condition in all groups.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Easy - hard							
Orbitofrontal cortex	47	L	204	-55	34	-2	3.09
Precuneus	7	L	27	-10	-69	45	3.23
	31	L	21	-7	-70	26	3.15
Superior temporal gyrus	40	L	204	-59	-47	22	3.70
Superior extending to middle temporal gyrus	22/39	R	159	55	-50	15	3.42
Fusiform gyrus extending to middle temporal gyrus	20/21	R	10	42	-11	-26	3.22

In the easy-hard subtraction, increased activity was measured in the left lateral OFC, left precuneus, right fusiform gyrus and bilateral temporal gyrus. In the hard-easy subtraction, no voxels exceeded the threshold for statistical significance.

Table 18: Foci of significant brain activations in the easy-hard condition in pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Easy - hard							
Orbitofrontal cortex	10	L	12	-38	54	-6	3.35
Inferior frontal gyrus	46/47	L	16	-42	31	8	3.25
Precuneus extending to posterior cingulate gyrus	31	L	1672	-7	-67	23	4.98
Inferior occipital gyrus	19	L	16	-38	-68	-2	3.41
Thalamus		R	80	21	-24	4	3.76

In the easy-hard subtraction, increased activation was reported in the left lateral OFC and VMPFC in addition to the posterior cingulate cortex, left precuneus, left

occipital gyrus and right thalamus. No significant voxels were measured in the hard-easy subtraction.

Table 19: Foci of significant brain activations in the easy-hard condition in non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Easy - hard							
Orbitofrontal cortex	11/10	L	142	-31	41	-2	3.82
	11/10	R	100	38	50	-11	3.50
	11	R	17	14	44	-11	3.11
Inferior frontal gyrus	45/47	L	41	-59	17	6	3.46
	44/9	L	161	-49	4	19	3.48
Postcentral gyrus	43/3	R	34	66	-16	20	3.58
Postcentral gyrus extending to inferior parietal gyrus	43/40	L	163	-66	-13	17	3.49
Middle temporal gyrus	22	L	43	-59	-41	5	3.23
Middle extending to superior temporal gyrus	40/22	R	109	55	-53	25	3.44

In the easy-hard subtraction, non-pathological gamblers showed increased activity in the bilateral OFC in addition to the bilateral postcentral gyrus and bilateral temporal gyrus. The hard-easy subtraction yielded no significant voxels.

Table 20: Foci of significant brain activations in the easy-hard condition in substance abusers

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Easy - hard							
Inferior parietal gyrus extending into superior temporal gyrus	40/22	L	315	-59	-40	25	3.63
Middle temporal gyrus extending into amygdala	21	R	231	59	-11	-11	3.82
Precuneus	7	R	63	10	-70	29	3.60
Medial occipital gyrus	18	R	88	21	-95	8	3.42

In the easy-hard subtraction, substance abusers showed increased activation in the left parietal cortex, right occipital gyrus, bilateral temporal cortex and right amygdala. No significant activation was measured within the prefrontal cortex. No significant voxels were found in the hard-easy subtraction.

Table 21: Foci of significant brain activations in the easy-hard condition in controls

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Hard - easy							
Orbitofrontal cortex	10/46	R	95	31	55	10	3.12
Superior frontal gyrus	9	R	34	28	46	33	3.29
Superior extending through middle frontal gyrus	9/10/8	L	1138	-38	39	27	3.87
Middle temporal gyrus	21	L	64	-45	2	-32	3.37
Inferior extending to middle temporal gyrus	37/21	L	21	-55	-38	-16	3.32
Angular gyrus	39	L	31	-42	-73	33	3.09
Inferior occipital gyrus	18	L	14	-28	-95	-4	3.09
Uncus	34/20	R	51	31	5	-27	3.11
Globus pallidus extending through caudate nucleus to thalamus		R	208	10	0	3	3.21
Cerebellum		L	61	-17	-52	-27	3.10
		R	48	14	-42	-24	3.38

In the hard-easy subtraction, controls showed increased activation in the right lateral OFC and bilateral DLPFC. Increased activity was also present in the left temporal gyrus, angular gyrus and occipital gyrus in addition to the right uncus, caudate nucleus, globus pallidus, thalamus and bilateral cerebellum.

Table 22: Foci of significant brain activations in the easy-hard condition: Comparison of pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-CO							
Inferior frontal gyrus	46/47	L	362	-42	34	8	4.03
Superior frontal gyrus	6	R	23	21	3	64	3.16
Postcentral gyrus extending to medial frontal gyrus	6	R	75	28	-11	52	3.45
Precentral gyrus extending into postcentral gyrus	6/3	L	53	-35	-11	52	3.16
Postcentral gyrus extending to inferior parietal gyrus	3/2/40	R	238	52	-22	37	3.75
Precuneus	19	L	29	-35	-76	36	3.17
Fusiform gyrus extending into inferior temporal gyrus	20	R	37	38	-18	-17	3.22
Inferior occipital gyrus extending into fusiform gyrus	19/37	L	255	-42	-71	-2	3.40
Caudate nucleus		R	858	7	0	10	3.72
Amygdala		R	54	21	-4	-17	3.32

Following the easy – hard comparison, pathological gamblers showed increased activity in the left inferior frontal cortex, dorso-medial frontal cortex, precentral gyrus, postcentral gyrus, left fusiform gyrus, right parietal cortex, occipital cortex and right amygdala compared to controls.

In the hard – easy comparison, controls had significantly higher activity in the left inferior frontal cortex, right fusiform gyrus, right temporal cortex and right caudate nucleus.

The CO-PG subtraction yielded no voxels that exceeded the threshold for statistical significance.

Table 23: Foci of significant brain activations in the easy-hard condition: Comparison of non-pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-CO							
Orbitofrontal cortex	11/10	L	2204	-31	40	-8	4.09
	11/10	R	21	10	47	-11	3.10
Inferior parietal gyrus	40	L	198	-45	-42	-38	3.82
Postcentral gyrus	43/3	R	29	62	-12	23	3.12
Precuneus	7	L	34	-7	-72	52	3.11
Superior extending to middle temporal gyrus	21/22/42	L	49	-59	-40	8	3.15
Inferior extending to superior temporal gyrus	20/38	L	71	-45	-2	-32	3.40
Supramarginal gyrus extending to superior temporal gyrus	40/22	R	30	59	-53	28	3.10
Fusiform gyrus extending to inferior temporal gyrus	37/20	R	505	38	-61	-6	3.62
Fusiform gyrus extending to hippocampus	20	R	148	49	-21	-20	3.42
Medial occipital gyrus	18/19	L	38	-28	-85	4	3.10
Cerebellum		L	256	-31	-58	-6	3.78
Pons		R	13	14	-29	-34	3.12

In the easy – hard choice comparison, non-pathological gamblers showed significantly higher activity in the left lateral OFC, postcentral gyrus, left parietal cortex, left precuneus, bilateral superior temporal gyrus, left cerebellum and brainstem compared to controls.

In the hard – easy comparison, controls showed increased activity in the left OFC, right inferior temporal gyrus, right fusiform gyrus, and left cerebellum compared to non-pathological gamblers.

Table 24: Foci of significant brain activations in the easy-hard condition: Comparison of substance abusers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
SA-CO							
Orbitofrontal cortex	47/46	L	125	-35	27	-1	3.55
Superior extending to middle frontal gyrus	6/8	L	412	-21	30	53	3.72
Inferior frontal gyrus	47	L	26	-24	9	-15	3.63
Medial frontal gyrus	6	L	12	-14	-4	55	3.29
Postcentral gyrus	4/5/7	L	35	-7	-37	70	3.16
Cuneus extending to precuneus	7	R	67	10	-70	29	3.21
Supramarginal gyrus	40	L	33	-42	-46	31	3.50
Middle temporal gyrus	39/19	R	29	49	-67	26	3.23
Superior extending to inferior temporal gyrus	38/21/20	R	297	31	2	-27	3.59
Inferior extending to superior temporal gyrus	20/22	L	114	-59	-31	-16	3.31
Middle temporal gyrus extending to uncus	21/38/28	L	142	-45	2	-32	3.58
Middle temporal gyrus extending to fusiform gyrus	22/37/20	R	97	49	-37	2	3.34
Inferior occipital gyrus	19	R	15	55	-68	0	3.09
Inferior occipital gyrus extending to cuneus	18/17	L	138	-28	-95	-4	3.83
Cuneus	18/17	R	92	28	-95	1	3.62
Fusiform gyrus extending to parahippocampal gyrus	37/19	L	180	-42	-45	-12	3.51
Cerebellum		R	43	10	-66	-38	3.23

When given easy opposed to hard choices, substance abusers showed higher activity in the left lateral OFC, right precuneus and cuneus, left supramarginal gyrus, right temporal cortex and right cerebellum compared to controls.

In the hard – easy comparison, controls had significantly higher activity in the left DLPFC, bilateral temporal cortex, left uncus, right cuneus, left fusiform gyrus and left parahippocampal gyrus compared to substance abusers.

The CO-SA subtraction yielded no supra-threshold voxels.

Table 25: Foci of significant brain activations in the easy-hard condition: Comparison of pathological and non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-NPG							
Precuneus	31	L	27	-7	-67	23	3.91
NPG-PG							
Orbitofrontal cortex	11	L	28	-31	40	-8	3.38
	10	R	69	38	51	-8	3.12
Medial frontal gyrus	10	R	25	10	55	13	3.68

In the easy - hard comparison, pathological gamblers showed higher activation in the left precuneus compared to non-pathological gamblers. In the same comparison, non-pathological gamblers showed significantly higher activation in the bilateral OFC compared to pathological gamblers.

Table 26: Foci of significant brain activations in the easy-hard condition: Comparison of pathological and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-SA							
Posterior cingulate	31	L & R	182	-3	-57	22	3.57
Precentral gyrus	6	R	12	28	-11	49	3.15
Postcentral gyrus	2	R	31	45	-29	37	3.41
Postcentral gyrus extending to cingulate cortex	2/23/31	L	191	-35	-22	30	3.65
Putamen		L	28	-31	-24	1	3.36
Globus pallidus		L	20	-17	-14	-5	3.19
SA-PG							
Superior temporal gyrus	22	L	28	-66	-37	8	3.70
Medial temporal gyrus	21	R	21	62	-11	-11	3.15

When given easy compared to hard choices, pathological gamblers showed significantly higher activity in the bilateral posterior cingulate, right precentral and postcentral gyrus, and left globus pallidus compared to substance abusers. In the same comparison, substance abusers showed higher activity in the bilateral temporal cortex compared to pathological gamblers.

Table 27: Foci of significant brain activations in the easy-hard condition: Comparison of non- pathological and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-SA							
Orbitofrontal cortex	11/10	L	90	-35	44	-8	3.37
Postcentral gyrus	3/43	R	15	66	-16	30	3.23

In the easy – hard comparison, non-pathological gamblers showed increased activity in the left lateral OFC and the right postcentral gyrus compared to substance abusers. The SA-NPG subtraction yielded no voxels that reached statistical significance.

Discussion

The delay discounting task was constructed to investigate the brain regions involved in decision-making when participants had to choose whether they wanted to act in a self-controlled manner in order to receive larger gains. The delays given in this task were real in order to make participants experience the consequences of their choices. There were two comparisons that were made from the results in the task, free vs. forced and easy vs. hard choices. There have been a handful of studies that have employed *f*MRI versions of a delay discounting task. In addition, there have been relatively few non-scanner delay discounting tasks that have provided realistic consequences associated with every trial.

When presented with free compared to forced choices, all groups showed significant activation in the prefrontal cortex, notably in areas posited to be involved in reward, decision-making and impulsive choice, i.e. the orbitofrontal cortex and the ventromedial and dorsolateral prefrontal cortex. Prefrontal activation was noticeably absent when given forced compared to free choices. These effects suggest that the free choices involve more strongly those areas of the brain found to be involved in decision-making and effortful processing.

Cumulating data from all four groups, the anterior cingulate cortex was found to be more active when given forced compared to free choices. At first, this may seem at odds with what we would expect as the ACC has been associated with voluntary choice (Rushworth et al., 2007). The ACC has been found not to have a role in impulsive choice (Cardinal et al., 2004). In this task, the ACC may be more active in the forced choice condition due to increased action monitoring. The forced trials asked the participant to make a specific button press whereas the free trials conferred a choice between two alternatives. Increased action monitoring may have been needed in the forced trials to make sure that the participant made the correct response.

Pathological gamblers and substance abusers have been found to reliably discount delayed rewards at a much faster rate compared to controls thus indicating their intolerance of delayed rewards and preference for immediate or short-term gratification. It has been suggested that these pathological groups may have biological abnormalities that underlie this decision-making bias, which may, in turn, cause or contribute to their addictive behaviour. It has been hypothesised that areas of the prefrontal cortex, especially the OFC, VMPFC and DLPFC, may function abnormally compared to healthy controls. When given forced compared to free choices, significantly higher prefrontal activity, including the VMPFC, was measured in the controls compared to the pathological gamblers. However, this was not the case when given free compared to forced choices. In fact, in this comparison, pathological gamblers showed higher activation in a small area of the right inferior prefrontal cortex compared to controls. This result gives evidence for some abnormalities in the functioning of the PFC in pathological gamblers compared to controls.

The same pattern of results was seen when comparing the substance abusers and controls. When given forced compared to free choices, higher activity was measured in a range of PFC regions including the VMPFC in controls. Higher activity was also measured in the ACC. However, in the free vs. forced choice comparison, higher activity was measure in the right lateral OFC in the substance abusers. It may be the case that the pathological gamblers and substance abusers are hypersensitive to choice and value the free choices more than the controls. Alternatively, the hyperactivation may reflect a characteristic of the samples. In experiment 3, no major differences were found between the pathological gamblers, substance abusers and controls in regards to delay and probability discounting. The majority of participants from experiment 4 were recruited from experiment 3. The hyper-stimulation of the OFC may have been underlying a forcible improvement in decision-making, i.e. if the OFC was not hyper-stimulated, behavioural deficits would have been measurable. It is interesting to note that the right OFC activity

was present in both addictive groups and that both performed similarly on the delay discounting task (and similarly to controls). Another interesting finding was that similar right OFC activity was measured in non-pathological gamblers, i.e. gamblers who show no addiction. This finding bolsters the conclusion outlined above in that some gambling and substance abusing groups may require hyper-activation of areas critical to reward processing in order to minimise potential decision-making deficits. This is opposed to when there is no choice (which could be construed as a baseline condition) in which decreased BOLD signal was measured in the prefrontal cortex in the pathological groups compared to the controls. As a side note, this seems to be an excellent example of how functional imaging can provide interesting information that cannot be picked up solely from neuropsychological testing.

A hypothesis was presented at the beginning of this project that posited that there might be a continuum between non-gambler and pathological gambler along which a series of biological abnormalities are exacerbated and when these cross a certain threshold, addictive gambling behaviour is exhibited (thus non-pathological gamblers will mimic the abnormalities found on pathological gamblers but to a lesser extent). Experiment 3 found little evidence to support this hypothesis. However, the possibility of a continuum regarding other behaviours was not ruled out. If a continuum were present, we would expect to see some functional differences in the non-pathological gamblers mirror those measured in the pathological gamblers but to a significantly lesser extent. When given free vs. forced choice trials, pathological gamblers showed increased activity in the VMPFC compared to non-pathological gamblers but higher activity was measured in the OFC in non-pathological gamblers compared to pathological gamblers. Higher frontal and ACC activity was also measured in pathological gamblers when given forced compared to free choices. In addition, in the free vs. forced choice comparison, non-pathological gamblers showed higher activity in the right OFC compared to controls. These results suggest that for brain regions underlying decision-making in environments involving delay, there is little evidence for a

continuum of increasing abnormalities from non-gambler to pathological gambler as, although non-pathological gamblers did show an increase in OFC function, the pathological gamblers showed increased function in other frontal areas involved in emotional processing and decision-making.

In every group, high activity was measured in the posterior parietal cortex when given free compared to forced choices. This supports that suggestion by McClure et al., (2004) that the posterior parietal cortex has a role in determining self-control or is involved in instrumental learning associated with the delay discounting task. This is an area that requires more attention to uncover its role in delay discounting.

All groups, except the pathological gamblers, showed increased activity in the visual cortex when given free compared to forced choices. This may be indicative of increased visual processing of the free choices. It could be argued that the forced choices would receive significantly less visual processing because the same information is given for each alternative.

The easy vs. hard choice comparison yielded some interesting results. Perhaps surprisingly, supra-threshold voxels were only measured in the easy – hard comparison and not the hard – easy comparison in the pathological gamblers, non-pathological gamblers and substance abusers. It could be expected that a higher number of brain areas, especially frontal areas, would be more active when given hard opposed to easy choices, as was found in the controls. The two gambling groups showed higher activity in the OFC and left inferior prefrontal gyrus when given easy compared to hard questions. No significant frontal activity was measured in the substance abusers. This may be indicative of a functional abnormality in substance abusers. The results from the controls conformed more to what was expected. When given hard compared to easy choices, controls showed high prefrontal activity, especially in the OFC and DLPFC. Significant activity was also measured in the dorsal striatum (more specifically, the caudate nucleus and globus pallidus), thalamus and visual cortex. The caudate nucleus has been

associated with the preference for immediate rewards rather than delayed rewards (Wittman et al., 2007) and the dorsal striatum has been linked to instrumental learning (O'Doherty et al., 2004). These differences between groups may be due to different circuits in the brain of gamblers/substance users responding to different stimuli compared to controls.

There were a number of interesting findings when comparing controls with gambling and drug abusing samples on the hard vs. easy contrast. Controls showed increased BOLD signal within prefrontal areas compared to the other groups. Pathological gamblers exhibited lower activation within the inferior prefrontal cortex, an area posited to be involved in the modulation of response inhibition (Chambers et al., 2007; Chikazoe et al., 2008; Kemmotsu et al., 2005; Kumari et al., 2007; Menon et al., 2001). This finding suggests that pathological gamblers may exhibit some degree of functional impairment when making relatively cognitively-demanding choices. Controls also showed significantly increased BOLD signal within the OFC and DLPFC compared to non-pathological gamblers and substance abusers respectively. These are areas with critical roles in modulating impulsivity and choice behaviour[16]. In addition to differences in prefrontal activity, temporal activity was commonly increased in controls compared to the other groups. Compared to pathological and non-pathological gamblers, controls exhibited higher BOLD signal within the right inferior temporal cortex whereas compared to substance abusers, controls exhibited higher signal within bilateral inferior, middle and superior regions. The temporal cortex has been posited to be included in fronto-temporo-limbic circuitry that modulates impulsivity (Hoptman et al., 2004). Surgical excision of regions of the temporal cortex have been found to lead to the production of behavioural and cognitive impairments in impulsivity, irratibility, social skills and executive functioning (Frayne et al., 1999) and patients with bipolar disorder or anti-social personality disorder who show impulsive behaviours exhibit significantly lower regional cerebral blood flow in prefrontal and temporal cortices (Goethals et al., 2004). The

[16] See section 7 of the introduction.

specific role of the temporal cortex in impulsivity is still under question but it has been posited to be involved in the processing of outcomes entailing losses (Vollm et al, 2007), however, direct functional imaging of the experience of losses does not corroborate this theory (Tom et al., 2007). Another area that was was found to exhibit significantly higher BOLD activity in controls compared to other groups was the fusiform gyrus. Interestingly, the fusiform gyrus has been found to be significantly active in pathological gamblers, drug users, alcohol abusers and addicted smokers during cue-reponse tasks (in which cues related to the addiction are presented) which has led to the hypothesis that the fusiform gyrus forms part of a dysfunctional system involved in visual perception (which links with other possible dysfunctional areas involved in emotion and reward) within these groups (Crockford et al., 2005; David et al., 2005; Due et al., 2002; Park et al., 2007; Wrase et al., 2002). The findings from this task extend previous research and finds that these groups also show dysfunction of the fusiform gyrus in non-passive choice situations.

Taking, as a whole, the findings from the easy vs. hard subtraction, it appears that pathological gamblers and substance abusers, in addition to non-pathological gamblers, exhibit significant widespread differences in neural function in areas involved in cognition and impulsivity. When considering the differences in function between groups, it is important to note that choice behaviour on the behavioural delay discounting task did not differ significantly. Two alternatives can be put forward as to explain the existence of the functional differences. One explanation is that they reflect widespread neural circuitry that is impaired within these groups compared to controls but not to a level which allows expression of impaired behavioural output. The second alternative suggests that the functional differences represent not impairments, but the existence of altered neural pathways within these groups, which has previously been suggested to occur in abstinent marijuana abusers (Padula et al., 2007). This hypothesis fits in with the heightened BOLD signal within the OFC measured within these groups in the free-forced subtraction. Therefore, altered neural pathways within these groups mask, to some

degree, deficits in behavioural output even though these groups still express significantly increased levels of impulsivity[17].

One concern regarding the task was the time it took for participants to complete. The task took a maximum of 12 minutes although all participants except one completed it in 10-11 minutes. Subjectively, the task may have felt lengthy as it contained a number of periods in which the participant had to wait until a delay was complete. As the task progressed, participants may have altered their decision-making strategy so that their preference switched to the sooner rewards in order to decrease task length. However, when analysing the results this did not appear to be the case.

Conclusions

In addition to uncovering brain areas involved in delay discounting, the task was designed to compare neurological function between groups exhibiting addictive behaviour (pathological gamblers and substance abusers), individuals showing similar behaviours but in a non-addicted state (non-pathological gamblers) and healthy controls. It was hypothesised that the addicted groups would show differences in neurological function compared to controls that had a role in the behavioural differences in delay discounting behaviour reliably exhibited by these groups in previous research. Although there was some evidence that controls showed slightly elevated prefrontal activity compared to pathological gamblers and substance abusers, this was not in the expected comparison (it was in the forced – free choice comparison). Instead, the two addicted groups, in addition to the non-pathological gamblers, showed elevated activity in the right lateral OFC in the free – forced comparison compared to controls. The second comparison again yielded interesting data. The results showed that in the hard compared to the easy choices, controls showed increased activation in a wide circuit of areas involved posited to

[17] See experiment 3.

modulate impulsivity and choice behaviour. No significant differences in choice behaviour were measured between groups, therefore, these results suggest that pathological gamblers, substance abusers, and even non-pathological gamblers, recruit altered neural pathways compared to controls when making cognitively-demanding choices in which participants must take account of delayed outcomes.

Probability discounting task

The probability discounting task had two conditions, free-forced and easy-hard[18].

Free vs. Forced choices

[18] See the "Materials" section of experiment 4 for a description

Table 28: Foci of significant brain activations in the free-forced condition taken from all groups.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free- forced							
Orbitofrontal cortex	10	L	100	-45	48	7	3.35
	47	L	75	-38	24	-4	3.38
	10	L	32	-21	58	-3	3.32
Medial frontal gyrus	8/9/46	L	1351	-3	26	41	5.75
Medial extending to inferior frontal gyrus	9	L	218	-45	9	35	4.01
Inferior frontal gyrus	47	R	102	35	17	-7	5.25
Inferior extending to superior parietal gyrus	40/7	R	1285	49	-35	44	6.46
Inferior parietal gyrus extending through precuneus to superior occipital gyrus	40/7/19	L	1062	-42	-46	41	5.6
Inferior extending to medial temporal gyrus	19/37	R	186	49	-61	-3	4.67
Globus pallidus extending to subthalamic nucleus and red nucleus		L/R/L	343	10	-3	3	4.65
Cerebellum		L	51	-35	-63	-29	3.47
		R	13	38	-62	-23	3.20
Forced – free							
Medial frontal gyrus	6	R	128	3	-8	46	3.62
Postcentral extending to precentral gyrus	5/4	L	145	-24	-38	60	3.94
Superior parietal gyrus	7	R	23	21	-41	73	3.58
Precuneus	7	L	31	-14	-46	38	3.67
Cuneus	18	R	225	17	-94	21	4.16
Lingual gyrus extending to inferior occipital gyrus	18/17	R	96	14	-65	-3	3.39
Superior temporal gyrus extending to angular gyrus	39	L	58	-49	-57	19	3.67
Parahippocampal gyrus extending to caudate nucleus	30	R	30	24	-47	9	3.51
Caudate nucleus		L	36	-17	15	22	3.55
Hippocampus extending to postcentral gyrus	40/3	R	3663	28	-18	-14	5.52
Cerebellum		L	14	-17	-83	-28	3.09
		R	46	17	-86	-28	3.84

The free-forced subtraction yielded many voxels within the prefrontal cortex, mostly within the left hemisphere. Increased activity was noted in the left medial and lateral OFC, left VMPFC and left DLPFC. Notable activity was measured in the posterior section of the brain including the bilateral parietal cortex, right temporal gyrus and left superior occipital gyrus. Bilateral cerebellar activity, sited within the anterior part of the posterior lobes, was also measured. Several limbic structures showed increased activity, notably the left globus pallidus, left red nucleus and right subthalamic nucleus.

When given forced compared to free choices, increased activity was notably absent from frontal areas except the medial dorsal region (BA 6). Increased activity was also present in medial areas of the brain such as the bilateral postcentral and precentral gyrus. Some activity was also measured in the most posterior sections of the brain including the left precuneus and right cuneus. Some limbic structures, namely the hippocampus and caudate nucleus, also showed increased activity. There was also increased bilateral cerebellar activity sited within the posterior section of the posterior lobes.

Table 29: Foci of significant brain activations in the free-forced condition in pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free- forced							
Orbitofrontal cortex	10	L	83	-17	54	-3	3.84
	10/46	R	240	24	61	3	3.81
Inferior frontal gyrus	9	L	21	-59	18	22	3.40
Medial frontal gyrus	9/8/6	R	116	7	29	40	3.17
	6	R	28	28	10	61	3.14
Postcentral gyrus	40	R	23	52	-32	47	3.09
Inferior parietal cortex	40	R	19	35	-39	37	3.14
Superior parietal cortex extending to precuneus	7	R	27	17	-65	61	3.15
Forced – free							
Precentral extending to postcentral gyrus	6/4	R	150	35	-8	42	3.20
Precuneus	7	L	33	-14	-46	38	3.23
Medial temporal gyrus	22	R	31	35	-50	12	3.09
Globus pallidus		L	48	-17	0	-6	3.89
Amygdala extending to hippocampus		R	167	31	-5	-23	3.58
Cerebellum		L	16	-21	-32	-25	3.30

When given free compared to forced choices, pathological gamblers showed increased activity throughout the prefrontal cortex including bilateral OFC and VMPFC. Increased activity was also present in the posterior sections of the right hemisphere, namely the postcentral gyrus, parietal cortex and precuneus.

In the forced-free subtraction, there was higher activity in limbic structures, namely the globus pallidus, amygdala and hippocampus. High amounts of activity was also measured in the left precuneus, right precentral to postcentral gyrus and right temporal gyrus.

Table 30: Foci of significant brain activations in the free-forced condition in non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free- forced							
Inferior frontal gyrus	44	R	76	55	15	19	4.23
	9	L	66	-55	12	32	3.52
	47	R	20	38	17	-7	3.25
Inferior extending to medial frontal gyrus	46/10	R	91	45	41	11	3.98
Medial frontal gyrus	6	R	81	31	9	45	4.00
Medial extending to superior frontal gyrus	8/6	L	87	-4	25	46	4.17
Inferior extending to superior parietal gyrus	40/7	R	843	38	-52	48	5.21
Inferior parietal gyrus extending to postcentral gyrus	40/2	L	359	-42	-45	51	4.14
Inferior extending into superior temporal gyrus	19/37/22	R	148	49	-61	-3	4.09
Thalamus		R	36	3	-17	1	3.34
Forced – free							
Anterior cingulate cortex	32	L	16	-24	28	15	3.13
Anterior cingulate cortex extending to orbital gyrus	32/11	L	201	-14	27	-4	3.67
Anterior cingulate cortex extending to caudate nucleus	32	R	63	10	27	-7	3.23
Precentral gyrus	6	L	11	-42	-14	62	3.53
Paracentral lobe	6	R	28	7	-28	50	3.48
Medial occipital gyrus extending to cuneus	18/19	R	73	14	-101	15	3.77
Lingual gyrus	18	L	16	-10	-99	-4	3.26
Parahippocampal gyrus	28/38	R	152	24	-18	-14	4.02
Parahippocampal gyrus including hippocampus	35	L	193	-21	-21	-11	3.69
Caudate nucleus		R	16	14	1	23	3.15
Cerebellum		R	16	3	-48	-1	3.20

When given free compared to forced choices, non-pathological gamblers showed increased activity in the bilateral VMPFC and bilateral DLPFC. Activity was also measured in bilateral posterior areas including the bilateral parietal cortex, right temporal gyrus. The right thalamus also showed increased activity.

When given forced choices compared to free choices, activity was reported in the anterior cingulate cortex, bilateral caudate nucleus, orbital gyrus, lingual gyrus, bilateral parahippocampal gyri including hippocampus and right cerebellum.

Table 31: Foci of significant brain activations in the free-forced condition in substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free- forced							
Inferior frontal gyrus	47	R	16	38	17	-7	3.29
Inferior extending to superior parietal gyrus	40/7	R	399	45	-39	44	4.63
Precuneus extending to inferior parietal gyrus	7/40	L	373	-28	-45	44	4.00
Medial occipital gyrus	19	R	37	49	-55	-6	3.44
Globus pallidus extending to subthalamic nucleus		L	30	-14	0	-3	3.24
Putamen extending to globus pallidus		R	79	17	7	9	3.55
Forced – free							
Orbitofrontal cortex	11	L	63	-3	47	-17	3.48
Precentral gyrus	6	L	14	-59	-2	36	3.23
Postcentral extending to precentral gyrus	3/6	R	46	52	-14	56	3.72
Superior temporal gyrus extending to parahippocampal gyrus	22/36	L	848	-52	-7	-6	4.30
Uncus extending into parahippocampal gyrus including hippocampus	28	R	872	31	6	-24	4.56
Caudate nucleus		L	158	-17	15	22	4.80
Cerebellum		L	68	-7	-69	-26	3.49
		L	31	-17	-55	-9	3.29

When give free compared to forced choices, the only activity measured in the PFC of substance abusers was in right BA47. Most activity was located within posterior areas including the bilateral parietal cortex, precuneus and occipital gyrus. Increased activity was also measured in the right putamen, bilateral globus pallidus, and left subthalamic nuclei.

In the forced-free subtraction, substance abusers showed increased activation in the left medial OFC in addition to more dorsal areas including the temporal gyrus, bilateral parahippocampal gyrus, right uncus and right hippocampus.

Table 32: Foci of significant brain activations in the free-forced condition in controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free- forced							
Medial frontal gyrus	10/9/8	R	901	3	29	37	5.01
Medial frontal gyrus extending to precentral gyrus	9	L	194	-42	5	35	3.99
Inferior frontal gyrus	47	R	49	35	17	-7	3.88
Inferior extending to superior frontal gyrus	40/7	R	750	49	-39	44	5.29
Inferior parietal gyrus extending to occipital gyrus	40/19	L	523	-49	-52	58	5.30
Inferior extending to medial temporal gyrus	37	L	28	-52	-55	-3	3.12
Inferior temporal gyrus extending to fusiform gyrus	20/37	R	106	55	-48	-12	4.01
Globus pallidus extending to thalamus		L	574	-10	-14	-5	4.40
Forced – free							
Orbitofrontal cortex	11/10	R	51	3	27	-10	3.75
Precentral gyrus	6	L	19	-62	-2	26	3.70
Postcentral extending to precentral gyrus	3/6	R	83	49	-18	56	3.18
Postcentral gyrus extending to superior temporal gyrus	40/21	R	520	55	-26	17	3.70

In the free-forced subtraction, controls showed increased activity in the prefrontal cortex including the left DLPFC. Increased activity was also present in posterior regions including the left parietal to occipital gyrus, bilateral temporal cortex and fusiform gyrus. Increased activity was also measured in the globus pallidus and thalamus.

When give forced compared to free choices, controls showed increased activity in the dorsal medial OFC, in addition to the bilateral precentral and right postcentral gyri.

Table 33: Foci of significant brain activations in the free-forced condition: Comparison of pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-CO							
Cingulate gyrus	24	L	13	-10	5	38	3.15
Precentral gyrus	6	L	10	-62	-2	-29	3.74
CO-PG							
Inferior frontal gyrus	47	L	54	-38	13	-15	3.85
Inferior parietal gyrus	40	L	29	-49	-52	48	3.51
Inferior extending to medial temporal gyrus	37/21	L	16	-52	-51	0	3.29
Globus pallidus extending to subthalamic nucleus		L	48	-14	0	-3	3.62

Pathological gamblers, when give free compared to forced choices, show increased activity in the cingulate cortex compared to controls. When given forced compared to free choices, pathological gamblers showed increased activity in the left globus pallidus and subthalamic nucleus.

When given free compared to forced choices, controls showed increased activity in the left inferior frontal gyrus, parietal gyrus and temporal gyrus. In the forced-free subtraction, greater activity within the left precentral gyrus was present in controls compared to pathological gamblers.

Table 34: Foci of significant brain activations in the free-forced condition: Comparison of non-pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-CO							
Precentral extending to postcentral gyrus	4/43	L	29	-62	-6	23	3.30
Superior temporal gyrus	21	R	16	55	-24	-2	3.27
Insula extending the superior temporal gyrus	41	L	80	-38	-30	21	3.51
CO-NPG							
Medial extending to superior frontal gyrus	8/9	R	35	28	40	46	3.67
Caudate nucleus extending to insula		R	40	24	20	-1	3.31
Uncus	28	L	18	-21	6	-24	3.09
Cerebellum		R	40	14	-28	-10	3.32

When given free compared to forced choices, non-pathological gamblers showed increased activity in the left posterior insula and temporal gyrus compared to controls. When given forced compared to free choices, non-pathological gamblers showed increased in the caudate nucleus and right anterior insula in addition to the right cerebellum.

From the free-forced subtraction, controls showed higher activity in the right DLPFC and uncus compared to non-pathological gamblers. When given forced compared to free choices, there was increased activity in the bilateral superior temporal gyrus and left posterior insula in controls.

Table 35: Foci of significant brain activations in the free-forced condition: Comparison of substance abusers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CO-SA							
Superior frontal gyrus	9	R	14	28	49	36	3.52
Middle frontal gyrus	8/6	R	34	10	26	44	3.12
	6	L	13	-45	6	51	3.25
Inferior parietal gyrus	40	L	42	-52	-52	48	3.54
Superior temporal gyrus extending to uncus	38/28	L	227	-42	6	-18	3.66
Uncus extending to superior temporal gyrus	28/38/21	R	99	31	6	-21	4.18
Caudate nucleus		L	24	-10	21	15	3.48

The SA-CO subtraction yielded no voxels that met the threshold for statistical significance. When given free compared to forced choices, controls (compared to substance abusers) showed higher amounts of frontal activity, notably in the right DLPFC in addition to the inferior parietal gyrus. Conversely, substance abusers showed higher activation in bilateral temporal cortex and bilateral uncus in addition to the left caudate nucleus in the forced-free subtraction.

Table 36: Foci of significant brain activations in the free-forced condition: Comparison of pathological and non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-NPG							
Orbitofrontal cortex	47	R	49	14	30	-13	3.09
NPG-PG							
Insula		L	111	-35	-24	4	3.12

When given free compared to forced choices, non-pathological gamblers showed increased activity in the left insula compared to pathological gamblers. When given forced compared to free choices, non-pathological gamblers showed higher activity in the right medial OFC.

Table 37: Foci of significant brain activations in the free-forced condition: Comparison of pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-SA							
Orbitofrontal gyrus	47	R	34	21	30	-10	3.36
	10	L	260	-17	54	-3	3.67
Anterior cingulate cortex	32/24	L	46	-14	18	22	3.30
Superior temporal gyrus	38	R	15	35	2	-21	3.22
Cerebellum		L	12	-17	-31	-16	3.22
SA-PG							
Globus pallidus		L	28	-14	0	-3	4.26

When given free compared to forced choices, pathological gamblers (relative to substance abusers) show increased left OFC activity. When given forced compared to free choices, pathological gamblers show increased activity in the left globus pallidus.

Substance abusers, when given forced compared to free choices show higher activity in the right OFC and anterior cingulate cortex in addition to the right temporal cortex and left cerebellum.

Table 38: Foci of significant brain activations in the free-forced condition: Comparison of pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-SA							
Precentral gyrus	6	L	16	-55	-5	42	3.60
Insula extending to superior temporal gyrus	41	L	179	-38	-17	4	3.69
Medial temporal gyrus	39	R	35	42	-54	9	3.24
Caudate nucleus		L	39	-17	15	22	3.55

When given free compared to forced choices, non-pathological gamblers showed significantly higher activity within the left precentral gyrus and right medial

temporal gyrus compared to substance abusers. When given forced choice trials compared to free choice, substance abuser showed increased activity in the left insula, superior temporal gyrus and left caudate nucleus.

Easy vs. hard choices

Table 39: Foci of significant brain activations in the easy-hard condition taken from all groups.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Easy – hard							
Medial frontal gyrus	6	L	25	-45	16	48	3.46
	6	R	26	10	-1	52	3.22
Fusiform Gyrus	36	L	21	-42	-38	-19	3.56
Cerebellum		R	59	21	-83	-28	3.10
Hard – easy							
Anterior cingulate cortex	24/32	L	36	-3	31	18	3.13
Superior occipital gyrus	19	R	59	35	-83	33	3.78
Medial occipital gyrus	18	R	36	38	-88	1	3.49
Medial occipital gyrus extending to cuneus	19	L	97	-38	-84	20	3.80

Data collated from all groups shows that when given easy, compared to high choices, higher activation is noted within the bilateral DLPFC in addition to the left fusiform gyrus and right cerebellum. Conversely, when give hard compared to easy choices, increased activity is present within the anterior cingulate cortex in addition to bilateral occipital regions.

Table 40: Foci of significant brain activations in the easy-hard condition in pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Easy – hard							
Medial frontal gyrus	6	R	42	10	-27	69	3.29
Precentral gyrus	4	L	18	-14	-31	69	3.12
Precuneus	7	R	21	14	-66	36	3.10
	31/7	L	23	-14	-60	32	3.45
Superior temporal gyrus	22	L	26	-42	-24	-8	3.23
Fusiform gyrus	36	L	18	-42	-35	-19	3.16
Insula		R	10	38	-33	21	3.39
Uncus	28	R	25	28	2	-27	3.13
Hard - easy							
Medial frontal gyrus	10	L/R	20	-3	65	13	3.19
Insula		R	51	38	14	12	3.53

The easy-hard subtraction yielded significant clusters within the right DLPFC, left precentral gyrus, left temporal gyrus, left fusiform gyrus, right posterior insula, right uncus and bilateral precuneus. When given hard compared to easy choices, higher activity was present in the bilateral VMPFC and right anterior insula.

Table 41: Foci of significant brain activations in the easy-hard condition in non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Hard – easy							
Anterior cingulate cortex	24	L	31	-3	31	18	3.21
Inferior parietal gyrus	40	L	26	-49	-29	24	3.47
Precuneus	19/7/31	R	375	28	-77	33	4.16
Medial occipital gyrus	19	L	163	-38	-84	20	3.88
Fusiform gyrus	37	R	168	38	-58	-6	3.51
Putamen extending to insula		L	22	-24	1	16	3.77

The easy-hard subtraction yielded no voxels that exceeded the threshold for statistical significance. When given hard compared to easy choices, non-pathological gamblers showed increased activity in the anterior cingulate cortex in addition to more posterior regions, namely the left parietal gyrus, left occipital gyrus and right precuneus. The right fusiform gyrus also showed increased activity in addition to the left anterior insula and left putamen.

Table 42: Foci of significant brain activations in the easy-hard condition in substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Easy - hard							
Insula		L	14	-38	-40	25	3.62
Hard – Easy							
Anterior cingulate gyrus	32	R	18	14	15	22	3.38
Inferior parietal gyrus	40	L	55	-24	-42	38	3.28
Medial occipital gyrus	18	R	49	38	-82	1	3.60
Cuneus	19	L	37	-21	-87	37	3.21
	17/18	L	99	-24	-81	11	3.68

The easy-hard subtraction yielded a significant cluster within the left insula. When given hard compared to easy choices, substance abusers showed activation in the anterior cingulate gyrus in addition to posterior regions such as the left parietal gyrus, right medial occipital gyrus and left cuneus.

Table 43: Foci of significant brain activations in the easy-hard condition in controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Easy - hard							
Inferior frontal gyrus	45/46	R	51	45	18	12	3.71
Precentral extending to postcentral gyrus	4/3	R	63	24	-24	69	3.17
Fusiform gyrus	20/37	L	18	-42	-35	-16	3.32
Insula		R	294	42	-6	16	4.06
Putamen		L	50	-24	-3	3	3.36

When given easy compared to hard choices, controls showed increased activity in right frontal areas in addition to the left fusiform gyrus, right insula and left putamen. The hard-easy subtraction yielded no significant voxels.

Table 44: Foci of significant brain activations in the easy-hard condition: Comparison of pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-CO							
Inferior parietal gyrus	40	L	18	-31	-52	41	3.24
CO-PG							
Insula		R	122	42	14	15	4.08

Pathological gamblers showed higher activation in the right insula in the hard-easy subtraction whilst controls reported higher activation in the right insula when give easy compared to hard choices.

Table 45: Foci of significant brain activations in the easy-hard condition: Comparison of non-pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CO-NPG							
Medial frontal gyrus	10	R	35	45	48	10	3.10
Inferior frontal gyrus	45	R	24	45	18	15	3.21
Inferior extending to superior parietal gyrus	40/22	L	77	-45	-29	24	3.45
Medial occipital gyrus	18	R	25	35	-85	4	3.21
Medial occipital gyrus including lingual gyrus	18	L	84	-28	-85	-2	3.34
Cuneus	19	L	78	-38	-80	23	3.23
Precuneus extending to cuneus	31/7/19	R	185	3	-70	33	3.46
Insula extending to putamen		R	238	42	-29	24	3.42
Putamen		L	94	-24	1	19	3.65
Parahippocampal gyrus extending through fusiform gyrus to lingual gyrus	37/19	R	93	28	-45	-7	3.27

The NPG-CO subtraction yielded no voxels that reached statistical significance. When given easy compared to hard choices, controls (relative to non-pathological gamblers) showed increased activity in the right VMPFC and posterior frontal areas in addition to the right insula and putamen. Non-pathological gamblers, when given hard compared to easy choices, showed increased activity in more posterior regions relative to controls, namely the left parietal gyrus, bilateral occipital cortex, bilateral cuneus in addition to right parahippocampal gyrus, fusiform gyrus, lingual gyrus and left putamen.

Table 46: Foci of significant brain activations in the easy-hard condition: Comparison of substance abusers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CO-SA							
Inferior frontal gyrus	9	R	69	42	-6	23	3.31
Postcentral extending to precentral gyrus	3/4	R	114	21	-31	53	3.24
Inferior parietal gyrus	40	R	47	42	-29	24	3.25
Inferior occipital gyrus	18	L	21	-28	-92	-1	3.20

The SA-CO subtraction yielded no voxels that met statistical significance. When given easy compared to hard choices, controls showed higher activity in the right inferior frontal gyrus, right precentral and postcentral gyrus, and right inferior parietal gyrus.

Table 47: Foci of significant brain activations in the easy-hard condition: Comparison of pathological and non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-NPG							
Precuneus	31/7/19	R	668	10	-70	36	4.22
Medial occipital gyrus extending to lingual gyrus	19/18	L	159	-31	-81	11	3.48
Insula		L	120	-49	-36	21	3.55
Insula extending to caudate nucleus		L	41	-28	-2	23	3.38
Parahippocampal gyrus	37	R	18	31	-41	-7	3.11
Putamen		R	58	28	-16	14	3.32

When given hard compared to easy choices, non-pathological gamblers (compared to pathological gamblers) showed increased activity in posterior regions, namely the right precuneus and left occipital and lingual gyri in addition to the left insula

and caudate nucleus. Pathological gamblers, when given easy compared to hard choices, showed higher activity in the right precuneus.

Table 48: Foci of significant brain activations in the easy-hard condition: Comparison of pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-SA							
Medial frontal gyrus	6	R	51	10	-27	69	3.12
Precentral gyrus	4	L	32	-14	-31	69	3.12
	6	L	26	-35	1	29	3.36
Medial occipital gyrus	19	L	139	-28	-81	11	3.82
Cerebellum		R	24	42	-49	-30	3.12
SA-PG							
Insula		R	26	38	18	12	3.24

When given easy compared to hard choices, pathological gamblers (compared to substance abusers) showed increased dorso-medial frontal activity in addition to activity in the left occipital gyrus and right cerebellum. Conversely, when given hard compared to easy choices, substance abusers showed increased activity in the left occipital gyrus. In the easy-hard subtraction, substance abusers, relative to pathological gamblers show increased activity in the right insula.

Table 49: Foci of significant brain activations in the easy-hard condition: Comparison of non-pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
SA-NPG							
Cuneus extending to precuneus	7/31	R	85	14	-70	33	3.13
Insula		L	33	-38	-36	24	3.43

No voxels met the threshold for statistical significance in the NPG-SA subtraction. When given easy compared to hard choices, substance abusers showed increased activity in the left insula. In the hard-easy subtraction, higher activity in the precuneus, cuneus and left insula was measured in non-pathological gamblers.

Discussion

The probability discounting task had two comparisons. The first explored brain areas involved in probabilistic decision-making and the second investigated probabilistic decision-making when faced with choices in which there was an obvious choice and choices where the alternatives were situated around the mean indifference point, thus making the decision more difficult. To our knowledge, no previous studies have utilised a *f*MRI version of a probability discounting task in humans. The task included real consequences, i.e. the participants experienced outcomes that randomly decided whether they won or did not win.

Clusters of activation noted between the free-forced and forced-free comparisons were extremely segregated. In the free-forced choice comparison, if the results from all groups were collated, there was widespread activation in the prefrontal cortex when given free opposed to forced choices, notably in the OFC, VMPFC and DLPFC, three areas that have important roles in decision-making. There was also activation in bilateral posterior parietal areas. In decision-making tasks involving risk activation of the left parietal cortex has been associated with analysis of risk and posterior parietal activation has been linked to judgement between choices in a delay discounting task. Bilateral posterior parietal activation in this task could be associated with judgement of the mathematical properties of each probabilistic outcome. There was also significant activation of the dorsal striatum, an area linked with instrumental learning.

When given forced compared to free choices there was a notable absence of prefrontal activity, which was expected. There was some activation in posterior

dorsal frontal areas (BA6) in addition to the precentral and postcentral gyri. There was also activation in the medial posterior visual cortex. Compared to the free-forced comparison, the forced-free comparison yielded highly significant voxels in the anterior parietal cortex. This may represent a functional dissociation between anterior and posterior regions of the parietal cortex with posterior regions involved in judgement and the anterior regions involved in behaviour in a non-choice environment. There also appeared to be dissociation within the cerebellum. In the free-forced choice situation, there were significant clusters within the anterior regions of the posterior lobe in the cerebellum. In comparison to this, the forced-free comparison yielded clusters in the posterior regions of the posterior lobe.

In the free-forced choice comparison, all groups, when explored individually, exhibited a wide range of activity in the prefrontal cortex as expected. The VMPFC and DLPFC were commonly activated across most groups. Interestingly, the substance abusers showed less activation in more anterior regions of the prefrontal cortex. Previous research has found that there are significant differences in BOLD signal in substance abusers on neuropsychological tasks compared to controls[19]. In the free-forced choice subtraction, substance abusers showed significant decreases in prefrontal BOLD response compared to controls. This may provide evidence for impaired prefrontal activation in substance abusers when making decisions involving risk. This possible deficit may underlie an abnormality in risk processing and, furthermore, potentially influence their addictive behaviour. The substance abusers reported higher levels of venturesomeness compared to other groups, suggesting that this group were more inclined to take part in activities regarded as risky. This may be linked to their acceptance of the high risks involved with drug use. However, if this is correct, one must then explain why substance abusers did not show higher risk-taking on the probability discounting task. One explanation is that the provision of real rewards (compared to hypothetical rewards, which have been previously used in other studies) may have caused the substance abusers to 'upgrade' their behaviour into a more risk-aversive state, thus gaining more money

[19] See section 7.4 of the introduction for more detail

and thus masking any apparent behavioural impairment. Another explanation is that levels of risk-taking are not significantly different but altered neural pathways are recruited in this task by substance abusers compared to controls.

One hypothesis of this project suggested that pathological gamblers may have shown significant abnormalities in brain activity in areas involved in decision-making compared to controls. Controls did show an increased BOLD signal in inferior frontal regions and the parietal cortex. Decreased functional activity within the inferior frontal cortex compared to controls was also found in the delay discounting task providing greater evidence for altered neural function in areas playing a role in response inhibition and impulsivity in pathological gamblers.

One of the aims of this project was to investigate whether there was a continuum along which gamblers progressed from healthy gambler to pathological gambler. The group comparison reveals that non-pathological gamblers showed increased activity in the right medial OFC compared to pathological gamblers but only in the forced-free comparison. Compared to controls, non-pathological gamblers showed significantly less activity in the DLPFC but, again, only in the forced-free condition. This provides some support to the theory that there is a continuum of exacerbating neuro-functional abnormalities between controls and pathological gamblers (but not in choice situations).

In the forced-free comparison, the precentral and postcentral gyrus were reliably activated across all groups suggesting that these areas are involved in forced choice behaviour. In the same comparison, the hippocampus was also active in all groups (except the controls). The hippocampus is involved in memory consolidation and instrumental learning. The reason for its higher activation during the forced choice condition is unknown as all responses, regardless of choice type, led to a rewarding outcome. Finally, compared to controls, all groups showed increased activation in the dorsal striatum, notably the caudate nucleus.

In the hard choice – easy choice comparison it could be expected that regions involved in decision-making and judgement would be more active when presented with a hard choice compared to an easy choice. When data from all groups were collated, significantly higher activity was measured in the anterior cingulate cortex in the hard condition compared to the easy condition. The ACC has a role in the processing of probabilistic rewards. This increased activity is likely to be associated with increased processing of risk in the hard choices compared to the trials where the choice was obvious and where less processing would occur. There was also increased activity in the visual cortex, which may be related to increased visual processing of the hard choices compared to the easy choices (where the choices could be viewed briefly and a decision would then be reached).

When choices were hard compared to easy, pathological gamblers showed increased activity in the VMPFC, suggesting increased processing of the hard choices. In addition, increased activity was measured in the anterior insula, which has been associated with risk-aversion. Activation of these areas may be associated with heightened emotional processing of salient, risky, choices and their high chance of leading to negative outcomes. In the group comparisons, controls exhibited significantly increased BOLD response in the VMPFC and inferior frontal gyrus compared to non-pathological gamblers and substance abusers. These results are similar to those from the delay discounting task in which decreased function within prefrontal areas modulating response inhibition was found in the gambling and drug-abusing groups. However, in the probability discounting task, the pathological gamblers exhibited no such decreased function within prefrontal areas compared to controls on this subtraction analysis. However, decreased inferior frontal signal was measured in the free-forced condition again suggesting that the three gambling/drug abusing groups show impaired functioning within this area. A previous study providing choices between small, likely rewards and large, unlikely, rewards has been found to recruit orbitofrontal and inferior frontal gyri (Rogers et al., 1999) suggesting that these areas are involved in response selection for probabilistic outcomes. However, it again must be noted that although

functional impairments were found in the gambling/drug abusing groups compared to controls, there were no significant differences in choice behaviour on the behavioural probability discounting task, suggesting that the gambling/drug abusing groups do not exhibit functional impairments but utilise altered neural pathways compared to controls in decision-making environments or, alternatively, express anomalous neural function that masks any apparent behavioural impirments.

A question could be raised as to the efficacy of the forced choices. Although measures were taken to ensure that there was no choice whatsoever (participants were even instructed which button to press), participants may have expressed a conscious or unconscious preference dependent on such factors as position on the screen or based on previous actions. However, the experimenter is confident that this confound would not have occurred enough times to significantly affect the results.

It could be questioned as to how easy and hard the choices actually were. The choices were designed so that the easy choices were extremely self-evident whilst the hard choices were situated around the mean IPs (calculated from experiment 2). One concern could regard the use of mean IPs from experiment 2, which recruited healthy controls. Although previous research has found that substance abusers and pathological gamblers reliably discount delayed rewards at a higher rate than controls, differences in behaviour on the probability discounting task are still under question with studies investigating risk-taking behaviour in these groups finding contrasting results. Therefore, it may be the case that some groups (such as the pathological gamblers) had significantly different IPs to the controls recruited in experiment 2. Results from study 3 indicate that there are group differences in IPs with non-pathological gamblers showing significantly different IPs to controls. In further studies, measuring each participant's IPs beforehand with a behavioural probability discounting task and then matching the task to suit each participant's behaviour would be advisable to ensure that this confound cannot occur. IPs from

experiment 2 were used because the tasks were designed following the results from experiment 2 and during the initial stages of recruitment for experiment 3 and it was felt to be more advantageous to complete the tasks before experiment 3 got underway.

Conclusions

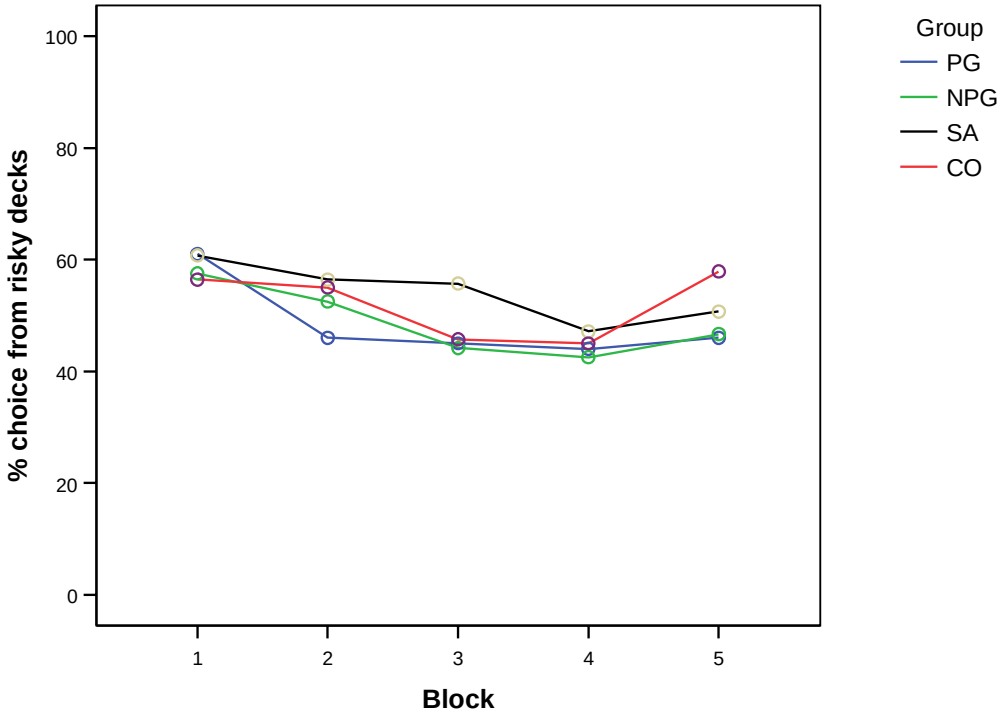
The behavioural version of a probability task has been used sparingly in psychological research and a *f*MRI version that provides real consequences has (as far as we are aware) not been utilised before. Therefore, although previous research could be used to gain ideas, the areas brain areas employed in probability discounting behaviour were unknown. The free-forced choice comparison yielded some very interesting results. As expected, the free choices recruited a wide range of prefrontal areas, which was not the case for the forced choice trials. In the free choice vs. forced choice comparison, pathological gamblers did show some differences in BOLD signal compared to controls. Substance abusers, on the other hand, showed significantly lower BOLD response in prefrontal areas compared to controls. Evidence for a continuum between non-gamblers and pathological gamblers was present in these tasks suggesting that a continuum of exacerbating abnormalities may occur.

Iowa task

Behavioural Iowa Task

Due to problems with the software used to present the Iowa task, results were obtained from five pathological gamblers, five non-pathological gamblers, six substance abusers and seven controls. Figure 18 shows the behaviour of each group over the course of the task.

Figure 18: Behaviour of each group over the time course of the behavioural Iowa task



There was no group difference in behaviour on the Iowa task, $F(3,21) = 0.32$, $p = .81$. There was a significant effect of block, $F(3.80, 79.77) = 5.19$, $p = .001$ which was caused by the trend for each group to decrease their choices from the risky decks over the course of the task. There were no group effects on Iowa score, $F(2,24) = .32$, $p = .81$, or winnings, $F(3,24) = .20$, $p = .90$.

fMRI Iowa task

No participant was excluded because they met the exclusion criteria[20].

[20] Described in the "Methods" section of experiment 4.

High – low risk choice

Table 50: Foci of significant brain activations in the high-low condition taken from all groups.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
High – low							
Middle frontal gyrus	8/9/46	R	70	42	19	31	3.16
Middle frontal gyrus extending to precentral gyrus	6	L	34	-45	6	45	3.12
	6/4	R	171	45	-8	52	3.84
Cingulate gyrus extending to superior frontal gyrus	32/6	R	282	3	22	34	4.16
Precuneus	7/31	R	76	7	-76	39	3.18
Superior temporal gyrus	38	L	81	-45	3	-18	3.18
Middle temporal gyrus	20	L	47	-52	-41	-7	3.67
Lingual gyrus	30	L	42	-17	-41	-1	3.56
Lingual gyrus extending to cuneus	18/17	L	735	-17	-82	-5	4.86
Caudate nucleus extending to globus pallidus		L	72	-3	14	-1	3.10
Thalamus		R&L	266	7	-13	7	4.46
Low – high							
Precentral gyrus extending to medial frontal gyrus	6	L	24	-14	-17	69	3.09
Inferior parietal cortex extending to postcentral gyrus	40/7/2	L	218	-42	-41	57	4.10
Cuneus	18	L	21	-7	-98	21	3.53
Lingual gyrus extending to fusiform gyrus and cerebellum	18/19	R	358	21	-78	-5	4.85
Cerebellum		L	10	-10	-87	-31	3.59

When data from all groups were collated, significantly higher activations were measured in the bilateral DLPFC in addition to right medial BA 6, cingulate gyrus, left temporal cortex, left visual cortex, left caudate nucleus, left globus pallidus and bilateral thalamus when presented with high vs. low risk choices.

When given low compared to high risk choices, increased activity was noted in the left medial BA 6, left parietal cortex, left cuneus, right lingual gyrus, right fusiform gyrus and posterior lobe of the right and left cerebellum.

Table 51: Foci of significant brain activations in the high-low condition taken from pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
High – low							
Middle frontal gyrus	6/9	R	331	52	6	48	4.22
Medial frontal gyrus extending to anterior cingulate cortex	9/32/24	L	100	-21	35	24	3.64
Inferior frontal gyrus	47/45	R	25	45	23	-7	3.22
	47	L	221	-35	17	-10	3.39
Precuneus	7	L	41	-10	-59	42	3.17
Fusiform gyrus	37	L	29	-49	-38	-10	3.70
Inferior occipital gyrus extending through lingual gyrus to fusiform gyrus	19/17	L	186	-38	-75	-5	3.35
Lingual gyrus	18	R	22	35	-68	-2	3.30
Parahippocampal gyrus	28	R	106	24	-21	5	3.32
Thalamus		L	19	-24	-24	-2	3.11
Thalamus and caudate nucleus		R&L	169	7	-13	7	3.60
Low – high							
Medial frontal gyrus	10	R	32	14	65	6	3.10
Precentral gyrus	6/4	L	162	-14	-20	69	4.28

When given high compared to low risk choices, pathological gamblers showed increased activity in the right DLPFC, VMPFC and right inferior PFC in addition to the left precuneus, left visual cortex, left fusiform gyrus, right parahippocampal gyrus, left caudate nucleus and bilateral thalamus.

In the low – high choice comparison, pathological gamblers showed increased activity in the right VMPFC and left precentral gyrus.

Table 52: Foci of significant brain activations in the high-low condition taken from non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
High – low							
Cingulate gyrus	32	R	28	3	22	34	3.22
Postcentral gyrus extending to precentral gyrus	3/6	R	66	45	-18	56	3.20
Low - high							
Cerebellum		L	75	-45	-66	-35	3.31

When presented with high vs. low risk choices, non-pathological gamblers showed increased activity in the cingulate gyrus in addition to the precentral and postcentral gyrus.

When given low compared to high risk choices, increased activation was measured in the left cerebellum.

Table 53: Foci of significant brain activations in the high-low condition taken from substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
High – low							
Cuneus extending to lingual gyrus	17/18	L	855	-10	-84	11	4.76
Cerebellum		L	53	-17	-56	-30	3.14
		L	53	-10	-25	-22	3.18
Low – high							
Orbitofrontal cortex	11	R	23	28	40	-17	3.09
Precentral gyrus	6	R	18	66	-9	33	3.38

In the high – low comparison, substance abusers showed increased activity in the left cuneus, left lingual gyrus and left cerebellum. When presented with low vs.

high risk choices, increased activity was measured in the right OFC and right precentral gyrus.

Table 54: Foci of significant brain activations in the high-low condition taken from controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
High – low							
Medial extending to superior frontal gyrus	8/6	R	505	3	26	37	3.86
Temporal gyrus extending to inferior frontal gyrus	21/47	R	304	52	-1	-15	3.63
Precentral gyrus	6	L	53	-49	2	45	3.77
Inferior parietal cortex	40	R	39	59	-35	40	3.13
Superior temporal gyrus	38	L	22	-38	2	-21	3.37
	38	L	19	-42	13	-12	3.31
Lingual gyrus extending to fusiform gyrus	18/19	L	77	-21	-79	-8	3.64
Thalamus extending to caudate		L&R	113	0	-17	7	3.49
Low – high							
Orbitofrontal cortex	11	R	13	3	47	-20	3.53
Middle frontal gyrus	46	L	22	-38	31	15	3.52
Inferior parietal gyrus extending through postcentral gyrus to precentral gyrus	40/2/4	L	187	-49	-35	57	3.65
Postcentral gyrus	7	L	15	-24	-48	64	3.11
Middle extending to superior temporal gyrus	22	R	16	59	-37	8	3.50
Superior temporal gyrus extending to insula	41/40	L	84	-52	-20	7	3.62
Middle occipital gyrus	18	R	17	24	-94	18	3.28
Lingual gyrus	18	R	507	21	-75	1	5.03

In controls, presentation of high vs. low choice trials caused increased activity in the right dorso-medial and right inferior PFC in addition to the left precentral gyrus, bilateral temporal cortex, right posterior parietal cortex, lingual gyrus, fusiform gyrus, right caudate nucleus and bilateral thalamus.

In the low – high comparison, increased activity was measured in the right OFC, ventrolateral PFC, left parietal cortex, left precentral and postcentral gyrus, bilateral temporal gyrus, left posterior insula and right visual cortex.

Table 55: Foci of significant brain activations in the high – low condition: comparison of pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-CO							
Cingulate gyrus extending to middle frontal cortex	32/9	L	36	-14	25	28	3.39
Precuneus	7	L	44	-14	-52	45	3.43
Superior temporal gyrus	22/41	R	11	66	-33	11	3.09
Lingual gyrus extending to fusiform gyrus	18/19	R	112	24	-75	1	3.55
Thalamus		L	12	0	-3	0	3.32
Parahippocampal gyrus	28	R	11	21	-24	-5	3.16
Claustrum		L	16	-38	-24	-2	3.14
Cerebellum		L	23	-24	-52	-12	3.19
CO-PG							
Cerebellum		R	10	49	-66	-32	3.33

When given high vs. low risk choices, pathological gamblers showed higher activity in the left middle frontal gyrus, cingulate gyrus, and left parahippocampal gyrus compared to controls. In the low – high risk choice comparison, controls showed increased activity in the right lingual gyrus and right fusiform gyrus.

Table 56: Foci of significant brain activations in the high – low condition: comparison of non-pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CO-NPG							
Cingulate gyrus	30	R	13	31	-67	16	3.12
Middle temporal gyrus	21	R	15	52	-4	-15	3.26
Cerebellum		L	30	-45	-66	-35	3.11
		R	31	5	-66	-35	3.49

In the high – low comparison, controls showed higher activity in the right temporal gyrus compared to non-pathological gamblers. In the low – high risk choice comparison, non-pathological gamblers showed increased activity in the cingulate gyrus and cerebellum compared to controls. There were no voxels in the NPG – CO comparison that exceeded the threshold for statistical significance.

Table 57: Foci of significant brain activations in the high – low condition: comparison of substance abusers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
SA-CO							
Middle temporal gyrus	39/37	L	30	-38	-54	3	3.09
Lingual gyrus extending to cuneus	18/17	R	49	21	-75	1	3.47
Cerebellum extending to cuneus	18	L	220	-3	-66	-20	4.11
CO-SA							
Orbitofrontal cortex	11	R	21	24	40	-17	3.16
Superior frontal cortex	6	R	33	14	16	54	3.18
Postcentral gyrus	3	R	11	66	-12	26	3.28
Superior temporal gyrus	21	R	13	52	-4	-12	3.09

When given high risk vs. low risk choices, higher activity was measured in the left temporal cortex in addition to the left cuneus and left cerebellum in substance

abusers compared to controls. In the same comparison, controls showed higher activity in the right medial BA 6 and right temporal cortex.

When give low compared to high risk choices, controls showed higher activity in the right lingual gyrus, bilateral cuneus and left cerebellum.

Table 58: Foci of significant brain activations in the high – low condition: comparison of pathological gamblers and non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-NPG							
Posterior cingulate gyrus	31	R	35	31	-64	16	3.44
Lingual gyrus extending to fusiform gyrus	19/17	R	43	31	-71	1	3.14
Cerebellum		L	47	-21	-32	-25	3.39
NPG-PG							
Precentral gyrus	6	L	18	-17	-20	69	3.57

When given high risk vs. low risk choices, pathological gamblers showed significantly higher activity in the right lingual gyrus and fusiform gyrus. When given low compared to high risk choices, pathological gamblers show increased activity in the left precentral gyrus. In the same comparison, non-pathological gamblers show increased attention in the posterior cingulate gyrus compared to pathological gamblers.

Table 59: Foci of significant brain activations in the high – low condition: comparison of pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-SA							
Orbitofrontal cortex	47/11	R	29	49	40	-14	3.48
Middle frontal gyrus	6	R	18	52	6	48	3.57
	9	R	115	28	25	31	4.12
Superior temporal gyrus	38	L	61	-42	19	-22	3.62
SA-PG							
Precentral gyrus	6	L	26	-14	-17	69	3.39
Cuneus	18/19	L	63	0	-88	17	3.16

When given high vs. low risk choices, pathological gamblers showed increased activity in the right PFC including the DLPFC in addition to the left temporal cortex. In the same comparison, substance abusers showed increased activity in the left cuneus compared to pathological gamblers.

In the low – high risk comparison, pathological gamblers showed significantly higher activity in the left precentral gyrus. In the same comparison, substance abusers showed increased activity in the right lateral OFC compared to pathological gamblers.

Table 60: Foci of significant brain activations in the high – low condition: comparison of non-pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
SA-NPG							
Posterior cingulate cortex	31	R	28	31	-64	19	3.38
Cerebellum		L	48	-21	-28	-22	3.38

When given high vs. low risk choices, substance abusers showed significantly higher activity in the left cerebellum. In the low – high risk comparison, non-pathological gamblers showed increased activity in the posterior cingulate cortex compared to substance abusers.

Free – forced choice

Table 61: Foci of significant brain activations in the free - forced comparison taken from all groups.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free – forced							
Orbitofrontal cortex	11	L	30	-35	43	-14	3.11
Medial frontal gyrus extending to anterior cingulate cortex	10/32	L&R	57	-3	58	7	3.23
Middle temporal gyrus	21	L	39	-52	-1	-29	3.30
Cerebellum		R	39	49	-66	-26	3.58
Forced – free							
Inferior frontal gyrus	47/44	L	206	-35	14	3	3.28
Cingulate gyrus extending to precentral gyrus	32/6	L	311	-17	22	34	3.74
Superior temporal gyrus	41	L	90	-49	-34	8	3.27
Caudate nucleus extending to putamen		R	1205	17	8	25	3.85

When the data was cumulated from all groups, significantly higher activity was measured in the left lateral OFC, bilateral VMPFC, ACC, left temporal gyrus and right cerebellum when given free vs. forced choices.

When given forced compared to free choices, significantly higher activity was measured in the left inferior PFC, left precentral gyrus, cingulate gyrus, left temporal gyrus, right caudate nucleus and right putamen.

Table 62: Foci of significant brain activations in the free – forced comparison taken from pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Forced – free							
Precentral gyrus extending to medial frontal gyrus	4/6	R	463	45	-15	46	4.10
Postcentral gyrus	3	L	46	-35	-28	47	3.15
Middle temporal gyrus	21	L	25	-52	6	-18	3.27
	21	R	23	62	-4	-20	3.37
Fusiform gyrus	20	R	23	42	-38	-16	3.25
Thalamus		R	96	24	-23	11	3.41

When given forced opposed to free choices, pathological gamblers showed increased activity in the right dorso-medial frontal gyrus, right precentral gyrus, left postcentral gyrus, bilateral temporal gyrus, right fusiform gyrus and right thalamus. The free – forced comparison yielded no voxels that exceeded the threshold for statistical significance.

Table 63: Foci of significant brain activations in the free - forced comparison taken from non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free – forced							
Orbitofrontal cortex	11/10	R	50	45	44	-11	3.24
	11/47	L	114	-35	43	-14	3.45
Orbitofrontal cortex extending to medial frontal gyrus	10	L	89	-24	54	1	3.43
Precuneus	7	L	66	-17	-69	42	3.41
Middle temporal gyrus	38	L	49	-42	8	-36	4.04
Middle extending to superior temporal gyrus	38	R	22	38	5	-36	3.22
Fusiform gyrus	20	R	16	42	-38	-16	3.69
Cuneus	17	L	33	-7	-99	-1	3.49
Cerebellum		R	21	49	-66	-26	3.45
Forced – free							
Putamen extending to caudate nucleus		R	88	31	-13	10	3.21

When given free vs. forced choices, non-pathological gamblers showed higher activity in the bilateral OFC, left VMPFC, left precuneus and cuneus, right temporal cortex, right fusiform gyrus and right cerebellum.

Table 64: Foci of significant brain activations in the free – forced comparison taken from substance abusers.

There were no voxels from this comparison that exceeded the threshold for statistical significance.

Table 65: Foci of significant brain activations in the free – forced condition taken from controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Free – forced							
Superior extending to middle occipital gyrus	19	R	48	31	-80	27	3.12
Forced – free							
Middle frontal gyrus extending to precentral gyrus	6/3	L	77	-38	-1	48	3.12
Superior frontal gyrus	6	L	81	-17	13	51	3.87
Medial frontal gyrus	25	L	56	-7	6	-18	3.78
Postcentral gyrus	2	R	104	38	-29	30	3.69
Inferior parietal gyrus	40	L	55	-45	-42	34	3.09
	40	R	23	66	-39	28	3.31
Superior temporal gyrus	38	R	13	59	10	-9	3.45
Middle extending to superior frontal gyrus	21/38	L	23	-49	6	-15	3.16
Cingulate gyrus	24	R	45	14	11	25	3.63
Fusiform gyrus	20	R	32	42	-24	-13	3.17

When given free vs. forced choices, higher activity was measured in the right occipital gyrus in controls. In the forced – free comparison, higher activity was measured in the left PFC including the DLPFC, right cingulate gyrus, right postcentral gyrus, bilateral parietal gyrus, bilateral temporal gyrus, and right fusiform gyrus.

Table 66: Foci of significant brain activations in the free – forced condition: comparison of pathological gamblers and non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CO-PG							
Inferior frontal cortex	47	R	34	35	30	-10	3.14
Postcentral extending to precentral gyrus	40/3/4	R	63	38	-25	53	3.75
Fusiform gyrus	20	R	19	42	-38	-16	3.33
Cuneus	19	R	34	28	-80	30	3.46
Thalamus		R	17	3	0	10	3.25

When given free vs. forced choices, controls showed higher activity in the right cuneus compared to pathological gamblers. Pathological gamblers showed higher activity in the right precentral and postcentral gyrus compared to controls in the forced-free choice comparison. The PG-CO subtraction yielded no significant voxels.

Table 67: Foci of significant brain activations in the free – forced condition: comparison of non-pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-CO							
Orbitofrontal cortex	10	L	63	-24	54	1	3.25
	47	R	22	17	27	-13	3.44
Middle temporal gyrus	38/21	L	50	-38	8	-36	3.76
	38	R	26	38	5	-36	3.46
Superior extending to middle temporal gyrus	38/21	L	56	-49	9	-18	3.68
Cuneus	17	L	29	-7	-99	-1	3.30

When given free vs. forced choices, non-pathological gamblers showed significantly higher activity in the bilateral OFC, left temporal gyrus and left cuneus compared to controls. In the forced – free comparison, controls showed

increased activity in the left temporal gyrus compared to non-pathological gamblers. The CO-NPG subtraction did not yield any supra-threshold voxels.

Table 68: Foci of significant brain activations in the free – forced condition: comparison of substance abusers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
SA-CO							
Medial frontal gyrus	25	L	41	-7	6	-18	3.27
Cingulate gyrus	32	R	23	17	15	25	3.13
Postcentral gyrus	2	R	20	42	-26	30	3.21
Superior temporal gyrus	38	R	28	55	13	-9	3.67

In the free – forced choice comparison, substance abusers showed significantly higher activity in the right temporal gyrus. In the opposite (forced – free) comparison, controls showed higher activity in the posterior medial frontal gyrus (BA 25), cingulate gyrus, postcentral gyrus and right temporal cortex.

Table 69: Foci of significant brain activations in the free – forced condition: comparison of pathological and non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-PG							
Inferior frontal gyrus	47	L	100	-45	23	-16	3.43
Precuneus	7/19	L	61	-17	-69	45	3.26
Middle extending to inferior temporal gyrus	38/20	L	63	-42	8	-36	4.23
Middle extending to superior temporal gyrus	38	R	60	42	1	-38	3.55
Fusiform gyrus	20	R	28	42	-38	-16	4.58
Lingual gyrus extending to cuneus	18/17	L	28	-14	-99	-4	3.80

When given free compared to forced choices, non-pathological gamblers showed significantly higher activity in the left inferior PFC, bilateral temporal cortex, right fusiform gyrus, left precuneus and left visual cortex compared to non-pathological

gamblers. When given forced vs. free choices, pathological gamblers showed increased activity in the right fusiform gyrus. The PG-NPG comparison yielded no supra-threshold voxels.

Table 70: Foci of significant brain activations in the free – forced condition: comparison of pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
SA-PG							
Medial frontal gyrus	6	R	59	10	-21	46	3.71
Precentral gyrus	4	R	100	42	-14	52	4.01
Inferior temporal gyrus	20	R	25	62	-8	-20	3.40
Middle extending to inferior temporal gyrus	38/20	R	17	42	1	-38	3.10
Cerebellum		R	48	-7	-48	-12	3.18
Red nucleus		L	12	0	-21	-5	3.18

When presented with forced vs. free choices, pathological gamblers showed higher activity in medial BA 6, right precentral gyrus and right temporal cortex. The PG-SA subtraction yielded no voxels that met the threshold for statistical significance.

Table 71: Foci of significant brain activations in the free – forced condition: comparison of non-pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-SA							
Inferior parietal gyrus	40	L	19	-35	-42	47	3.13
Precuneus	31	L	12	-21	-38	57	3.11
Cuneus	17	L	28	-7	-99	-1	3.35
SA-NPG							
Cerebellum		R	40	10	-45	-18	3.69

In response to free vs. forced choices, non-pathological gamblers showed significantly higher activity in the left parietal cortex, precuneus and cuneus compared to substance abusers. In the forced – free comparison, non-pathological

gamblers expressed higher activity in the anterior lobe of the right cerebellum compared to substance abusers.

Discussion

The Iowa task was designed to explore decision-making in situations where the probability of a positive or negative hypothetical monetary outcome was not explicitly specified. Two versions of the Iowa task were used in this experiment, a behavioural version and a *f*MRI version. The behavioural task was based upon the standard Iowa task that has been used in previous research (e.g. Bechara et al., 1994). The *f*MRI version presented, in each trial, a choice from only two, out of four, decks. There were two comparisons; the high vs. low risk comparison investigated brain areas utilised in high risk and low risk choices and the free vs. forced choice comparison compared brain areas utilised in choices between a high risk vs. low risk deck to choices where both alternatives were high or low risk.

The behavioural Iowa task revealed no group differences in behaviour. Previous research found that pathological gamblers (Orford, 2005) and substance abusers (Dom et al., 2005) preferred the risky decks compared to controls with this strategy ultimately culminating in decreased monetary outcome. The results from this experiment indicated that the pathological gamblers and substance abusers did not show significantly different decision-making strategies compared to controls. One confound that has to be taken into account is the low sample sizes. Unfortunately, the program used to run the task repeatedly suffered from technical problems resulting in loss of data. Therefore, the results from this task only provide an indication of the behaviour exhibited by each group. However, the task does indicate that all groups learnt the contingencies of the decks to some degree and, as the task progressed, preferred to choose from the safer decks.

One interesting observation from the group behaviour from the behavioural Iowa task was the increased number of choices from the risky decks that occurred in the

final block of the task. This effect occurred in every group and was most pronounced in the controls. In the final block, decision-making strategies employed by the participants appeared to alter significantly from the tendency to choose from the safer decks to a tendency to prefer the risky decks. This behaviour seems contradictory seeing as all groups appeared to learn the contingencies of the tasks and adjust their behaviour accordingly to obtain increased winnings. This behaviour may have occurred due to a transient tendency to attenuate the potential negative aspects of losses and increase the value of potential gains. In other words, it may have reflected a 'get rich quick' approach where the potential negative consequences were largely ignored, which arguably was a poor strategy to employ. The task was fairly lengthy, usually taking approximately 17 minutes to complete. By the last section, participants may have experienced higher degrees of boredom thus prompting a temporary shift in decision-making strategy to include higher amounts of risk and excitement. Added to the fact that the rewards were hypothetical and therefore of relatively little value this shift in strategy may have been associated with relatively few negative consequences. In future tasks, a debrief questionnaire would be useful in order to probe participants about their decision-making strategies. In addition, a real rewards Iowa task could be created. Of course, this would mean that the rewards per trial would be very small. As has been shown in experiment 3, creating variants of tasks that provide small rewards appears to significantly alter behaviour when compared to performance of hypothetical tasks. However, a difference in behaviour may occur if playing for real rewards.

In the high vs. low risk choice comparison, when data from all groups was cumulated there was a significant increase in BOLD response in the bilateral thalamus and dorsal striatum when given high risk rather than low risk choices. Activity within the bilateral thalamus may reflect a higher physiological response that has been associated with the choice from the risky decks (Goudriaan et al., 2006). The dorsal striatum has been linked to the formation of predictions utilised in instrumental learning. Previous studies have found that structures within the

dorsal striatum are active during the creation of stimulus-response outcomes (O'Doherty, 2004). Structures of the dorsal striatum have previously been found to be active in controls when performing the Iowa task (Krain et al., 2006), which has been linked to the learning of contingencies between stimuli and outcomes. In addition to the creation of stimulus-reponse rules, it has been posited that the dorsal striatum has a major role in maintaining information about stimuli on-line in order to improve current decision-making frameworks (O'Doherty et al., 2004). In this research, the activity of the dorsal striatum may be linked to the maintenance of the learned expectation that the selection of a high risk deck may lead to a highly salient punishing outcome.

The pathological gamblers showed higher VMPFC activity, in addition to bilateral thalamus activity, when given high risk compared to low risk choices. Only the controls showed similar bilateral thalamus activity suggesting neural activity in this area did not differ in pathological gamblers. Compared to controls, pathological gamblers showed higher activity in the left lateral PFC when given high risk vs. low risk choices. This provides further evidence abnormal prefrontal function in pathological gamblers. Another area in which differences were noted between gamblers and controls was the middle temporal gyrus. Controls exhibited higher BOLD signal in this area on the high-low contrast compared to both groups of gamblers. The temporal cortex has reliably been associated with memory and patients with damage to the temporal lobe associated with amnesia show severely impaired behaviour on the Iowa task, in fact they perform at chance level, and exhibit no anticipatory skin conductance response when choosing high risk choices (Gutbrod et al., 2006). This impairment has been linked to a deficit in explicit memory which impairs capability for reversal learning. One could conclude that, in this project, this finding suggests that the gamblers exhibited significantly impaired function within the temporal cortex when faced with high risk choices, which may be linked to abnormalities in reversal learning. However, choice behaviour on the behavioural task did not differ significantly between groups suggesting that although the gambling groups may present deficits in brain function in areas

involved in reversal learning, this did not impair behavioural output. This could be taken as evidence that these groups utilise altered neural mechanisms compared to controls when faced with high risk decisions.

Substance abusers, another group to show altered decision-making on this task in previous research, showed higher OFC activity in the low risk compared to the high risk choices in a similar way to controls. This is contrary to previous studies that have found impaired OFC function in substance abusers when performing this task (Dom et al., 2005). The discrepancy in results may reflect the type of task utilised in this research. This task provided cues as to the contingencies of the decks. In addition, participants completed a behavioural Iowa task previous to performing the fMRI task. This would have significantly decreased the amount of learning needed to learn the contingencies of the decks in the fMRI Iowa task. Decreases in OFC function found in previous studies may be linked to deficicts in reversal learning rather than impairments in risk processing.

Non-pathological gamblers did not show significant differences in the pattern of brain activity used in high or low risk choices although high risk choices did activate more the precentral and postcentral gyrus. Non-pathological gamblers did show higher activity in the posterior cingulate compared to pathological gamblers, which may be indicative of increased calculation of reward probabilities by non-pathological gamblers. Except this difference, there were no other major differences in the activation patterns of pathological and non-pathological gamblers.

When data from all groups was cumulated in the free vs. forced choice comparison, higher PFC activity was measured in the free choices vs. forced choices, especially in the VMPFC, OFC and ACC. This could have reflected the increased level of stimulus processing when choosing between a high and low risk choice as opposed to two alternatives that are both high or low risk.

Compared to controls, pathological gamblers and substance abusers did not show any significant difference in BOLD signal in areas of the brain laid out in our hypotheses. However, an increase in OFC activity was measured in non-pathological gamblers compared to controls.

Conclusions

No group showed significantly altered decision-making strategies on the standard Iowa task despite previous research that has suggested the contrary. However, due to the small sample sizes these effects can only be seen as showing indications. No group showed significant differences in BOLD signal in hypothesised areas compared to controls on the *f*MRI version. In fact, pathological gamblers showed increased VMPFC and thalamic activation to high risk choices possibly indicating higher affective response to the high risk choices. Pathological gamblers also tended to show slightly elevated PFC response to high risk choices compared to controls. In another condition, non-pathological gamblers showed elevated OFC response compared to gamblers. However, differences in temporal function were measured between controls and both groups of gamblers. These results suggest that in choice situations where probabilities of winning and not winning are not obvious, and where learning takes place, although pathological gamblers and substance abusers can utilise decision-making strategies that are comparable to controls, the gamblers especially, may be utilising altered neural mechanisms to make these choices.

Go/no-go task

Go – No-go responses

There were no group differences in performance on the go-no/go task, $F(3.41) = 0.44$, $p = .73$.

Table 72: Foci of significant brain activations in the Go – No-go condition: data from all groups.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Go – No-go							
Orbitofrontal cortex	11/47	L	149	-3	37	-11	4.64
Inferior frontal gyrus	46	L	40	-49	31	8	3.66
Medial frontal gyrus	8	L	62	-24	29	37	4.34
Paracentral lobe	5	L	15	-21	-38	50	3.23
Cingulate gyrus	24	L	22	-10	1	26	3.90
Hippocampus extending to medial frontal gyrus	6	R	3115	28	-31	-4	6.12

The Go – No-go subtraction yielded widespread activity in the prefrontal cortex including the left medial OFC and left DLPFC. In addition, the cingulate gyrus and hippocampus showed significant activity.

Table 73: Foci of significant brain activations in the Go – No-go condition in pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Go – No-go							
Medial frontal gyrus	9	L	17	-31	19	35	3.48
Medial frontal gyrus extending to cingulate gyrus	6/24	L	103	-3	-1	48	3.93
Cingulate gyrus	24	L	13	-24	2	35	3.16
Precentral extending to postcentral gyrus	6/1	L	65	-59	1	29	3.49
Postcentral gyrus	4	L	14	-38	-18	43	3.24
Insula extending to precentral gyrus	4	R	229	31	-2	19	4.54
Medial temporal gyrus	21	R	22	38	2	-27	3.63
	21	L	52	-38	-41	2	3.41
Lingual gyrus	19	R	80	28	-61	0	3.67
Parahippocampal gyrus including hippocampus		R	40	28	-34	-4	3.73
Thalamus		R	20	3	-4	-3	3.10
Pons		L	30	-10	-29	-37	4.19

Pathological gamblers showed significantly increased activity in the left prefrontal cortex including the DLPFC. Other areas showing high activity were the cingulate cortex (dorsal BA24), left precentral and postcentral gyri, right insula, bilateral temporal gyri including right lingual gyri, right hippocampus and thalamus, and the pons.

Table 74: Foci of significant brain activations in the Go – No-go condition in non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Go – No-go							
Inferior frontal gyrus	47	R	32	45	24	2	3.41
Anterior cingulate cortex extending to orbitofrontal cortex	32/11	L	111	-7	34	-8	4.24
Medial frontal gyrus extending to precentral gyrus	6/4	L	230	0	-8	49	4.00
Precentral gyrus	4/6	L	63	-38	-14	52	3.27
Superior temporal gyrus	38/22	L	195	-35	3	-15	3.74
Superior temporal gyrus extending to inferior frontal gyrus	22/21/44	R	262	62	-17	1	3.50
Hippocampus extending to parahippocampal gyrus	35/36	R	111	28	-31	-4	3.61

There was a high amount of activity in bilateral prefrontal areas including the left medial OFC in addition to the anterior cingulate cortex. Increased activity was also measured in the bilateral temporal gyrus and right parahippocampal gyrus including the hippocampus.

Table 75: Foci of significant brain activations in the Go – No-go condition in substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Go – No-go							
Orbitofrontal cortex	11	L & R	28	-1	30	-13	3.12
Precentral gyrus	6	L	14	-35	-17	65	3.82
Posterior cingulate gyrus	31/30/23	L	100	-7	-57	25	3.46
Parahippocampal gyrus	30/35/19	L	137	-10	-37	-1	3.77
	35	R	58	17	-38	-7	3.75
Insula		L	17	-35	-16	20	3.13

Substance abusers showed moderate activity in the prefrontal cortex. Increased activity was measured in the bilateral OFC and left precentral gyrus. Increased activity was also noted in some posterior regions of the brain including the posterior cingulate cortex, left posterior insula and bilateral parahippocampal gyri.

Table 76: Foci of significant brain activations in the Go – No-go condition in controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
Go – No-go							
Orbitofrontal cortex	11	R	11	28	37	-2	3.30
Precentral gyrus	6/4	L	122	-35	-14	62	4.51
	6	R	14	38	-1	42	3.13
Precentral gyrus extending to insula	6	R	281	49	-13	10	3.97
	6	L	400	-55	-3	7	4.55
Postcentral gyrus	1	R	43	52	-18	43	4.01
	3/4	L	21	-21	-32	47	3.41
Posterior cingulate gyrus	31	R	42	24	-29	37	4.55
	31	R	83	21	-53	25	3.53
	30	L	60	-17	-47	15	4.09
Inferior occipital gyrus	19	L	18	-31	-75	-2	3.37
Caudate nucleus		L	51	-17	-12	30	3.57
Uncus	34	L	155	-10	-8	-23	4.20
Cerebellum		R	417	17	-48	-9	4.52

Significant activity was reported in the right OFC and bilateral precentral and postcentral gyri in controls. Increased activity was also reported in posterior regions including the bilateral posterior cingulate gyrus, left occipital cortex, left uncus and right cerebellum. The left caudate nucleus also showed increased activity.

Table 77: Foci of significant brain activations in the Go – No-go condition: Comparison of pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-CO							
Medial frontal gyrus	9	R	37	10	42	33	3.20
Precentral extending to postcentral gyrus	4	R	28	38	-15	46	3.30
Cerebellum		L	10	-28	-60	-38	3.41
Medulla oblongata		L	22	-10	-29	-37	3.94
CO-PG							
Superior frontal gyrus extending to precentral gyrus	6/4	L	67	-31	-7	65	3.52
Paracentral lobe	7	L	57	0	-35	57	3.33
Lingual gyrus extending to cuneus	18/17	R	61	18	-89	-10	3.94
Medial temporal gyrus	39	R	35	55	-67	16	3.39
Insula		L	34	-42	-7	4	3.33
Cerebellum		L	227	-17	-38	-10	3.97
		R	27	38	-49	-24	3.62

In the go – no-go subtraction, pathological gamblers showed increased activity in the precentral and postcentral gyri and left brainstem.

In the go – no-go subtraction, controls had increased activity in the left superior frontal gyrus and prefrontal gyrus in addition to the left insula and cerebellum compared to pathological gamblers. In the no-go – go subtraction, controls reported higher activity in the right VMPFC compared to pathological gamblers.

Table 78: Foci of significant brain activations in the Go – No-go condition: Comparison of non-pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-CO							
Inferior extending to medial frontal gyrus	45/46	R	41	59	21	12	3.28
Anterior cingulate cortex	32	L	216	-7	34	-8	3.83
CO-NPG							
Inferior parietal gyrus	40	L	31	-59	-45	44	3.29

In the go – no-go subtraction, non-pathological gamblers had increased activity within the right lateral prefrontal cortex and left anterior cingulate cortex. In the no-go – go subtraction, non-pathological gamblers showed higher activity in the left parietal cortex compared to controls.

Table 79: Foci of significant brain activations in the Go – No-go condition: Comparison of substance abusers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CO-SA							
Inferior frontal gyrus	47	L	26	-21	17	-10	3.47
Cingulate gyrus extending to thalamus	24	L	62	-10	-12	30	3.26
Postcentral gyrus	2/3	R	32	28	-29	37	3.94
Superior temporal gyrus	22	L	104	-55	0	6	4.42
Lingual gyrus	18	R	18	17	-89	-10	3.27
Lingual gyrus extending to cuneus	18/17	L	52	-7	-86	-10	3.27
Uncus	20	L	100	-28	-5	-35	3.83
Cerebellum		R	18	24	-46	-33	3.32

The SA-CO yielded no voxels that were above threshold for statistical significance. In the Go – No-go subtraction, controls showed higher activity in the cingulate gyrus, right postcentral gyrus, left temporal gyrus, right lingual gyrus, left thalamus

and left uncus. Substance abusers, compared to controls, showed higher activity in the left inferior frontal gyrus, left lingual gyrus, cuneus, and right cerebellum when given no-go compared to go trials.

Table 80: Foci of significant brain activations in the Go – No-go condition: Comparison of pathological and non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-NPG							
Insula		R	12	31	-2	19	3.09
NPG-PG							
Inferior frontal gyrus	45/46	R	63	45	24	2	3.70
Precentral gyrus extending to paracentral lobe	6/4/5	L	303	-24	-24	66	3.57
Medial temporal gyrus	21	R	15	52	-21	-8	3.09
Cuneus	17	R	21	7	-95	5	3.10
Lingual gyrus	18	R	18	14	-89	-10	3.25
Thalamus		L	32	-3	-24	1	3.52
Cerebellum		L	48	-31	-72	-17	3.13

When given go compared to no-go conditions, pathological gamblers showed increased activity in the right anterior insula. This was the only cluster showing a significant difference in this subtraction. Non-pathological gamblers, compared to pathological gamblers, showed increased activity in frontal and posterior regions including the right inferior frontal gyrus, precentral gyrus, paracentral lobe, right temporal gyrus and right cuneus. In the reverse comparison (no-go – go), higher activity was measured in ventral areas including the lingual gyrus, left cerebellum and left thalamus in pathological gamblers.

Table 81: Foci of significant brain activations in the Go – No-go condition: Comparison of pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-SA							
Medial frontal gyrus extending to cingulate cortex	6/24	R	68	-3	-1	48	3.36
Postcentral gyrus	2/40	R	172	42	-22	30	3.85
Middle temporal gyrus	37	L	24	-42	-44	-4	3.43
SA-PG							
Posterior cingulate cortex	31	L	19	-24	-47	22	3.44
Middle extending to inferior temporal gyrus	21	L	25	-55	2	-21	3.10
Cerebellum		L	106	-17	-38	-7	3.81

In the go – no-go subtraction, pathological gamblers showed higher activation in the dorsal medial frontal gyrus, cingulate cortex, postcentral gyrus and left temporal gyrus. In the no-go – go subtraction, pathological gamblers showed increased activation in the left temporal gyrus.

In the go – no-go subtraction, substance abusers showed higher activation in the posterior cingulate cortex and left cerebellum compared to pathological gamblers.

Table 82: Foci of significant brain activations in the Go – No-go condition: Comparison of non-pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-SA							
Medial frontal gyrus	10	R	70	38	54	-3	3.23
Medial frontal gyrus extending to cingulate gyrus	6/24/31	R	131	3	6	61	3.37
Inferior frontal gyrus	47	R	49	45	24	-1	3.31
	47	L	27	-21	24	-4	3.32
Precentral gyrus	6	R	24	52	-12	36	3.09
Anterior cingulate cortex	32	L	22	-3	34	-5	3.56
Superior temporal gyrus	22/42	L	133	-59	-3	7	3.85
Cuneus	17	R	101	7	-95	8	3.22

The SA-NPG subtraction yielded no voxels that were above the threshold for statistical significance. In the go – no-go subtraction, non-pathological gamblers showed higher activity in the right inferior frontal gyrus, anterior cingulate cortex, precentral gyrus and left temporal gyrus compared to substance abusers. There was also a significant difference in activation in the right lateral OFC between groups.

Discussion

The go/no-go task was designed to assess brain areas involved in behavioural inhibition. When the results were collated across groups there was found to be wide activation of the prefrontal cortex when given go compared to no-go trials, especially in the OFC and DLPFC, two areas involved in inhibitory control, decision-making and cognitive processing.

All groups showed high activation of the OFC in this task except the pathological gamblers. This may be indicative of a possible impairment in OFC function in pathological gamblers associated with inhibitory control. Compared to controls, pathological gamblers did show significantly lower OFC function but in the no-go – go subtraction. This is, again, suggestive of a possible impairment in OFC

function in pathological gamblers. However, in this task and in the stop task from study 3 there were no significant performance differences between pathological gamblers and controls. Therefore, if the results from the go/no-go task do reflect a functional impairment then it does not appear to affect their level of inhibitory control in a significant way.

It could be hypothesised that substance abusers would show decreased BOLD signal in areas posited to be involved in inhibitory control compared to controls. No area previously associated with inhibitory control was found to differ in BOLD signal between these groups, suggesting that this group of substance abusers did not show any noticeable abnormalities in brain areas involved in inhibitory control. In contrast to this hypothesis, substance abusers exhibited significantly increased signal within the inferior frontal gyrus compared to controls, a region previously posited to be involved in response inhibition. This increase in function may be related to a masking effect whereby increased function is necessary to alter behavioural output to a level comparable to that of controls.

Considering the continuum theory, non-pathological gamblers showed higher activation in a number of areas compared to pathological gamblers including the right inferior frontal gyrus. However, non-pathological gamblers also showed higher activity in a number of areas compared to controls including the right lateral prefrontal cortex and anterior cingulate cortex. Increased ACC activity in non-pathological gamblers may indicate increased action monitoring in this group. This evidence runs counter to the continuum theory.

Interestingly, the two gambling groups showed increased activity in the hippocampus while the substance abusers and controls did not. This may be indicative of a circuit that is preferentially active in gamblers and not in non-gamblers. The hippocampus is purported to be involved in memory consolidation and instrumental learning. Activation in the pathological groups may reflect a hyper-activation of memory circuits in these groups.

One possible criticism of this task concerns the construction of the different blocks. There were four blocks that contained 26 go trials and four blocks that contained 13 go trials and 13 stop trials. These two blocks created the go and no-go blocks respectively. Due to the construction of the no-go blocks, the inclusion of 13 go trials may have diluted the possible effects measured on these trials. Future tasks could utilise an event related design but, if this method is used, care must be taken to ensure enough no-go trials were present.

Conclusions

No group showed major differences in BOLD signal in hypothesised areas compared to controls although pathological gamblers showed some hypo-function of the VMPFC. Non-pathological gamblers tended to show the highest amounts of activation especially in the anterior cingulate cortex. These differences were not related to behavioural performance on the go/no-go or stop task.

Urge to Gamble task

The ratings from each group were compared to investigate whether there were any group differences in reaction to the stimuli. In the casino gambling condition, there was a significant main effect of group when questioned about urge to gamble, $F(3,38) = 7.51$, $p = .001$, and excitability, $F(3,38) = 6.85$, $p = .001$. Post-hoc testing was performed using Tukey's HSD test. In ratings of urge to gamble, non-pathological gamblers had significantly higher scores compared to substance abusers, $p = .001$, and controls, $p = .001$. For ratings of excitability non-pathological gamblers reported higher scores than controls, $p = .02$. Pathological, $p = .02$, and non-pathological gamblers, $p = .002$, also reported significantly higher excitability scores compared to substance abusers. There were no significant group effects in the neutral condition.

In the horse gambling condition there was a group effect when questioned about urge to gamble, $F(3,40) = 5.62$, $p = .003$. In post-hoc testing, pathological gamblers, $p = .04$, and non-pathological gamblers, $p = .02$, reported higher scores than controls. Non-pathological gamblers also had higher scores compared to substance abusers, $p = .02$. There were no significant group effects in the neutral condition.

In the internet gambling condition there was a significant group effect on ratings of urge to gamble, $F(3,40) = 7.67$, $p < .001$, and excitability, $F(3,40) = 8.62$, $p < .001$. Post-hoc testing revealed that, for ratings of urge to gamble, pathological gamblers, $p = .01$, and non-pathological gamblers, $p = .002$, reported higher ratings compared to controls. In addition, pathological gamblers, $p = .04$, and non-pathological gamblers, $p = .008$, reported higher scores compared to substance abusers. For ratings of excitability, pathological, $p = .03$, and non-pathological gamblers, $p = .001$, reported higher ratings than controls. Pathological gamblers, $p = .03$, and non-pathological gamblers, $p = .001$, also scored higher than substance abusers. In the neutral condition, there were no significant effects.

Gambling – Neutral stimuli (GAMB – NEUT)

For this condition neurological activity from the CG, HG and IG stimuli were grouped and compared to the group effects of the CN, HN and IN stimuli. The activations measured when the data were collated for all groups is not given as it would combine data from groups who are very sensitive and extremely insensitive to the stimuli, thus the combined data was thought not to provide useful information.

Table 83: Foci of significant brain activations in the GAMB-NEUT condition in pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
GAMB - NEUT							
Orbitofrontal cortex	45/47	R	34	52	34	-2	3.14
Claustrum		R	19	28	20	-1	3.22
Insula		L	12	-35	-3	16	3.28
NEUT - GAMB							
Postcentral gyrus	3	R	121	10	-31	66	3.22

In the GAMB-NEUT contrast, pathological gamblers showed increased activation in the right lateral OFC, right claustum and left insula. In the NEUT-GAMB contrast, increased activation was measured in the postcentral gyrus.

Table 84: Foci of significant brain activations in the GAMB-NEUT condition in non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
GAMB - NEUT							
Inferior frontal gyrus	44/45	R	22	49	24	5	3.23
Superior frontal gyrus	6	L	29	-1	-7	68	3.19
Cerebellum		L	32	-7	-63	-32	3.53
		R	23	3	-38	-22	3.44
NEUT - GAMB							
Medial frontal gyrus	8	R	18	3	26	41	3.20
Precentral gyrus	6	L	29	-49	-10	13	3.64
Inferior parietal lobe	40	L	10	-55	-29	27	3.16

In the GAMB-NEUT contrast, non-pathological gamblers showed activity in the right inferior frontal gyrus and left dorso-medial frontal gyrus (posterior BA 6). Activation was also measured in the anterior lobe of the right cerebellum and posterior lobe of the left cerebellum. In the NEUT-GAMB subtraction, increased activation was reported in the right dorso-medial frontal gyrus, left precentral gyrus and inferior parietal lobe.

Table 85: Foci of significant brain activations in the GAMB-NEUT condition in substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
GAMB - NEUT							
Cerebellum		R	15	14	-52	-27	3.36
NEUT - GAMB							
Superior frontal gyrus extending to medial frontal gyrus	8/9	R	99	3	36	43	3.61
Inferior frontal gyrus extending to medial frontal gyrus	44/9/8	R	38	55	4	16	3.28
Medial frontal gyrus	6	R	17	45	2	48	3.11
Precentral gyrus extending to medial frontal gyrus	4/6	R	138	35	-18	52	3.92
Precental gyrus	4	L	10	-42	-15	39	3.75
Cingulate gyrus	32	L	10	-7	18	28	3.60
Cingulate gyrus extending to medial frontal gyrus	24/6	R	31	14	-1	45	3.53
Posterior cingulate	30/23/31	R	59	3	-50	15	3.39
Thalamus		R	21	21	-20	4	3.63
Uncus including amygdala extending into fusiform gyrus	20	R	48	31	-8	-29	3.24
Uncus	20	L	63	-31	-5	-35	3.30

In the GAMB-NEUT subtraction, substance abusers showed activation only in the right cerebellum. In the NEUT-GAMB, widespread activity was seen in the right frontal cortex including the VMPFC and DLPFC in addition to bilateral cingulate cortex. Increased activity was also reported in the right thalamus, right amygdala and bilateral uncus.

Table 86: Foci of significant brain activations in the GAMB-NEUT condition in controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
GAMB - NEUT							
Orbitofrontal cortex	11	L	10	-7	47	-11	3.14
Precentral gyrus	6	L	11	-42	-2	26	3.09
Postcentral gyrus	2	R	76	49	-19	33	4.42
Insula		R	67	35	4	19	3.95
Uncus		L	26	-21	-4	-25	3.87
NEUT – GAMB							
Cuneus	17	R	16	17	-92	5	3.30
	17/18	L	22	-14	-78	-5	3.10
Caudate nucleus		R	24	14	-2	23	3.29

In response to gambling vs. neutral stimuli, controls showed higher activation in the left medial OFC, precentral gyrus, postcentral gyrus, anterior insula and uncus. When given neutral vs. gambling stimuli, higher activation was measured in the bilateral cuneus and right caudate nucleus.

Table 87: Foci of significant brain activations in the GAMB-NEUT condition: Comparison of pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-CO							
Insula		L	20	-38	-9	17	3.30
CO-PG							
Medial frontal cortex, extending to cingulate gyrus	6/24	R	39	17	-5	39	3.34
Postcentral Gyrus	2/3/5	R	115	14	-37	70	3.28

In response to gambling vs. neutral stimuli, pathological gamblers showed higher activation in right insula compared to controls. In the NEUT-GAMB comparison, pathological gamblers showed increased activation in the right postcentral gyrus, cingulate cortex and dorso-medial frontal cortex compared to controls.

Table 88: Foci of significant brain activations in the GAMB-NEUT condition: Comparison of non-pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-CO							
Cerebellum		L	15	-7	-63	-32	3.40
CO-NPG							
Superior frontal gyrus	9	R	26	38	35	27	3.26
Precentral gyrus	6	L	32	-42	2	32	3.30
	4	L	10	-14	-31	63	3.81
Inferior parietal gyrus	40	L	16	-55	-29	27	3.11
Cingulate gyrus		R	24	17	5	42	3.35
Midbrain, red nucleus		L	12	0	-24	-11	3.09

Non-pathological gamblers showed increased activation in the left cerebellum when presented with gambling stimuli compared to neutral stimuli. Significant differences in activity in the right dorsolateral prefrontal cortex, left inferior parietal cortex, right cingulate gyrus, left precentral gyrus and left red nucleus located within the midbrain were also measured.

Table 89: Foci of significant brain activations in the GAMB-NEUT condition: Comparison of substance abusers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CO-SA							
Inferior frontal gyrus extending to medial frontal gyrus	44/6/9	R	91	55	4	19	3.52
Medial frontal gyrus	8/9	R	57	10	36	37	3.41
Orbitofrontal cortex	11	R	19	35	40	-14	3.13
Postcentral gyrus	4/3/2	R	189	35	-21	46	4.07
	4	L	15	-42	-18	40	3.80
Superior parietal lobe	7	R	22	17	-62	61	3.32
Cingulate gyrus	24	R	43	14	-1	45	3.54
Posterior cingulate	29/30	R	63	7	-40	18	3.43
Hippocampus extending to parahippocampal gyrus	36	L	37	-31	-11	-23	3.16
Amygdala extending into uncus	28	R	102	28	-4	-20	3.54
Midbrain			30	0	-25	-19	3.66

In the SA-CO subtraction, there were no supra-threshold voxels. When given gambling compared to neutral stimuli, controls showed higher activation in the right postcentral gyrus and left hippocampus and parahippocampal gyrus compared to substance abusers. When presented with neutral compared with gambling stimuli, substance abusers showed higher activation in the right inferior prefrontal cortex and VMPFC in addition to the postcentral gyrus, right cingulate and posterior cingulate gyrus, left hippocampus and parahippocampal gyrus, right amygdala, right uncus and the midbrain.

Table 90: Foci of significant brain activations in the GAMB-NEUT condition: Comparison of pathological and non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-NPG							
Inferior parietal lobe	40	R	26	53	-46	28	3.42
	40/43	L	25	-55	-29	27	3.23
Caudate nucleus		L	18	-3	7	6	3.26
Insula		L	35	-45	-3	13	3.29
Cerebellum		R	17	21	-73	-38	3.30
NPG-PG							
Medial frontal gyrus	6	L	120	-3	-10	65	3.33
Cerebellum		R	76	7	-38	-22	3.87
		L	31	-7	-63	-32	3.76

When given gambling opposed to neutral stimuli, pathological gamblers (compared to non-pathological gamblers) showed increased activation in the left caudate nucleus. When given gambling compared to neutral stimuli non-pathological gamblers showed increased activation in the right cerebellum compared to pathological gamblers. When given neutral stimuli opposed to gambling stimuli, pathological gamblers showed higher activation in the left medial frontal gyrus and bilateral cerebellum compared to non-pathological gamblers.

Table 91: Foci of significant brain activations in the GAMB-NEUT condition: Comparison of pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-SA							
Medial frontal gyrus extending to superior frontal gyrus	9/10	R	27	14	45	24	3.45
Inferior frontal gyrus	44	R	22	55	4	16	4.02
	45	R	21	45	18	12	3.21
Inferior parietal lobe	40	R	26	55	-33	27	3.16
Lingual gyrus	18	L	31	-3	-68	3	3.46
Cingulate gyrus	24	L	42	-3	15	28	3.62
Cingulate gyrus extending into precuneus	31/7	R	53	21	-47	22	3.25
Insula		L	11	-31	29	9	3.23

In the GAMB-NEUT subtraction, pathological gamblers showed higher activation in the right VMPFC, right inferior parietal gyrus and left cingulate gyrus. In the NEUT-GAMB subtraction, substance abusers showed significantly higher activation in the left lingual gyrus. There were no voxels that met statistical significance in the SA-PG subtraction.

Table 92: Foci of significant brain activations in the GAMB-NEUT condition: Comparison of non-pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-SA							
Inferior frontal gyrus	45	R	32	45	18	12	3.79
	44	R	25	55	4	16	3.78
Orbitofrontal cortex	47	R	12	49	33	-11	3.43
Medial frontal gyrus	6	L	45	-3	14	62	3.30
Thalamus		R	23	21	-20	-2	3.31
Cerebellum		L	23	-7	-63	-32	3.4
		R	66	14	-28	-16	3.28
SA-NPG							
Precentral gyrus	6	L	14	-49	-10	10	3.15

In the GAMB-NEUT subtraction, non-pathological gamblers showed significantly higher activation in the right inferior frontal gyrus (BA 45) and left dorso-medial frontal gyrus (BA 6). In the NEUT-GAMB subtraction, non-pathological gamblers reported significantly higher activation in the left precentral gyrus. In the NEUT-GAMB subtraction, substance abusers (compared to non-pathological gamblers) reported significantly higher activation in the right inferior frontal gyrus (BA 44) and right thalamus.

Casino Gambling – Neutral condition (CG-CN)

Table 93: Foci of significant brain activations in the CG-CN condition in pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CG-CN							
Inferior frontal gyrus	9/47/44	R	202	55	17	9	3.64
Caudate nucleus extending to cingulate cortex	32	L	214	-7	11	12	3.39
Insula		L	23	-35	21	5	3.13
Inferior occipital gyrus	18	L	10	-35	-85	-2	3.12

In the CG-CN subtraction, pathological gamblers showed increased activity in the right inferior frontal gyrus, left caudate nucleus and insula. There were no voxels in the CN-CG subtraction that reached statistical significance.

Table 94: Foci of significant brain activations in the CG-CN condition in non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CG-CN							
Inferior occipital gyrus extending to medial occipital gyrus	18/17	L	80	-35	-89	-4	4.01

In the CG-CN subtraction, the only areas that reached statistical significance for showing activation were the inferior and medial occipital gyrus. There were no voxels in the CN-CG comparison that reached statistical significance.

Table 95: Foci of significant brain activations in the CG-CN condition in substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CG-CN							
Transverse temporal gyrus extending into superior temporal gyrus	41/22	L	44	-45	-27	11	3.77
CN-CG							
Superior frontal gyrus	10	R	13	28	45	17	3.2
Inferior frontal gyrus	47	L	19	-38	27	-1	3.77
	45	R	12	59	21	5	3.45
Cingulate gyrus extending to medial frontal gyrus	32/9	R	124	17	22	31	4.79
Precentral gyrus extending to superior frontal gyrus	4/6	R	63	35	-18	49	3.52
Uncus including amygdala	20	R	17	31	-1	-23	3.47
Middle temporal gyrus	37/39/19	L	36	-35	-57	16	3.14
Left cerebellum		L	36	-10	-63	-32	3.35
		L	12	-17	-76	-29	3.32

In the CG-CN subtraction, substance abusers showed significant levels of activation only in the transverse and superior temporal gyrus. In the CN-CG subtraction, there was significant activation in the right superior temporal gyrus, cingulate gyrus and bilateral inferior prefrontal cortex. In addition, the right uncus, amygdala and left cerebellum showed an increase in activity.

Table 96: Foci of significant brain activations in the CG-CN condition in controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CG-CN							
Orbitofrontal cortex	10	L	36	-7	44	-11	3.18
	47	L	22	-38	40	-8	3.45
Middle frontal gyrus extending to precentral gyrus	9/8	R	16	38	29	28	3.11
Precentral gyrus	4	R	28	14	-27	72	3.71
	6	R	20	31	5	22	3.5
Postcentral gyrus	3/5	L	134	-14	-34	66	4.31
Superior temporal gyrus extending into inferior parietal gyrus	39/40	L	53	-45	-53	28	3.84
Medial temporal gyrus	21	L	18	-59	-54	0	3.65
	21	L	12	-52	-1	-26	3.24
	21	R	17	52	6	-18	3.40
Medial occipital gyrus	19	R	12	55	-61	-6	3.39
Fusiform gyrus	37	R	64	35	-51	-6	3.47
Paracentral lobe extending into cingulate gyrus and thalamus	31/23	L	97	-1	-28	43	3.48
Hippocampus extending into amygdala		L	63	-31	-15	-23	3.26
Cerebellum		L	90	-38	-55	-18	3.27
CN-CG							
Inferior parietal gyrus	40	R	17	66	-23	24	3.54
Cerebellum		R	25	14	-66	-20	3.76

In the CG-CN, controls showed significant activation in the left medial and lateral OFC in addition to the right DLPFC. Activation was also reported in the precentral and postcentral gyrus, bilateral temporal gyrus, fusiform gyrus, left thalamus, hippocampus and anterior and posterior lobe of the right cerebellum. In the CN-CG comparison, increased activation was reported in the right posterior lobe of the cerebellum.

Table 97: Foci of significant brain activations in the CG-CN condition: Comparison of pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-CO							
Inferior frontal gyrus	45	R	97	62	17	2	4.46
Insula		R	31	45	3	0	4.14
		L	39	-42	-6	7	3.36
Caudate nucleus		L	51	-7	11	12	3.57
CO-PG							
Postcentral gyrus	3/5/7	L	34	-21	-47	70	3.54
Middle temporal gyrus	21	L	49	-55	-51	-3	3.50

In the CG-CN subtraction, pathological gamblers reported increased activity in the right lateral inferior frontal gyrus, bilateral insula and caudate nucleus. In the same subtraction, controls showed higher activity in the left postcentral gyrus and left temporal cortex.

In the CN-CG subtraction, pathological gamblers showed increased activation in the left temporal cortex compared to controls.

Table 98: Foci of significant brain activations in the CG-CN condition: Comparison of non-pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CO-NPG							
Postcentral gyrus	3	L	12	-35	-19	30	3.52
Insula		L	46	-35	-46	25	3.48

The NPG-CO subtraction yielded no supra-threshold voxels. In the CG-CN subtraction, controls showed increased activation in the left posterior insula compared to non-pathological gamblers.

Table 99: Foci of significant brain activations in the CG-CN condition: Comparison of substance abusers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CO-SA							
Orbitofrontal cortex	11	R	27	35	37	-14	3.45
	11	L	58	-1	40	-14	3.21
Superior frontal gyrus extending to medial frontal gyrus	10/9	R	44	28	45	24	3.76
Inferior frontal gyrus extending through medial frontal gyrus	10/47	L	156	-28	44	4	3.65
Medial frontal gyrus extending to cingulate gyrus	9/32	R	133	14	36	30	4.37
Postcentral gyrus extending to precentral gyrus	3/4	R	66	35	-21	46	3.89
Middle temporal gyrus	21	R	72	52	12	-30	3.48
Superior temporal gyrus	38	L	13	-42	19	-25	3.11
Middle temporal gyrus extending to inferior parietal gyrus	39/40	L	107	-35	-53	25	3.50
Precuneus	7	L	16	-3	-69	49	3.27
Uncus	28	R	30	21	2	-30	3.64
Cerebellum		L	57	-21	-56	-38	3.77
		R	31	24	-76	-17	3.48
Midbrain extending through substantia nigra		R	20	3	-21	-17	3.34

The SA-CO subtraction yielded no supra-threshold voxels. Following the CG-CN comparison, controls showed higher activation in the left medial OFC, left parietal gyrus, bilateral temporal cortex, uncus and right cerebellum. In the CN-CG subtraction, substance abusers showed increased activation in the right lateral OFC, bilateral ventro-lateral prefrontal cortex, precentral and postcentral gyrus and bilateral cerebellum.

Table 100: Foci of significant brain activations in the CG-CN condition: Comparison of pathological and non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-NPG							
Inferior frontal gyrus	44	R	20	62	14	3	3.21
Middle frontal gyrus extending to superior frontal gyrus	6	R	22	14	-1	52	3.16

Following the CG-CN subtraction, pathological gamblers showed increased activation in the right inferior, middle and superior medial frontal gyri. There were no voxels in the NPG-PG subtraction that reached statistical significance.

Table 101: Foci of significant brain activations in the CG-CN condition: Comparison of pathological gamblers and substance abuser.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-SA							
Inferior frontal gyrus	45/47	R	60	62	21	5	3.84
Inferior frontal gyrus extending through putamen	47	L	119	-38	27	-1	3.41
Middle frontal gyrus extending through superior frontal gyrus	6/8	L	20	-24	23	54	3.11
Medial frontal gyrus	6	R	37	14	3	55	3.74
Superior frontal gyrus	6	R	18	17	-10	65	3.12
Cingulate gyrus extending to medial frontal gyrus	32/9	R	426	17	22	31	4.02
Cerebellum		R	16	28	-60	-35	3.13

Following the CG-CN comparison, pathological gamblers showed widespread activation in the bilateral prefrontal cortex and cingulate gyrus compared to substance abusers. In the CN-CG comparison, substance abusers showed increased activity in the right lateral inferior frontal gyrus, medial frontal gyrus and cingulate

gyrus compared to pathological gamblers. There were no significant voxels in the SA-PG subtraction.

Table 102: Foci of significant brain activations in the CG-CN condition: Comparison of non-pathological gamblers and substance abuser.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-SA							
Inferior occipital gyrus	17/18/19	L	45	-35	-85	-5	3.48
Cerebellum		L	13	-7	-63	-32	3.13
SA-NPG							
Insula		L	13	-42	-26	14	3.16

Following the CG-CN comparison, non-pathological gamblers, compared to substance abusers, showed increased activation in the inferior occipital gyrus. From the CN-CG comparison, substance abusers showed higher activity in the left cerebellum compared to non-pathological gamblers.

Horse racing – neutral stimuli (HG – HN)

In this comparison, only the horse racing and corresponding neutral stimuli were compared. The tables below show the activated areas reported in each group followed by the group subtractions.

Table 103: Foci of significant brain activations in the HG-HN condition in pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
HG-HN							
Caudate nucleus		R	13	17	-36	18	3.44
		L	14	-21	-5	29	3.11
Hippocampus		L	33	-38	-37	5	3.33
Precentral gyrus	4	R	39	42	-15	46	3.17
HN-HG							
Orbitofrontal cortex	11	L	33	-35	40	-14	3.20
	10/11	L	64	-21	54	1	3.46
Orbitofrontal cortex extending to superior frontal cortex	11/10	R	201	17	54	1	4.00
Inferior frontal gyrus	46/9	L	36	-42	34	8	3.31
Medial frontal gyrus extending to precentral gyrus	6/4	L	3776	-21	0	61	4.36
Superior temporal gyrus	22	L	49	-66	-40	8	3.30
	22	R	21	66	-47	22	3.23
Middle temporal gyrus extending to inferior temporal gyrus	37/21	R	23	66	-48	-1	3.46
Middle temporal gyrus	21	R	71	55	6	-12	3.55
	21	R	40	45	-41	-7	3.13
Putamen extending to thalamus		L	495	-28	0	10	3.67
Uncus		L	10	-35	-15	-29	3.56
Cerebellum		R	705	7	-32	-25	3.80
		L	21	-10	-58	-6	3.28

In the HG-HN subtraction, pathological gamblers showed increased activation the left hippocampus and bilateral caudate nucleus. Following the HN-HG subtraction, many clusters were reported in the bilateral OFC and left DLPFC in addition to the bilateral temporal gyri in addition to the left putamen, thalamus, and uncus and the right cerebellum.

Table 104: Foci of significant brain activations in the HG-HN condition in non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
HG-HN							
Inferior frontal gyrus	44/45	R	18	49	14	9	3.70
Postcentral gyrus extending into medial frontal gyrus	5/6	R	21	3	-44	70	3.27
Hypothalamus extending into uncus		R	170	7	-7	-6	3.68
Cerebellum		R	76	3	-42	-27	3.41

Non-pathological gamblers showed significant activation within the right lateral inferior frontal gyrus, medial frontal gyrus, hypothalamus, uncus and cerebellum in the HG-HN subtraction.

Table 105: Foci of significant brain activations in the HG-HN condition in substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
HN-HG							
Medial frontal gyrus	8	R	58	10	29	40	3.58
Parahippocampal gyrus extending into amygdala	28	R	74	21	-21	-17	3.32
Lingual gyrus	12	L	12	-35	-68	-5	3.29
Cerebellum		R	118	3	-75	-8	4.02
		L	11	-7	-28	-16	3.14

There were no areas that showed enough activation to meet statistical significance in the HN-HG subtraction. In the HN-HG subtraction, areas showing increased activation included the medial frontal gyrus, amygdala and bilateral cerebellum.

Table 106: Foci of significant brain activations in the HG-HN condition in controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
HG-HN							
Middle frontal gyrus	6	R	17	45	9	45	3.3
Middle temporal gyrus extending into medial occipital gyrus	39/37/19	R	32	45	-71	16	3.50
Cerebellum		L	18	-7	-35	-22	4.13

In the HG-HN subtraction, controls showed activation in the right DLPFC and left cerebellum in addition to the medial temporal gyrus and medial occipital gyrus.

Table 107: Foci of significant brain activations in the HG-HN condition: Comparison of pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-CO							
Precentral gyrus	4	R	31	45	-11	52	3.36
CO-PG							
Orbitofrontal cortex	10	R	43	17	54	1	3.33
	11	R	69	35	47	-2	3.78
Medial frontal gyrus	9/8	L	26	-35	26	41	3.32
	6	L	313	-17	13	57	3.63
Precentral gyrus extending through medial frontal gyrus to posterior cingulate cortex	4/6/23	R	1483	31	-21	53	4.39
Inferior parietal gyrus	40	L	59	-55	-39	37	3.26
Angular gyrus	39	L	20	-28	-59	38	3.25
Supramarginal gyrus	40	R	25	52	-49	35	3.17
Middle temporal gyrus	21	R	12	66	-44	-4	3.09
Putamen		R	56	21	4	9	3.29
Uncus extending into parahippocampal gyrus	28/35	R	39	31	-8	-29	3.18
Cerebellum		R	57	7	-32	-25	4.21
		L	66	-7	-76	-20	3.12

Following the HG-HN comparison, pathological gamblers showed increased activation in the right precentral gyrus compared to controls. In the HN-HG subtraction, pathological gamblers showed increased activity in the right lateral OFC and left DLPFC in addition to the posterior cingulate cortex, precentral gyrus, parietal gyrus, temporal gyrus, angular gyrus, supramarginal gyrus, putamen, uncus, parahippocampal gyrus and right cerebellum.

Table 108: Foci of significant brain activations in the HG-HN condition: Comparison of non-pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-CO							
Hypothalamus extending to thalamus		R	23	7	-7	-6	3.31
Cerebellum		R	172	7	-39	-39	3.79
CO-NPG							
Middle frontal gyrus	46	L	11	-42	39	27	3.16
Precentral gyrus	6	L	20	-42	2	32	3.30
Cingulate gyrus	24	L	11	-14	-12	39	3.36
Middle temporal gyrus	19	R	28	42	-74	20	3.51

When viewing HG images compared to HN images, non-pathological gamblers showed higher activation in the hypothalamus, thalamus and right cerebellum. In the HN-HG comparison, non-pathological gamblers showed higher activation in the right temporal gyrus in addition to the left DLPFC and cingulate cortex.

Table 109: Foci of significant brain activations in the HG-HN condition: Comparison of substance abusers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
CO-SA							
Middle frontal gyrus extending to inferior frontal gyrus	6/9	R	45	49	9	48	3.43
Medial frontal gyrus extending to cingulate gyrus	8/32	R	53	10	33	40	3.97
Posterior cingulate	23	R	14	10	-36	18	3.12
Parahippocampal gyrus extending through hippocampus to amygdala	28	R	35	21	-21	-17	3.14
Lingual gyrus	18	R	64	17	-72	-5	3.24
Medial occipital gyrus	19	L	10	-35	-68	-5	3.51
Cerebellum		L	24	-7	-28	-16	3.41

No voxels from the SA-CO subtraction met statistical significance. In the HG-HN condition, controls showed increased activity in the right DLPFC. Following the HN-HG condition, substance abusers showed increased activity in the right DLPFC in addition to the right medial frontal gyrus (BA8), cingulate and posterior cingulate cortex. Increased activity was also measured in the lingual gyrus, hippocampus and amygdala compared to controls.

Table 110: Foci of significant brain activations in the HG-HN condition: Comparison of pathological and non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-PG							
Orbitofrontal cortex	10	R	14	17	54	1	3.22
Inferior frontal gyrus	44	R	17	55	11	12	3.54
Superior frontal gyrus	6	L	340	-17	-10	68	3.98
Precentral gyrus	4	R	102	3	-44	70	3.6
Precentral extending to postcentral gyrus	4/1	L	63	-45	-11	49	3.14
Inferior parietal gyrus	40	L	77	-28	-35	44	3.34
Precuneus	7/31	R	146	14	-72	49	3.55
Medial temporal gyrus	21	R	41	55	6	-12	3.47
	21	R	12	66	-18	-11	3.28
Medial extending to superior frontal gyrus	21/22	L	55	-55	-21	-11	3.32
Hypothalamus extending to thalamus		R	39	7	-7	-6	3.38
Putamen		R	27	17	14	3	3.13
Caudate nucleus		R	38	35	-27	1	3.28
Cerebellum		R	359	7	-35	-25	3.95
		L	54	-21	-62	-20	3.36

The PG-NPG subtraction yielded no voxels that met statistical significance. When viewing gambling images opposed to neutral images, non-pathological gamblers showed increased activity in the right lateral inferior frontal gyrus, hypothalamus, thalamus and right cerebellum. In the HN-HG subtraction, pathological gamblers showed increased activation in a number of areas including the right OFC, right lateral inferior frontal and superior frontal (BA6) gyrus, precentral and postcentral gyrus, right temporal gyrus, hypothalamus, thalamus, putamen and bilateral cerebellum.

Table 111: Foci of significant brain activations in the HG-HN condition: Comparison of pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-SA							
Precentral extending to postcentral gyrus	6/4/3	R	36	49	-4	55	3.56
Lingual gyrus	18	R	78	3	-78	-5	3.53
Posterior cingulate	23	R	15	10	-33	21	3.17
SA-PG							
Orbitofrontal cortex	11	R	34	35	47	-11	3.10
Medial frontal gyrus	10	R	32	17	54	1	3.76
Anterior cingulate cortex	24	R	28	7	31	18	3.19
Cingulate cortex	24	L	16	0	-19	36	3.09
Precuneus	19/7	R	76	7	-83	40	3.57
Caudate nucleus		L	25	0	0	3	3.27

In the HG-HN subtraction, pathological gamblers showed increased activity in the precentral and postcentral gyri and lingual gyrus compared to substance abusers. In the HN-HG subtraction, pathological gamblers reported increased activation in the VMPFC, lateral right OFC, anterior cingulate cortex, cingulate cortex (posterior BA24), precuneus, and left caudate nucleus.

Table 112: Foci of significant brain activations in the HG-HN condition: Comparison of non-pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-SA							
Inferior frontal gyrus	45/44	R	17	49	24	5	3.2
Substantia nigra		L	68	-17	-27	-5	3.22
Cerebellum		R	62	3	-75	-8	3.78
		L	336	-3	-39	-30	3.67

When viewing gambling images compared to neutral images, non-pathological gamblers showed increased activity in the right inferior frontal gyrus and left cerebellum compared to substance abusers. In the HN-HG subtraction, substance abusers showed increased activity in the right cerebellum compared to non-pathological gamblers. The SA-NPG subtraction yielded no voxels that met statistical significance.

Internet gambling – neutral stimuli (IG-IN)

Table 113: Foci of significant brain activations in the IG-IN condition in pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
IG-IN							
Orbitofrontal cortex	10/11	R&L	156	10	37	-14	3.49
Medial frontal gyrus	10	L	123	-3	48	14	3.46
Inferior frontal gyrus	47	R	13	49	27	-13	3.41
Transverse temporal gyrus	41	R	31	35	-37	8	3.16
Hippocampus		R	15	28	-11	-23	3.11
Thalamus		L	15	-10	-24	4	3.43
Claustrum		R	27	31	-13	14	3.27

In response to the IG-IN subtraction, pathological gamblers showed high levels of activity in the medial OFC and VMPFC, inferior frontal gyrus, claustrum, hippocampus, thalamus and temporal gyrus. No voxels reached statistical significance in the IN-IG subtraction.

Table 114: Foci of significant brain activations in the IG-IN condition in non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
IG-IN							
Orbitofrontal cortex	47	R	11	52	30	-13	3.29
	11/47	L	11	-38	40	-17	3.26
IN-IG							
Precentral gyrus	6	L	19	-35	-5	26	3.33
Precentral extending to paracentral gyrus	4/6	L	23	-14	-27	63	5.04
Posterior cingulate extending to lingual gyrus	30/18	L	22	-7	-54	6	3.15
Inferior parietal cortex	40	R	17	59	-39	28	3.53
Precuneus extending into cuneus	31/7/19	L	68	-24	-77	26	3.2
Caudate nucleus		R	19	21	21	5	3.26
Cerebellum		L	55	-31	-45	-18	3.67
		L	24	0	-82	11	3.95

In the IG-IN subtraction, non-pathological gamblers showed high levels of activation in the bilateral OFC. In the IN-IG comparison, increased activity was reported in the posterior cingulate cortex, lingual gyrus, precentral and paracentral gyri, precuneus and cuneus, right caudate nucleus and left cerebellum.

Table 115: Foci of significant brain activations in the IG-IN condition in substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
IG-IN							
Caudate nucleus		L	20	-7	1	23	3.37
Insula extending to caudate tail		L	18	-35	-30	18	3.54
IN-IG							
Orbitofrontal cortex	10/11	R	23	42	47	-5	3.09
Superior frontal gyrus	8	R	14	31	26	50	3.09
Medial extending to superior frontal gyrus	6	R	37	21	-1	45	3.14
Inferior extending to medial frontal gyrus	44/9/6	R	85	55	4	16	4.29
Posterior cingulate	30	L	11	0	-50	15	3.11
Precentral extending to postcentral gyrus	4/1	R	43	35	-17	59	3.34
Inferior parietal gyrus	40/7	R	55	52	-45	44	3.39
Medial extending to inferior temporal gyrus	21/20	L	67	-55	-1	-23	3.45
Globus pallidus extending to amygdala		R	64	24	-20	1	3.73
Uncus	20	R	17	28	-2	-38	3.11

In response to the IG-IN comparison, substance abusers reported high activity in the caudate and insula. In the IN-IG subtraction, increased activity was widespread in the prefrontal cortex including the right lateral OFC and right DLPFC in addition to the right globus pallidus, amygdala and uncus, posterior cingulate, precentral and postcentral gyri, parietal, and temporal gyri.

Table 116: Foci of significant brain activations in the IG-IN condition in controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
IN-IG							
Cuneus extending to the lingual gyrus	19/17	R	290	28	-91	24	4.00
Cerebellum		L	37	-21	-51	-9	3.39

No voxels met statistical threshold in the IG-IN comparison. In the IN-IG subtraction, significant activity was present in the cuneus, lingual gyrus and the anterior lobe of the left cerebellum.

Table 117: Foci of significant brain activations in the IG-IN condition: Comparison of pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-CO							
Orbitofrontal cortex	47	R	11	49	27	-13	3.26
Medial frontal gyrus	10	L	12	-38	52	20	3.09
Inferior parietal gyrus	40	R	10	42	-32	31	3.18
Medial extending to superior temporal gyrus	21/38	R	28	52	-1	-15	3.13
Medial occipital gyrus	18	R	33	24	-81	4	3.18
Insula		L	17	-38	18	12	3.15
Claustrum extending through putamen to insula		R	36	38	-13	7	3.26

In response to the gambling versus neutral stimuli, pathological gamblers showed increased amounts of activity in the right lateral OFC, temporal cortex, claustrum, putamen and bilateral insula. Following the IN-IG subtraction, controls showed significantly higher activation in the occipital cortex compared to pathological gamblers. In the CO-PG subtraction, no voxels reached statistical significance.

Table 118: Foci of significant brain activations in the IG-IN condition: Comparison of non-pathological gamblers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-CO							
Orbitofrontal cortex	11/47	L	19	-45	26	-16	3.36
Medial occipital gyrus	18	R	24	24	-94	21	3.10
CO-NPG							
Precentral gyrus	4	L	14	-14	-27	63	4.59
Caudate nucleus		R	19	21	21	9	3.23

In the IG-IN comparison, non-pathological gamblers showed significantly higher activation in the left lateral OFC compared to controls. In the same comparison, controls showed increased activity in the caudate nucleus and precentral gyrus compared to non-pathological gamblers.

Following the IN-IG comparison, controls showed higher activation in the occipital cortex compared to non-pathological gamblers.

Table 119: Foci of significant brain activations in the IG-IN condition: Comparison of substance abusers and controls.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
SA-CO							
Superior temporal gyrus	38	L	18	-35	2	-24	3.24
Cuneus extending through medial occipital gyrus	17/18/19	R	95	17	-88	8	3.47
Cuneus extending to lingual gyrus	17/18	R	32	-14	-84	11	3.65
CO-SA							
Orbitofrontal cortex	10	L	17	-10	54	-9	3.22
Superior frontal gyrus	8/6	R	21	17	37	53	3.28
	6	R	17	28	-7	68	3.38
Medial frontal gyrus	6	L	15	-10	-24	72	4.55
Middle frontal gyrus extending to precentral gyrus	6	R	21	52	9	45	3.45
Inferior frontal gyrus	44	R	27	55	4	16	4.77
Posterior cingulate cortex	30	L	10	0	-50	15	3.10
Putamen extending to globus pallidus		R	32	28	-7	4	3.28

In the IG-IN comparison, substance abusers showed increased activity in the right prefrontal cortex including the DLPFC in addition to the putamen and globus pallidus. Following the IN-IG comparison, controls showed increased activity in the cuneus, occipital gyrus and lingual gyrus compared to substance abusers.

Table 120: Foci of significant brain activations in the IG-IN condition: Comparison of pathological and non-pathological gamblers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-NPG							
Medial frontal gyrus	10	L&R	59	-3	45	11	3.24
Middle frontal gyrus	6	R	13	24	6	48	3.25
Medial frontal gyrus extending to cingulate gyrus	8/32	L	53	-3	22	31	3.53
Precentral gyrus extending to insula	6	L	32	-38	-2	29	3.48
Inferior parietal extending to superior temporal gyrus	40/22	R	167	59	-39	28	3.80
Precuneus	7/19	L	70	-17	-69	39	3.10
Precuneus extending into cingulate gyrus	7/31	R	32	24	-60	32	3.36
Posterior cingulate gyrus	29/30	L	77	-10	-47	18	3.23
Insula extending to claustrum		R	20	35	-20	14	3.20
Caudate nucleus		R	37	21	24	5	3.34
		L	17	-3	7	6	3.20
Hypothalamus		R	25	7	0	-9	3.22
NPG-PG							
Medial temporal gyrus	20	R	14	52	-41	-10	3.33
Cerebellum		L	21	-10	-42	-19	3.18

When viewing gambling vs. neutral stimuli, pathological gamblers showed increased activation in the bilateral VMPFC, posterior cingulate cortex, right posterior insula, left caudate nucleus and hypothalamus compared to non-pathological gamblers. In contrast to this, when viewing neutral opposed to gambling stimuli, non-pathological gamblers showed increased activation in the cingulate gyrus, left precentral gyrus, left insula, precuneus and right caudate nucleus.

Table 121: Foci of significant brain activations in the IG-IN condition: Comparison of pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
PG-SA							
Medial and superior frontal gyri including orbitofrontal cortex	9/10	L&R	295	-3	48	14	3.74
Medial frontal gyrus	6	R	26	17	3	64	3.25
Inferior frontal gyrus	44	R	13	55	4	16	3.72
Inferior parietal gyrus extending to superior temporal gyrus	40/39	R	259	62	-36	31	3.82
Medial temporal gyrus	21	R	83	45	2	-32	3.39
Medial temporal gyrus extending into supramarginal gyrus	39/40	L	20	-38	-53	28	3.16
Posterior cingulate cortex	30	R/L	47	3	-50	19	3.10
Globus pallidus extending through claustrum to thalamus		R	43	24	-20	0	3.95
Claustrum extending into insula		L	24	-24	21	12	3.29
Caudate		L	24	-3	7	6	3.34
Hippocampus		R	163	28	-11	-23	3.62

Following the IG-IN comparison, pathological gamblers showed significantly higher activation in the bilateral VMPFC and OFC in addition to the right parietal cortex, right temporal cortex and left caudate nucleus compared to substance abusers. In the IN-IG comparison, substance abusers showed increased activation in the right DLPFC, right lateral inferior prefrontal cortex, globus pallidus, thalamus and hippocampus.

Table 122: Foci of significant brain activations in the IG-IN condition: Comparison of non-pathological gamblers and substance abusers.

Area	BA	Left/Right	Cluster size	Talairach co-ordinates			z score
				x	*y*	*z*	
NPG-SA							
Orbitofrontal cortex	11/47	L	19	-42	30	-19	3.64
Superior frontal gyrus	8	R	17	35	30	50	3.77
Precentral gyrus	6	R	18	55	1	19	3.79
Inferior parietal gyrus	40/7	R	37	45	-56	41	3.52
Middle temporal gyrus	L	L	14	-38	-53	28	3.22
SA-NPG							
Precuneus extending into cuneus	31/18	L	32	-24	-70	29	3.33
Posterior cingulate	30	L	13	-7	-54	6	3.37
Insula		L	13	-35	-30	21	3.66
Caudate nucleus		R	20	17	24	5	3.30

When viewing gambling vs. neutral images, non-pathological gamblers showed significantly higher activation in the left OFC, right DLPFC, precentral gyrus, right parietal cortex and left temporal cortex. In the IN-IG comparison, non-pathological gamblers showed increased activation in the precuneus, cuneus and caudate nucleus compared to substance abusers.

Following the IN-IG comparison, substance abusers showed increased activation in the right DLPFC, precentral gyrus, parietal and temporal cortex.

Discussion

This task was designed to explore brain areas that are active when provided with gambling cues. Groups of gamblers and non-gamblers were compared to discover whether the gambling groups expressed any abnormalities in neurological function in response to these cues.

During the task, after each set of images were shown, five questions were asked asking participants to rate their urge to gamble, excitability, happiness, anxiety and sadness during the previous set of images. This was performed in order to explore the arousal caused by each set of images. It could be expected that the two gambling groups would have expressed higher excitability and stronger urge to gamble following the gambling images compared to the two non-gambling groups. In addition, it could be expected that the neutral stimuli would evoke similar levels of arousal in each group. The results upheld these expectations. Both groups of gamblers gave significantly higher self-reports of excitability and urge to gamble in response to the horse and internet gambling images compared to controls. However, during presentation of the casino gambling stimuli only the non-pathological gamblers, and not the pathological gamblers, reported significantly higher excitability and stronger urge to gamble compared to controls. This suggests that cues relating to casino gambling were not as arousing to the pathological gamblers compared to the non-pathological gamblers. This finding may be related to the number on individuals engaging in each type of gambling activity. Every pathological gambler and non-pathological gambler recruited in this project reportedly used internet gambling sites but a lower proportion visited casinos and bet on horses. This could lead to the conclusion that the most valid comparisons are those from the internet gambling condition. This may also explain why casino images did create as much arousal in the pathological gamblers. A number of pathological gamblers reported that they were 'professional' gamblers. Participants who described themselves as professional gamblers reported that they were more likely to pursue gambling activities in which knowledge and skill could be utilised in order to gain an advantage. Some professional gamblers reported that they bet on certain events (e.g. horse racing) because certain knowledge (e.g. course conditions, previous history of horse's performance) could be utilised to choose individuals who had subjectively higher chances of winning. These gamblers reported that they, most of the time, did not engage in games which involve a high element of luck such as 'Lucky Numbers' or 'Wheel of Fortune'. Therefore, many of the pathological gamblers may not have frequented casinos as most of the games

involve high amounts of luck. Non-pathological gamblers may have been more likely to visit a casino because they reportedly gambled for fun or because of social reasons.

The results from the ratings showed that the stimuli from the task had the desired effect with gamblers reporting the gambling stimuli as highly arousing compared to non-gamblers. There was no difference in ratings of neutral stimuli, which was expected.

Comparisons from all conditions reliably showed high PFC activity measured in gamblers in response to all gambling images. PFC activity in controls displayed a similar pattern. Substance abusers reliably showed higher PFC activity in response to neutral compared to gambling stimuli, which would fit with their responses on the ratings. The substance abusers reported SOGS scores similar to controls so the effects of the gambling stimuli should, as shown by this task, be minimal.

As mentioned above, the internet gambling condition could be determined to be the most valid for group comparison. Therefore, this condition will be considered first. In response to the internet gambling stimuli, pathological gamblers and non-pathological gamblers showed significantly increased PFC activity compared to controls. High activity in the bilateral OFC, VMPFC and right inferior PFC was measured in pathological gamblers in response to the internet gambling cues. This suggests that these cues were highly salient to the pathological gamblers. Compared to controls, increased activity was measured in the OFC in pathological gamblers and non-pathological gamblers. This suggests that the OFC in the pathological and non-pathological gambler may be overly responsive to salient gambling cues.

In the casino condition, higher activity was measured in the right inferior PFC, caudate and bilateral insula in pathological gamblers compared to controls. Although the pathological gamblers did not report significantly higher excitability

or urges to gamble compared to controls they did show elevated BOLD response in the PFC. Interestingly, controls also showed a relatively high high BOLD response within the PFC in response to the casino stimuli compared to the other gambling images. This leads to the supposition that cues relating to casinos are arousing in non-gamblers, and to a higher extent, in gamblers.

In the horse racing condition, pathological gamblers exhibited significantly higher PFC activity compared to controls but in response to the neutral vs. gambling images. This result is interesting considering that pathological gamblers reported significantly higher ratings of excitability and urge to gamble during the horse gambling images and reported no significant differences in ratings in the neutral condition compared to controls. Therefore, in this instance, BOLD response was not correlated with self-ratings of arousal.

In addition to the OFC, the insula may be part of a circuit that is abnormally active in response to gambling cues in pathological gamblers compared to controls. In both the casino and internet gambling conditions, the bilateral insula was found to be more active in pathological gamblers compared to controls. More research is needed to uncover any role of this area in responding to gambling cues.

These results support the findings from Crockford et al. (2005), which found that pathological gamblers showed hyperactivity in the PFC in response to gambling cues. However, the areas found by Crockford et al.'s study are different to the areas found in this project. In the Crockford study, the VMPFC and DLPFC were found to be hyperactive in response to gambling cues whereas this project found the OFC and insula to be hyperactive. Differences may be due to methodological dissimilarities between the studies. This task utilised still images whereas the Crockford et al. study utilised videos. This task provided images because it was easier to control potential confounding problems such as size and quality compared to videos. Evidence from both the previous and current study suggests that there is a circuit of frontal areas that are hyperactive in response to salient gambling

stimuli. These areas are involved in reward valuation, emotion processing and inhibitory control. Abnormal activity in these areas may lead to disruption of these behaviours, causing gambling stimuli to be given high rewards and, in addition, inhibition of responses to these cues to be impaired. The results from Crockford et al. (2005) and this study are contrary to Potenza et al.'s (2003) findings, which indicated hypo-activity in frontal and somatosensory areas in pathological gamblers in response to gambling videos. The difference in results may be due to variances in methodologies. Potenza et al. compared activations on the same videos overlaid by an actor relating a happy or sad gambling experience whereas the Crockford et al. study presented muted videos involving gambling or scenes of nature. Therefore, it could be disputed that the two tasks were measuring slightly different concepts. The Potenza et al. study measured empathic response to happy or sad gambling experiences experienced by a third-party in addition to reaction to gambling cues whereas the Crockford et al. study compared response to gambling vs. control stimuli.

Conclusions

In summary, evidence from this task builds upon a previous study finding hyper-activity in the prefrontal cortex in pathological gamblers compared to controls in response to gambling cues. In addition, a circuit of hyper-active brain regions may also encompass the insula cortex in addition to prefrontal areas, especially the orbitofrontal cortex. Results from this study also suggest that non-addicted gamblers also show hyperactivity in the orbitofrontal cortex in response to gambling cues.

General discussion of results from experiment 4

In this project, five tasks were utilised in order to investigate and compare neurological activity of pathological gamblers, non-pathological gamblers, substance abusers and controls. Three of the tasks were new and created by the

researcher (delay discounting, probability discounting and urge to gamble) and two had been used extensively in previous research (Iowa task and go-no/go task). The main aims were to compare brain activity across the groups to see whether there were any differences that may underlie the addiction and altered behaviour shown by pathological gamblers and substance abusers that have been measured in previous research. In addition, non-pathological gamblers were investigated to see whether pathological gambling is brought about by a progression of neurobiological changes.

Firstly, we will consider the new delay and probability discounting tasks and their validity. The data obtained from each task was as expected in many of the subtractions. In the free-forced choice comparison, significant PFC activity was measured in the PFC when activity in the free trials was compared with that in the forced trials.

Considering any possible abnormalities in neurological function of the pathological gamblers and substance abuser compared to the controls, there were significant differences in the probability discounting task. Substance abusers significantly lower BOLD response in the PFC compared to controls. This difference in BOLD response may underlie their addiction and their attitude towards drugs. Pathological gamblers also showed some impairments but in smaller, more specific areas, which were the inferior PFC and parietal cortex. This difference in BOLD response between the substance abusers and pathological gamblers may underlie the reason why they are addicted to different stimuli. In contrast to these findings, no significant differences in BOLD response were measured on the Iowa task. At first, these results may appear contradictory as they both measure risk-taking; however, the tasks do measure different constructs. The probability discounting task measures how an individual reacts to risk and is a more direct measure of risk-taking. The Iowa task measures an individual's ability to incorporate previously learned information into working memory and predict the best decision-making strategy to use in order to increase one's overall gains. In addition, the Iowa task

provided the participant with some training in the task, which may have masked any major functional abnormalities.

Pathological gamblers and substance abusers also showed decreased BOLD response within the PFC in the delay discounting task but only in the forced-free choice comparison. The forced choice condition presented the participants with no choice, only a simple button press. In the free-forced comparison, no difference in BOLD function was found. In fact, pathological gamblers and substance abusers showed increased OFC activity compared to controls. This suggests that in choice situations that are associated with delay, these groups show hyper-activity of the OFC compared with controls. However, when the situation requires relatively little effortful processing, an decreased BOLD function within the PFC can be measured in pathological gamblers and substance abusers. This condition could be seen as a baseline condition. Thus, at baseline when relatively little processing is needed, the addicted groups show decreased PFC function. However, when a situation requiring effortful processing is presented, the OFC is hyperactive. This may denote an OFC that has to function at increasing levels of activity in order for the individual to behave in a similar way to controls.

In the easy-hard condition of the delay discounting task, the pathological gamblers, non-pathological gamblers and substance abusers showed completely different patterns of activation to the controls suggesting that the brain circuits within these groups may also function in a different manner to controls.

Pathological gamblers also showed decreased BOLD function within the OFC in the go/no-go task. Interestingly, the performance of pathological gamblers on the go/no-go task and stop task (in experiment 3) was comparable to that of the controls, indicating that this functional difference did not significantly affect their levels of inhibitory control.

When reviewing all the results from these tasks, brain regions that have commonly been identified as having significantly different levels of BOLD signal within the drug abusing and gambling groups compared to controls can be identified. Most interestingly, the most common areas that show dysfunction are the OFC, VMPFC and inferior frontal gyrus in addiction to the middle temporal gyrus. This can be taken as evidence to suggest that there exists widespread regional differences in neural function in pathological gamblers, substance abusers and non-pathological gamblers compared to non-gambling non-drug taking controls. To a lesser extent, the fusiform gyrus and insula also show dysfunction within gambling and drug abusing groups. Dysfunction of fronto-temporo-limbic structures has previously been linked to heightened levels of impulsivity (Hoptman et al., 2004), which the groups recruited for this study have exhibited on self-report measures.

Taken as a whole, the evidence suggests that pathological gamblers and substance abusers do show altered neurological activity compared to controls in situations that require toleration of delay (self-control) and evaluation of risk. Both groups showed significant decreases in BOLD response in areas of the PFC when making decisions that are associated with risk. However, when making decisions involving self-control, pathological gamblers and substance abusers showed hyper-activity of the OFC, which may indicate that this area has to function at an increased rate in order to 'upgrade' behaviour leading to maximisation of gains.

A hypothesis was put forward at the beginning of the project that put forward the idea that there may be a progressive element in the development of pathological gambling such that there may be exacerbating neurological (and behavioural) changes that come about as one progresses from non-gambler, through non-pathological gambler to pathological gambler. It was expected that pathological gamblers would show a significant difference in BOLD response in specific areas of the brain and some, but not all, of these differences would be measured in non-pathological gamblers. In the areas that did not mirror those in pathological gamblers it was also expected that non-pathological gamblers would show similar

BOLD response compared to controls. In a minority of tasks, non-pathological gamblers did mirror some of the differences measured in pathological gamblers and, generally, did mirror the activity shown by the controls. However, it must be noted that the results from these tasks could only indicate if the BOLD response within certain areas was significantly *different* and could not validly indicate if the BOLD response was similar.

The urge to gamble task investigated brain areas that were active when gambling cues were presented. Pathological and non-pathological gamblers showed high PFC activity when given gambling cues compared to controls and substance abusers, especially in the OFC. Interestingly, at some times, this high OFC activity was not linked to self-reports of urges to gamble or excitability following the cues. In one condition pathological gamblers did not report a significantly higher urge to gamble or level of excitability following the cues yet still showed an elevated BOLD signal within the OFC. In addition to increased OFC activity, pathological gamblers showed elevated bilateral insula activity. This suggests that these two regions may be part of a circuit that responds to gambling cues in pathological gamblers.

Concern may be expressed over the control sample. In many of the behavioural tasks, there have been no significant differences in performance between the controls and the other groups. It would be expected that there would be significant differences in performance between the pathological gamblers/substance abusers and the controls. However, this was not the case. The control sample was picked from respondents from the University of Manchester and care was taken to make sure that they expressed no behavioural disorder that would affect the results. Instead of a problem with the control sample, it is felt more likely that the participants from the other groups reflect a less abnormal section of their population. Perhaps if the substance abusers were recruited from treatment programs or all the pathological gamblers were currently not seeking any treatment then the results may have been different. Alternatively, it could be that many of the participants from the addicted groups did not have any major neurological

abnormalities but were instead influenced by environmental factors. In fact, this theory is put forward in the pathways theory of gambling. This theory states that the development of pathological gambling can occur through alterations in behaviour caused by biological abnormalities, vulnerabilities in personality (e.g. depression, anxiety), conditioning through environmental factors or any mix of the three (Blaszczynski & Nower, 2002).

These tasks have shown that pathological gamblers and substance abuser do show abnormalities in neurological activity in tasks assessing factors of impulsivity. In addition, the abnormalities shown by pathological gamblers and substance abusers are separately identifiable, which may underlie the choice of addictive stimulus by these groups.

General Discussion

The main aims of this project were to investigate the behavioural and neurological factors involved in self-control and risk-taking. The project was split into four main sections. The first section piloted novel delay and probability discounting tasks in humans to assess their applicability in testing our hypotheses. The second and third sections utilised the new tasks to explore self-control and risk-taking in healthy controls, individuals with addictive disorders (namely substance abusers and pathological gamblers), individuals showing similar non-addicted behaviour (non-pathological gamblers) and individuals with Generalized Anxiety Disorder or Social Phobia (anxiety-disordered). The fourth section explored the brain areas involved in impulsive behaviours, including self-control and risk-taking, in pathological gamblers, non-pathological gamblers, substance abusers and controls to investigate further these behaviours and search for abnormalities in neural function between these groups.

A number of hypotheses were generated at the beginning of the project. The first hypothesis was concerned with differences in performance between discounting tasks giving real vs. hypothetical rewards. More specifically, it was hypothesised that the provision of real rewards would cause participants to become more self-controlled on the delay discounting task and decrease their risk-taking tendencies on the probability discounting task compared to when hypothetical rewards were given. The small number of studies that have previously compared performance on delay discounting tasks giving real vs. hypothetical rewards have provided contrasting results for a difference in discounting behaviour. In this project, experiment 2 contrasted performance exhibited by healthy controls on delay and probability discounting tasks giving real vs. hypothetical monetary rewards. As predicted by the hypothesis, participants acted in a more self-controlled manner when faced with real compared to hypothetical rewards. This was thought to be due to increased tolerance of delay in order to gain maximal gains when given the opportunity of receiving real rewards. Performance differences were found not to

be due to K^+ or Q^+, questioning the applicability of the Multiplicative Hyperbolic Model of Choice to human behaviour. Reward type also affected performance on the probability discounting task but not in the hypothesised direction. In fact, participants took more risks when provided with real rewards. Alterations in Q^+ were found to partially explain these results with sensitivity to the difference of the real rewards being higher than with the hypothetical rewards. In addition to this effect, it was suggested that because of the small reward sizes utilised, when potential losses were offset compared to potential wins, participants may have attenuated the punishing aspects of the potential loss compared to the reward aspects of the potential win. In experiment 3, the same tasks were given to pathological gamblers, non-pathological gamblers, substance abusers and anxiety-disordered individuals. Reward type had no effect on choice behaviour on the delay discounting task. In the probability discounting task, substance abusers and, to a lesser extent, pathological gamblers showed increased risk-taking when provided with real vs. hypothetical rewards. This suggests that these individuals are more sensitive to tasks giving real probabilistic rewards rather than hypothetical ones. Researchers utilising a delay or probability discounting task in addiction-disordered or healthy control samples must take account of the ramifications of providing real or hypothetical rewards as this project has found evidence to suggest that task design can significantly alter the outcome of the results.

The second hypothesis stated that pathological gamblers and substance abusers would exhibit higher impulsivity compared to controls. Results form the self-report scales supported this hypothesis with pathological gamblers and substance abusers reporting higher scores than controls on the impulsivity subscale of the IVE and the impulsiveness and disorderliness subscales of the TCI. These results fall in line with previous studies reporting that these populations reported higher levels of impulsivity compared to controls. The hypothesis also stated that the higher impulsivity shown by pathological gamblers and substance abusers would be reflected by the expression of lower self-control on the delay discounting task and higher risk-taking on the probability discounting task compared to controls. Several

previous studies have found that pathological gamblers and substance abusers discounted delayed rewards at a significantly higher rate compared to controls on delay discounting tasks providing hypothetical rewards and delays. Our results showed that non-pathological gamblers exhibited the highest levels of self-control and there was a similar trend for substance abusers. Levels of self-control expressed by pathological gamblers did not significantly differ from controls. Choice behaviour on the probability discounting task expressed by the pathological gamblers and substance abusers did not significantly differ from controls although non-pathological gamblers showed significantly higher risk-taking compared to controls. The differences in results between this project and previous studies may have been due to task design. Only one other study has utilised a discounting task in a non-control sample (addicted smokers) employing real consequences for each choice (Reynolds, 2006). This study found that behaviours that were correlated with a hypothetical pen-and-paper delay discounting task were not correlated to performance on the real rewards task. Combined with the results from this project this suggests that the provision of real consequences in a discounting task may cause individuals to significantly alter their behaviour compared to a hypothetical discounting task. The experience of the consequences of each choice may cause individuals to employ different decision-making strategies that take account of cost-benefit attributes. It may be disputed that these tasks may more validly measure real-life discounting behaviour as they provide real consequences as opposed to the traditional hypothetical discounting tasks.

It was also hypothesised that there would be behavioural differences between the substance abusers and pathological gamblers that would reflect their differences in preferred addictive stimulus. More specifically, substance abusers would express lower self-control and greater risk-taking compared to pathological gamblers. There were no significant differences in choice behaviour on the discounting tasks between the two groups. However, substance abusers did consistently report higher scores on self-report scales measuring the tendency to engage in new or risky activities, i.e. the venturesomeness scale from the IVE and openness to experience

scale on the Big 5. This suggests that, although both groups report comparable levels of impulsivity (including self-control, risk-taking and inhibitory control) the substance abusers are more willing to engage in behaviours that are novel and involve relatively high elements of risk. This may underlie their tendency to prefer drugs, which would provoke new sensory experiences, compared to gambling (and vice-versa for the pathological gamblers).

It was hypothesised that anxiety-disordered individuals would show significantly higher self-control and lower risk-taking compared to controls. In fact, choice behaviour between these two groups did not significantly differ in either the delay or probability discounting tasks. Therefore, self-control and risk-taking may not be characteristics that influence levels of problematic anxiety although they may be affected by transient mood-induction techniques in a healthy sample (as has been found in previous studies[21]). In no previous study had these tasks had been utilised to measure behaviour in anxiety-disordered individuals.

Previous research has suggested that there are differences in neurological function that may underlie biases in decision-making inherent within pathological gamblers and substance abusers, which may underlie their addictive disorders. In this project, tasks were given to assess brain activity involved in self-control (delay discounting task), risk-taking (probability discounting task and Iowa task), inhibitory control (go/no-go task) and gambling urges (urge to gamble task). Substance abusers did show significantly decreased BOLD function in frontal activity in the probability discounting task compared to controls. However, there was found to be no significant differences in choice behaviour between the substance abusers and controls in the probability discounting task, therefore, this difference did not appear to be linked to a performance difference. One explanation is that when risk-taking is directly assessed using a task providing real consequences, substance abusers will behave in a similar way to controls in order to maximise gain. However, in general, substance abusers are more tolerant of the risks associated with highly

[21] See section 6.4 of the introduction for more details

valued outcomes such as using drugs. This may indicate a discrepancy between measuring risk-taking using behavioural techniques and risk-taking exhibited in real-world environments. Evidence for this view is provided by the performance of the substance abusers on the 'venturesomeness' subscale of the IVE and 'openness to experience' subscale of the Big 5 questionnaires which measured an individual's propensity to engage in new and risk-related experiences. On these subscales, substance abusers reported significantly higher scores indicating that they have a general tendency to engage in novel, risk-oriented, experiences.

Substance abusers and pathological gamblers also showed decreased prefrontal activity in the delay discounting task but only in the condition where no choice was presented and only a simple button press was needed. This suggests that when a situation requires minimal processing, controls show a significantly higher BOLD response. In contrast to this finding, when making choices involving delayed rewards, these two groups showed significantly higher activity in the right inferior prefrontal cortex including the orbitofrontal cortex. Considering that pathological gamblers and substance abusers did not show significant differences in delay discounting behaviour, it could be suggested that hyper-activity in these areas may occur due to a compensatory mechanism expressed by these two groups that allows them to match performance with controls.

Pathological gamblers did show decreased BOLD response within the PFC compared to controls on the go/no-go task. However, this impairment did not lead to performance deficits on the go/no-go task or stop task. This may have been due to factors within the lifestyles of the pathological gamblers that have altered their behaviour. Many of the pathological gamblers had experienced serious negative life events caused by their gambling such as job loss, legal trouble and divorce. Therefore, although a neurological deficit may have been present in these groups, social and environmental factors had caused them to compensate for this deficit and significantly alter their behaviour.

One hypothesis also questioned whether substance abusers would show a different response in the prefrontal cortex compared to the pathological gamblers, which would underlie the inter-group differences in preferred addictive stimulus. Following the free-forced choice comparison in the probability discounting task, there were significant differences in OFC activity between the two groups with pathological gamblers showing increased left OFC activity but substance abusers showing higher right OFC activity. In addition, when given high vs. low risk choices on the Iowa task, pathological gamblers showed higher right PFC activity, including the DLPFC. However, when given low vs. high risk choices, substance abusers showed higher OFC activity. These results suggest that choice situations involving the analysis of risk activate different prefrontal circuits in pathological gamblers compared to substance abusers. It has already been suggested that abnormalities in brain activity exhibited by the substance abusers may be associated with increased tendency to engage in risky endeavours. It is possible that differences in brain activity when assessing risk may be linked to differences in preferred addictive stimulus. Therefore, although the differences did not fit with the original hypotheses, some differences in neural function were measured between pathological gamblers and substance abusers.

The urge to gamble task revealed interesting results concerning the response of gamblers to gambling cues. Only two studies had previously investigated response to gambling cues on pathological gamblers and they found contrasting results. Both gambling groups showed significantly high brain activity when presented with gambling stimuli. Compared to controls, pathological and non-pathological gamblers showed an increased BOLD response in a wide variety of prefrontal areas including the orbitofrontal cortex. Pathological gamblers also showed increased activity in the insula. Interestingly, increased activity was not always associated with self-report measures. Even when pathological gamblers reported that the gambling cues caused no increase in gambling urges or excitability, significantly increased prefrontal activity was still measured. Combined with results from a previous study, this could suggest that pathological gamblers, and to a lesser extent

non-pathological gamblers, have a circuit of brain areas that are hyper-responsive to gambling cues and that this hyper-responsiveness may underlie gambling urges.

The final hypothesis questioned whether non-pathological gamblers would mirror functional activity measured in pathological gamblers but to a lesser extent, thus questioning whether pathological gambling occurs as a result of progressive changes in behaviour and brain function. Overall, some evidence was found for this hypothesis. Evidence for this hypothesis came from a subset of self-report questionnaires. The imaging experiment showed that non-pathological gamblers did mirror (in some of the tasks) impairments shown by pathological gamblers.

This project assessed self-control and risk-taking in controls, individuals with addictive disorders (pathological gambling or substance abuse), individuals exhibiting similar but non-addicted behaviour (non-pathological gamblers) and those with anxiety disorders. The results provided extensive evidence for differences in choice behaviour and also impairments in brain activity which may underlie these differences. The information provided by this project influences such areas as addiction, impulsivity (more specifically self-control and risk-taking), decision-making and validity of methodologies in use in decision-making research.

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Appendix 1: Standardised instructions given by the pilot discounting tasks

You will be asked to complete two tasks. The tasks will involve you choosing between two alternatives. Each alternative will have a different hypothetical monetary reward.

In the first task, each alternative will carry a delay, which you will have to wait through. Alternative A will have a small reward but a smaller delay. Alternative B will have a larger reward but a larger delay. Please make your choice as quickly as possible by stating out loud “A” or “B”. The researcher will then immediately start a stopwatch that will count out the delay associated with the alternative you chose. You will not be able to do anything at this time. When the delay has ended the researcher will show you the next choice.

The second task is similar but there are no delays. Instead, each alternative will carry a chance of winning the money. Alternative A will have a smaller reward but a larger chance of winning. Alternative B will have a larger reward but a lower chance of winning. Please make your choice as quickly as possible by stating out loud “A” or “B”. You will be handed a spinner at the start of the task. Place the spinner onto the outline shown and spin the arrow. The arrow must travel around the spinner three times for it to be considered legal. If it does not spin around three times then you will be asked to spin again. If the arrow lands in the white section you win. If it lands in the black section, you do not win.

In both tasks choose whichever alternative you prefer. There are no right or wrong answers.

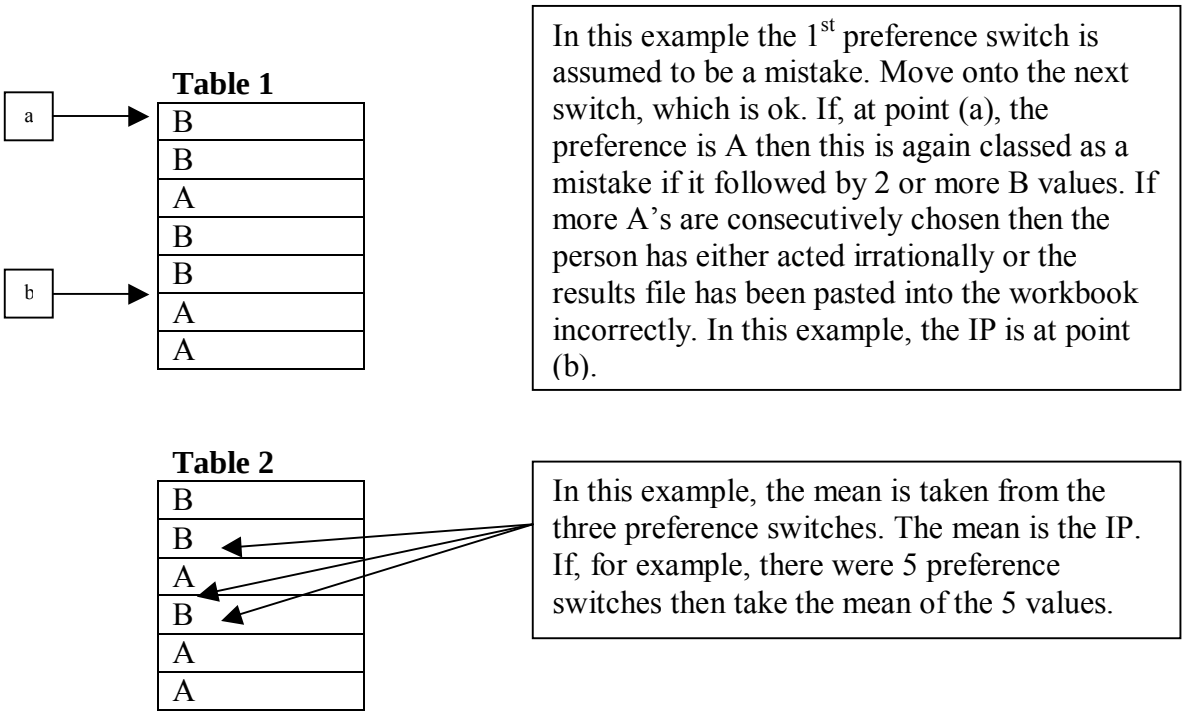
After you have completed these tasks you will be given two short questionnaires to complete. These tasks will give instructions to you before you attempt them.

Appendix 2: Algorithm used to calculate indifference points on the delay and probability discounting tasks

The following rules assume that choice behaviour is following a rational model, i.e. when dA = dB, choice = B.

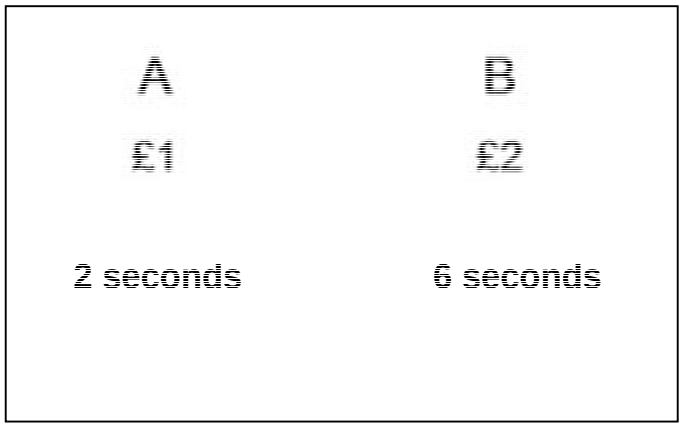
1. From dA=dB/pA=pB, move down the choices until preference switch (i.e. when B switches to A)
2. Is this switch followed by at least 2 choices of A?
3. If yes, obtain IP at mean between switch values (e.g. if switch occurs when dB changes from 4-6 seconds then IP=5). (END) If no, go to 4.
4. Is switch followed by at least 2 B choices (see table 1). If yes go to 5. If no go to 6.
5. Move to next preference switch and go to 2.
6. Does preference continuously switch for at least three consecutive d/p values (see table 2). Go to 7.
7. Take the mean of all preference switches to obtain IP. (END)

Example of how indifference points were calculated in non-simple cases



Appendix 3: Screen shots of the behavioural delay discounting and probability discounting tasks

Delay discounting task

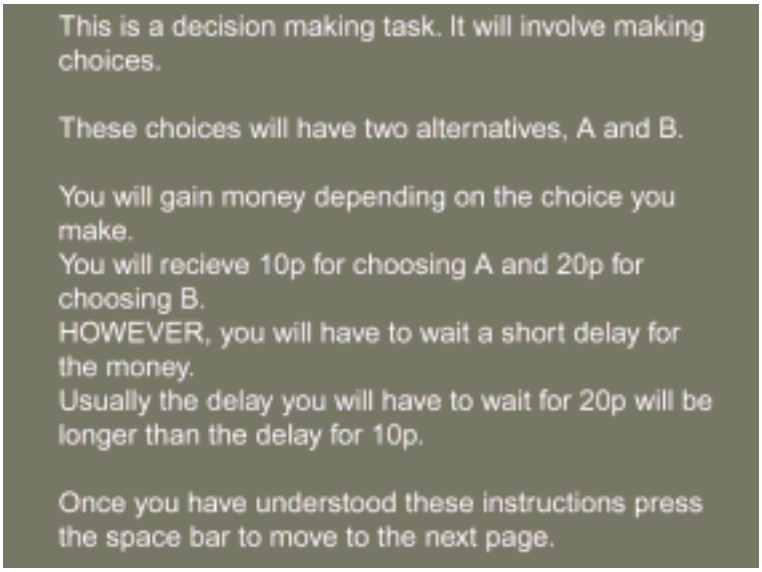


Probability discounting task

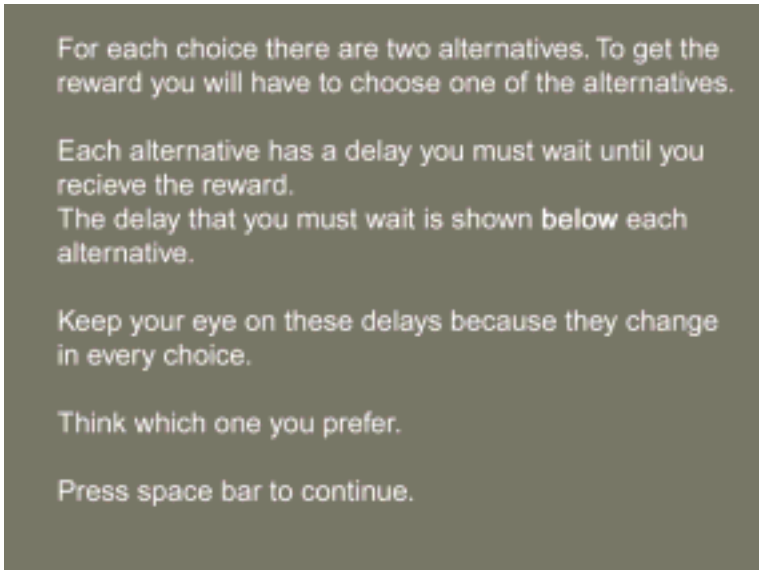
Appendix 4: Instructions given in the behavioural versions of the delay and probability discounting tasks

Delay discounting task

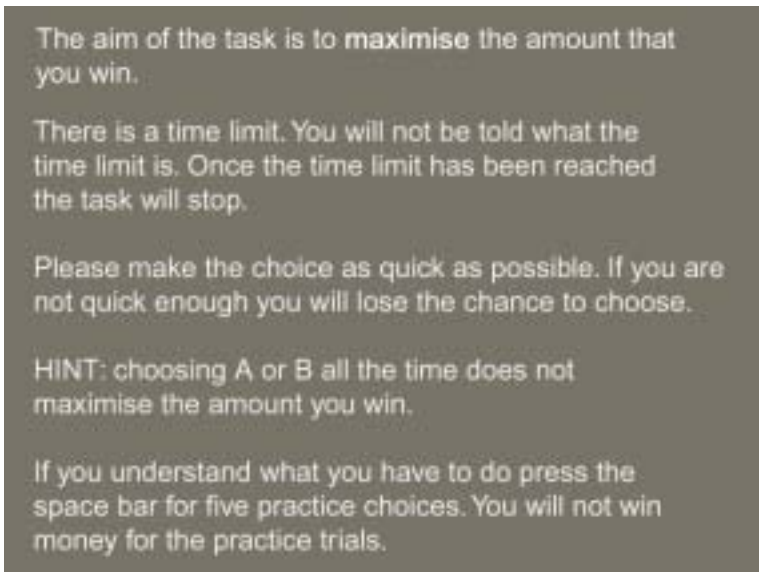
Screen 1



Screen 2

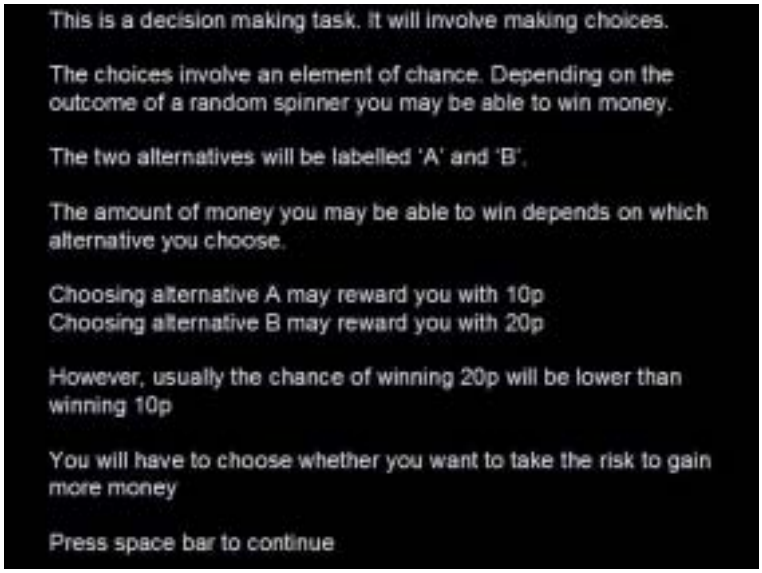


Screen 3

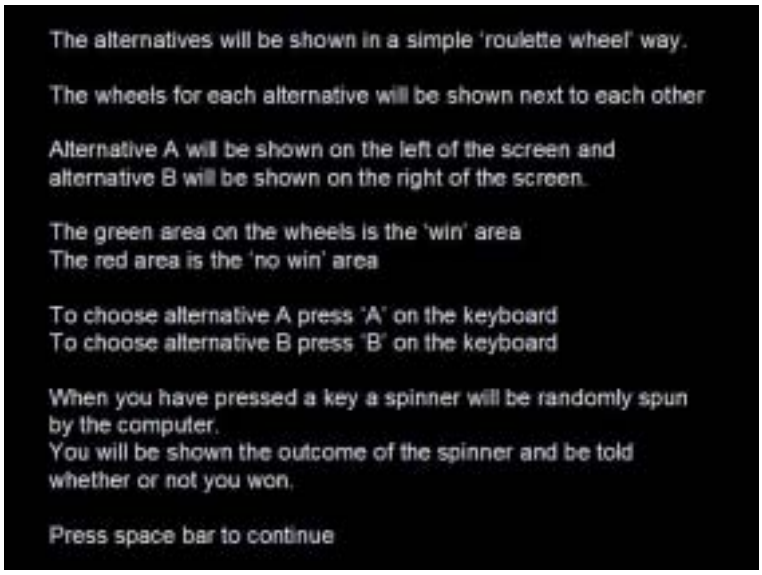


Probability discounting task

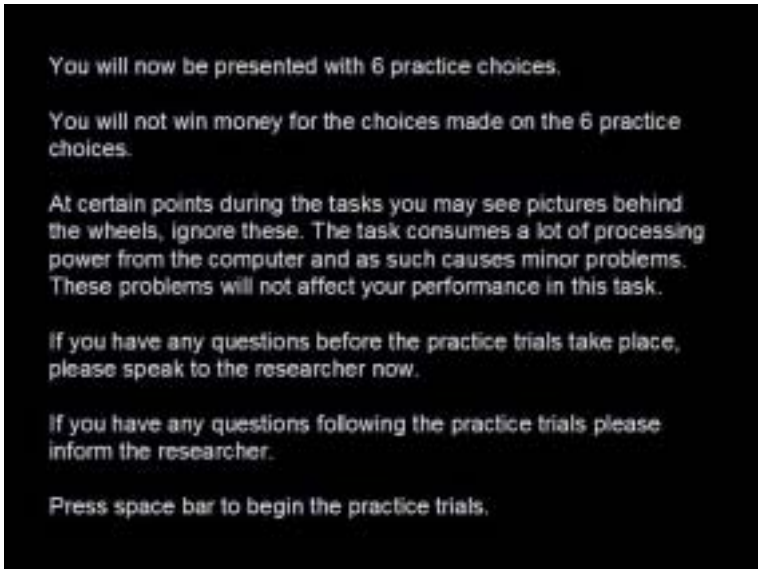
Screen 1



Screen 2



Screen 3


You will now be presented with 6 practice choices.
You will not win money for the choices made on the 6 practice choices.
At certain points during the tasks you may see pictures behind the wheels, ignore these. The task consumes a lot of processing power from the computer and as such causes minor problems. These problems will not affect your performance in this task.
If you have any questions before the practice trials take place, please speak to the researcher now.
If you have any questions following the practice trials please inform the researcher.
Press space bar to begin the practice trials.

Appendix 5: Mean scores from the neuropsychological tasks and self-report questionnaires from study 3

In some questionnaires, only selected sub-scales of interest are shown. Standard deviations are shown in brackets.

Impulsivity Venturesomeness Empathy questionnaire (IVE)

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
Impulsivity	**11.93** (3.03)	**9.93** (3.97)	**10.55** (4.39)	**6.09** (4.06)	**6.86** (3.67)
Venturesomeness	**9.86** (3.88)	**12.20** (3.83)	**12.91** (2.43)	**8.18** (4.13)	**10.44** (2.59)

Barratt Impulsiveness Scale (BIS-11)

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
Total score	**73.97** (13.61)	**73.73** (9.43)	**76.73** (7.74)	**65.46** (14.91)	**65.97** (9.64)
Attention	**20.71** (4.16)	**18.79** (3.12)	**21.09** (4.23)	**18.82** (3.16)	**17.58** (3.75)
Motor	**25.07** (6.23)	**25.57** (4.29)	**25.36** (5.18)	**22.00** (4.36)	**22.89** (3.97)
Non-planning	**28.14** (5.87)	**29.79** (4.66)	**30.00** (5.88)	**24.64** (8.29)	**25.61** (5.20)

Stop task

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
Stop errors	**8.36** (5.52)	**4.80** (3.45)	**5.09** (4.06)	**4.64** (4.46)	**5.03** (6.81)
Go RT	**541.52** (111.37)	**651.96** (101.09)	**696.75** (129.28)	**676.27** (123.74)	**691.76** (185.24)

Temperament and Character Inventory (TCI)

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
Novelty seeking	**24.58** (5.83)	**26.33** (5.53)	**26.91** (6.78)	**17.00** (6.42)	**21.43** (5.40)
Exploratory excitability	**5.31** (2.47)	**7.93** (3.04)	**7.36** (2.11)	**5.33** (2.45)	**7.54** (1.89)
Impulsiveness	**6.75** (1.92)	**6.13** (1.77)	**5.91** (2.77)	**3.22** (1.30)	**3.81** (2.28)
Extravagance	**6.31** (2.58)	**5.40** (2.67)	**6.64** (2.58)	**4.89** (3.26)	**4.97** (2.27)
Disorderliness	**6.19** (1.87)	**6.87** (0.92)	**6.91** (1.14)	**3.56** (2.19)	**5.11** (1.90)

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
Harm avoidance	**17.50** (7.01)	**9.80** (6.77)	**17.91** (7.99)	**26.00** (8.32)	**11.76** (7.82)
Anticipatory worry	**5.63** (2.28)	**2.67** (1.88)	**4.91** (2.81)	**7.11** (4.40)	**3.78** (2.74)
Fear of uncertainty	**3.63** (2.00)	**2.00** (2.17)	**2.73** (2.20)	**4.78** (2.22)	**2.16** (2.02)
Shyness	**3.69** (2.98)	**3.40** (2.80)	**4.91** (2.70)	**6.00** (2.74)	**2.68** (2.24)
Fatigability	**4.56** (2.78)	**1.73** (1.94)	**5.36** (5.00)	**7.11** (1.97)	**3.22** (2.78)

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
Reward dependence	**15.00** (3.76)	**13.40** (5.05)	**15.00** (4.49)	**16.11** (3.01)	**15.68** (3.76)
Sentimentality	**6.00** (2.07)	**4.93** (2.19)	**5.91** (2.34)	**7.22** (1.48)	**7.16** (1.91)
Attachment	**4.75** (1.95)	**4.87** (2.72)	**4.82** (2.60)	**4.44** (2.30)	**5.11** (2.11)
Dependence	**4.25** (1.44)	**3.60** (1.55)	**4.27** (1.74)	**4.44** (0.88)	**3.41** (1.55)

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
Persistence	**5.63** (1.89)	**5.07** (2.19)	**3.82** (1.54)	**4.00** (2.45)	**5.62** (1.98)

Big 5

Scores from each subscale are totalled and then divided by the number of items within that subscale giving a score from 0-5.

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
Extraversion	**3.42** (1.47)	**3.83** (0.68)	**3.60** (0.72)	**2.77** (1.23)	**3.56** (0.66)
Agreeableness	**3.65** (0.85)	**3.37** (0.53)	**3.60** (0.31)	**3.82** (0.43)	**3.87** (0.52)
Conscientious-ness	**3.50** (0.76)	**3.39** (0.80)	**3.09** (0.38)	**3.43** (1.10)	**3.73** (0.64)
Neuroticism	**3.21** (0.79)	**2.50** (0.96)	**3.01** (0.72)	**4.03** (0.50)	**2.76** (0.90)
Openness	**3.32** (0.54)	**3.65** (0.49)	**4.23** (0.50)	**3.53** (0.69)	**3.86** (0.52)

Quick Test of IQ (QT)

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
IQ	**91.36** (8.08)	**90.87** (10.23)	**97.55** (8.79)	**99.00** (9.59)	**95.17** (9.77)

State Trait Anxiety Inventory

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
Trait anxiety	**34.23** (8.17)	**28.13** (4.82)	**32.09** (6.81)	**37.09** (8.69)	**28.17** (4.27)
State anxiety	**39.85** (11.04)	**30.73** (4.56)	**37.45** (7.62)	**44.18** (11.91)	**32.00** (4.87)

Nback task

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
Total correct	**21.38** (2.22)	**21.47** (3.14)	**19.81** (2.27)	**20.56** (1.13)	**20.28** (3.29)

South Oaks Gambling Screen (SOGS)

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
Total	**12.69** (5.59)	**3.00** (1.72)	**1.27** (2.01)	**1.00** (1.90)	**0.81** (1.42)

Alcohol Use Disorder Identification Test (AUDIT)

	Pathological gamblers	Non-pathological gamblers	Substance abusers	Anxiety-disordered	Controls
Total	**6.50** (5.57)	**8.33** (6.94)	**13.82** (6.16)	**4.82** (3.37)	**6.19** (4.61)

Appendix 6: Instructions from the *f*MRI discounting tasks

Delay discounting task

Screen 1

This is a decision making task.

You will be given several choices between two alternatives called 'A' and 'B'.

Each alternative has a monetary reward.

Each choice carries a delay that you have to wait through in order to get the reward.

The aim of the task is to **maximise the amount that you can win**.

Press the key under your forefinger to continue.

Screen 2

There is a time limit to the task.

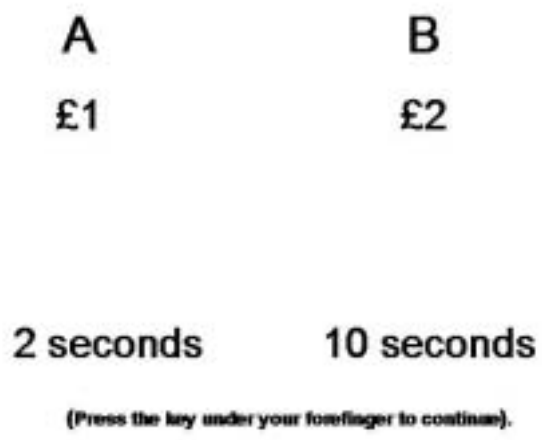
You will not be told how long the time limit will be.
Once the time limit is over the task will stop.

HINT: choosing A or B all the time will not maximise your winnings.

You will now be shown what a typical choice screen will look like.

Press the key under your forefinger to continue.

Screen 3



Screen 4

Sometimes you will be told which choice to make.

In these situations simply follow the onscreen instructions.
When you need to respond, the instructions will say "Choose alternative X". X will be the alternative you have to choose.

In the other choices you will be free to make your own decisions.
When it is time to make a choice the instructions will say "Make your choice now".

Please pay close attention to the amounts you can win and the delays as these will frequently change.

Press the button under your forefinger to continue.

Screen 5

You will be shown each choice for a short time. You will not be able to choose at this time.

A prompt to make your choice will then appear on the screen. Make your choice at this time.

Make the choice quickly or you will lose the chance to gain money.

To choose alternative **A** use the button under your **1st (fore-) finger**.
To choose alternative **B** use the button under your **2nd (middle-) finger**.

Press the key under your forefinger to start the task.

Probability discounting task

Screen 1

This is a decision making task.

You will be given several choices between two alternatives called 'A' and 'B'.

Each alternative has a monetary reward.

The choices involve an element of chance. Depending on the outcome of a random spinner you may be able to win money.

The aim of the task is to **maximise the amount that you can win**.
Press the key under your forefinger to continue.

Screen 2

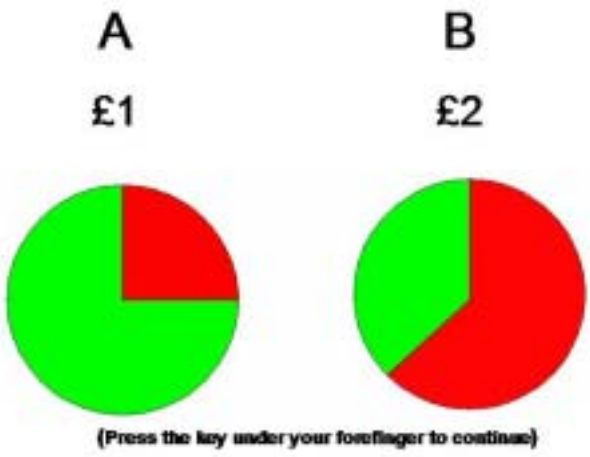
The chances of winning for each alternative are shown in a simple "roulette wheel" style.
The green area in the wheel is the 'win' area.
The red area shows the 'no win' area.

When you have made a choice a random spinner will be spun by the computer.
Depending on where it lands you will either win/not win.

You will now be shown what a typical choice screen will look like.

Press the key under your forefinger to continue.

Screen 3



Screen 4

Sometimes you will be told which choice to make.

In these situations simply follow the onscreen instructions.
When you need to respond, the instructions will say "Choose alternative X". X will be the alternative you have to choose.

In the other choices you will be free to make your own decisions.
When it is time to make a choice the instructions will say "Make your choice now".

Please pay close attention to the amounts you can win and the delays as these will frequently change.

Press the button under your forefinger to continue.

Screen 5

You will be shown each choice for a short time.
You will not be able to choose at this time.

A prompt to make your choice will then appear on the screen. Make your choice at this time.

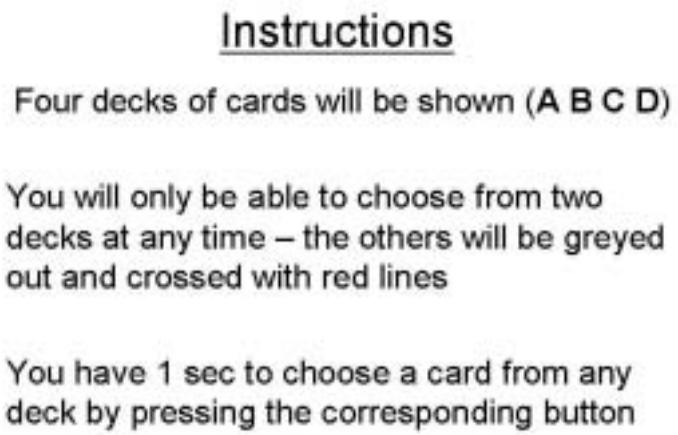
Make the choice quickly or you will lose the chance to gain money.

To choose alternative **A** use the button under your **1st (fore-) finger**.
To choose alternative **B** use the button under your **2nd (middle-) finger**.

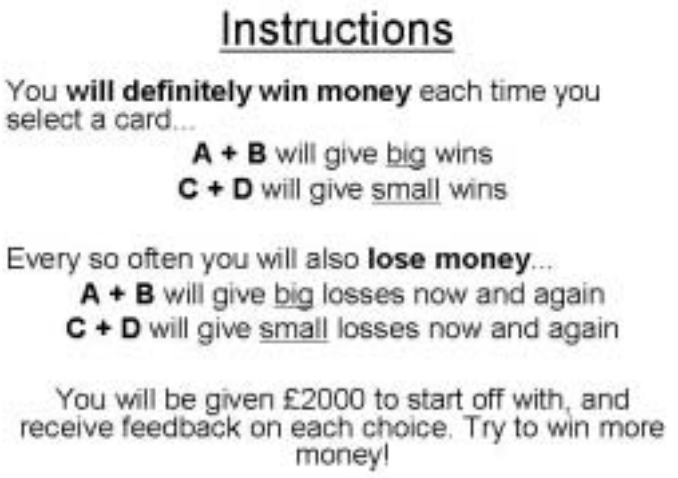
Press the key under your forefinger to start the task.

Appendix 7: Instructions for the fMRI version of the Iowa task

Screen 1



Screen 2



Appendix 8: Examples of the self-rating questions in the Urge to Gamble task

Urge to gamble rating

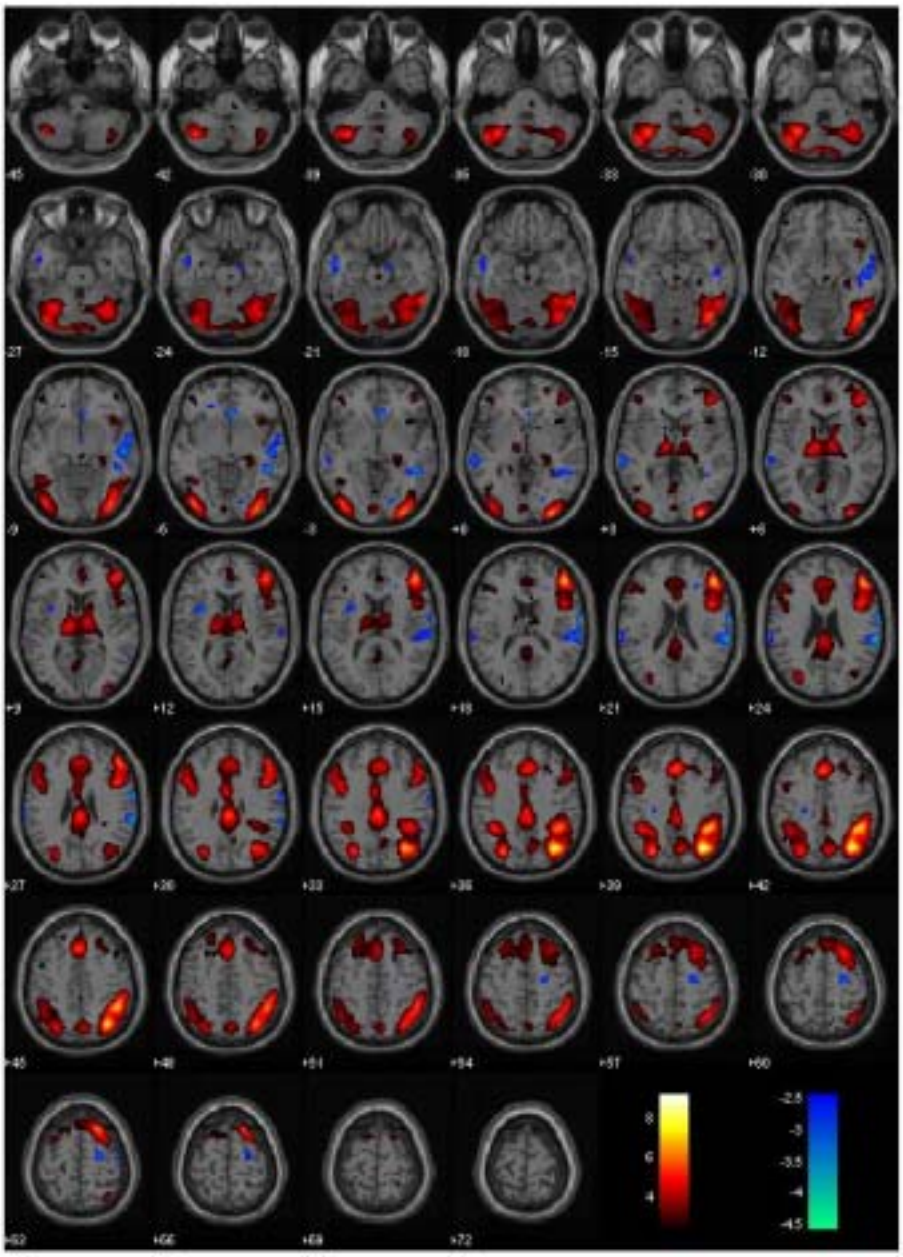
Rating of excitability

Appendix 9: Slice overlays obtained from the *f*MRI tasks

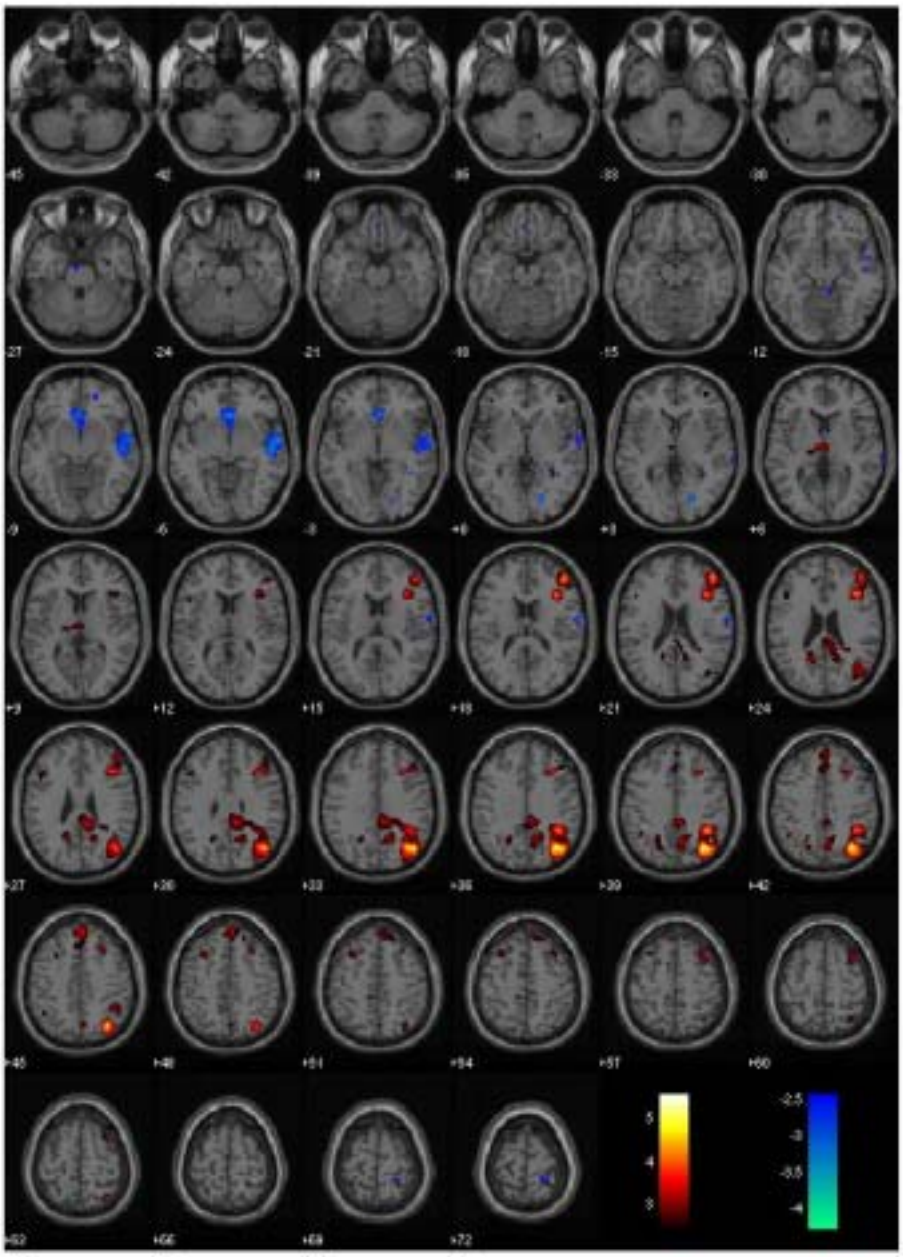
The slice overlays show the activity measured from each subtraction. Red areas indicate activity measured from the first comparison whereas blue areas show the activity measured from the opposite comparison. For example, if pathological gamblers are compared against controls then the PG-CO subtraction will be in red and the CO-PG subtraction will be in blue.

Delay discounting task: Free – forced choice

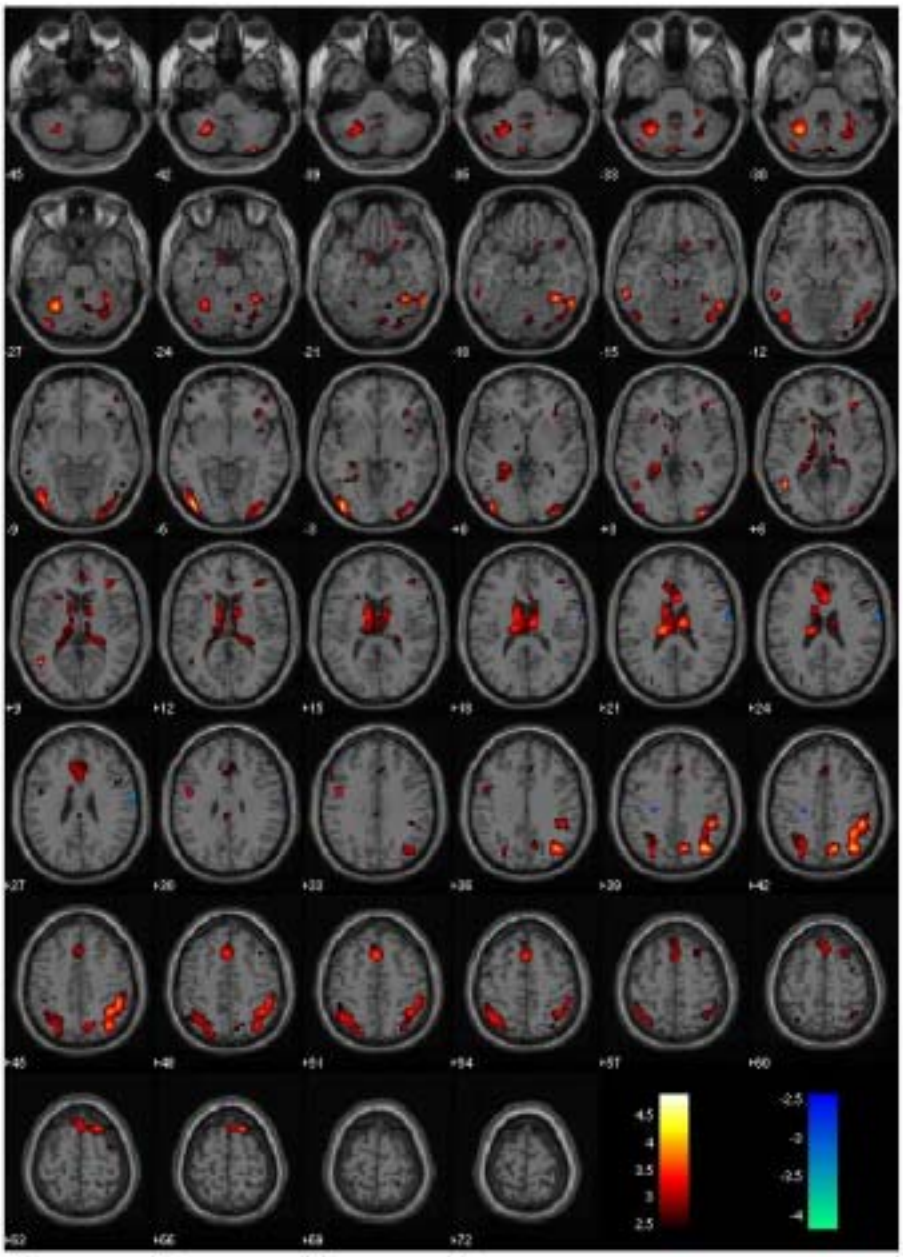
Data collated from all groups



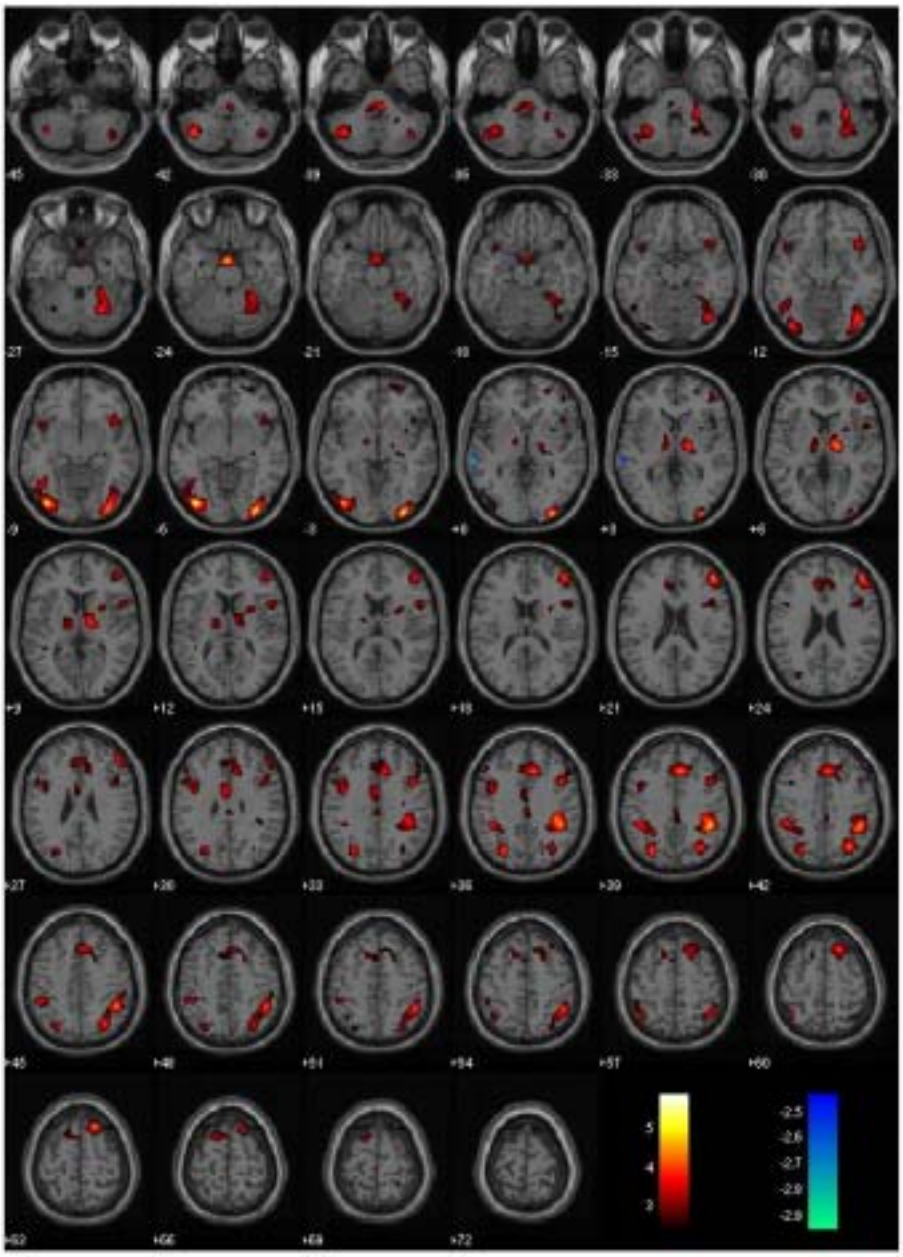
Pathological gamblers



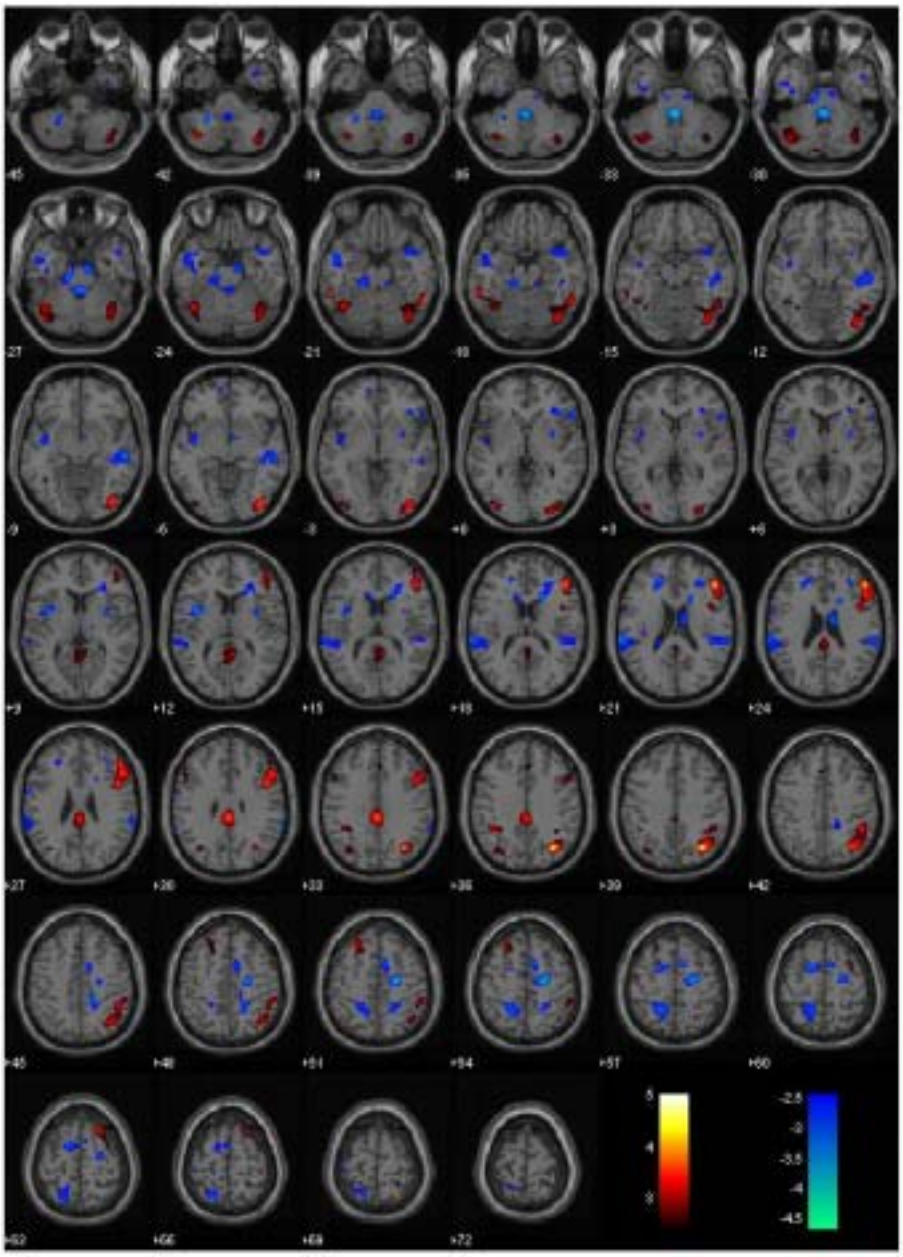
Non-pathological gamblers



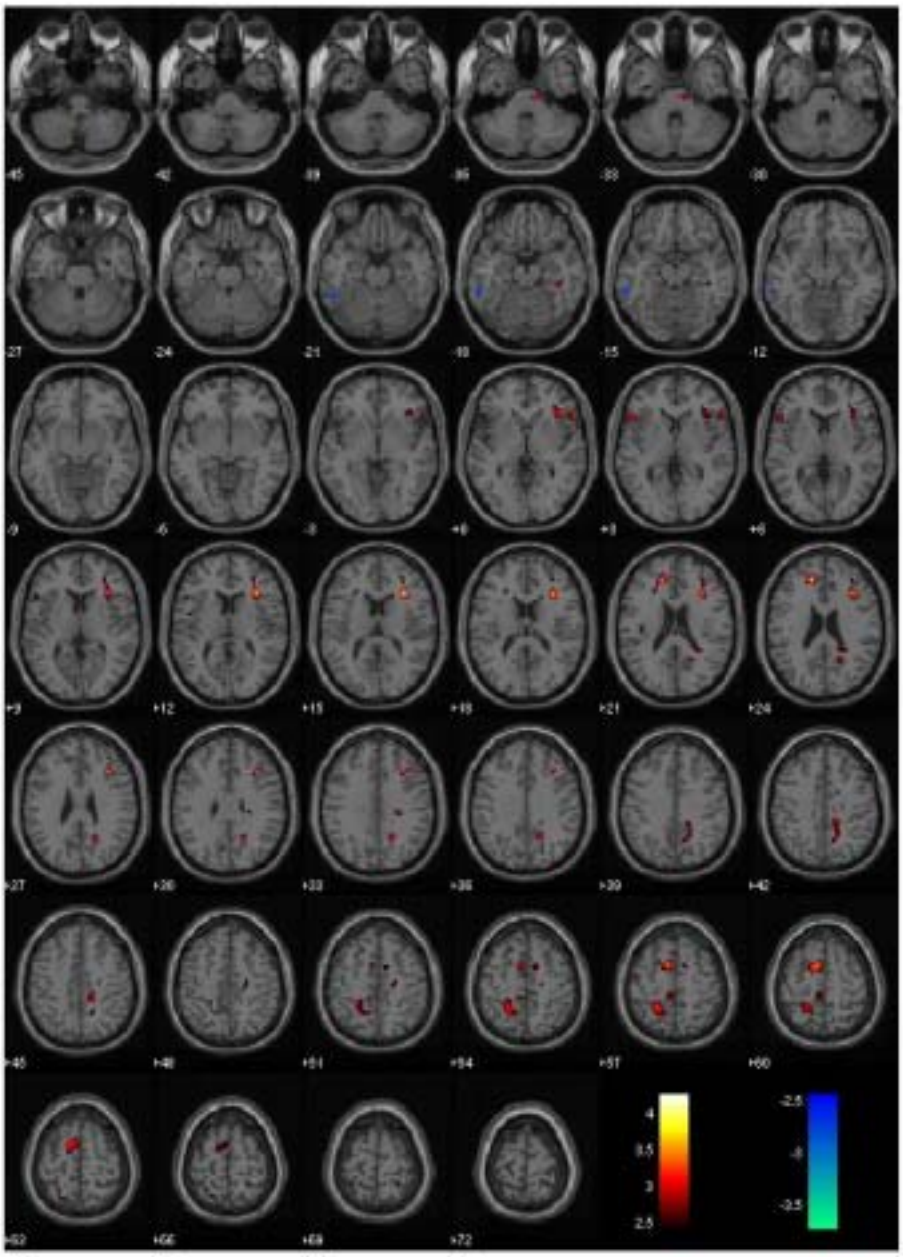
Substance abusers



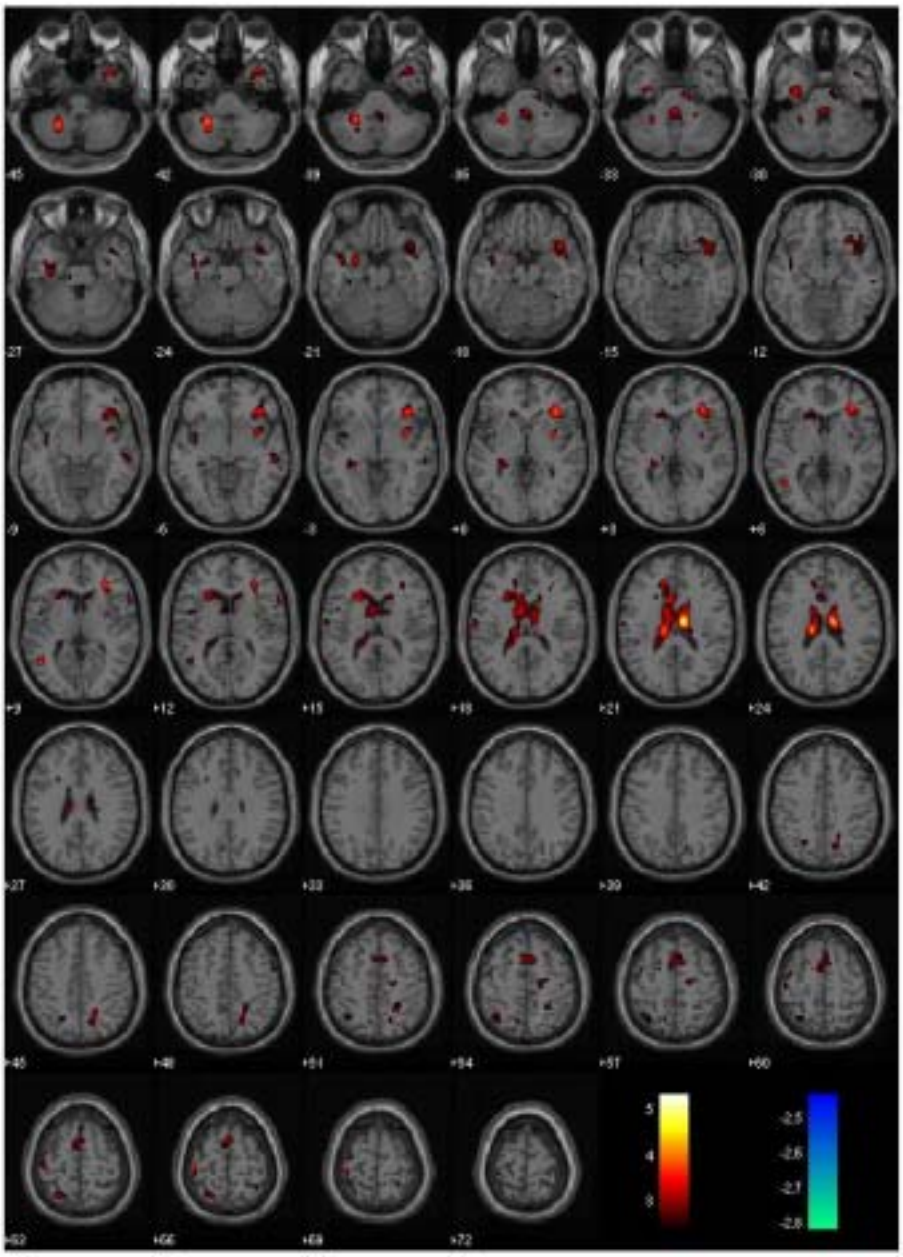
Controls



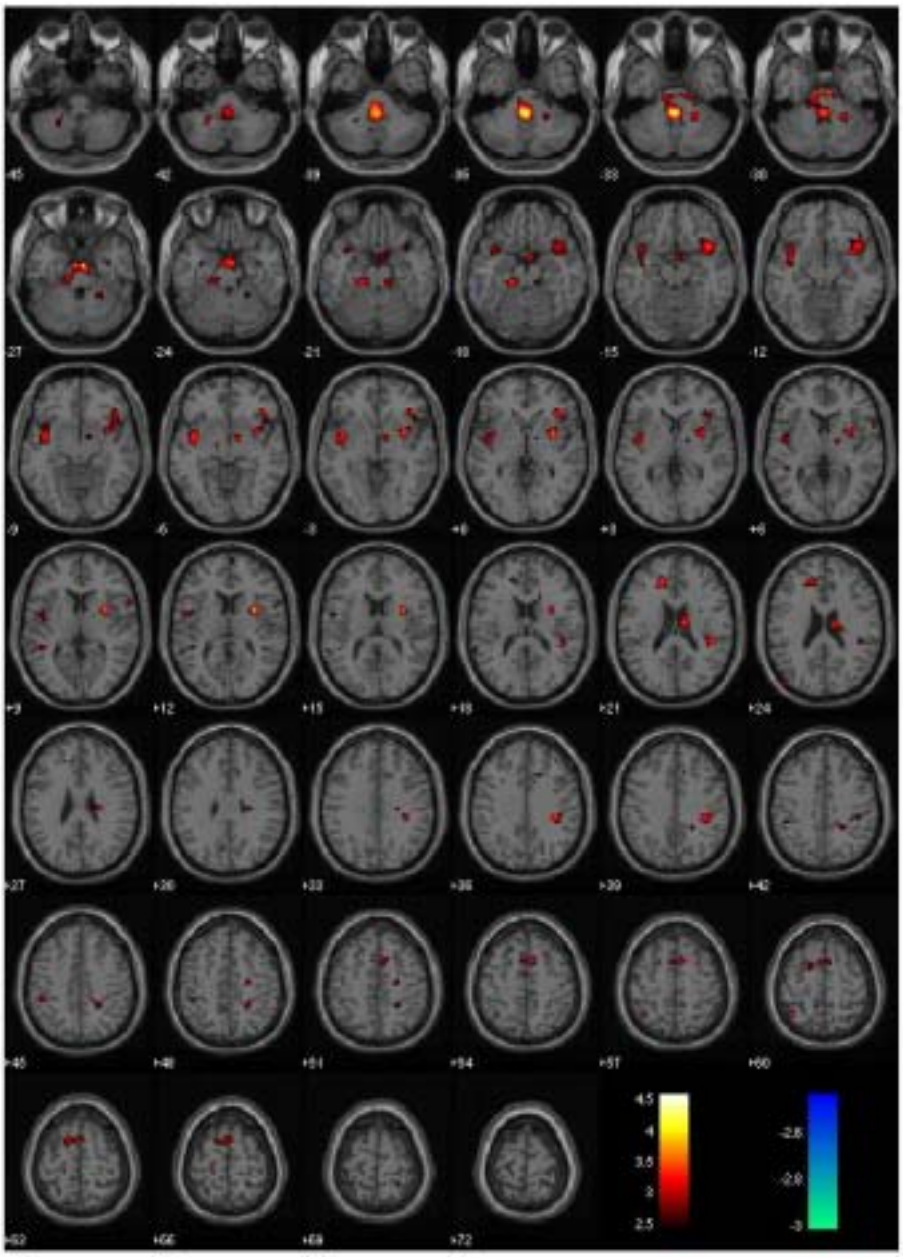
PG – CO



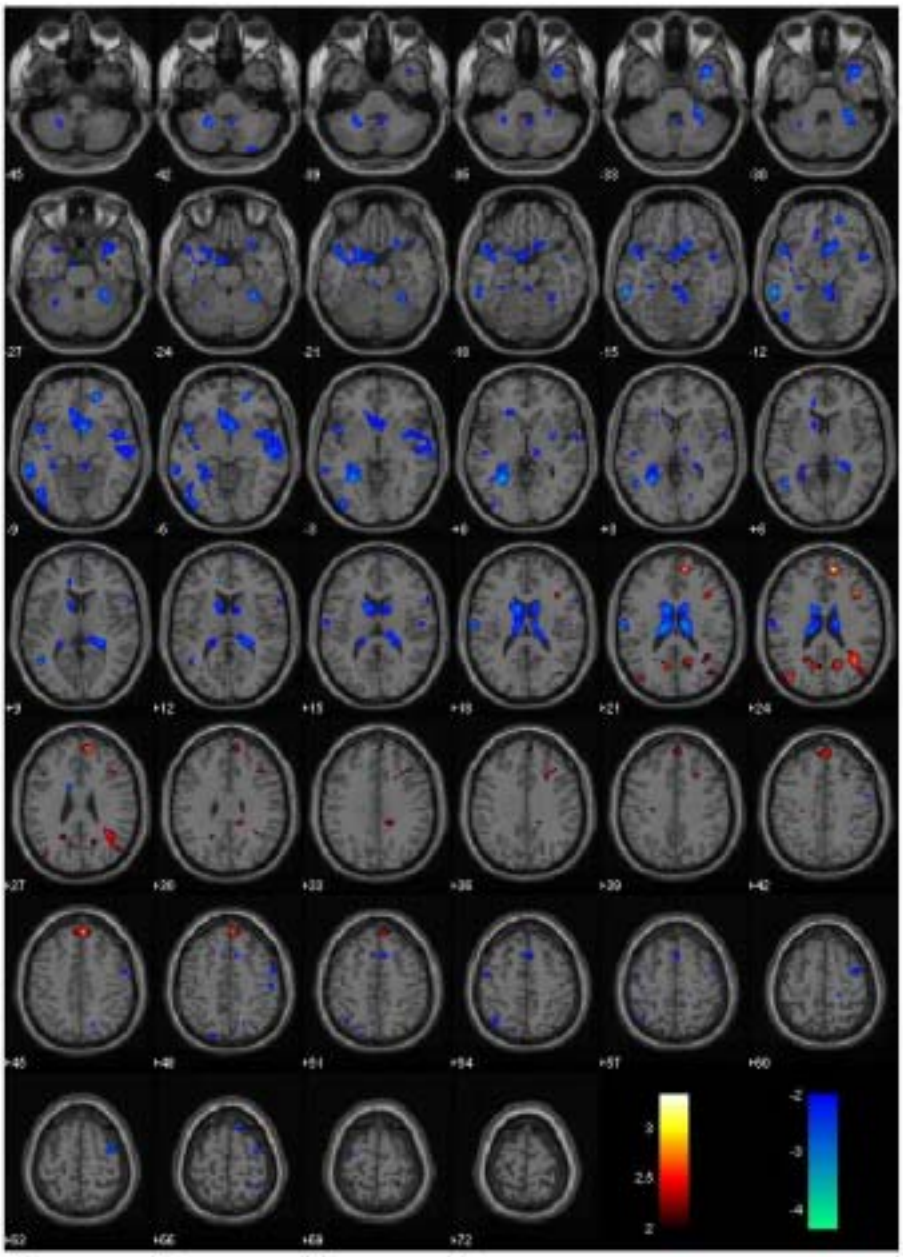
NPG – CO



SA – CO

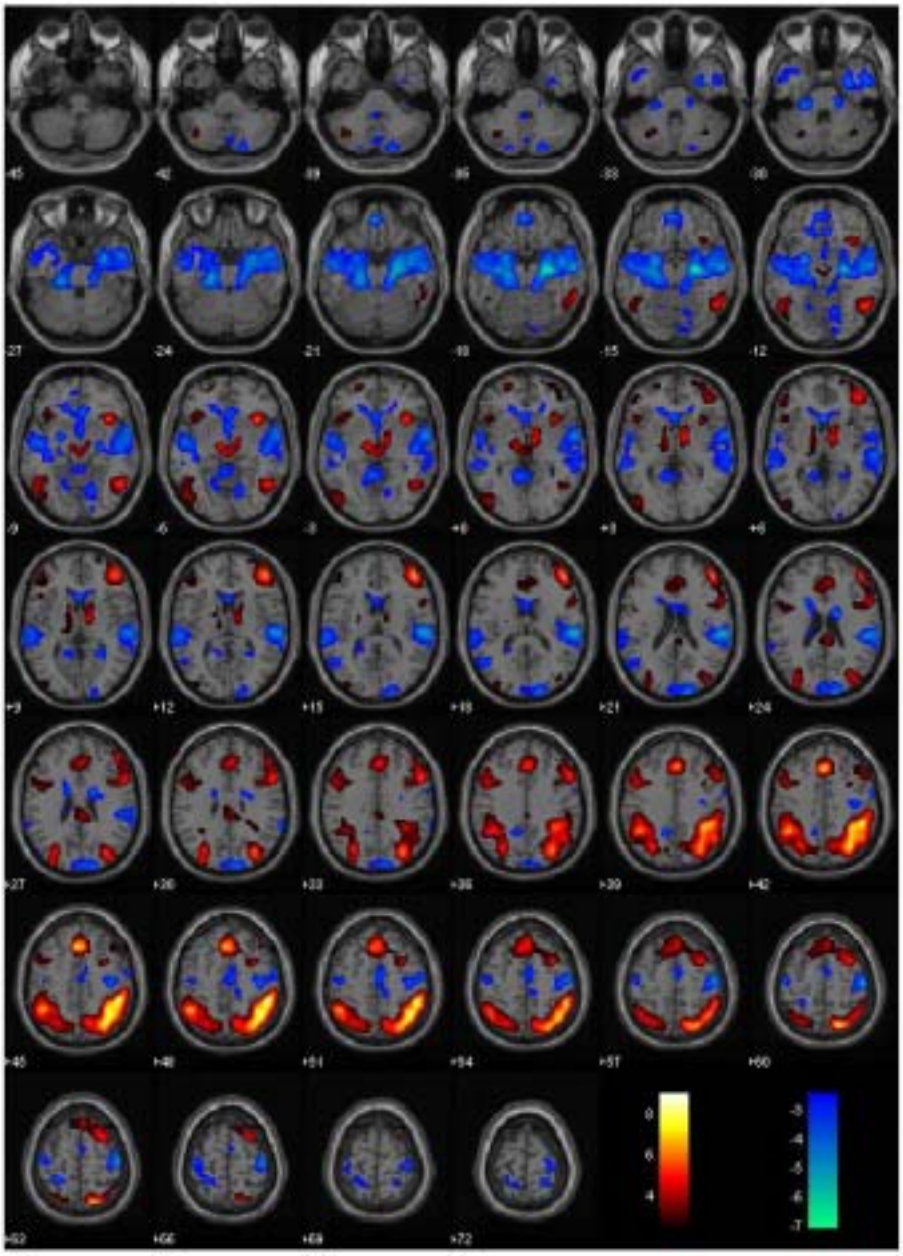


PG – NPG

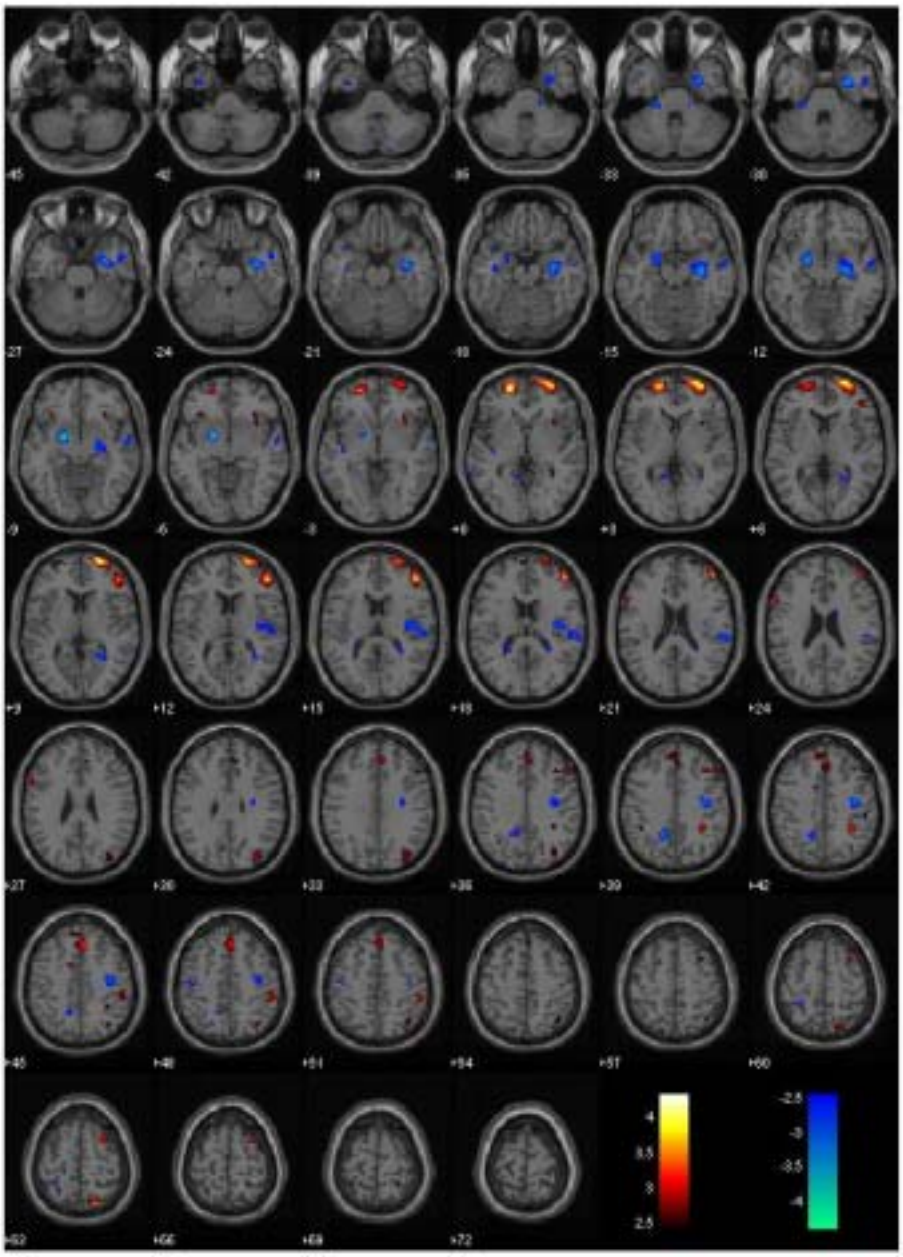


Probability discounting task: Free - forced

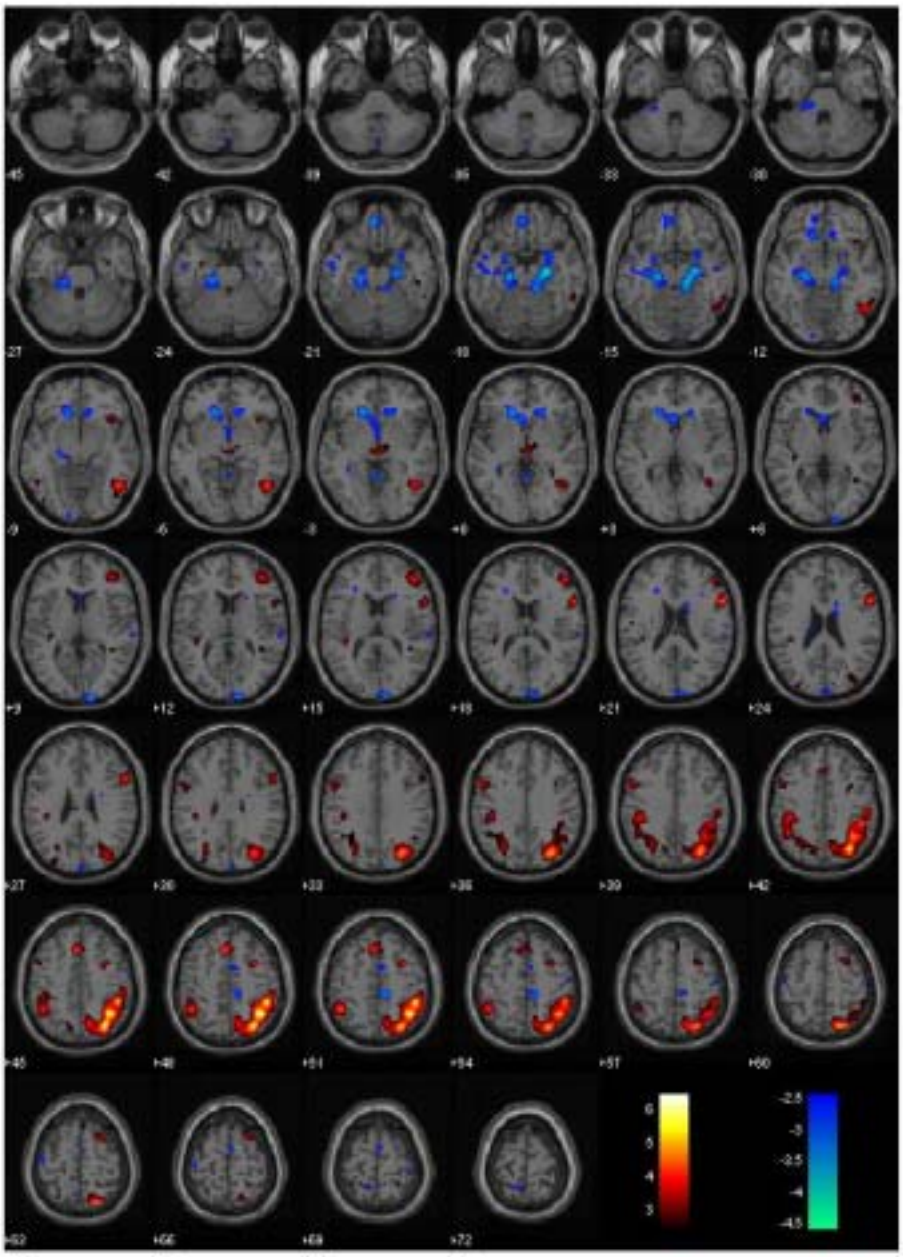
All groups



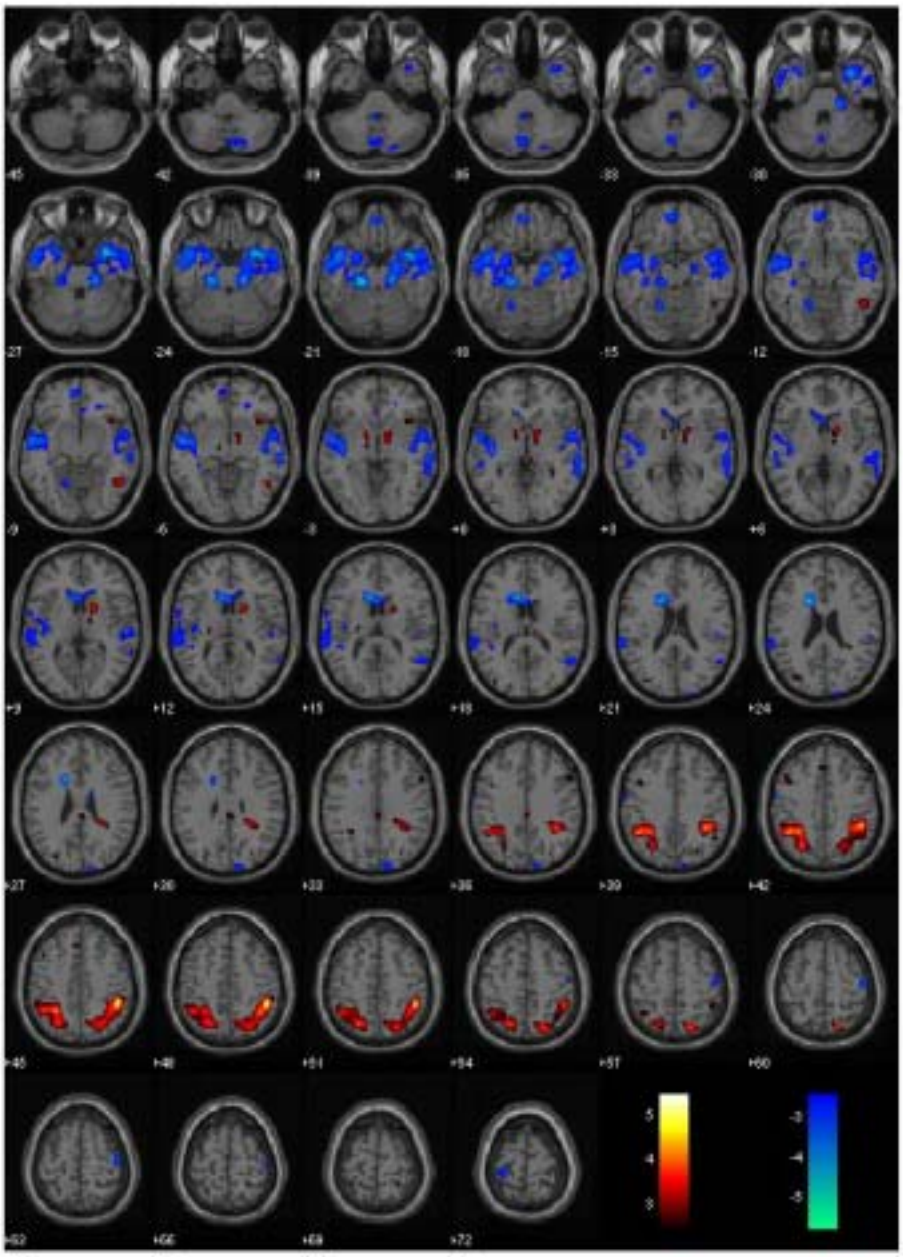
Pathological gamblers



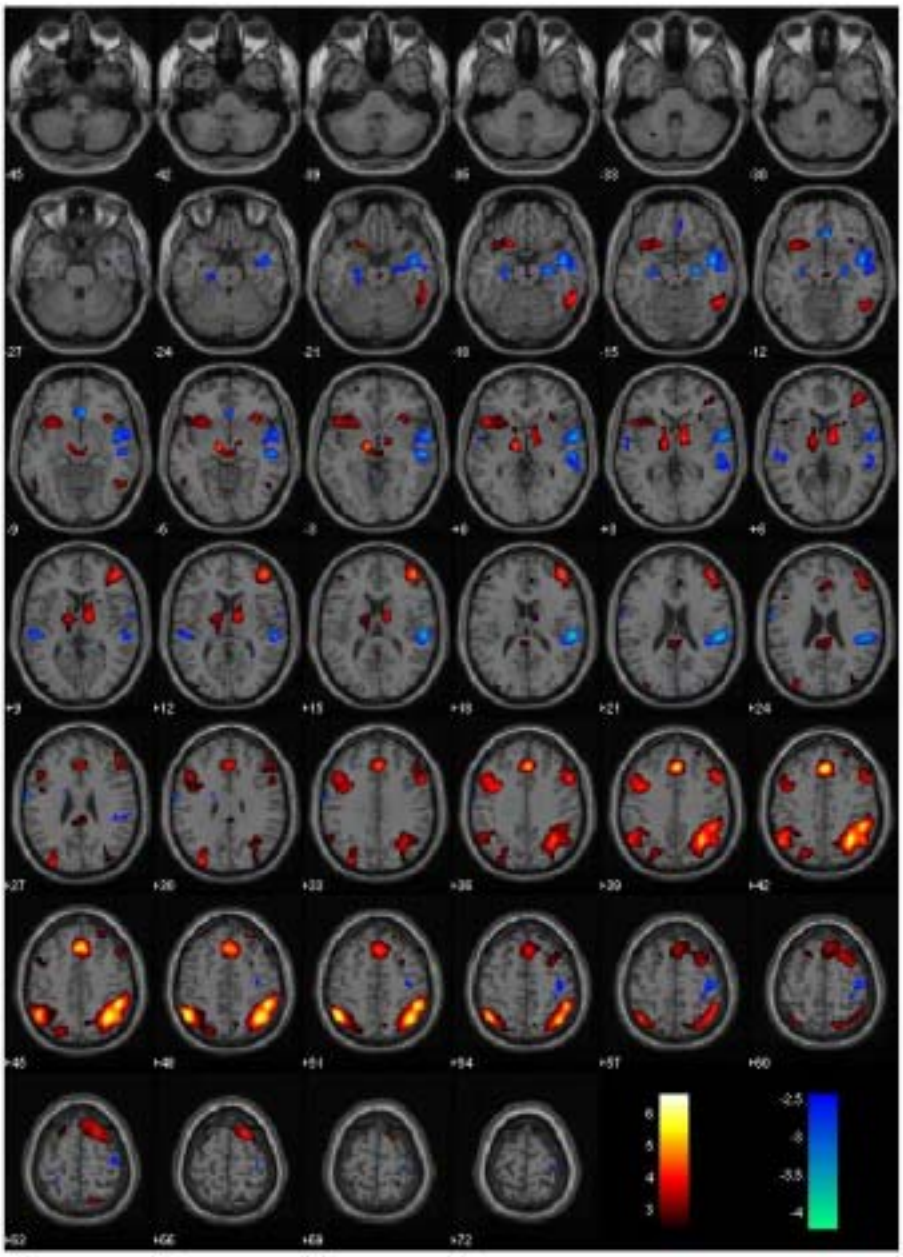
Non-pathological gamblers



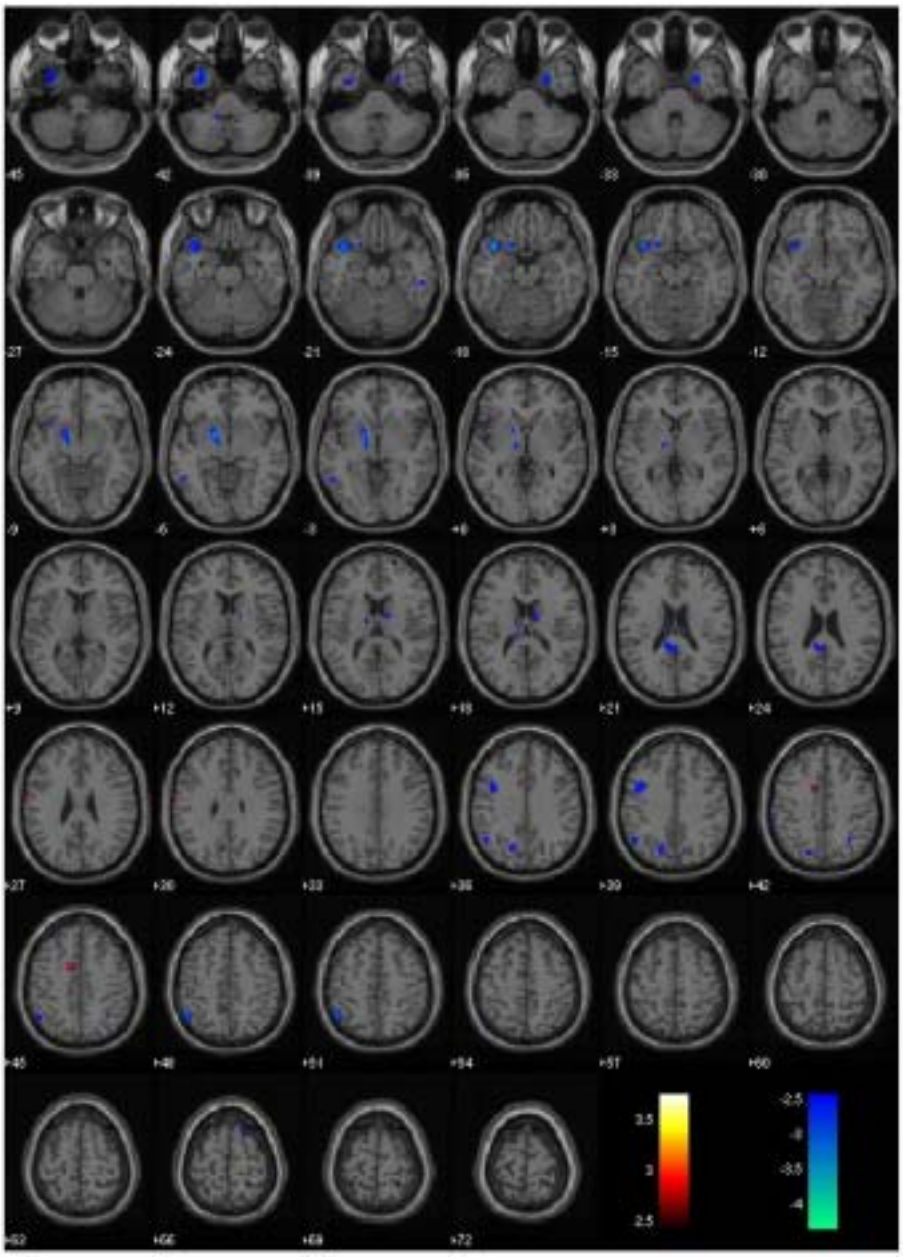
Substance abusers



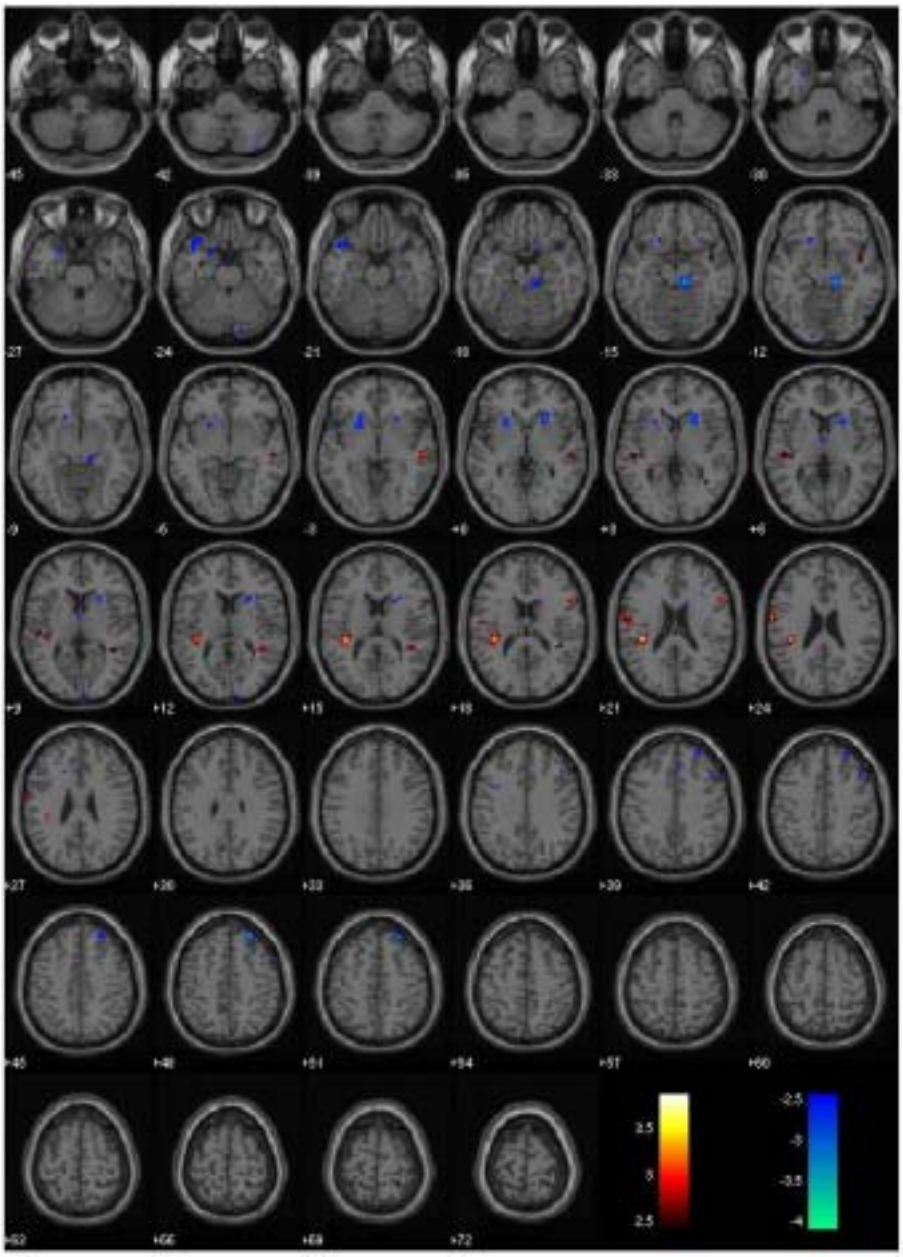
Controls



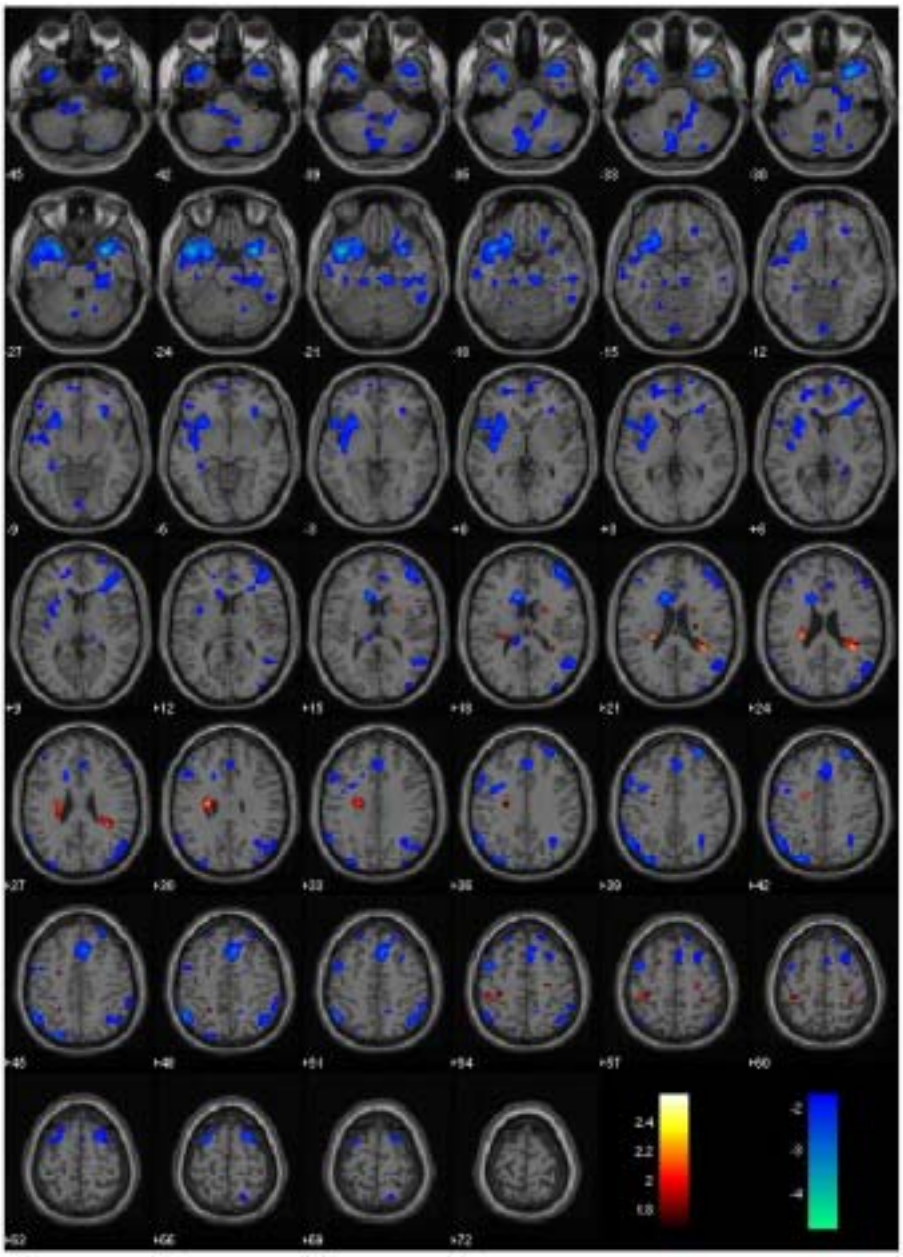
PG – CO



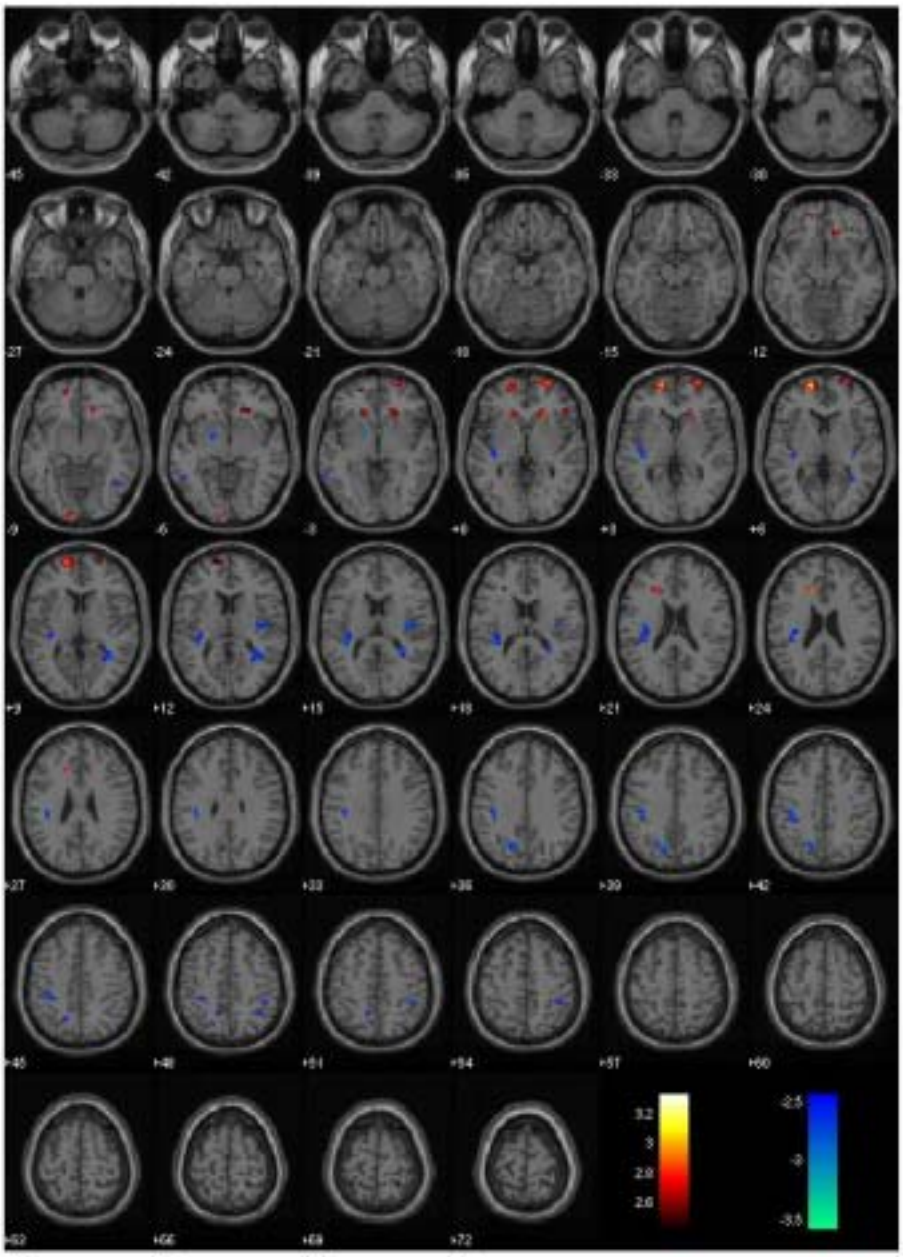
NPG – CO



SA – CO

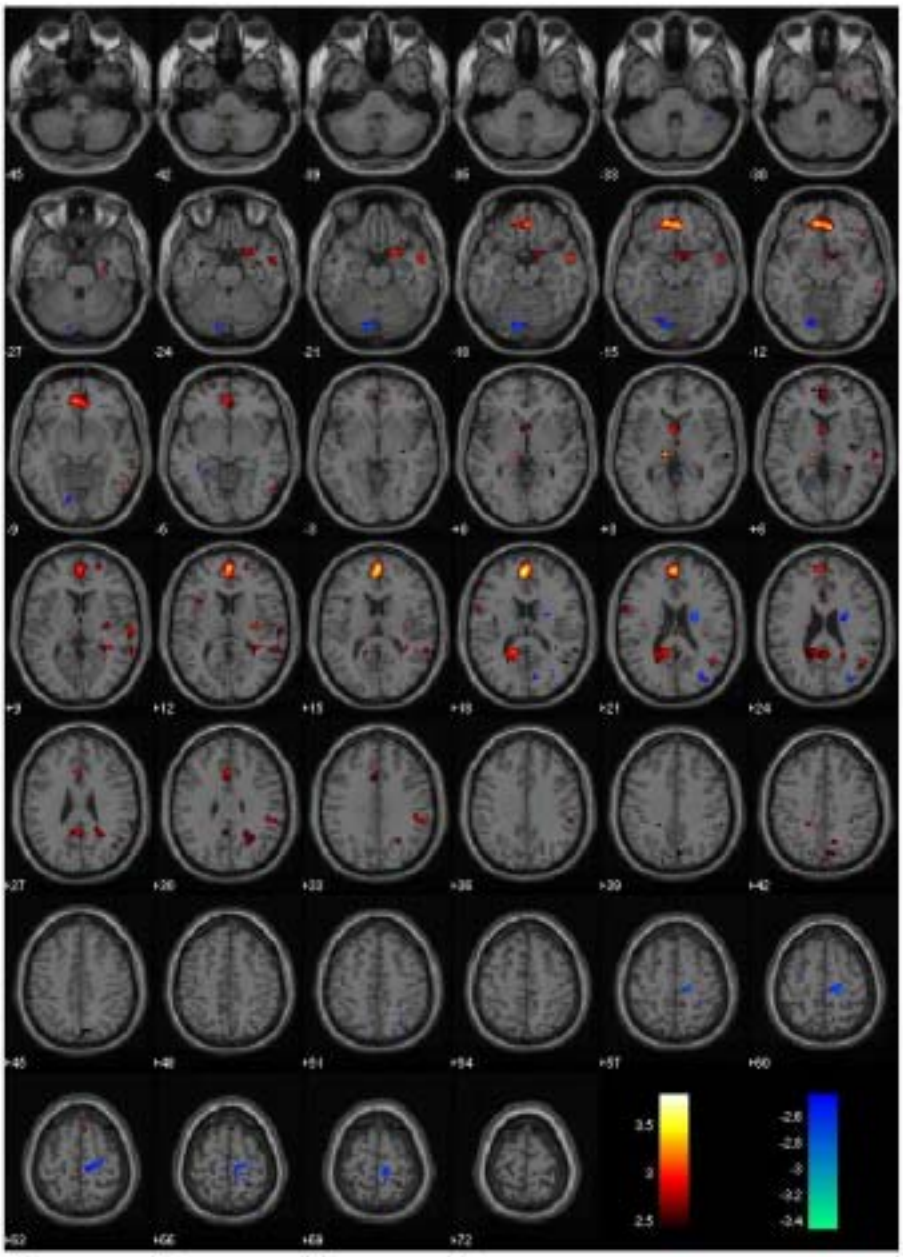


PG – NPG

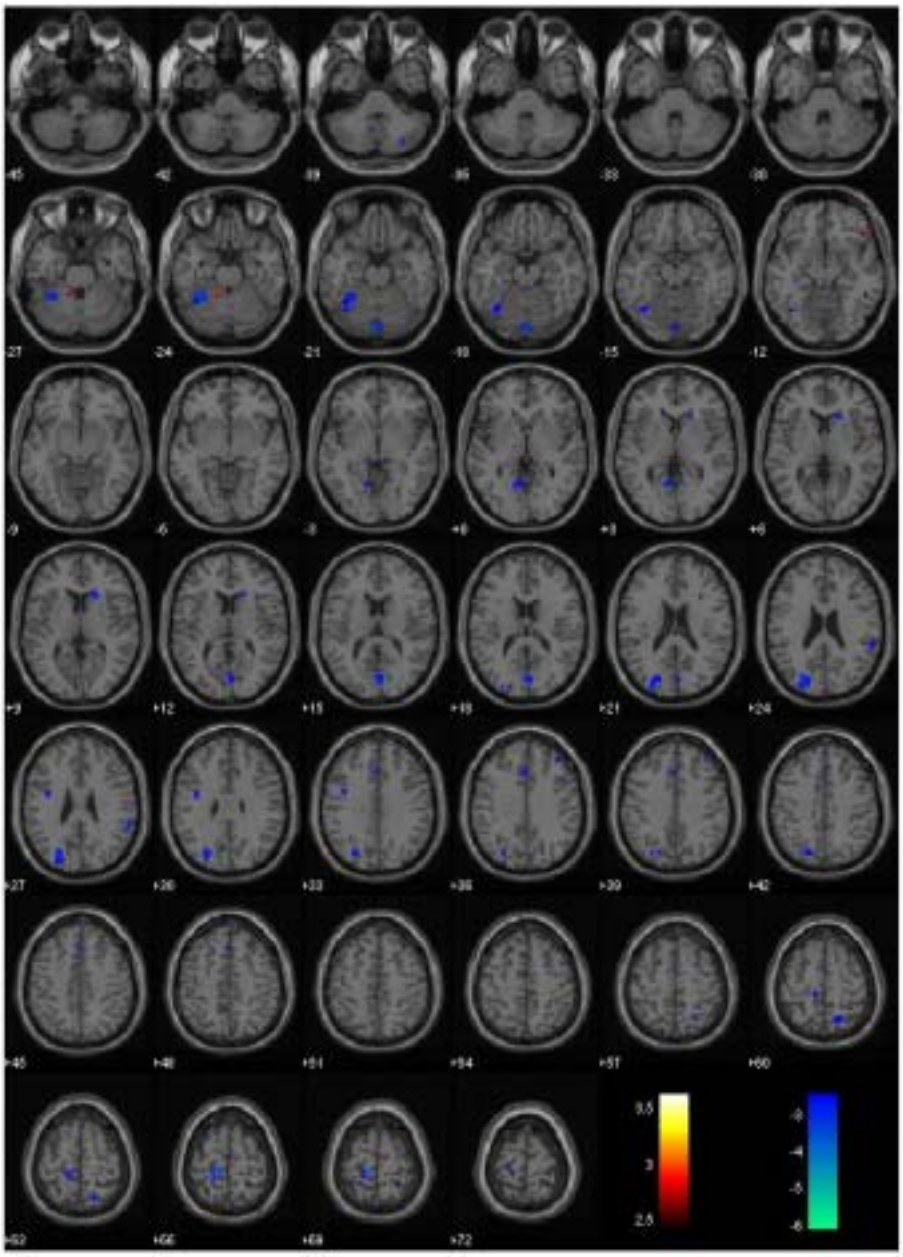


Urge to Gamble task: Internet gambling vs. neutral stimuli

Pathological gamblers

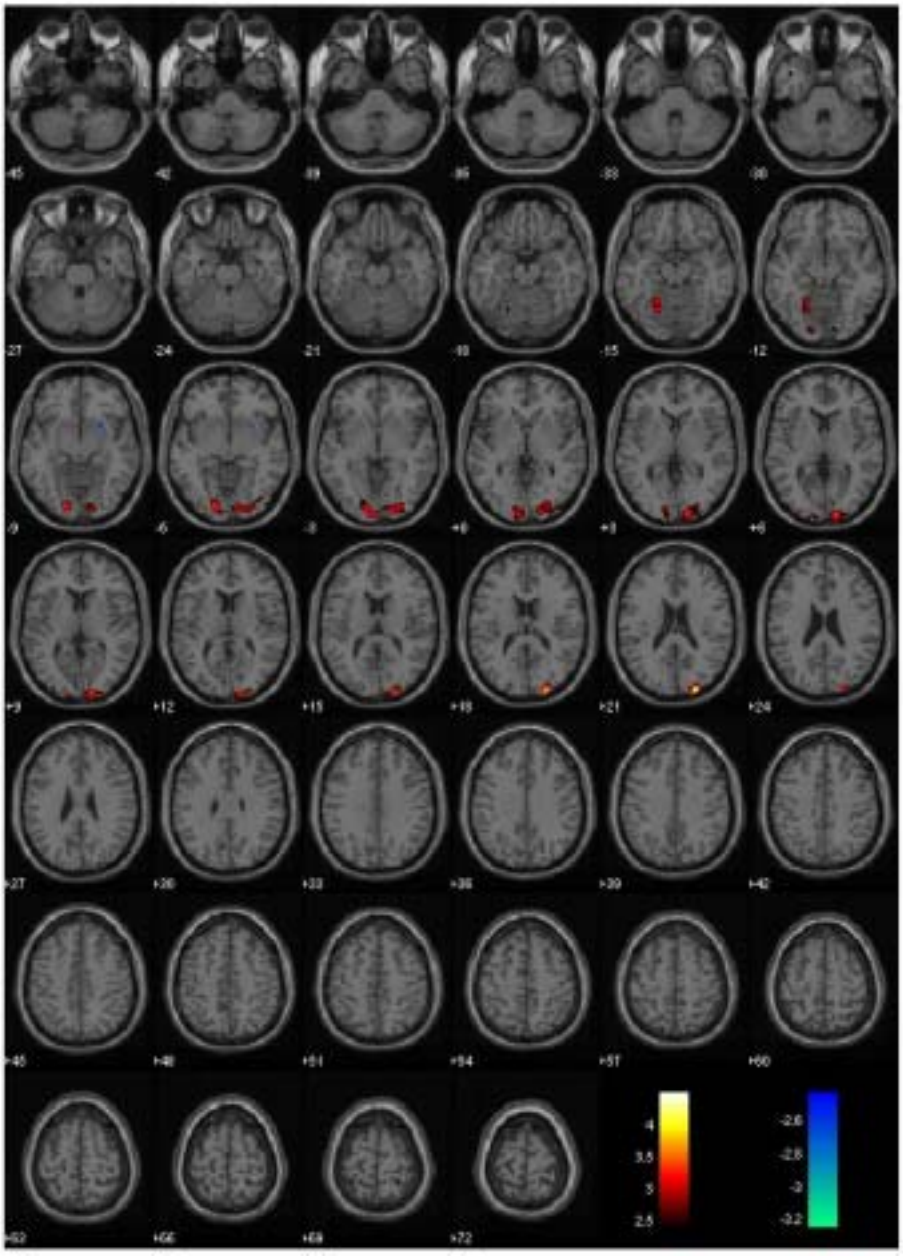


Non-pathological gamblers

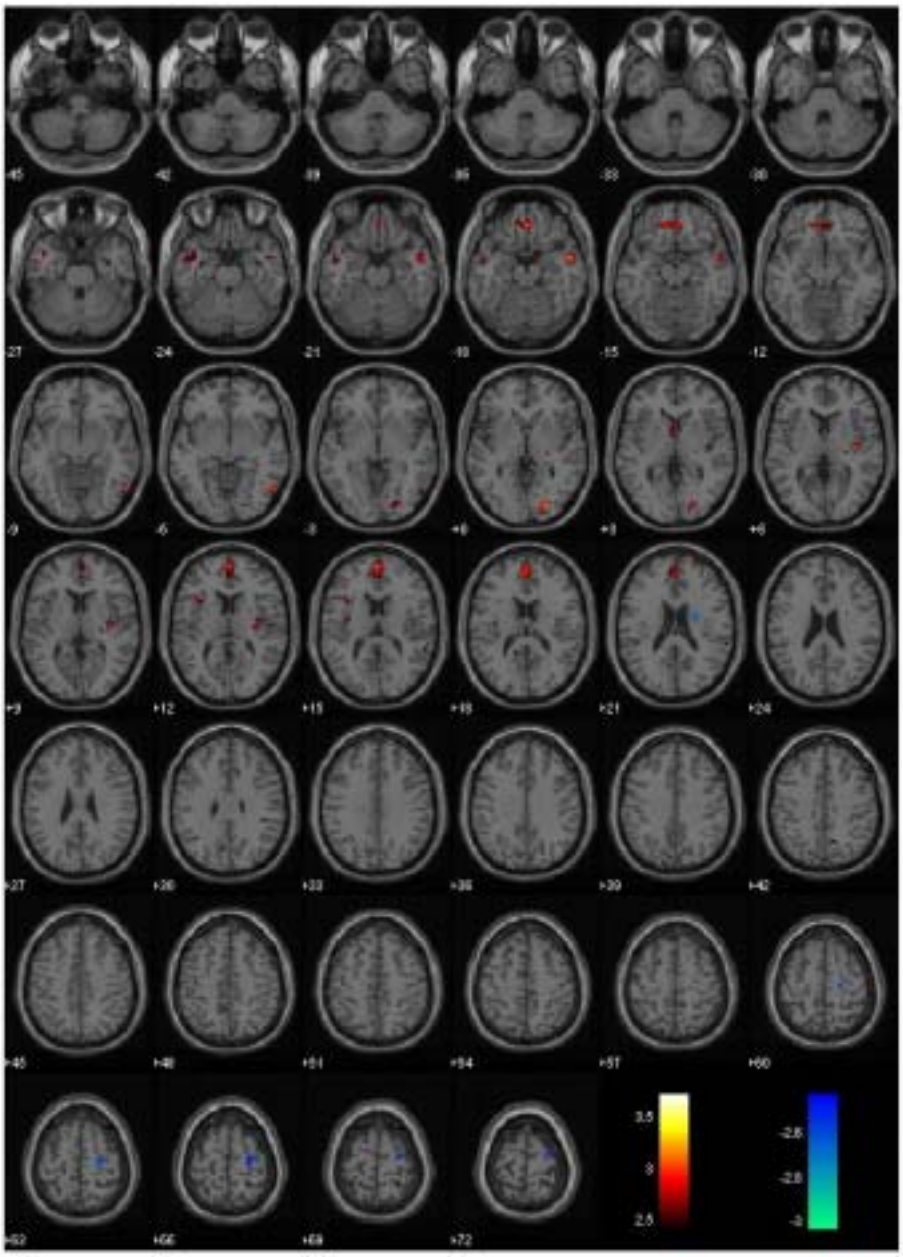


Controls

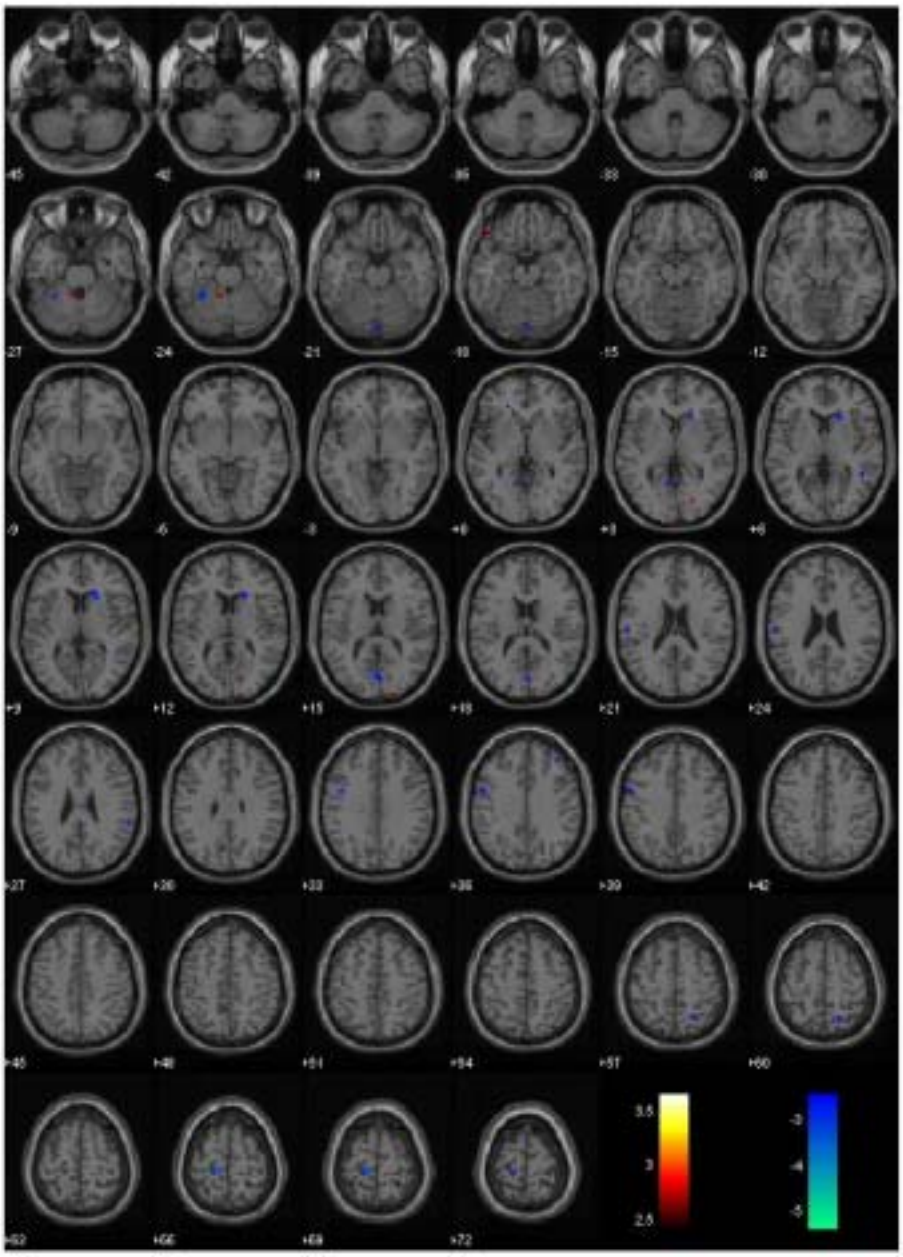
Please note that for this comparison only the colours are reversed.



PG – CO



NPG – CO



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