

*The Economics, Neurobiology and  
Pharmacology of Intertemporal Choice in  
Humans*

*A thesis submitted for the degree of Doctor of Philosophy*

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September 2009

## **Preface**

I, Alexander J Pine confirm that the work presented in this thesis is my own. Where information has been derived from other sources I confirm that this has been indicated in the thesis.

AJ Pine

## Abstract

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In intertemporal choice, decision-makers must choose between options whose outcomes occur at different times in the future and are associated with different magnitudes of gain or loss. Previous neuropsychological research on this problem is dominated by a behavioural-economic model which proposes that choice outcome is solely determined by a process of devaluing rewards with time, termed temporal discounting.

This thesis investigates the veracity of this assumption by developing a new mathematical model of choice which takes into account another fundamental feature of human preference, namely the non-linearity of the relationship between the utility and magnitude of gains.

Using behavioural data, methodologies are developed to demonstrate that this model is superior to previous models in accounting for human intertemporal choices. Specifically, using existing terminologies 'impulsive' and 'self-controlled' to describe preference in choices between smaller-sooner and larger-later monetary rewards, it is shown that the discounting of increasing magnitudes implied by the law of diminishing marginal utility exerts a significant effect in determining choice outcome. In addition to high rates of temporal discounting, it is shown that impulsivity can be engendered by higher rates of diminishing marginal utility and vice-versa.

A neuronal account of this model is delineated using neuroimaging techniques, revealing fundamental properties of the brain's value systems. It is shown that sub-components of value relating to time and magnitude are evaluated by distinct systems and then integrated to furnish an overall metric of utility used to guide choice – in accordance with utility theory.

Finally, the ability of the neurotransmitter dopamine to modulate these features of preference and neurobiological systems is investigated using pharmacological manipulation, where it is shown that enhancing dopamine activity engenders impulsivity. These behavioural and neural findings are shown to offer a compelling account of the pathological impulsivity observed as a feature of disorders associated with aberrant dopamine function.

To Opi and Elian

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## Acknowledgements

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First I would like to thank Val Curran and Ray Dolan for being outstanding supervisors. Their support, guidance and encouragement made it all possible. Thank you also to the Medical Research Council for granting me the opportunity to research this fascinating area of neuroscience.

Thank you to everyone who helped me along the way, particularly Jon Roiser, Tamara Shiner, Hanneke den Ouden, Chloe Hutton and the radiographers for help with testing and analyses. Special thanks to Ben Seymour for help with everything, for endless discussions, for being a great mentor and for all the g-chats! Thanks to Karl Friston for being so patient. Thanks to Peter Bossaerts for help with economics and to Anna Remington for all the coffee fueled study sess's. Thanks to everyone at the FIL and psychopharmacology unit for making them such great places to work.

I would also like to thank the researchers who took time to answer a stranger's questions so thoroughly, in particular Chris Bradshaw, Leonard Green and Yang Ho.

Finally, thanks to my family and to Elian for everything.

## Abbreviations used in this thesis

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5-HIAA	5-hydroxyindoleacetic acid
5-HT	5-hydroxytryptamine (serotonin)
5,7-DHT	5,7-dihydroxytryptamine
6-OHDA	6-hydroxydopamine
8-OH-DPAT	8-Hydroxy-N,N-dipropyl-2-aminotetralin
ACC	Anterior cingulate cortex
ACPC	Anterior cingulate – posterior cingulate
ADHD	Attention-deficit/hyperactivity disorder
AIC	Akaike information criterion
ANOVA	Analysis of variance
ASAP	As soon as possible (model)
BIS	Barratt impulsiveness scale
BLA	Basolateral amygdala
BOLD	Blood-oxygen-level-dependent
COMT	Catechol-O-methyltransferase
CSF	Cerebrospinal fluid
<i>D</i>	Discount factor
DA	Dopamine
DAT	Dopamine transporter
DAT KO	Dopamine transporter knock-out (mice)
DDS	Dopamine dysregulation syndrome
DLPFC	Dorsolateral prefrontal cortex
DS	Dorsal striatum
DSM	Diagnostic and statistical manual
DU	Discounted utility
EPI	Echo-planar images
EU	Expected utility
fMRI	Functional magnetic resonance imaging
FWE	Family-wise error
FWHM	Full-width at half-maximum
GABA	$\gamma$ -aminobutyric acid
HRF	Hemodynamic response function
<i>K</i>	Discount rate parameter
L-Dopa	Levodopa
<i>M</i>	Magnitude
MEU	Maximization of expected utility
MHM	Multiplicative hyperbolic model
MLE	Maximum likelihood estimation

MNI	Montreal Neurological Institute
MPFC	Medial prefrontal cortex
MSADHD	Motivational style attention-deficit/hyperactivity disorder
NA	Noradrenaline
NAc	Nucleus accumbens
OCD	Obsessive-compulsive disorder
OFC	Orbitofrontal cortex
$P$	Probability
$P(A B)$	Probability of A given B (conditional)
PCC	Posterior cingulate cortex
pCPA	para-Chlorophenylalanine
PD	Parkinson's disease
PIT	Pavlovian - instrumental transfer
PFC	Prefrontal cortex
$r$	Utility concavity (/convexity)
RT	Reaction time
SHM	Simple hyperbolic model
SHR	Spontaneously hypertensive rat
SPM	Statistical parametric map
SSRI	Selective serotonin reuptake inhibitor
SSRT	Stop-signal reaction time
TR	Repetition time
$U$	Utility
$V$	Value
VBM	Voxel based morphometry
VMOFC	Ventromedial orbitofrontal cortex
VS	Ventral striatum
VTA	Ventral tegmental area

## **Publications**

To date the following publications have arisen as a result of work directly presented in this thesis:

Pine A, Seymour B, Roiser JP, Bossaerts P, Friston KJ, Curran HV, Dolan RJ. (2009). Encoding of Marginal Utility across Time in the Human Brain. *The Journal of Neuroscience* **29**:9575-81.

Pine A, Shiner T, Seymour B, Dolan RJ. (In Press). Dopamine, time and impulsivity in humans. *The Journal of Neuroscience*.

# Chapter 1.

## Introduction

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### Overview

This thesis investigates a fundamental category of decision-making which human beings engage in on a daily basis – intertemporal choice. In simple terms, this is the decision-making which is required when we are faced with a choice of two or more options whose outcomes both occur at different times in the future, and are associated with different magnitudes of gain or loss. Specifically, I will consider intertemporal choice in the context of three related disciplines – economics, psychology and neurobiology – tied together by a single theme, namely the development and corroboration of a new model of choice. This model changes a number of fundamental assumptions about how humans arrive at such decisions and in turn illuminates each of the three disciplines respectively.

The problem of intertemporal choice has been deliberated for two hundred years and until recently has been confined to the field of economics. It now forms a major topic within this field and especially in the newer discipline of decision-theory. Since the greatest influence on thinking about this problem has come from decision theory, as well as most of the early empirical observations, I shall first give a brief overview of the field. I will start by considering normative decision theory and the framework it provides for studying choice. Particularly I will focus on utility theory and the axioms it describes regarding fundamental features of preference humans should possess in order to make rational, stable and optimal choices. Next, decision theory will be considered from the perspective of

descriptive and empirical theorists, and how their aims and methods relate to those of normative theorists. Subsequently I will summarize the development of intertemporal choice models, starting from the earliest thinkers, moving on to the ideas of normative theorists and finally considering a wealth of observations catalogued by behavioural economists, which have led to current models of choice.

When behavioural economists started to investigate human and animal intertemporal choice, a number of psychologists became interested in the problem and how it relates to the trait of impulsivity. A brief review of this literature will show how modern theorists fractionate impulsivity into a number of component behavioural processes, one of which is amenable to study by intertemporal choice paradigms. Impulsivity therefore became linked to the economic models describing this process. In the last twenty years this interest in intertemporal choice spread to neurobiologists and neuroeconomists who have attempted to provide a neural basis for intertemporal choice behaviour and impulsivity. Before reviewing this literature I will discuss the methodology of intertemporal choice experiments and how standard models are evaluated.

Finally, I will return to consider some concepts from decision theory which form the basis of a number of concerns with standard intertemporal choice models and much of the experimental work carried out to date. These ideas lead to the development of a new model of choice which is subsequently investigated.

## **Introduction to decision theory**

Decision theory concerns goal directed behaviour in the presence of options, and as such, is fundamental in accounting for higher-order motivated behaviour. It is tacitly assumed that organisms are designed to select courses of action whose outcome is most beneficial to their survival – in economic terms this principle is

known as maximizing utility. At any one time, there are myriad available decisions one could take. When we consider an agent who must decide between a number of possible actions, the information used to guide choice is extremely varied and complex. Decision theory therefore provides a framework for the identification and determination of value – and the variables relating to this concept – which enables organisms to make optimal and stable choices. It also allows us to make specific predictions about the behaviour of agents in choice environments.

### *Normative decision-making and axioms of utility theory*

Decision theory spans a number of disciplines but is traditionally split into two branches – normative and descriptive. Normative or prescriptive theory, addresses how decisions *should* be made. There is almost unanimous agreement that the main desideratum of such a theory is rationality in choice. In other words a normative decision theory is a theory about how decisions should be made in order to be rational. The term rational is somewhat contentious (Arrow, 1989; Becker, 1978; Green and Shapiro, 1994; Sen, 1987) but in this context can be traced to formal utility theory which delineates a number of axioms that define attributes of preference which perfectly rational agents should possess (von Neumann and Morgenstern, 1947; see Arrow, 1989; Becker, 1978; Russell and Norvig, 1995). The three most important axioms are completeness, reflexivity and transitivity.

Suppose that  $A$  and  $B$  are two bundles of goods (for example, apples and oranges). We can describe an agent's preferences with the following binary relations:

$A \geq B$      $A$  is at least as good as  $B$

$A > B$      $A$  is preferred to  $B$

$A \sim B$  The agent is indifferent between  $A$  and  $B$  (they are equally preferred)

Completeness requires that one and only one of the relations  $A \geq B$  and  $B \leq A$  should always hold true. In other words an agent should always be able to state a preference between two bundles such that  $A > B$ ,  $B > A$  or  $A \sim B$ . Reflexivity posits that for any bundle,  $A \sim A$  holds true. Transitivity implies that if  $A > B$  and  $B > C$  then it must be true that  $A > C$ .

Other axioms include independence – if  $A > B$  then  $[A + C] > [B + C]$ . It is easy to see how violation of these axioms can lead to unstable and irrational choice. For example, violation of transitivity can lead to a 'money pump' scenario – if an agent's preference relation is  $A > B > C > A$ , an observer could offer  $C$  in exchange for  $A$  and a small monetary payment; similarly  $B$  for  $C$  and  $A$  for  $B$ . The agent ends up in its original state but with less money, which – assuming money is desirable – is irrational.

If an agent's preferences satisfy the axioms, then there must exist a utility function  $U$  that assigns a real number to every action such that if  $X > Y$  then  $U(X) > U(Y)$ . This utility function will be a continuous function whereby the agent is able to rank the utility of all possible goods (or outcomes of actions)  $X_1, X_2, \dots, X_n$  such that  $Utility = U(X_1, X_2, \dots, X_n)$ .

In addition to assigning value to outcome states, goal directed action also requires knowing the consequences of actions. Allowing for the fact that actions do not always have predictable consequences, an agent's knowledge about the causal nature of the world can be represented in the form  $p(action \rightarrow outcome_n | evidence)$ , assigning the probability, given the available evidence that *action* causes *outcome<sub>n</sub>*. The *expected utility* (von Neumann and Morgenstern, 1947) of an action is therefore determined as follows:

$$EU(action|evidence) = \sum_n p(action \rightarrow outcome_n|evidence) \cdot U(outcome_n)$$

Selection of the outcome which maximizes expected utility on the part of the agent entails rational decision-making – the MEU principle. This theory does not specify the utility function itself, nor does it specify the way the decision is arrived at, which may be implicit or explicit. Furthermore utility could either be a cardinal measure, whereby each action outcome could be assigned a number in *utils*, or it could be an ordinal measure where the utility function simply specifies rank orderings of the expected utilities of each action. In either case, when choosing between options which differ in nature – for example, food versus mating – it is necessary to compare them on a single valuation dimension. Utility functions achieve this by converting multifactorial alternatives to real numbers (or ranks).

Note that utility is an undefined term, roughly translating to desirability or happiness, although in neoclassical economics it serves as a purely behavioural measure based on revealed preference, without the need to invoke mental states. In the moral philosophy of Bentham (1789) and Mill (1863), Utilitarianism sought the greatest happiness for the greatest number of people – in other words, the maximization of global utility – as a moral criterion for the organisation of society and a basis for moral decisions.

Finally, normative decision theory entails a number of *ceteris paribus* assumptions such as perfect knowledge on the part of the agent about the outcome of its actions (or sufficient evidence to compute probabilities in the case of uncertainty). Additionally it is assumed that the agent has sufficient time and cognitive resources to compute the expected utilities of each course of action (in artificial intelligence this has proved a difficult problem (Russell and Norvig, 1995).

### *Descriptive decision theory*

Whereas normative decision theory aims to provide a framework for an idealized system of decision-making which is based on a set of axiomatic principles, leading to stable, predictable and rational (utility maximizing) choice, descriptive theory characterizes how humans and animals actually do make decisions. The empirical science of behavioural economics investigates the circumstances under which behaviour is consistent and inconsistent with the assumptions of normative theory. Amos Tversky, Daniel Kahneman and a number others founded this field of research by cataloguing an array of cognitive biases and irrationalities in human decision-making, particularly decision-making under risk and uncertainty (Kahneman et al., 1982; Kahneman and Tversky, 2000; Tversky and Kahneman, 1974). This research culminated in the publication of prospect theory (Kahneman and Tversky, 1979) which replaced expected utility theory to become the dominant model of choice under uncertainty. One of the main themes discussed in behavioural economics is the use of heuristics – or rules of thumb – used by humans to aid and speed up the decision-making process. This is also linked to the concept of bounded-rationality (Simon, 1991; Kahneman, 2003) which focuses on the fact that the rationality of agents is limited by the time and computational power which would be required to calculate the expected utilities of every possible course of action. Rather than arriving at the optimal (utility maximizing) solution, decision-makers apply their rationality only after having greatly simplified the choices available using heuristics.

Descriptive decision theory does not aim to do away with the axioms of utility theory but attempts to modify neoclassical equations using behavioural insights, to be able to make accurate predictions where classical models fail, and to theorize about the cognitive underpinnings of underlying decision and value systems. A

particular focus of behavioural economics is the role emotion plays in decision-making.

More recently, the field of neuroeconomics (e.g. Camerer et al., 2005; Glimcher, 2003; Loewenstein et al., 2008; Montague, 2007; Rangel et al., 2008) attempts to investigate the neural bases of valuation and decision-making in the brain by using mathematical models and insights taken from decision-theory. The aim of this endeavor is to assess how these models may be implemented neuronally and whether evidence from brain function corroborates them. Once a satisfactory understanding of these processes has been reached neuroeconomists hope to explain why actual behaviour deviates from normative models, why individuals differ in traits associated with decision-making, and how these systems go awry in cases of aberrant decision-making associated with various disorders. One of the most dominant and contentious proposals in neuroeconomics claims that there are two decision-making systems – one, a rational, deliberative system which functions according to the principles of normative theory, based in high-order executive and cognitive areas such as the prefrontal cortex (PFC) whereas the other is an irrational, affective system based in more primitive regions such as the limbic system, which can lead behaviour to stray from rational principles (e.g. Rustichini, 2008; Sanfey and Chang, 2008). Neuroeconomics also seeks to impact on behavioural economics by providing a new source of data with which to inform models of decision-making.

The response of some normative theorists to descriptive theorists' observations of axiom violation and failure of their models is varied. Some claim that what humans actually do is irrelevant to their goal of building an idealized framework of decision making that leads to perfectly rational and optimal behaviour. Others remain skeptics with regard to putative biases in decision-making and irrationalities which have been observed, insisting that they only appear under

unique experimental settings or that they disappear after prolonged testing or when pointed out to the subject (e.g. Myagkov and Plott, 1997; Plott, 1996). It could also be argued that our underlying valuation systems do conform to the axioms, however it is a faulty decision-making system which leads to non-optimal choices.

Decision-making research has focused on a number of foundational areas which are relatively easy to study, where the key variables are (parametrically) quantifiable and where rewards or punishment are usually monetary. These include decision making under risk and uncertainty – an attempt to understand and model humans' risk-taking behaviour and probabilistic reasoning systems under different circumstances. Game theory and social decision-making forms another core area. The present thesis is primarily concerned with intertemporal choice or decision making over time.

## **Intertemporal choice and the discounted utility model**

As noted earlier, choice can be simple when the options differ in one particular dimension – it's obvious (from a utility maximizing approach) to choose £100 over £50 or an 80% chance of acquiring a piece of cheese over a 25% chance – but in real life organisms must make choices between rewards (and punishments) that differ in more than one valuation dimension. Choices where the options differ in both magnitude and the delay to their receipt (or consumption) are known as intertemporal choices and form one of the most important and common classes of decisions that humans engage in on a daily basis. Examples of these may include deciding whether to save some income into a pension scheme (a large delayed reward) versus using the money to buy a new flat-screen TV (a small immediate reward), paying off a credit card bill now (a small immediate punishment) versus allowing the interest to accrue and paying it off at a future date (a larger delayed

punishment), and eating a highly calorific dessert (small, soon reward) versus dieting to improve one's health (larger later reward). In experimental settings, these choices are often presented in the form of a smaller-sooner versus a larger-later amount of money. This decision class can range from the prosaic, spanning short delays, to life changing decisions involving health, education, family and finances that can span multiple years. Indeed the ability to make choices over such long time frames is a uniquely human activity that sets us apart from other species – Stevens et al. (2005) report that our nearest evolutionary relatives such as cotton-top tamarin monkeys, are unable to wait more than eight seconds to triple the value of an immediately available food reward and are unable to consider rewards delayed by more than a minute.

### *Temporal discounting: reasons for caring less about the future*

It is both natural and rational to reason that future rewards should not be as desirable as current rewards. Therefore to decide between rewards and punishments of differing magnitudes and delays, an agent should devalue or discount their value in accordance with their delay. This process is termed temporal discounting. Economists in the 19<sup>th</sup> and 20<sup>th</sup> centuries posited a number of psychological and economic reasons as to why this should be the case.

John Rae, the Scottish economist who first considered the problem of intertemporal choice in the context of explaining differences in the wealth of nations, proposed two reasons as to why desire for the “accumulation of wealth” should be limited. The first reason was that waiting for future rewards entails a risk that those rewards will not be received due to the “uncertainty of human life”. As he put it:

When engaged in safe occupations, and living in healthy countries, men are much more apt to be frugal, than in unhealthy, or hazardous occupations, and in climates pernicious to human life. Sailors and soldiers are prodigals. In the West Indies, New Orleans, the East Indies, the expenditure of the inhabitants is profuse. The same people, coming to reside in the healthy parts of Europe, and not getting into the vortex of extravagant fashion, live economically. (Rae, 1834; p. 57).

Thus, just as we discount the value of probabilistic rewards in accordance with their risk of non-occurrence, we should devalue future rewards on similar grounds. This uncertainty is reflected in modern financial markets where borrowing costs measured by interest rates (i.e. the time value of money) are larger for companies and individuals with lower credit ratings and increase with the length of time a loan is made for. Indeed modern debate continues as to whether temporal discounting is a special case of probabilistic discounting and whether they share the same psychological and neural mechanisms (e.g. Green and Myerson, 2004; Luhmann et al., 2008).

Rae also reasoned that the excitement produced by the prospect of immediate consumption and the concomitant discomfort of deferring such available gratifications is another motivation in temporal discounting:

Such pleasures as may now be enjoyed generally awaken a passion strongly prompting to the partaking of them. The actual presence of the immediate object of desire in the mind by exciting the attention, seems to rouse all the faculties, as it were to fix their view on it, and leads them to a very lively conception of the enjoyments which it offers to their instant possession. (Rae, 1834; p. 120).

Eugen von Böhm-Bawerk, another major figure in the development of the economic and psychological perspective on intertemporal choice, submitted a new motive to the list, arguing that humans suffer from a systematic tendency to underestimate or perhaps have an inability to imagine future wants:

It may be that we possess inadequate power to imagine and to abstract, or that we are not willing to put forth the necessary effort, but in any event we limn a more or less incomplete picture of our future wants and especially of the remotely distant ones. And then there are all those wants that never come to mind at all. (Böhm-Bawerk, 1889; pp. 268–69).

Von Böhm-Bawerk also considered the problem of intertemporal choice to be a technical one, regarding it as a problem of how best to allocate resources to oneself over different points in time. This approach was crystallized by Fisher (1930) who postulated that rational agents will borrow or lend so that their marginal rate of substitution between present and future money will equal the market interest rate. Here, marginal rate of substitution means the rate at which it can be exchanged while keeping utility constant. To see why this should dictate a rate of 'pure time preference' consider an environment where the interest rate is 5%, so £100 lent will yield £105 in a year's time. If an impatient individual who is indifferent between £100 offered today and £130 in one year, were offered a choice of £100 today and £110 in one year what should he choose? According to Fisher, he should choose the larger reward and subsequently borrow £100 at the 5% rate. In a year's time he can then collect the £110 and use it to pay back the £105 he owes, to pocket £5 difference. A similar logic can be made for a patient individual who is indifferent between £100 today and £102 in a year. If they were offered a choice between £100 today and £104 in one year, they should choose the sooner option and lend it at the market rate to receive £105 in a year. Thus, all rational agents should make the same intertemporal trade-offs for money. Note this does not tell us how impatient the individuals are, consequently it does not inform us about their consumption decisions. Fisher deemed the marginal rate of substitution an objective (or pure) factor contributing to temporal preference but he also considered a number of subjective, psychological motivations to be important, as previous economists had done.

Fisher and von Böhm-Bawerk's insights in to the causes of discounting can more generally be described as opportunity cost arguments. Discounting future rewards compensates for the fact that opportunity costs grow over time. In the example of the 5% interest rate world, waiting one year for £104 would cost the agent £1 in interest (risk-free). Opportunity cost is what can be earned from the best alternative use of resources. In general most people grow wealthier over time (or have the opportunity to do so) and so it would make sense to prefer to receive resources sooner in order to invest them for the future – the farmer should prefer one bushel today than one next year because from one grow many (Read, 2003). Similarly a given loss now will be worth less in the future so we should want to defer losses as long as possible. Opportunity cost is also reflected in financial markets as the risk-free or official central bank rate, which increases with duration of the treasury bond.

Psychological factors such as risk, visceral states and a deficiency in imagining future wants, as well as opportunity cost arguments provide cogent reasons for discounting the future. These themes are still present in modern theories of discounting (e.g. Berns et al., 2007; Kacelnik, 1997; Kagel, 1987; Read, 2003) However economists also single out *impatience* (also termed pure time preference by some authors) as another basis for temporal discounting (e.g. Frederick et al., 2002; Read, 2003). Frederick et al. (2002) clarify this distinction as follows:

We distinguish *time discounting* from *time preference*. We use the term *time discounting* broadly to encompass *any* reason for caring less about a future consequence, including factors that diminish the expected utility generated by a future consequence, such as uncertainty or changing tastes. We use the term *time preference* to refer, more specifically, to the preference for immediate utility over delayed utility." (p. 352).

We can take impatience to mean that a given amount of utility is preferred the earlier it arrives, such that an individual who expects to obtain two future amounts of utility will be willing to exchange a unit increase in the earlier of the expected utilities for a decrease of more than one unit in the later. Uncertainty, or utility of anticipation are not time preference, under this scheme, because they pertain to the expected amount of utility consequences confer, and not the weight given to utility at different moments. Impatience has the overall effect of reducing lifetime utility, and as such caring more about current than future utility may be considered irrational. Parfit (1971, 1982, 1984) uses a Humean view of personal identity to rationalize such behaviour. He argues that there is no enduring self or 'I' over time, to which future utility can be ascribed. Since future selves are related to current selves only by psychological continuity, which diminishes over time, our descendent future selves have a status of other people, making their utility less than fully 'ours' and giving us a reason to count it less. In other words, you are not entirely the same person tomorrow as you were today. Economists have debated whether this concept of time impatience really exists (Peart, 2000), or whether caring about when something occurs is only attributable to an amalgamation of the factors previously recounted (Frederick et al., 2002). If a distinction can be made, it is not immediately obvious where to draw the line between factors that operate on utility and factors that make up time impatience, especially when considering some of the psychological motivations mooted by the early theorists.

*Normative models of intertemporal choice: the discounted utility framework*

Whilst 19<sup>th</sup> and early 20<sup>th</sup> century thinkers considered time preference to be a summary of various intertemporal motives playing out, Samuelson (1937)

introduced a revolutionary new model (which was axiomatically derived) known as the discounted utility (DU) model, whereby all these motives underlying temporal discounting were condensed into a single parameter known as the *discount rate*. The DU model specifies a decision-maker's intertemporal preferences over consumption profiles  $(C_t, \dots, C_T)$  which can be represented by an intertemporal utility function  $U^t(C_t, \dots, C_T)$  – under the normal axiomatic assumptions. The specifies the functional form of a person's intertemporal utility function accordingly:

$$U^t(C_t, \dots, C_T) = \sum_{k=0}^{T-t} D(k)u(C_t + k)$$

Where

$$D(k) = \left(\frac{1}{1+\rho}\right)^k$$

The term  $U(C_t + k)$  in this formulation is interpreted as the individual's cardinal instantaneous utility function (or well being over the time period  $t + k$ ), and  $D(k)$  is the individual's discount function.  $\rho$  here represents the individual's discount rate which is meant to reflect the amalgamation of intertemporal motives discussed above. The simplicity and elegance of Samuelson's DU model engendered its adoption as the framework by which to analyze intertemporal choice. This was despite his insistence that DU should not be considered a descriptive model of choice, remarking that "it is completely arbitrary to assume that the individual behaves so as to maximize an integral of the form envisaged in [the DU model]" (Samuelson, 1937; p. 159). One attractive feature of the formulation was its similarity to the compound interest formula, by which we can calculate, given a constant rate of increase, the future value of a given amount of money. Working backwards with the compound interest formula allows for the calculation of the present value of a future amount of money, given a certain interest rate.

In modern, practical (and experimental) settings this normative model is referred to as exponential discounting, and is usually functionalized more simply in the form:

$$V = M \cdot e^{-K \cdot t}$$

Thus the present (discounted or subjective) value  $V$ , of a reward or punishment of magnitude  $M$ , decreases exponentially in accordance with its delay  $t$  (e.g. Ainslie, 1975; Ainslie and Haslam, 1992; Cardinal et al., 2004; Green et al., 1994a; Mazur, 1987; Rodriguez and Logue, 1988). In this formulation  $K$  is a free parameter which represents the individual's discount rate. Thus  $K$  quantifies an individual's tendency to discount the future, or more accurately, discount future rewards/punishments. An individual with a high  $K$  value devalues rewards more quickly as they become more distant in time.

Exponential discounting is intuitively sensible and rational because it assumes a constant proportional devaluation per unit time (Figure 1). Just as the exponential decay of a radioactive compound represents the constant probability per unit time that an atom will decay, so too the exponential discount function assumes a constant devaluation per unit time which is based on a number of constant factors (probability of losing the reward, opportunity cost etc.). This leads to a constant per-period rate of discounting for all time periods ( $K_n = K$  for all  $n$ , where  $K_n$  is the discount rate applied between time periods  $n$  and  $n+1$ ).

Thus we now have a formal and normative model of how we should devalue future rewards, so as to be able to compare the present or subjective value of all the available options when faced with an intertemporal choice. The DU model facilitates choice by allowing the multidimensional aspects of delayed rewards to be compared on a unidimensional plane of measurement ( $U$ ) according to

axiomatic principles, thus allowing for utility maximization. In this regard, DU is the normative counterpart of the EU model for choice with probabilistic outcomes.

The DU model comes with a number of assumptions. These state that outcomes occur with certainty and are consumed instantly, discounting is independent from consumption, outcome utility is stationary (timing-independent), and so on (see Frederick et al., 2002; Read, 2003 for reviews).

### **Behavioural economics of intertemporal choice: DU anomalies**

Empirical research in intertemporal choice has catalogued a number of inadequacies of the DU model as a descriptive model of behaviour. Some of these ‘anomalies’ are robust findings whilst others are only occasionally observed and may depend on context or hypothetical choice scenarios. Nevertheless, it should be stressed that the term anomaly in this context exists only by reference to a normative model that was constructed without regard to its descriptive validity. Whether these anomalies are mistakes or irrationalities may just depend on the reference model, and whether the subject would persist in their anomalous behaviour after it has been pointed out to them – perhaps a better description of the term irrational. Some of the major anomalies are now considered (for a full review see Frederick et al., 2002; Loewenstein and Prelec, 1992; Loewenstein and Thaler, 1989; Read, 2003; Thaler, 1981).

#### *The sign effect*

The sign effect relates to the observation that gains are discounted more than equivalent losses. This has been well documented in many studies and it is thought that it relates to a lower discount rate ( $K$  value) when discounting future

losses. Thaler (1981) told subjects to imagine they had received a parking ticket and asked them how much they would be willing to pay if they could defer payment by three, six or nine months. When comparing the implied discount rate to one calculated from choices involving the same magnitude of monetary gains, he found the discount rate to be significantly lower in the loss condition. Indeed in some studies, some subjects have preferred to take an immediate monetary loss rather than defer it (Benzion et al., 1989; Loewenstein, 1987; Yates and Watts, 1975) and extremely low discount rates are especially observable in choices concerning bad health outcomes (Mackeigan et al., 1993; Redelmeier and Heller, 1993). One could argue that this asymmetry could reflect a different functional form for the discounting of losses versus gains (rather than different discount rates per se) but similar functional forms have been found to fit both (Estle et al., 2006; Murphy et al., 2001). A recent study (Xu et al., 2009) described a neural basis for this phenomenon by showing that discounting of delayed losses was associated with greater activity of regions which correlate with negative emotions such as the insula and anterior cingulate cortex (ACC). Indeed the finding that ‘losses loom larger than gains’ is a well documented one in most fields of decision-making (Kahneman and Tversky, 1979; Tversky and Kahneman, 1992) and it is thought that the negative emotions associated with losses – and additionally in this instance, their negative *anticipation* utility – can account for these effects (Loewenstein, 1987).

Though this anomaly is well documented, a number of studies have cast doubt on its reliability. Specifically, the effect has been found to reverse or disappear when tested in conjunction with other factors leading to anomalous choice. Shelley (1993, 1994) observed an interaction with the direction effect (see below), whereby the discount rate when delaying a loss was greater than that for delaying an equivalent gain. In another study examining the intertemporal preferences of

smokers (Odum et al., 2002) it was found that current and ex-smokers, discounted future health losses more steeply than future health gains and that non-smokers did not discount gains and losses differently. Finally, Estle et al. (2006) found that the sign effect was apparent in choices between small amounts but disappeared in choices between larger magnitudes – thus interacting with the magnitude effect (see below).

### *The direction effect: 'the delay, speed-up asymmetry'*

In decision-making under uncertainty it has been reliably shown that the way a choice is framed can affect the outcome (e.g. Kahneman and Tversky, 2000). Similarly in intertemporal choice, people tend to discount future rewards at different rates depending on how the choice is framed. Loewenstein (1988) showed that discount rates can be affected by whether the change in delivery time of a previously endowed outcome is framed as an acceleration, or a delay. For example, subjects who were told they would receive a VCR immediately demanded on average \$126 to delay its receipt by a year, whereas subjects who were initially told they would receive the VCR in one year were willing to pay on average \$54 to receive it immediately. Thus, higher discount rates are engendered when a choice is framed as a delay relative to one framed as an expedition. The reverse pattern has been found for losses (Benzion et al., 1989; Shelley, 1993).

### *The magnitude effect*

A common finding in the intertemporal choice literature is that small magnitudes are discounted more than large ones (over a given delay). This has been shown in numerous studies involving both real and hypothetical rewards (e.g. Ainslie and

Haendel, 1983; Benzion et al., 1989; Green et al., 1997, 1999a; Green, Fristoe and Myerson., 1994; Green, Fry and Myerson., 1994; Holcomb and Nelson, 1992; Johnson and Bickel, 2002; Kirby, 1997; Kirby et al., 1999; Kirby and Marakovic, 1995; Loewenstein, 1987; Myerson and Green, 1995; Raineri and Rachlin, 1993; Thaler, 1981). Thaler (1981) for instance, found that \$4000, \$350 and \$60 amounts were discounted by 29%, 34% and 139% respectively, when delayed by a year (based on the immediate amounts they would accept to be indifferent between the two options). However, the magnitude effect has not been reliably observed in the loss domain (Estle et al., 2006) and in some (but not all) studies seems to level off when the magnitudes involved are fairly large (Shelley, 1993; Green et al., 1997).

Although the magnitude effect has also been documented in non-monetary reward domains such as medical treatments, drugs, job choices, vacations and restaurant tips (Baker et al., 2003; Chapman 1996; Chapman and Elstein, 1995; Chapman and Winquist, 1998; Raineri and Rachlin, 1993; Schoenfelder and Hantula, 2003) it has not been documented in species other than humans, for example in rats and pigeons using food rewards (Grace, 1999; Green et al., 2004; Richards et al., 1997a) or in the domain of losses (Estle et al., 2006).

## **Hyperbolic discounting and dynamically inconsistent preferences**

The greatest challenge to the normative account – and one of the most important behavioural economic discoveries – has come from the observation that the discount rate is not constant but seems to decrease with time. Numerous studies have shown this to be the case (e.g. Benzion et al., 1989; Chapman, 1996; Chapman and Elstein, 1995; Kirby, 1997). In a simple demonstration, Thaler (1981) asked subjects to specify the amount of money they would require in one month, one year or ten years, to make them indifferent between that option and receiving \$15

now. Their median responses implied an average annual discount rate of 19% over a ten year horizon, 120% over a one year horizon and 345% over a one month horizon. Similar observations have been demonstrated in non-monetary domains such as health and in credit markets (Chapman 1996; Chapman et al., 2001; Chapman and Elstein 1995; Pender, 1996; Redelmeier and Heller, 1993). This pattern also emerges from a meta-analysis of discount rates computed from studies using different time spans (Frederick et al., 2002).

Moreover, when mathematical functions are fit to such data, a multitude of studies have demonstrated that hyperbolic or quasi-hyperbolic discount functions provide a superior fit compared to exponential functions in both humans and animals, for monetary and other forms of delayed reward and punishment (e.g. Estle et al., 2006; Frederick et al., 2002; Green and Myerson, 2004; Green et al., 1994a, 1994b; Green et al., 1997, 1999a, 1999b; Ho et al., 1999; Kirby, 1997; Kirby and Marakovic, 1995; Kirby and Santiesteban, 2003; Kirby et al., 1999; Myerson and Green, 1995; Ostaszewski et al., 1998; Rachlin et al., 1991; Richards et al., 1997a,b; Simpson and Vuchinich, 2000 – and most of the studies reviewed below in the pharmacology, neurobiology and psychiatry of intertemporal choice). The standard and most widely used functional form for hyperbolic discounting in the behavioural literature, was proposed by Mazur (1987) and based on earlier work by Ainslie and Herrnstein (e.g. Ainslie, 1975; Ainslie and Herrnstein, 1981; Herrnstein, 1981). Using the same terminology as the exponential discounting model, the discounted value of a delayed reward or punishment is calculated as follows:

$$V = \frac{M}{(1+K \cdot d)}$$

Here delay is represented by  $d$ . It is important to note that other functional forms which capture decreasing rates of discounting have also been proposed (see

Chapter 3, Frederick et al., 2002; Green and Myerson, 2004; Loewenstein and Prelec, 1992; Phelps and Pollak, 1968). Therefore, unlike exponential discounting, where the reward is devalued at a constant proportion per unit time, in hyperbolic discounting the reward loses a gradually smaller proportion of its value per increasing unit time – so it will lose a large proportion of its value in the initial stages of the delay and less throughout the later stages (see Figure 1).

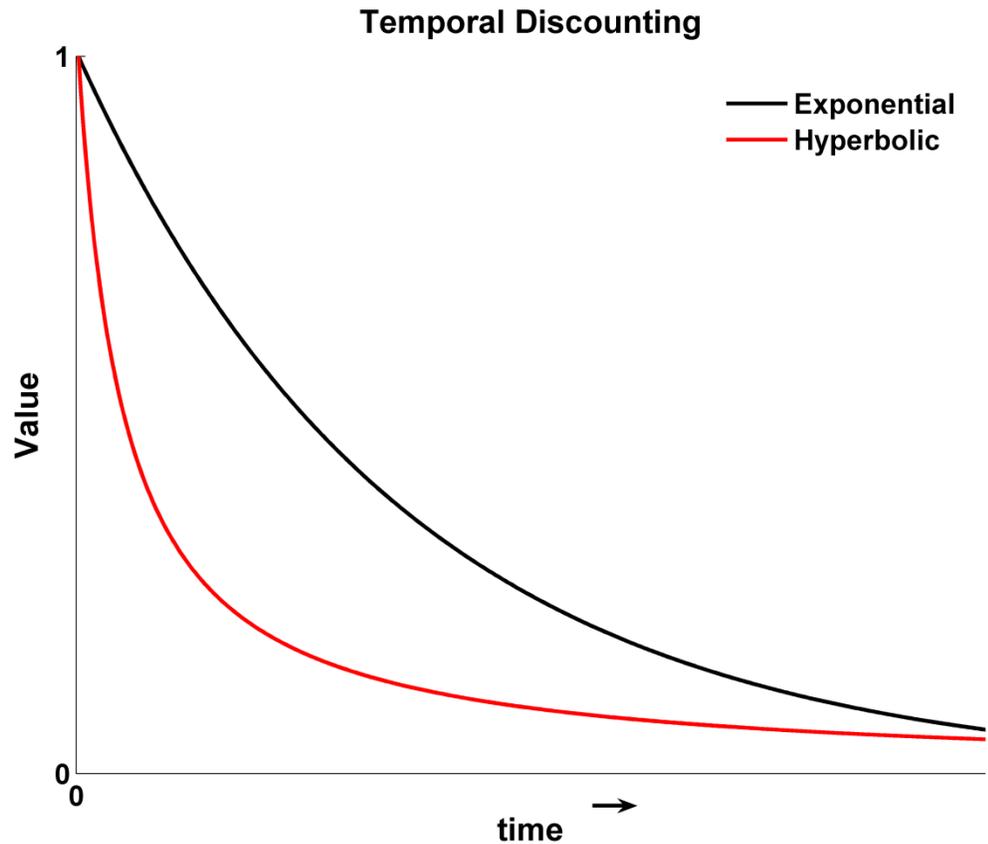
One interesting prediction that emerges from hyperbolic (but not exponential) models is that preference in intertemporal choice should be observed to reverse depending on the time that the choice is made. Thus a person may prefer \$1 today to \$1.50 tomorrow but prefer \$1.50 in 51 days to \$1 in 50 days (Figure 2). Such ‘preference reversal’ is a reliable experimental finding in both humans and animals (Ainslie and Haendel, 1983; Ainslie and Haslam, 1992; Ainslie and Herrnstein, 1981; Bradshaw and Szabadi, 1992; Green and Estle, 2003; Green et al., 1981, 1994; Herrnstein, 1981; Kirby and Herrnstein, 1995; Mazur, 1987; Millar and Navarick, 1984; Rachlin, 1974; Rachlin and Green, 1972; Rachlin and Raineri, 1992; Rodriguez and Logue, 1988; Solnick et al., 1980). Green et al. (1994) for example, asked subjects whether they would prefer \$20 now or \$50 in 1 month. In this case, most respondents said they preferred the \$20 option. They then added a constant delay to each option, in increasing increments – increasing the delay to the first option while keeping the delay between the two options constant. Thus, subjects had to subsequently choose between \$20 in six months and \$50 in seven months, \$20 in one year and \$50 in one year and one month, and so on. As the delay to the first option increased, subjects increasingly switched their preference to the larger-delayed option, such that most participants preferred \$50 in one year and one month to \$20 in one year. In an analogous experiment (Green et al., 1981) pigeons were given a choice between a smaller-sooner pellet of food and a larger-later pellet. To make the choice they had to peck one of two response keys. They found

that if the choice was presented two seconds before the outcome of either option was initiated, the pigeons most often opted for the smaller-sooner option, whereas if the choice outcome occurred after 28 seconds, they opted for the larger-later option. Holt et al., (2008) also observed preference reversals in the loss domain.

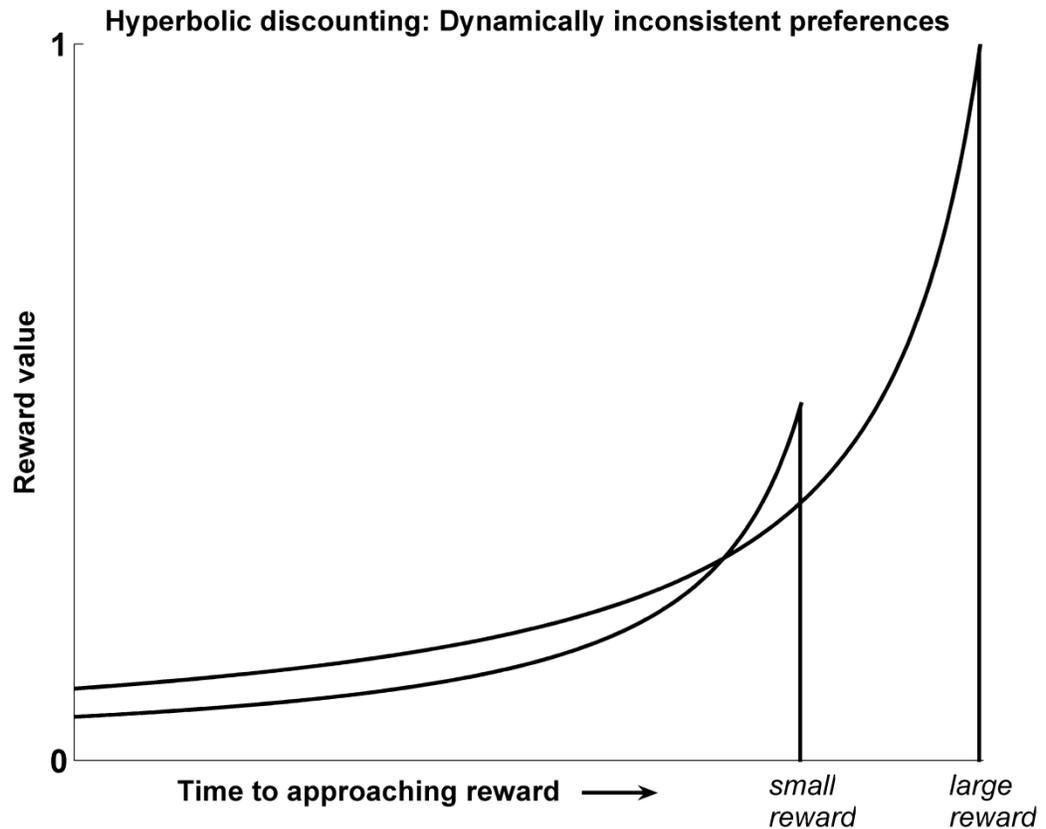
Preference reversals are consistent with most functional forms of discounting where the discount rate decreases over time. They occur because the subjective value of the larger-later reward decreases more slowly, as it becomes more delayed, than the subjective value of the smaller-sooner reward. In exponential discounting such a scenario is not possible since the rate of discounting is constant across all time periods. Introspection and simple anecdotal observation of human behaviour confirms the existence of preference reversals. Take the classic example of a smoker or dieter who says that from now on they intend to quit smoking, or refrain from eating highly calorific foods. When the decision is made at time  $t_1$  they are stating their decision intention about a future choice between a larger-later (quitting smoking, health and financial benefits etc.) and a smaller-sooner (enjoying the next cigarette) option. Their statement at  $t_1$  indicates that they value the larger-later option as the greater option (higher utility). Yet when the decision gets closer they often succumb and instead choose the smaller-sooner option, indicating (assuming they have a decision-making system which is based on their value systems) that they now value the smaller-sooner option as the greater – thus constituting a preference reversal. It is during the brief period, close to the possible receipt of the smaller-sooner option that values can cross and a lifetime's resolve can be overcome by a moment's weakness (Figure 2).

This key feature of hyperbolic discounting has led to its being described as irrational (e.g. Ainslie, 1992, 2001; Olson and Bailey, 1981; however see Becker and Murphy, 1988 for a rational and exponential take on preference reversals). As Strotz (1955) argues, if we make plans for future consumption, we should stick to

them unless we have a good reason to do otherwise. Moreover, dynamically inconsistent choices may be seen as a violation of the independence axiom (see above).



**Figure 1. Temporal discounting.** Rewards lose value with increasing delay. In the exponential model (black line) rewards lose a constant proportion of their value per unit time. Hyperbolic discounting (red line) implies that the reward loses a decreasing proportion of its value per unit time and is characterized by a steeper loss in the initial phases of the delay and a shallower loss in later phases.



**Figure 2. Dynamically inconsistent choice.** Hyperbolic but not exponential discounting can lead to preference reversals. When the agent makes a decision between a smaller-sooner reward and a larger-later reward when both options are far away, the larger-later option may be valued more (e.g. a smoker says he intends to quit rather than smoke the next cigarette). As time approaches the sooner option, its value may increase above that of the larger-later option, leading to a preference reversal.

## Akrasia and weakness of the will

That people engage in self-destructive and irrational behaviours – particularly in the period where choice is imminent – is a perplexity for economists. This is seen in the consumption of drugs and food, in relationships, gambling, procrastination, investments – for example paying high-interest credit card bills whilst simultaneously holding investments earning 5% (Harris and Laibson, 2001) – and in generally failing to carry out their future intentions and plans.

This human characteristic puzzled the ancient Greek philosophers who used the term *akrasia* or incontinence to describe the state of acting against one's better judgment (commonly translated as weakness of will or lack of self control). Socrates (Plato, 380 BC / 2004) considered it implausible that if one considered a certain action to be the best course of action, he could do otherwise – “no one goes willingly toward the bad” (358d). He thought that man never chooses to act against his better judgment and such actions arise as a product of being ignorant of facts or knowledge of what is best or good. In a different approach Aristotle acknowledged *akrasia* as a real characteristic, an inability to suppress one's desires in favour of more rational, high-minded resolutions:

The incontinent man, knowing that what he does is bad, does it as a result of passion, while the continent man, knowing that his appetites are bad, refuses on account of his rational principle to follow them. (Aristotle, 350 BC / 1925, book 7, Chapter 1.)

It is plain, then, that incontinent people must be said to be in a similar condition to men asleep, mad, or drunk. (Book 7, Chapter 3.)

Now incontinence and continence are concerned with that which is in excess of the state characteristic of most men; for the continent man abides by his resolutions more and the incontinent man less than most men can. (Book 7, Chapter 10.)

Ainslie (1975) summarized 3 guesses as to why people may be prone to obey impulses:

1. In seeming to obey impulses, people do not knowingly choose the poorer alternative but have not really learned the consequences of their behavior. Socrates said something like this. Those who hold this kind of theory prescribe education or "insight" as the cure for impulsiveness.
2. In obeying impulses, people know the consequences of their behavior but are impelled by some lower principle (the devil, repetition compulsion, classical conditioning) to act without regard for differential reward. Those who hold this kind of theory prescribe some means of exorcising the lower principle, such as abreaction or desensitization.

3. In obeying impulses, people know the consequences of their behavior, but their valuation of the consequences is innately distorted so that imminent consequences have a greater weight than remote ones. Those who hold this kind of theory prescribe devices that serve to commit future behavior to courses decided on well in advance.

The third option would equate to hyperbolic discounting. Some have tried to explain these behaviours as being consistent with rational choice behaviour (Becker and Murphy, 1988). Ainslie (1975, 1992, 2001) attributes these momentary relapses to a breakdown in will.

Ainslie (Ainslie, 1992; Ainslie and Haslam, 1992) and others (Elster, 1979; Nozick, 1993; Read, 2001; Schelling, 1984; Strotz, 1955; Thaler and Shefrin, 1981; Winston, 1980) envisage intertemporal choice as a struggle between multiple selves who have competing interests and alternately take control of behaviour. Most multiple-self models postulate a myopic self which is in conflict with a farsighted self. The interests of these selves lie in the welfare of one's immediate self and one's future self respectively. These models (though not usually formalized in any way) capture an important strategy known as precommitment, which is often implemented to ensure that when the decision approaches, an agent will stick to his/her prior preference. For example the alcoholic might pour all his vodka down the drain so the next time the temptation arises, the decision will have already been made. This can be viewed as the farsighted self taking steps to prevent tomorrow's self from taking control. The main problem with this approach is that it fails to specify why either type of agent emerges when it does, nor the asymmetry of behaviour – the myopic self rarely takes steps to ensure that tomorrow's self will have access to the alcohol he will then crave. While these models are rarely used to derive testable predictions that go far beyond the intuitions that inspired them, they have been used to make sense of the wide range of self-control strategies that people engage in to regulate their future behaviour.

## **Impulsiveness and self-control**

### *Fractionating impulsivity*

A large and wide-ranging body of research aims to define and understand the causes of impulsive behaviour. Impulsivity is generally thought to comprise behaviour in the absence of adequate foresight which, “encompasses a range of actions which are poorly conceived, prematurely expressed, unduly risky or inappropriate to the situation and that often result in undesirable consequences” (Daruna & Barnes, 1993). As mentioned above, impulsivity is considered a normal feature of human personality which varies amongst individuals (Barratt & Patton, 1983; Eysenck, 1993; Eysenck & Eysenck, 1977) however, like all such characteristics, it can become pathological, and forms a central feature of a number of clinical disorders. The diagnostic and statistics manual of the American Psychiatric Association (DSM-IV, 1994) for example, cites impulsiveness as a behavioural tendency exhibited by patients suffering from various psychiatric conditions and also lists a number of impulse control disorders where it is considered a key clinical feature. Here impulsiveness is loosely defined as, amongst other things, “the failure to resist an impulse, drive or temptation to perform an act that is harmful to the person or others” (p. 609). The adult disorders listed as most associated with impulsive symptoms are mania, substance abuse and personality disorders. Since DSM is primarily concerned with providing physicians with useful rule-of-thumb guidelines for obtaining a diagnosis, such definitions lack specificity and the quantitative means to study its basis (for example, using operant measures).

A common technique employed by clinical psychologists and personality theorists to measure and identify different aspects of behaviour is the use of self-report questionnaires, a number of which were devised to quantify and qualify

impulsivity in both normal and clinical populations (Barratt 1981, 1983, 1994; Eysenk, 1993; Eysenck et al., 1985). For example, a typical question from the Barratt Impulsiveness Scale (BIS) (Barratt, 1994; Patton et al., 1995) involves the respondent having to say with what frequency the statement “I Buy things on impulse” is true. By applying factor analysis to the responses of such questionnaires, variability in the answers can be accounted for by one or more statistical factors. The BIS for example is thought to distinguish 3 different types (factors) of impulsivity; motor, cognitive and non-planning, which are elaborated to describe acting without thinking, making quick cognitive decisions and present orientation, respectively. One flaw with this method is the risk that the researchers own opinions are reflected in the questions posed and that with the addition and deletion of questions over time factors may change. In addition, some of these questions can be circular in nature (e.g. I am self-controlled?) or describe behaviour in complex social situations. Nevertheless, factor analysis suggests that impulsive behaviour comprises a number of independent dimensions, with considerable variation as to the precise definition of these constituent parts (see Evenden, 1999a for a review). While some of these factors may correlate with biological variables (Barratt, 1983) they still do not provide an adequate description of the fundamental behavioural processes which contribute to impulsivity or a way of operationally measuring them, and are too reliant on introspection.

More recently, the broad phenotype of impulsivity is thought to subsume a diversity of distinct decision-making processes which relate to discrete features of the operant behaviour of humans and animals (Evenden, 1999a, 1999b; Ho et al., 1999; Moeller et al., 2001; Winstanley et al., 2004a, 2006a). Critically, it is thought that these specific features of impulsivity may be dissociated pharmacologically and neuronally (Chamberlain and Sahakian, 2007; Dalley et al., 2008; Evenden, 1999a, 1999b; Ho et al., 1999; King et al., 2003; Pattij and Vanderschuren, 2008;

Winstanley et al., 2004a, 2006a). The behavioural paradigms used to measure these separate aspects of impulsivity in humans and animals can broadly be bifurcated into those measuring behavioural or motor impulsiveness, and those measuring impulsive decision-making.

Motoric impulsivity is defined as the inability to withhold a prepotent behavioural response or as a failure to inhibit behavior, characterized by fast inaccurate responding (Brunner and Hen, 1997). Soubrié (1986) considered 'behavioural inhibition' to be a key determinant of impulsiveness. In this context, impulsiveness relates to a deficit in a putative impulse-control mechanism which modulates or suppresses the internally or externally driven pre-potent desire for reinforcers. This mechanism allows slower cognitive processes to take over from rapid conditioned responses and reflexes in controlling behaviour (see Nigg, 2000). Typical tasks used to measure behavioural inhibition (e.g. Winstanley et al., 2004a) are the go/no-go and the stop-signal reaction time (SSRT) task. In a typical go/no-go task, the subject learns to make a particular response on initiation of a trial, when cued to do so by the 'go' signal (e.g. press a key). In a subset of trials, a 'no-go' signal is presented prior to, or concurrently with the 'go' signal requiring the subject to withhold from making the response. In the SSRT a no-go signal is presented after presentation of the go signal, the earlier the stop signal is in time to the moment of responding, the more difficult it is for the subject to inhibit their behaviour. However these tasks themselves may incorporate multiple distinct behavioural processes.

Evenden's review (1999a) of the field categorizes a number of related and perhaps even more basic processes involved in such behavioural responses. Preparation impulsivity (Evenden, 1998) for example, refers to decisions being made before all relevant information is taken into account (a good paradigm for assessing this trait is the 5-choice serial reaction time task e.g. Winstanley et al.,

2004a). Evenden (1999a) also highlights premature responding as a unique impulsive process. This is responding when the opportunity is given, before discriminating available information, or an inability to restrain actions. A similar concept is 'reflection' impulsiveness (Clark et al., 2006; Kagan, 1966) a deficit in the gathering and evaluation of information – to increase accuracy – before making a decision. Similarly, Frank et al. (2007) argue that the ability to “hold your horses”, or to slow down in the face of decision-conflict is a determinant of impulsive decision-making. Decision conflict refers to the difficulty of making a choice when the options being considered are similarly valued, and occurs in order to slow down choice and adequately consider the options (e.g. Botvinick, 2007; Botvinick et al., 2004). Evenden then describes motor/execution impulsivity as the last stage in the decision-making process where impulsiveness can arise. This is as an inability to restrain actions and can also occur when a chain of behaviour is terminated before the outcome is reached.

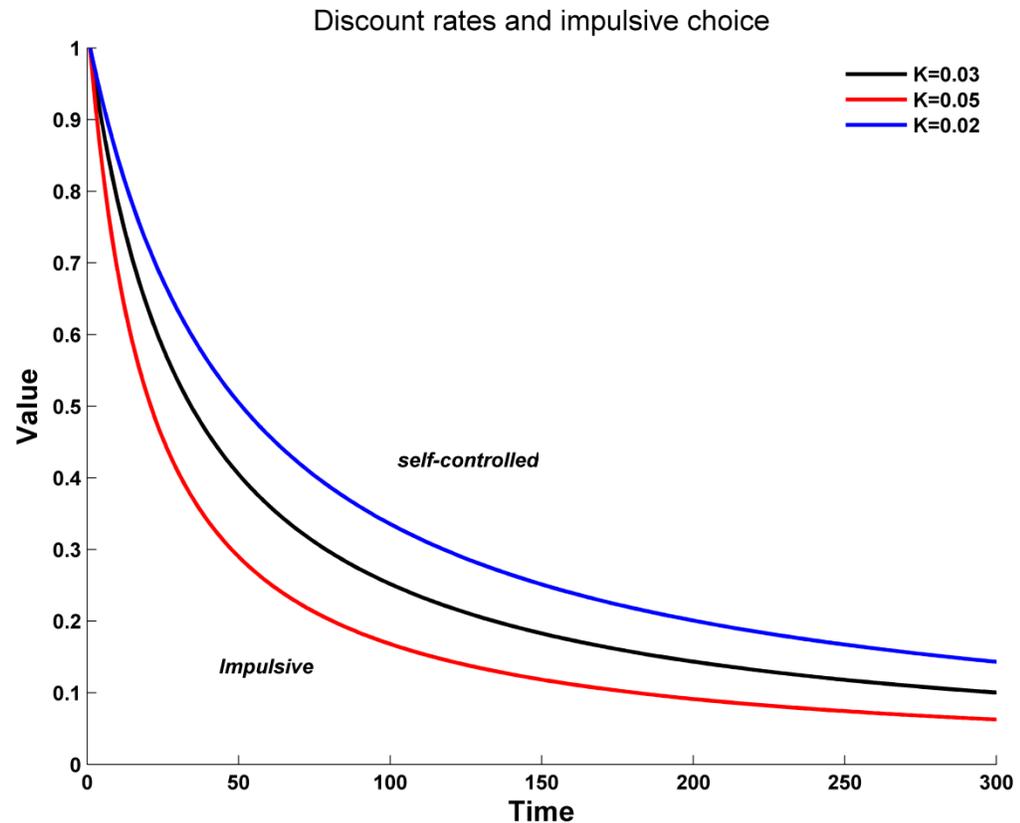
Other processes deemed important in behavioural tasks relevant to impulsiveness are behavioural 'switching' – the frequency of responding between response alternatives (Ho et al., 1998) and various aspects of timing behaviour which have been investigated by the Bradshaw group (e.g. Al-Zahrani et al., 1996; Ho et al., 1995; van den Broek et al., 1992) such as the ability to discriminate time intervals. In each of these cases specific tasks are used to break down impulsiveness into its fundamental components (see Evenden, 1999a; Ho et al., 1998 for reviews).

### *Impulsive choice*

Multifaceted though impulsivity is, the present thesis focuses exclusively on *impulsive choice* (outcome impulsiveness in Evenden's review) which refers to the

propensity to choose smaller-sooner gains in preference to larger-later gains and larger-later losses in preference to smaller-sooner losses (e.g. Ainslie, 1975, 1992, 2001; Deluty, 1981; Evenden, 1999a; Herrnstein, 1981; Ho et al., 1999; Logue, 1988, 1995; Mazur, 1987; Rachlin, 1995). This is also sometimes referred to as intolerance to delay, or delay of gratification (Logue, 1988; Mischel, 1966) and can be operationally measured using intertemporal choice paradigms, to assess how temporally impulsive an individual is.

In this context, the discount rate parameter ( $K$ ) in the discount functions above is thought to represent or correspond to an individual's impulsivity in choice. A person with a high  $K$  value can be said to be *more* impulsive and a low  $K$  person can be described as *more* self-controlled (e.g. Ainslie, 2001, Bickel and Marsch, 2001; Cardinal et al., 2004; Herrnstein, 1981; Logue, 1995) (Figure 3). This is because a higher discount rate will lead to greater preference of the smaller-sooner option in choice. Note that pathological impulsivity in this sense might be categorized as a hypersensitivity to delay, or by an abnormally high discount rate, but what is 'normal' in this new sense is undefined. This ability to identify and parametrically measure impulsivity using behavioural techniques marks a major step forward in impulsivity research. Moreover, the assumptions that the extent to which the discount rate parameter varies between individuals may be regarded as a personality dimension (Herrnstein, 1981; Herrnstein and Prelec, 1992), and that discounting rates are relatively stable properties of individuals (Ho et al., 1999), have made impulsivity amenable to study in animals, unlike many other personality dimensions.



**Figure 3. Impulsivity and the discount rate.**  $K$  values are thought to describe impulsivity in choice such that individuals with a high  $K$  value are said to be more impulsive and vice versa.

The identification of choice impulsiveness with the discount rate and the application of discount functions to intertemporal choice experiments have led to a vast literature of research into temporal discounting and impulsive choice. By measuring discount rates (or their proxy) researchers have probed the neurobiological, pharmacological and psychological basis of impulsive choice (and its regulation) as well as the neuropsychiatric basis of disorders of impulsivity and their pharmacological treatment. At a more basic level, researchers aim to uncover the neurobiological and pharmacological basis of the discount function, so as to be able to give a biological account of temporal discounting and the valuation systems which underpin its manifestation. This research also addresses the veracity of

different forms of the discount function, individual variations in discounting and the basis for hyperbolic versus exponential discounting.

Typical paradigms in rodents include pharmacological manipulation or lesions, and comparison of discount rates pre and post the manipulation. Primate studies usually involve single cell recordings while an intertemporal choice task is performed, and in humans the use of neuroimaging has become prevalent. Psychiatric, psychological and pharmacological research often involves comparison of discount rates between two groups, within a group across an experimental condition, or simply the correlation of individual discount rates with some other variable. The dominant theme in all of this research has been that any independent variable observed to change intertemporal behaviour can be reflected by a change in the discount rate. Thus, these variables tell us something both about impulsivity and about temporal discounting.

Before reviewing this literature it is necessary to first become familiar with the common methodologies utilized to assess discount rates in these experiments (for an overview of techniques used in economic field studies of intertemporal choice see Frederick et al., 2002).

## **Methodology of intertemporal choice and the measurement of discount rates**

### *Indifference point methodology*

The most common methodology used to quantify discounting is 'indifference point' methodology. The central theme of these techniques is that the subject is provided with a choice between two reinforcers, *A* (smaller-sooner) and *B* (larger-later), and the size or delay of one of them is varied until the subject comes to

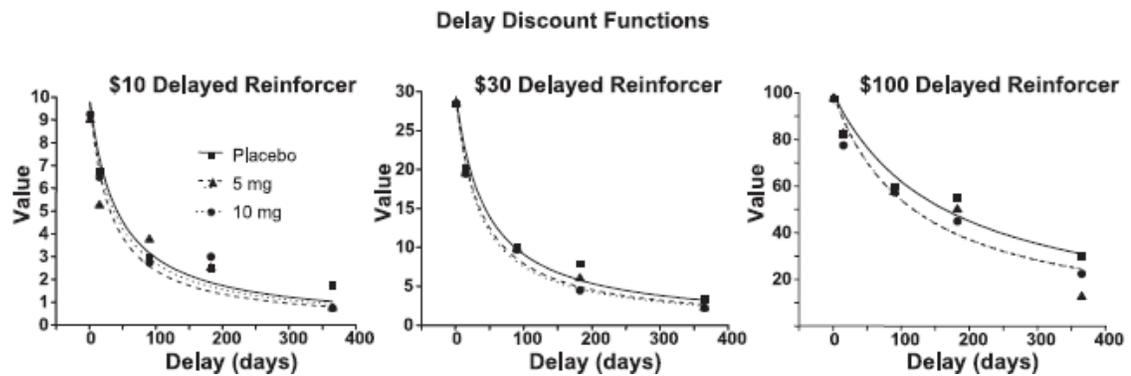
choose the two reinforcers with equal frequency (i.e. until the subject becomes indifferent between them). Under these conditions it is assumed that the values of the two reinforcers are equal –  $V_A = V_B$  (Mazur, 1987). A clear advantage of utilizing indifference points is that no assumptions are required with respect to the relation between reinforcer value and behavioural output – one need only assume that indifference implies equality of (subjective) value.

A number of different methods can be used to evaluate indifference points and the rate of discounting (e.g. see Ho et al., 1999). One common procedure (e.g. see Green and Myerson, 2004), known as an ‘adjusting amount’ procedure (Epstein et al., 2003; Kirby, 1999; Kirby and Marakovic, 1996; Mitchell, 1999; Rachlin et al., 1991; Richards et al., 1997a, 1999a) (originally developed for use in rodents) provides the subject with repeated opportunities to choose between a delayed reinforcer of fixed magnitude ( $B$ ) and an immediate reinforcer ( $A$ ), the size of which is adjusted in accordance with the subject’s choices. For example, on the first block,  $B$  might be £100 at 10 days and  $A$  is immediate. The size of  $A$  is varied until indifference (i.e. the subject chooses both options with equal frequency, or a switch in choice is caused by any further change in  $A$ ), and the indifference point is defined as the amount of  $A$  which is ‘equal’ to  $B$  at that delay. During the next block,  $B$  will be fixed at a different delay e.g. 20 days, and the new indifference point (value of  $A$ ) will be found. This process is repeated until there are enough indifference points (typically between 5 and 8) which can be plotted on a graph of delay to  $B$  along the  $x$  axis and value of  $A$  along the  $y$  axis (Figure 4). Essentially, because  $A$  is always immediate, this curve shows us the discounted (present) value of  $B$  at various delays into the future. In this procedure, the smaller the indifference point, the more impulsive is the subject and the steeper the curve will appear – in accordance with a higher  $K$  parameter.

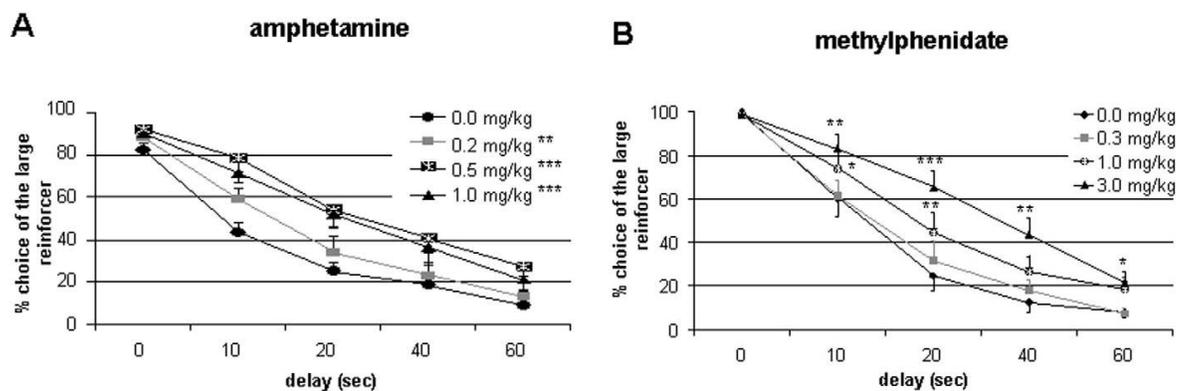
The subsequent use of indifference points is varied depending on the goal of the research. If the researcher wishes to estimate the discount rate or compare the fit of different discount functions, a regression can be performed to fit a curve to the indifference points according to a specified function (typically done using curve fitting software and using the Mazur (1987) hyperbolic function). This will yield a goodness of fit measure for the function as well as an estimate of the free parameters in the function (including  $K$ ) (e.g. de Wit et al., 2002; Green et al., 1999a, 1999b; Richards et al., 1997a, 1999a). The  $K$  parameter estimate can then be used to compare experimental groups or conditions, or to correlate with other variables. Myerson and Green (2001) also proposed a ‘theory neutral’ measure of discounting which involves calculating the area under the discount curve. This involves first normalizing the delay and subjective value for each data point so that they are expressed as a proportion of the maximum delay (on the  $x$  axis) and the nominal magnitude on the  $y$  axis. This measure can provide a useful proxy for discounting behaviour (impulsivity) (and/or the discount rate) which does not rely on any theoretical assumptions about the functional form of the discount function. This can be especially useful when comparing discounting across studies or species, particularly since the error associated with the estimated  $K$  value can often be high.

Often, when comparing two populations or a group of subjects pre and post a given experimental manipulation, it is not necessary to estimate the discount rate parameter (or rely on a particular discount function) to gauge how the experimental condition affects discounting – for example, one could simply statistically compare a set of indifference points to see if one group discounts more than the other (i.e. if their set of values for  $A$  significantly differs). In ‘systematic’ tasks of discounting it is not even common to use indifference point methodology. Here the experimenter will offer the subject the choice of a smaller-sooner ( $A$ ) versus a larger-later ( $B$ ) reward.  $A$  is kept constant throughout the experiment

(typically delivering an immediate payoff) the amount of  $B$  is also kept constant and the delay to  $B$  is increased throughout the experiment. This technique yields a measure of the proportion of choices of  $A$  versus  $B$  chosen for each block (delay to  $B$ ). When the percentage choice of  $B$  is plotted on the  $y$  axis and the delay to  $A$  on the  $x$ , the resulting curve appears similar to a standard discount curve (Figure 5). This approach is particularly prevalent in animal research (e.g. Evenden & Ryan, 1996; Mobini et al., 2000a,b; van Gaalen et al., 2006; Winstanley et al., 2003, 2004a; Wogar et al., 1993), where it is difficult to home in on an indifference point, as behaviour is more stochastic. Rats for example, tend not to just switch their preferences between two levers once an indifference point is crossed, rather they will proportionally press one more than another. These percentage choices of  $B$  at each delay can then be statistically compared to infer any change in discounting behaviour (e.g. van Gaalen et al., 2006). Note that this measure of discounting/impulsivity is also theory neutral in that it does not rely on a functional form for discounting or the use of estimates of a discount rate. It is possible to estimate indifference points by use of linear interpolation from these graphs – the delay to  $B$  corresponding to 50% choice of  $B$  (“indifference delay”) can be calculated by linear interpolation between the two delays which fall on either side of the point where  $B$  is chosen 50% of the time (e.g. Bradshaw and Szabadi, 1992; Mobini et al., 2000a) in each block. One could go on to compare or use these indifference points to estimate a value of the discount rate. It should be noted that indifference point methodology is in some ways superior because it does not assume a relationship between reinforcer value and behavioural output (Ho et al., 1999).



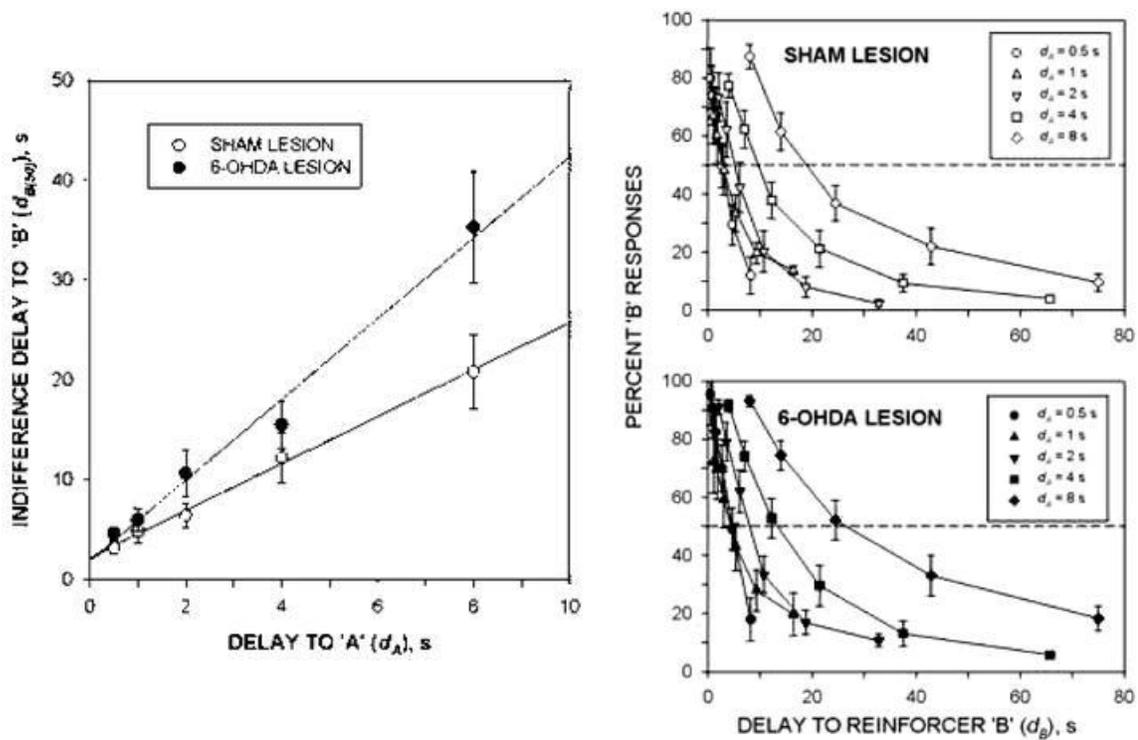
**Figure 4. Example of the adjusting amount procedure.** Indifference points (in this case value of  $A$  at indifference to 5 delays of  $B$ , where  $B$  is a \$10, \$30 and \$100 reward) are plotted and fit using a hyperbolic discount function to estimate  $K$  values. In this case results show that diazepam does not affect impulsive choice. From Reynolds et al. (2004).



**Figure 5. Probabilistic choice in rodent adjusting delay studies.** Here rather than plotting indifference points, researchers compare the %choice of the larger reinforcer at various delays. Indifference points can be calculated using linear interpolation. Here, stimulants are shown to increase %choice of the larger-later reinforcer. Taken from van Gaalen et al. (2006).

There have been a number of adjusting procedures developed to measure indifference points. One particularly important one is the adjusting delay procedure (Mazur, 1987, 1997) which has been extensively used by the Bradshaw and Szabadi group (e.g. Ho et al., 1999; Kheramin et al., 2002) but is uncommon in human studies. In this procedure the magnitudes of the larger-later and smaller-

sooner options are kept constant throughout. In each block the delay to the smaller sooner is kept constant and the delay to the larger-later is adjusted until indifference. On subsequent blocks the delay to the smaller-sooner is changed, until five or more indifference delays are found. These indifferent points can also be calculated using linear interpolation on a graph relating percentage choice of the larger-later option to its delay, for each block (delay to the smaller-sooner) (e.g. Kheramin et al., 2004). Thus, this approach yields indifference points relating the delay of one reinforcer to the other. These points can then be plotted on a graph where the  $y$  axis is the delay to the larger-later and the  $x$  axis the delay to the smaller-sooner. Such a graph yields a linear relationship between the two variables (Figure 6). Since more impulsive subjects will have smaller indifference points (delay to larger-later), they will have reduced intercepts and or gradients on this plot (Ho et al., 1999). One advantage of this technique is that (depending on the discount function assumed) one need not perform a curve fitting analysis to calculate  $K$ , rather it can be calculated from the slope and intercept of the line, requiring only a linear regression.



**Figure 6. Example of adjusting delay procedure.** Using linear interpolation on the right, indifference points are determined and plotted on a  $d_A \times d_B$  graph where they are modelled by a linear function. Here dopamine depletion of the orbitofrontal cortex leads to impulsive choice. From Kheramin et al. (2004).

### *Differences in animal and human studies*

In human studies the choices are carried out on paper or on a computer by selecting the preferred option. Typically, on adjusting amount tasks, in a given block, subjects will start with an immediate reward of the same value as the delayed option. This amount decreases on subsequent trials until choice switches from the sooner to the later option. An indifference point is calculated as the mean value of the sooner amount on trials immediately before and after the switch. Often there will be an ascending block (where choice is designed to switch from the later to the sooner) and a descending block (e.g. Rachlin et al., 2001), as indifference points are susceptible to ordering effects (just as they are to framing

e.g. the delay speed up asymmetry, above). On computer tasks, feedback from choices can be used to determine the next choice, to speed up estimation and remove redundant choices (e.g. Epstein et al, 2003). There are even a number of 'quick and dirty' methods for estimating the discount rate. Kirby (1999; Kirby and Marakovic, 1996) for example, has devised a 27 choice questionnaire (to be completed within 5 minutes) whereby one of 10 possible discount rates is assigned to the subject, depending on the answers. One should be wary of such measures as 27 choices are an extremely small number with which to estimate discount rates which vary widely in the population, and these estimates are highly likely to have a large error term associated with the fit. Furthermore, many people will lie outside of the range of the ten possible  $k$  values assigned. This measure has not been found to correlate well with an adjusting amount task within subjects (Epstein et al., 2003), indeed it is likely that most tasks using different methodologies for estimation are likely to yield significantly different estimates. Although there have been a number of studies examining the effect of different task methodology on discount rate estimates in humans, no clear view has emerged regarding differences engendered by task design. Task design is much more likely to be an important factor in animal manipulation studies (see below).

In rodent studies animals are usually presented with two levers which deliver the two choice options (smaller-sooner and larger-later). Typically one lever will deliver an immediate reward (food pellet or water) and the other will deliver a delayed but larger quantity of the reward. After the choice has been made the levers are retracted until the animal experiences the outcome. Other techniques have also been used to implement the choice. The most common of these alternate methods is to place the animal on a T-maze where one arm leads to a smaller-sooner reward and the other to the larger-later (e.g. Bizot et al., 1999; Denk et al., 2005; Poulos et al., 1996). Here, delays are implemented using a waiting chamber

on each arm, before the rat has access to the food. In all animal experiments animals must first learn the contingencies between their actions (e.g. lever presses) and the outcomes – this requires instrumental conditioning. Following learning, the adjusting techniques can then be implemented by changing the magnitude or delay associated with one of the levers. There is also an important distinction regarding the use of free-operant or discrete-trials schedules of reinforcement in animal studies (see Ho et al., 1999 for further elaboration).

Thus, human and animal studies of intertemporal choice differ in a number of important ways. Typically, in human studies, the choices are hypothetical whereas in rodent studies they are real in the sense that the animal must actually experience the delays and the rewards in each choice. More recently – due to scepticism of the validity of hypothetical choice tasks – human studies have attempted to attain greater ecological validity by typically selecting one of the chosen trials at random, for payment at the given delay (even if this occurs months away e.g. Kable and Glimcher, 2007 – see also later). Although this is not realistic in the sense that subjects must experience the rewards and delays between trials, it is nevertheless ecologically valid as most intertemporal choices made by humans (e.g. spend or save) also rely on past experience and prospective imagination (of delays and rewards). Other techniques in humans (Reynolds, 2006; Reynolds and Schiffbauer, 2004) have attempted to mimic animal studies by using very short delays and small monetary magnitudes on each trial, though these techniques have not had great success, are difficult to administer, and have not been adopted widely. One problem with using monetary rewards in this paradigm is that money can only be spent (consumed) following the experiment so any delays during testing are in a sense irrelevant. Such procedures have been more successfully used when employing primary reinforcers such as fruit juice (McClure et al., 2007) or when

used to study delayed reinforcement (learning to associate actions with delayed outcomes) (Tanaka et al., 2004).

In animal studies primary reinforcers (food, water) are used whereas human studies tend to use secondary reinforcers (money, health, vacations etc.) although there have been a small number of studies utilising food rewards (McClure et al., 2007) and hypothetical drug rewards (see later). The delays also differ significantly, with human studies employing a range from days to years and animal studies mostly utilising a range of roughly 1 to 60 seconds. These differences suggest caution is required when extrapolating results from animal to human studies and vice versa. Indeed, the very fact that primates discount to zero any rewards occurring after longer than a few minutes (Stevens et al., 2005) suggests that the decision processes in humans (when considering options months or years in advance) may be fundamentally different.

Possibly the most important difference between animal and human studies is that whereas humans can be offered explicit choices without prior experience of the situation (“pre-packaged” action-outcome contingencies, Cardinal et al., 2004) animals must learn these contingencies through experience, and so their behaviour is controlled by a number of psychological representations (goal-directed action, stimulus-response habits, conditioning, and so on) during and after learning. Therefore, animal studies where manipulations are carried out prior to learning should be treated with caution in relation to human studies as they may affect learning processes.

Neurochemical and neurobiological studies of intertemporal choice are reviewed below. As mentioned above, since actions are not always followed by their outcomes, in intertemporal choice animals (and in some cases humans) must learn to bridge this delay to reinforcement. Studies pertaining to this process of learning are not considered in detail in this thesis.

## **Pharmacological and neurochemical studies**

### *Dopamine*

#### **Evidence from Attention-Deficit/Hyperactivity Disorder and monoaminergic stimulants**

Dopamine (DA) is perhaps the natural choice of neurotransmitter for studying in relation to intertemporal choice. This is in part because of its ubiquity and importance in the reward and learning literature (e.g. Berridge, 2007; Berridge and Kringelback, 2008; Dayan, 2009; Dayan and Balleine, 2002; Doya, 2008; Iversen and Iversen, 2007; Robbins and Everitt, 1996; Robbins et al., 1989; Schultz, 2002, 2004, 2007; Spanagel and Weiss, 1999; Wise, 2004) and also because of a number of disorders featuring both impulsiveness and altered dopamine function, for example, addiction and Attention-Deficit/Hyperactivity Disorder (ADHD) (see below).

Much of the interest in the relationship between DA and impulsivity stems from the discovery that amphetamine and similar psychostimulants are an effective therapy for ADHD (Bradley, 1937; Porrino et al., 1983; Solanto, 1988; Spencer et al., 2001). The most widely prescribed drugs for treatment of ADHD are D-amphetamine (Adderall) and methylphenidate (Ritalin) (Safer et al., 1996; Swanson and Volkow, 2009), and though these drugs have many effects, their primary mode of action is to enhance monoaminergic neurotransmission – especially of DA and noradrenaline (NA) (e.g. Feldman et al., 1997; Koob and Bloom, 1988; Kuczenski and Segal, 1997; Ritz and Kuhar, 1989; Rothman et al., 2001; Seiden et al., 1993; Sulzer et al., 1995). These drugs are termed indirect agonists in that they do not stimulate catecholaminergic receptors directly; they facilitate the actions of DA and NA by increasing their synaptic concentration. Methylphenidate (Ritalin) acts like cocaine, blocking reuptake of DA whereas amphetamine also acts as a

powerful releaser of DA from presynaptic neurons. These effects are accomplished by a blocking of the presynaptic DA transporter in the case of methylphenidate and induction of a reverse transport process in the case of amphetamine (Bannon et al., 1995; Feldman et al., 1997; Groves and Tepper, 1983; Sonders et al., 1997 – for further references and reviews of the neuropharmacological basis of ADHD and its treatment with monoaminergic stimulants see Solanto, 1998, 2002; Swanson et al., 1998; Swanson and Volkow, 2009; Winstanley et al., 2006a).

ADHD is characterized by inattentive, hyperactive and impulsive behaviour (DSM-IV, APA 1994). One of the fundamental deficits underlying the disorder is reduced behavioural inhibition, as measured by a number of tasks such as the go/no-go and the SSRT (Solanto, 2002, Swanson et al., 1998, Winstanley et al., 2006a). Amphetamine is effective in reducing such deficits (Solanto, 1998). However, ADHD patients have also been shown, in some (but not all) cases to choose more impulsively than controls on intertemporal choice or delayed gratification tasks, preferring the smaller-sooner to the larger-later option (Barkley et al., 2001; Sagvolden et al., 1998; Schweitzer and Sulzer-Azaroff, 1995; Solanto et al., 2001; Sonuga-Barke et al., 1992, 1996 - however see Scheres et al., 2006; Sonuga-Barke et al., 1998). Such data, along with other observations, has led to the hypothesis that at least one subtype of ADHD – sometimes referred to as “Motivational Style” (MSADHD) (Sonuga-Barke, 2002, 2003) – is caused by abnormally steep temporal discounting, or a strong aversion to experiencing delays and that this is due to a putative hypofunctional mesolimbic DA system focused in the ventral striatum (e.g. Johansen et al., 2002; Sagvolden and Sergeant, 1998; Sagvolden et al., 1998). This theory is partly based on the idea that the deficit is ‘normalized’ by treatments which boost dopamine function, though whether ADHD is attributable to a hypodopaminergic or hyperdopaminergic state, and the pharmacological basis of its treatment is very controversial (Seeman and Madras,

1998, 2002; Solanto, 1998, 2002; Swanson et al., 1998; Zhuang et al., 2001). For example, a number of complex abnormalities in the dopamine transporter have been reported in ADHD patients along with functional and structural irregularities in the prefrontal cortex and striatum (Castellanos and Tannock, 2002; Dougherty et al., 1999; Krause et al., 2000; Solanto, 1998, 2002; Winstanley et al., 2006a). A number of authors posit that ADHD results from a hyperfunctioning dopamine system and that stimulants act to reduce DA activity in moderate doses (Seeman and Madras, 1998, 2002; Solanto, 1998, 2002).

Many of the inferences regarding neural and neurochemical abnormalities in ADHD have been drawn from studies of the spontaneously hypertensive rat (SHR), an inbred strain of rat that serves as an animal model of ADHD (e.g. Sagvolden, 2000; Sagvolden et al., 1992, 1993). This rat exhibits hyperactivity as well as a number of attentional deficits that resemble ADHD, including impulsiveness – for example, it exhibits a steeper ‘scallop’ of responding on fixed-interval schedules of reinforcement which can be interpreted as a high sensitivity to immediate reinforcement (Evenden and Meyerson, 1999; Sagvolden et al., 1992). The SHR also has a complex pattern of abnormalities in its DA system, particularly with respect to the nucleus accumbens (NAc) (e.g. Carey et al., 1998; Papa et al., 1998; Russell, 2000). The SHR is partially responsive to treatment with methylphenidate and amphetamine although the effects appear to be blunted (e.g. Sagvolden et al., 1992; van den Buuse and de Jong, 1989; Yang et al., 2003)). Dopamine transporter knockout mice (DAT KO) are also hyperactive and considered animal models of ADHD (see Solanto, 1998, 2002, for review of these animal models), supporting the view that DA is integral to the ADHD syndrome.

### **Human dopamine manipulation studies of intertemporal choice**

Though evidence from ADHD offers a compelling basis for a role of DA in intertemporal choice, the idea that psychostimulants help to promote self-control has somewhat mixed evidence when the effects of these drugs have been analysed in laboratory models of impulsive choice. Only four human studies have addressed this question. De Wit et al., (2002) gave oral doses of amphetamine (moderate or low dose) or placebo to individuals who subsequently performed an adjusting delay type task. Although the lower dose had no significant effect on choices, the moderate dose led to an increased preference for the larger-later option, as measured by imputed  $K$  values which were significantly lower than in the placebo condition. The effect however was slight and not observed in a follow up study with amphetamine by the same group (Acheson and de Wit, 2008). In another study, Pietras et al. (2003) tested eleven adults with a history of criminal behaviour on an (unusual) intertemporal choice task after having taken three doses of methylphenidate or placebo. The results of this study are not as clear cut. The authors reported that in over half the subjects one of the doses led to a significant decrease in impulsive choice. There was an overall effect of the medium dose but only a trend with the larger dose. They concluded that the effects varied widely but that overall, methylphenidate tended to promote self-control. More recently however, direct augmentation of the DA system by the mixed D2/D3 dopamine receptor agonist pramipexole was found to have no effect on intertemporal choice in healthy humans (Hamidovic et al., 2008).

More indirectly, in a human genetic study of intertemporal choice, different polymorphisms of the catechol-*O*-methyltransferase (COMT) gene – which is thought to be important in regulating frontal DA (e.g. Chen et al., 2004) – were found to predict discounting behaviour and neural activity in brain regions

involved in the task (Boettiger et al., 2007). However the manifestations of these polymorphisms with regard to dopamine function is unclear.

Finally, evidence from human studies for the involvement of DA in modulating impulsive choice comes from a number of disorders associated with altered dopamine function where impulsivity is a common feature (see below), particularly addiction where abusers of a variety of different drugs have been shown to be greater temporal discounters than controls (see below), and are thought by some to have a hypofunctioning DA system in addition to sensitized NAc dopamine release (e.g. Koob, 1992; Koob et al., 1998; Robinson and Berridge, 2000, 2008; Volkow & Li, 2004, 2005; Volkow et al., 2008). Furthermore, during a state of withdrawal – when DA levels in the NAc are markedly reduced and susceptibility to relapse is high (e.g. Hildebrand et al., 1998; Volkow & Li, 2005) – heroin and nicotine users have been shown to have a higher  $K$  value than when measured just after using their drug of choice (Field et al., 2006; Giordano et al., 2002). These observations lend weight to the theory that a hypofunctioning mesolimbic DA system can lead to impulsive choice.

In summary, there is evidence for a role of dopamine in temporal discounting and intertemporal choice, based on human laboratory studies. However, the evidence is limited to very few studies and it is far from conclusive that boosting dopamine activity leads to greater self-control. Similarly, whether monoaminergic stimulants act to enhance or suppress dopamine activity in ADHD is controversial. The human studies presented above as well as the evidence from dopamine related disorders are further discussed below and in Chapter 4.

## **Rodent dopamine manipulation studies**

Evidence from rodent studies also implicates dopamine's involvement in intertemporal choice. A number of studies have reported that boosting dopamine function with amphetamine or methylphenidate (Bizot et al., 2007; Cardinal et al., 2000; Floresco et al., 2008; Isles et al., 2003; Richards et al., 1999a; Sagvolden et al., 1992; van Gaalen et al., 2006; Wade et al., 2000; Winstanley et al., 2003) cocaine (Winstanley et al., 2007) and the selective dopamine reuptake inhibitor GBR 12909 (van Gaalen et al., 2006) leads to a reduction in impulsive choice (or  $K$ ). Similarly, a number of studies also demonstrate that by attenuating dopamine function using the selective D1 receptor antagonist SCH 23390 (van Gaalen et al., 2006), the D2 receptor antagonists raclopride and haloperidol (Denk et al., 2005; Wade et al., 2000) or the mixed D1/D2 antagonist flupenthixol (Cardinal et al., 2000; Floresco et al., 2008; Wade et al., 2000) impulsive choice is increased. Finally, Kheramin et al. (2004) also demonstrated that dopamine depletion of the orbital prefrontal cortex leads to an increase in  $K$  values.

One particularly comprehensive study (van Gaalen et al., 2006) used a variety of specific dopaminergic and noradrenergic drugs to give an account of the pharmacological basis of the psychostimulant effect. The authors first demonstrated that methylphenidate and amphetamine increased choice of the larger-later reward on a standard intertemporal choice task in rodents. To test whether this effect was mediated by dopamine or noradrenaline specifically, they compared the selective dopamine reuptake transporter inhibitor GBR 12909 and the selective noradrenaline reuptake inhibitor desipramine. Whereas GBR 12909 led to a reduction in impulsive choice, desipramine had mixed effects depending on the dose and the delay to the larger-later option. Furthermore the  $\alpha_2$  adrenoreceptor agonist clonidine caused an increase in choice of the sooner option and the  $\alpha_1$  adrenoreceptor agonist phenylephrine did not affect choice. This led the

authors to conclude that the beneficial effects of psychostimulants are mediated through dopamine, with noradrenaline playing only a minor role in control of impulsive choice (where boosting NA function leads to an opposite effect of boosting DA function). They speculate that an optimal noradrenergic tone is required to inhibit impulsive action through regulation of attentiveness or maintenance of behavioural organization under arousing conditions (Aston-Jones et al., 1991; Dalley et al., 2001). (NA has also been investigated using the more selective reuptake blocker atomoxetine (Robinson et al., 2008) which was found to reduce delay aversion). Finally to investigate the roles of specific DA receptors they compared the selective D1 receptor antagonist SCH-23390 with the D2 antagonist eticlopride. Whereas SCH-23390 increased impulsive choice, eticlopride had no effect on discounting. Interestingly, eticlopride attenuated the effects of amphetamine on impulsive choice whereas amphetamine retained its effect on impulsivity in animals pretreated with SCH-23390. This led the authors to conclude that tolerance to delay of reinforcement depends on the D1 receptor whereas the beneficial effects of amphetamine are mediated by the D2 receptor. This finding contrasts with an earlier study (Wade et al., 2000) where using an adjusting amount procedure, the D2 receptor antagonist raclopride was found to increase temporal discounting whereas SCH-23390 had no effect. Van Gaalen et al. (2006) speculate that the psychological mechanism by which dopamine receptor activation inhibits impulsive decision-making is likely dependent on dopamine's role in incentive salience and goal directed behaviour, with increased dopamine transmission enhancing the subjective value of the larger, delayed option. However they do not specify why such a mechanism would enhance the value of the larger relative to the smaller option.

Although these studies indicate that enhancing DA transmission increases self-control (or reduces the discount rate), closer inspection reveals that the reality is

much more complex. Often the actions of amphetamine and other dopaminergic agents are dose or delay dependent (delay dependent meaning that the change in percentage choice of the larger reinforcer is only significant, or has opposite effects at certain delay lengths e.g. see van Gaalen et al., 2006). For example, in some of these studies amphetamine at high doses actually increases impulsive choice or has no effect (Floresco et al., 2008; Isles et al., 2003; Richards et al., 1999a). Bizot et al. (2007) found that methylphenidate was only effective in young but not adult rats, and Denk et al. (2005) found that haloperidol caused rats to increase responding (relative to controls) for the smaller reward even when the delays to it were increased to match that of the larger-later option. Indeed the same psychostimulant can have opposite effects in different tasks designed to measure impulsivity (Richards et al., 1997b).

In another group of studies dopamine augmentation has been observed to have the outright opposite effect, increasing impulsive choice (Cardinal et al., 2000; Charrier and Thiébot, 1996; Evenden & Ryan, 1996; Helms et al., 2006; Logue et al., 1992).

### **Complicating factors in rodent and human dopamine manipulation studies**

These pharmacological manipulation studies demonstrate the critical involvement of dopamine in intertemporal choice however the nature of this relationship is extremely complex, with the effects of pharmacological intervention likely dependent on a number of key variables. These may include dosage (de Wit et al., 2002; Seeman and Madras 1998, 2002; Solanto, 1998, 2002), baseline level of dopamine activity, pre versus post-synaptic pharmacological effects (Seeman and Madras, 1998; Solanto, 1998), which receptor/transporter is targeted, delay effects (how delayed the larger reward is) and the behavioural paradigm used to assess

impulsive choice. Another factor which is likely to be critical is whether the manipulation takes place before or after the reinforcement *learning* has taken place as DA is known to play an important role in this process (e.g. Dayan, 2009; Schultz et al., 2002, 2004).

That animals must learn the action-outcome contingencies, is also likely to be a complicating factor, as a number of different psychological representations which contribute to their actions (e.g. goal directed actions, stimulus-response habits, etc. Cardinal et al., 2004) can influence their choices and potentially be influenced by pharmacological manipulations. In this vein, Cardinal et al. (2000) sought to test whether the presence of a cue during the delay may be able to explain discrepancies in the rodent dopamine manipulation literature. A cue is often presented during delay to reinforcement in free operant tasks as it increases the rate of responding and can promote choice of the delayed reinforcer (Lattal et al., 1987; Mazur, 1997). The authors reported that amphetamine promoted choice of the smaller-sooner option if a cue was not presented during delay to the larger-later (when selected) whereas it promoted choice of the larger-later if it was signaled. They hypothesized that the cue becomes associated with the reinforcer (Williams and Dunn, 1991) and acquires conditioned reinforcing properties which can affect choice. Since amphetamine has been shown to enhance the effects of conditioned reinforcement (e.g. Robbins, 1976, 1978) it is feasible that it would promote choice of the delayed reward in this paradigm. Remarkably, a later study from the same group (Winstanley et al., 2003) found that amphetamine increased choice of the larger reinforcer when no cue was present. These considerations demonstrate that there are major differences between animal and human studies and that one must be cautious when interpreting and extrapolating results.

A final consideration to bear in mind regarding dopaminergic manipulation studies, especially those employing non-selective agents is the possible

involvement of serotonin (5-HT). Amphetamine increases levels of 5-HT as well as dopamine and noradrenaline (Balcioglu et al., 2003; Kuczenski et al., 1987; Kuczenski and Segal, 1989, 1997). Enhancing serotonin function has been observed to alter preference in intertemporal choice (see below) therefore the therapeutic benefit derived from administration of amphetamine in ADHD, and some of the results observed in the studies above, may result in part from activation of the serotonergic system. In support of this suggestion, the hyperactivity observed in the DAT KO could be reduced by the 5-HT releasing agent fenfluramine (Gainetdinov et al., 1999). Furthermore, Winstanley et al. (2003, 2005, 2006b) have demonstrated an important interaction between the two systems particularly with regard to the self-control promoting effects of amphetamine (see below). In one case, the ability of amphetamine to reduce impulsive choice was abolished by destruction of 5-HT neurons.

### **In vivo studies of dopamine function during intertemporal choice**

A caveat with pharmacological manipulation studies is that they demonstrate necessity but not sufficiency, nor the normal function of dopamine neurons during intertemporal choice. To this end a number of other studies may be informative. Winstanley et al., (2006b) used in vivo microdialysis while rats performed a typical intertemporal choice task. They found that levels of a dopamine metabolite increased significantly in the orbitofrontal cortex (OFC) during task performance, but not in yoked rats which controlled for instrumental responding and reward delivery. Kobayashi and Schultz (2008) demonstrated more specifically that the activity of DA neurons in the striatum of primates tracks the discounted value of rewards in accordance with a hyperbolic discount function. Recording from single neurons in the midbrain, DA responses to Pavlovian conditioned stimuli predicting rewards of differing delays decreased with longer delays at a rate

similar to the animals behaviourally measured discount rate (from a separate choice task), and in a pattern similar to a hyperbolic decline. Some neurons were also responsive to the magnitude of the predicted reward. Surprisingly however, response of DA neurons to the reward itself actually increased when they were delayed further in time (see discussion there for possible explanations). The results suggest that temporal discounting can occur even at the Pavlovian stage, outside a choice context and that DA neurons are likely to provide important inputs to neural regions involved in intertemporal choice, possibly also encoding subjective (discounted) reward value. Dopamine neurons in the ventral tegmental area (VTA) of rats have also been shown to fire in accordance with the delay and magnitude of cues predicting rewards, again suggesting their possible role in encoding temporally discounted value (Roesch et al., 2007b). However, the usual caveats apply to these single unit studies which fuse reinforcement learning theory with intertemporal choice and discounting – especially given DA's known involvement in these processes.

## *Serotonin*

### **Evidence from behavioural inhibition and impulsive mood disorders**

The suggestion that 5-HT is involved in impulse control or inhibition of behaviour was first proposed by Soubrié (1986) following observations that drugs which suppress 5-HT function appear to reduce behavioural inhibition – for example on tasks measuring punishment-induced suppression of behaviour – making animals more impulsive in a motor sense (see Evenden, 1999a, 1999b; Pattij and Vanderschuren, 2008; Winstanley et al., 2004a for review and Dalley et al., 2002 for a counter observation). Further evidence of its involvement in impulse control comes from correlational studies where low cerebrospinal fluid (CSF) levels of the

5-HT metabolite 5-hydroxyindoleacetic acid (5-HIAA) are associated with greater risk taking and aggressive behaviour in monkeys (as observed in the longer and riskier leaps that they take) and rats (Evenden, 1998b; Mehlman et al., 1994) as well as impulsive aggression, alcoholism, violence and suicide in humans (e.g. Asberg et al., 1976; Brown and Linnoila, 1990; Linnoila et al., 1993a, 1993b; Mann, 2003; Ryding et al., 2008). Furthermore, altered serotonin function has been heavily linked to obsessive compulsive disorder (OCD) (Insel et al., 1990) depression (e.g. Caspi et al., 2003; Delgado et al., 1990) and mania (Shiah and Yatham, 2000), disorders of which impulsivity is a common symptom – especially in those prone to suicide (Asberg, 1997; Cremniter et al., 1999). Linnoila et al. (1983) for example found that CSF 5-HIAA of violent aggressive individuals was lower in those where the aggression was impulsive relative to those where it was premeditated. More recently there has also been speculation that aberrant serotonin function may be involved in ADHD (Oades, 2007).

### **Human serotonin manipulation studies of intertemporal choice**

Whereas evidence for the role of serotonin in behavioural inhibition and impulse control is well documented, its involvement in choice impulsiveness is less certain. Until recently, only one human study had manipulated serotonin to observe resulting effects on intertemporal choice. Crean et al., (2002) used a tryptophan depletion procedure to lower serotonin levels (Biggio et al., 1974) of participants who subsequently performed a computerized adjusting amount task and a task designed to measure behavioural inhibition. Whereas performance on the behavioural inhibition task was sensitive to 5-HT depletion, intertemporal choice was unaffected by the manipulation. However, Schweighofer et al. (2008) developed a new choice task which in some respects represents those used in rodent studies (i.e. using short time scales and experienced delays) and showed

that subjects had a greater discount rate after tryptophan depletion than under normal conditions. Serotonin was also found to modulate neural activity during task performance (see below). This result comes with a number of caveats however – the effect was small with only a 4% increase in choice of the smaller-sooner option, and no increase in self-control was observed post a dietary induced increase in serotonin. Furthermore in an earlier study (Tanaka et al., 2007) using a similar paradigm, no behavioural effect was observed. These studies also utilized a short time frame paradigm which had a learning component (though the authors argue this was accounted for).

### **Rodent serotonin manipulation studies**

A number of animal studies have shown that intertemporal choice is sensitive to serotonin manipulation. Although the findings are less conclusive than those in the motor impulsivity literature, rodent studies have associated reduced 5-HT function with greater impulsivity in choice. Wogar et al. (1993), Richards and Seiden (1995), Al-Ruwaitea et al. (1999) and Mobini et al. (2000a, 2000b) found that destruction of the ascending 5-HTergic pathways by intra-raphé injections of selective neurotoxins such as 5,7-dihydroxytryptamine (5,7-DHT), promoted choice of smaller, more immediate reinforcers on various adjusting or delay to reinforcement tasks. Mobini et al., (2000a, 2000b) and others ascribed this change in behaviour to an increase in the  $K$  parameter. Thiébot (1992) and Denk et al. (2005) observed similar findings when using a 5-HT depleting agent (*p*-chlorophenylalanine) in a T-maze procedure, where one arm leads to a small immediate food reward and the other leads to a large delayed one. Boosting 5-HT function, either by using selective 5-HT reuptake blockers such as clomipramine and zimeldine (Bizot et al., 1988), or by fenfluramine (a 5-HT releasing agent), has also been found to increase preference for the more delayed option in the T-maze

task and other procedures (Bizot et al., 1988; Poulos et al., 1996). In another T-Maze study, Bizot et al., (1999) found that 5,7-DHT lesions of the raphe nuclei and the 5-HT synthesis inhibitor para-Chlorophenylalanine (pCPA) increased choice of the smaller-sooner reward arm whereas the selective serotonin reuptake inhibitors (SSRIs) fluoxetine and fluvoxamine as well as a the 5-HT<sub>1A</sub> receptor agonist 8-Hydroxy-N,N-dipropyl-2-aminotetralin (8-OH-DPAT) had the opposite effect.

As with dopaminergic manipulation studies, these results should be treated with caution. For example, many of these effects may be dose or delay dependent. Wogar et al. (1993) found that 5-HT depletion increased discounting, but the effect was abolished when the sizes of the two rewards were doubled. Poulos et al. (1996) demonstrated that low doses of the 5-HT<sub>1A</sub> agonist 8-OH-DPAT promoted choice of the immediate reinforcer only to reduce it at higher doses. Moreover, the propensity of forebrain 5-HT depletion to promote impulsivity has sometimes been transient (Bizo et al., 1999) or not observed (Winstanley et al., 2003, 2004a) and a non-selective 5-HT antagonist (metergoline) has been observed to promote choice of the larger-later option (Evenden & Ryan, 1996). Furthermore, promotion of 5-HT function with SSRIs (Evenden and Ryan, 1996; Logue et al., 1992) and the partial 5-HT antagonist WAY 100635 has been found to have no effect whereas the partial 5-HT agonists buspirone, ipsapirone and MDL 73005EF were shown to increase impulsive choice (Bizot et al., 1999). Evenden and Ryan (1999c) showed that the 5-HT<sub>2</sub> agonist DOI increased choice of the smaller-sooner option whereas the 5-HT<sub>1A</sub> agonist 8-OH-DPAT had mixed effects and both had no effect at low doses. Results of the latter study led the authors to conclude that 5-HT may modulate impulsivity in different ways depending on the involvement of different receptor subtypes, where optimal behaviour may also require a subtle balance between pre and post synaptic receptors.

The factors which could explain these mixed observations are likely to mirror those discussed above in relation to dopamine. The mechanisms by which the 5-HT system modulates impulsive choice are not completely understood, partly owing to the complex nature of this system which contains at least 14 different receptor subtypes, each belonging to one of 7 receptor families (Barnes and Sharp, 1999; Smythies, 2005). Pre and post synaptic effects, dose and whether the manipulation is done pre or post learning are all likely to be important. For example 5-HT<sub>1A</sub> agonists may decrease serotonin efflux because of their effects on presynaptic autoreceptors (Blier and Ward, 2003, – see Pattij and Vanderschuren (2008) for references). One relevant factor in many of the serotonin studies performed by the Thiébot group is the use of the T-maze procedure (Thiébot et al., 1985). There are a number of problems associated with this procedure (See Evenden and Ryan, 1996), indeed Charrier and Thiébot (1996) using a standard lever paradigm failed to show any effect on choice of partial agonists, full agonists or SSRIs, where they had done using the T-maze.

### **In vivo studies of serotonin during intertemporal choice**

Winstanley et al. (2006b) observed enhanced 5HT efflux in the medial prefrontal cortex (mPFC) of rats performing an intertemporal choice task compared to yoked animals, controlling for reward, movement and other factors. More recently, Tanaka et al. (2007) used a novel choice task which required the learning of cues predicting monetary rewards at short and long timeframes. They discovered using functional magnetic resonance imaging (fMRI), a graded map of discount rates in the striatum such that the ventral striatum (VS) activity correlated with expected future rewards and steeper discount rates (short-term reward prediction) and dorsal striatum (DS) correlated with expected future rewards and slower discounting (long-term reward prediction). Furthermore, using tryptophan

depletion and enhancement techniques, they observed that this parallel organization is under differential modulation by the serotonergic system – the ventral striatum activity was enhanced under the tryptophan depletion condition, whereas activity in the dorsal striatum was enhanced under the tryptophan loading condition. This could be consistent with the notion that adequate 5-HT neurotransmission is required for the selection of longer term rewards (although no behavioural effect was observed in this study). The authors suggested that this differential modulation is likely facilitated by differently distributed 5-HT receptor subtypes in the VS and DS (see there for references).

### **Serotonin-dopamine interactions**

Another complicating factor in interpreting 5-HT experimental studies is that many of the effects of selective 5-HT manipulations on impulsivity – for example, produced by depleting brain 5-HT through intracerebroventricular infusions of the serotonergic neurotoxin 5,7-DHT or the administration of selective 5-HT receptor antagonists – appear to involve interactions with the brain DA systems (Harrison et al., 1997; Lucki and Harvey, 1979; McMahon et al., 2001; Segal, 1976). Indeed, DA/5-HT interaction in intertemporal choice has been addressed in a number of papers by the Winstanley group (see also above). In the first of these studies (Winstanley et al., 2003) 5,7-DHT infusions were shown to have no effect on intertemporal choice, despite depleting 85% of forebrain 5-HT. Animals treated with amphetamine were observed to become more self-controlled, however this effect was attenuated by forebrain 5-HT depletion. This demonstrates that 5-HT function is necessary for the self-controlling effect of amphetamine on impulsive choice. In a more anatomical analysis, Winstanley et al. (2005) first treated rats with intra-accumbens 6-hydroxydopamine (6-OHDA), which had the effect of depleting DA and NA in the nucleus accumbens (but did not alter task performance). They

were then either treated with systemic injections of amphetamine or the 5HT1A agonist 8-OH-DPAT. In sham operated rats the 5-HT1A agonist increased impulsive choice, an effect which was blocked by the 5-HT1A antagonist WAY 100635, however, 8-OH-DPAT had no effect on choice in the NAc lesioned rats. Moreover, 8-OH-DPAT blocked the effects of amphetamine in the sham control group. These studies demonstrate the critical interaction between dopamine and serotonin in the regulation of intertemporal choice.

In summary, serotonin is likely to play a role in intertemporal choice and temporal discounting, but it is far from clear how it acts as a modulatory influence on these processes and its study is complicated by interactions with other neurotransmitters, its large number of receptor subtypes and other widespread influences on mood, cognition, executive functioning and behaviour (e.g. Buhot, 1997; Lucki, 1998). Elucidation of its role is of particular importance given serotonin's involvement in aggression and other psychiatric disorders involving impulsivity.

### *Other pharmacological investigations*

Although most pharmacological studies of intertemporal choice have focused on serotonin and dopamine there is a small literature on other important neurotransmitter systems such as glutamate (e.g. Floresco et al., 2008) and gamma-Aminobutyric acid (GABA) (e.g. Cardinal et al., 2000). Acute effects of drugs such as alcohol (e.g. Dougherty et al., 2008; Oberlin and Grahame, 2009; Ortner et al., 2003; Reynolds et al., 2006; Richards et al., 1999b; Tomie et al., 1998) benzodiazepines (e.g. Acheson et al., 2006; Cardinal et al., 2000; Charrier and Thiébot, 1996; Reynolds et al., 2004a;) and ketamine (Floresco et al., 2008) have also been assessed with regards to intertemporal choice. Other studies have assessed

correlations between discount rates and blood plasma levels of hormones including testosterone (Takahashi et al., 2006, 2007) and cortisol (e.g. Takahashi, 2004). These studies are not the concern of the present thesis as no real consensus has formed on the roles of these other neurotransmitter systems and hormones. It is likely that their involvement in choice is mediated by indirect effects on DA and 5HT systems as well as widespread effects on critical brain regions.

## **Neuroanatomical studies of intertemporal choice**

### *Animal and lesion studies*

#### **Orbitofrontal cortex**

The orbitofrontal cortex (OFC) has long been recognised as an important region in decision-making and reward. Damage to this area in humans can cause severe deficits in decision-making abilities (e.g. Bechara, 2004; Bechara et al., 2000, 2005; Damasio, 1994; Lishman, 1998) rendering the patient more risk-prone and impulsive. Behaviour of such patients appears to be guided by immediate prospects and is insensitive to future outcomes – as exemplified by their performance on gambling tasks, where they are likely to choose options with a higher frequency of short-term rewards but larger long-term losses (Bechara et al., 1998, 1999; Rogers et al., 1999). More recently, it is thought that the OFC plays an important role in hedonic experience and in assigning value to reinforcers and conditioned stimuli (e.g. Cardinal et al., 2002; Kringelbach, 2005; Rolls and Grabenhorst, 2008) as well as decision-making based on the long term consequences of voluntary action (Bechara et al., 2000 ). As such the OFC is likely to be involved in temporal discounting.

Although hypothetical intertemporal choices taken by OFC lesioned patients have not demonstrated a specific deficit in impulsive choice (thought they did have a deficit in 'time framing', Fellows and Farah, 2005), it is interesting to note that drug addicts are abnormally impulsive discounters (as inferred from their high  $K$  values compared to controls) (see later) and it has been shown that the brain glucose metabolism of drug addicts is significantly reduced in the OFC (e.g. Volkow & Li, 2004, 2005). Certain populations of addicts also show a similar decision-making profile to OFC patients on gambling-tasks (Rogers et al., 1999). One could hypothesize that this hypoactivity may be one of the underlying causes of the severe impulsiveness seen in addicts, which keeps them chained to immediate gratification. ADHD patients are also thought to have abnormal OFC functioning (Swanson et al., 1998; Winstanley et al., 2006a – see above) and as noted earlier, Winstanley et al. (2006b) observed DA efflux in the OFC of rats during task performance. These observations together suggest a link between the OFC and regulation of temporal discounting.

In specific tests of this hypothesis, Mobini et al. (2002), Rudebeck et al. (2006) and Kheramin et al. (2002, 2003, 2004) found that lesions encompassing the OFC of rats, or dopamine depletion of the OFC, induced steeper devaluation of rewards on an adjusting delay and other intertemporal tasks (i.e. increasing  $K$ ). In contrast, Winstanley et al. (2004b) observed that OFC lesions induced the opposite effect – better self-control than shams, using an identical paradigm. Two explanations have been given for this discrepancy; both have important ramifications for the function of the OFC in intertemporal choice. One possible reason (Cardinal et al., 2004; Roesch et al., 2007a) is that the subjects in the Winstanley et al. study were trained before the OFC was destroyed and retested postoperatively, while Mobini et al. and Kheramin et al. trained and tested postoperatively. This may indicate a role for the OFC in the learning of delayed reinforcement contingencies.

In fact Roesch et al (2007a) review a number of studies to suggest that the OFC has two important functions in intertemporal choice. They first argue that the OFC is critical for maintaining representations of rewards over delays. Evidence for this comes from single unit recordings of a number of cells in the OFC of rats while they learned to press a lever for a reward which appeared after a variable delay (Roesch et al., 2006). They found that in the intervening period, activity in a number of cells rose in anticipation of the reward for the duration of the delay. This outcome-expectant activity, in maintaining representations of an imminent reward, could facilitate the formation of associative representations in other brain regions. Thus the effects on pre-training OFC lesions may reflect the absence of these expectancies when these associations must be learned – resulting in a weaker encoding of associations with the larger-later option. This would explain why after *both* rewards were delayed and the rats had experience with the larger-later option, lesioned animals in Rudebeck et al. (2006) lost the impulsive deficit observed initially, once the smaller option was subsequently made immediate. Interestingly, activity in the majority of OFC neurons tested in well trained rats did not bridge the gap between response and reward delivery, but instead declined as the delay to the reward increased (Roesch et al., 2006). This activity was correlated with a decreased tendency for rats to choose the larger-later option in future free-choice trials. Thus in post-learning lesioned rats the absence of discounting signals would bias the animal to the larger-later option without affecting the formation of associative representations formed prior to the lesion. This view critically implicates the OFC not only in the learning but also the temporal discounting of delayed reinforcers.

Another difference between the studies is that Winstanley et al. used a 1-pellet immediate reinforcer and a 4-pellet delayed reinforcer whereas Mobini et al. offered the rats a choice between a 1-pellet immediate reinforcer and a 2-pellet

delayed reinforcer. Kheramin et al. (2002, 2004) argue that OFC lesions, whilst causing an increase in temporal discounting, also increase the sensitivity of an animal to differences in reward magnitude. In the case of Winstanley et al., due to the relative magnitude of the rewards, this effect could have overpowered the effects of increased temporal discounting (see later and Chapter 2 for further elaboration on this point). Kheramin et al. propose that the OFC's involvement in discounting may be related to its role in the maintenance of the conditioned reinforcing value of intra-delay stimuli, as do Roesch et al. (2007a), although they do not opine as to whether the discounting of rewards *per se* is represented there.

While there is a general agreement that the OFC is involved in temporal discounting (both from animal and human studies), Roesch et al. (2007a) argue that the OFC is not a site of "common value currency". That is to say, the discounted magnitude of a delayed reward is not necessarily encoded there ("time discounted representation of absolute value", in their terminology). They found that neurons responding to delay did not also respond to reinforcer magnitude (a requirement if they encoded discounted value), and as a population, the OFC was not responsive to reward magnitude, indicating that these different types of value information may be represented in different regions. However, Kalenscher et al. (2005) recording from pigeon OFC analogue, and Roesch and Olson (2005) recording from primate OFC, do argue for an integration of time and magnitude information in the OFC, observing activity which is consistent with the time discounted value of delayed reward (see Roesch et al. 2007a for further discussion).

In summary, lesion and single unit recording studies both demonstrate that the OFC is necessary and sufficient for the temporal discounting of rewards in animals. However, the exact nature of its role is complicated by its involvement in learning for delayed options (necessary in animal studies) and other potential roles in value assignment such as magnitude sensitivity. The type of choice task is also

likely to be important in determining OFC lesion effects. These results accord well with human deficits in impulsivity and short term behaviours observed in a wide variety of disorders linked to frontal lobe damage and hypoactivity, although further studies to characterize the specific types of impulsivity implicated in these conditions should be carried out.

Although most research in animals has focused on the OFC, other parts of the prefrontal cortex are also likely to be involved in intertemporal valuations. Kim et al. (2008) for example, used a novel task in primates to show that neurons in the dorsolateral PFC (DLPFC) also encode or track the discounted value of delayed options. Winstanley et al. (2006b) observed 5-HT efflux in the medial PFC (mPFC) of rats during task performance, although lesions in this region do not appear to alter choice (Cardinal et al., 2001). A number of neuroimaging studies in humans (see below) also implicate mPFC, lateral OFC and DLPFC in intertemporal choice, as well as OFC.

It is also important to note that the usual caveats apply with regards to inferring normal function from lesion studies, necessity versus sufficiency, and comparison of animal and human brain regions.

### **Striatum and nucleus accumbens**

The NAc is by far the most ubiquitously identified brain region in studies of reward and motivation processes (e.g. Cardinal et al., 2002; Dayan, 2009; Parkinson et al., 2000; Robbins and Everitt, 1996; Robbins et al., 1989; Robinson and Berridge, 2008) and is thus a natural target for investigation. The NAc/ventral striatum (VS) is activated in response to the receipt of rewards, or cues signalling impending rewards in humans (e.g. Breiter et al., 2001; Knutson and Cooper, 2005; Knutson et al., 2001; O'Doherty et al., 2004; Yacubian et al., 2007). The NAc is also richly

innervated by dopaminergic and serotonergic afferents (e.g. Fallon & Loughlin, 1995; Halliday et al., 1995) and is interconnected to other major reward regions such as the ACC, OFC and amygdala (see Cardinal et al., 2002; Parkinson et al., 2000). In the SHR, differences in DA receptor density and gene expression have been observed within the core and shell regions of the NAc (e.g. Carey et al., 1998; Solanto, 1998, 2002) and drugs of abuse can produce chronic neuroadaptations (Koob et al., 1998; Robinson and Berridge, 2008 – see later) as well as reduced DA function in the striatum (Volkow & Li, 2004, 2005), especially during a state of withdrawal (e.g. Hildebrand et al., 1998).

In a seminal study, Cardinal et al. (2001) examined the effects of excitotoxic lesions of the NAc core on rats' ability to choose between rewards on a progressive delay schedule. To avoid confounding, no cues were present in the delay and subjects were trained preoperatively and tested postoperatively. The rats exhibited a marked preference for smaller-sooner options compared to controls, and they persisted on choosing impulsively even though they were made to experience the larger delayed reward at regular intervals. This effect was not due to an inflexible bias away from the lever producing the delayed reward or an inability to discriminate the reward magnitudes, as when the delays were removed the rats preferred the larger reward, and again switched preference to the smaller when the delays were re-introduced.

This study demonstrates that the integrity of the NAc is crucial for self-control and the ability to choose delayed rewards. In contrast, rats' discounting behaviour was not altered by lesions of the anterior cingulate cortex or medial PFC, two major reward related regions and afferents of the NAc. This ACC finding stands in contrast to previous reports of motor impulsivity or disinhibited responding in ACC lesioned rats, which have been found to over-respond to unrewarded stimuli and to respond prematurely in situations where they are required to wait (Bussey

et al., 1997; Parkinson et al., 2000). These observations suggest that ACC abnormalities in disorders of impulsivity (Bush et al., 1999; Rubia et al., 1999) do not contribute to steeper temporal discounting.

The finding that NAc is critical for rats' ability to select delayed rewards has been replicated a number of times using various tasks (Bezzina et al., 2007; Cardinal and Cheung, 2005; da Costa Araujo et al., 2009; Pothuizen et al., 2005, however see Acheson et al., 2006) some explicitly demonstrating an increase in estimated  $K$  values. Increased discount rates have also been produced by disconnecting the OFC and NAc (Bezzina et al., 2008) and in these studies no effect was found on the rats' ability to discriminate reinforcer magnitude. Cardinal and Cheung (2005) actually observed an increase in sensitivity to reward differences following NAc lesioning, strongly indicating that the deficit is produced by greater temporal discounting.

It is difficult to conclude from these studies what the exact role of the NAc is as no single unit recordings have been carried out, however Cardinal et al (2001) speculate that the NAc could also be involved in maintaining the value of, or expectation of reinforcement over delay (though this would stand in contrast to the hypothesis of Roesch et al. (2007a) that post-learning, once the animal has already formed the association between the response and the delayed reward, such signals are not required). Such a role may accord with findings previously discussed regarding VTA single unit recordings (Kobayashi and Schultz, 2008; Roesch et al., 2007b) as there is a direct projection of these neurons to the NAc. The ventral striatum and nucleus accumbens are also observed to be involved in temporal discounting in the majority of neuroimaging studies in humans (see below).

### **Amygdala and other regions**

The basolateral amygdala (BLA) is highly interconnected with the NAc and OFC, innervated with dopamine neurons and serves as an important emotional learning centre (Cardinal et al., 2002; Parkinson et al., 2000). Winstanley et al. (2004b) found that excitotoxic lesions of the BLA also promote impulsive responding on a delayed reinforcement choice task. Amygdala activity has also been observed in human neuroimaging discounting studies (see below). In addition, this study demonstrated that lesions of the subthalamic nucleus decreased impulsive choice. Other medial temporal lobe structures are not commonly implicated in temporal discounting however Cheung and Cardinal (2005) observed increased impulsive choice following hippocampal lesions.

Taken together, from these animal lesion and single unit studies it appears a fronto-striatal-limbic network comprising the amygdala, OFC, mPFC and NAc is critically involved in choice between reinforcers differing in magnitude and delay. These regions are all interconnected and comprise a substantial part of the limbic system and (associated) ventral basal ganglia loops (Alexander and Crutcher, 1990; Alexander et al., 1990). Moreover, they are richly innervated by DA and 5-HT afferents, suggesting that natural modulation of temporal discounting could be mediated by the action of these neurotransmitters on these regions. However, the precise manner in which these structures and the neurochemical modulators interact in a choice situation is far from clear (Cardinal, 2006). For example, the fact that neurons recorded from the OFC, DLPFC and possibly also VTA have all been found or hypothesized to track temporally discounted values of rewards makes the individual contribution of each region unclear. In addition, elucidation is likely to be complicated by the learning which is required in animal studies.

### *Human neuroimaging studies of intertemporal choice*

In recent years, fMRI has contributed an enormous amount to the understanding of neurobiological mechanisms of temporal discounting and intertemporal choice. Of course, the usual caveats apply with regard to inferences from correlational data.

#### **Single or dual systems for evaluating delayed rewards**

McClure et al. (2004) performed the first neuroimaging study of intertemporal choice to provide a neurobiological account of temporal discounting and preference reversals. The disproportionate valuation of rewards available in the immediate future, and other evidence, led them to postulate that the discrepancy between short-run and long-run preferences may reflect the differential activation of distinguishable neural systems – specifically, that short-run impatience is driven by the limbic system which responds to immediate rewards and is less sensitive to the value of future rewards, whereas long-run patience is mediated by the lateral PFC which is able to evaluate trade-offs between more abstract rewards, including those in the more distant future. Such an account is reminiscent of current versus future self struggles discussed above, however here it is termed as a struggle between an affective and a deliberative decision-making system.

They proposed that two parameters of a quasi-hyperbolic time discounting function (which has been used to capture aspects of human behaviour under various circumstances, Laibson, 1997) could represent the joint influence of these distinct neural processes. This beta-delta function (Laibson, 1997; Phelps and Pollack, 1968) splices together two different discounting functions, one exponential (delta) and another which distinguishes sharply between present and future rewards (beta). This beta parameter represents a special value placed on

immediate rewards relative to those received at any other time. The hypothesis then was that activity in lateral PFC areas should correspond with this rational, deliberative delta function, and limbic activity should represent the beta parameter. To test this hypothesis, they scanned the brains of subjects using fMRI as they made a series of different hypothetical choices between smaller-sooner monetary amounts and larger-later amounts. Critically, they split the trials into two trial types – those where both rewards were delayed in the future, and those where the small reward could be received today.

When they compared these two conditions in their analysis, they found that whereas lateral PFC (dorsal and ventral) and intraparietal regions (regions they defined as delta voxels) were similarly active across all trial types, limbic structures including the ventral striatum (NAc), mPFC, posterior cingulate and medial OFC (regions they defined as beta voxels) were preferentially activated in response to choices where there was an option for immediate reward. If this theory is correct, it makes an additional strong prediction – the relative strength of activation of the two regions should be able to predict what choice the subject made (in choices where there was an immediate component). Indeed, they found that when they analysed all the choices where there was an immediate component, they could predict the outcome – a greater activation of limbic areas led to choice of the immediate small reward, whereas choice of the delayed reward followed a greater activation of the lateral PFC areas relative to the limbic ones.

McClure et al. argue for a dual-core decision-making system in the brain. A rational, deliberative, cognitive system, implemented in the lateral PFC – which devalues rewards exponentially – and an irrational, emotionally driven system implemented in the limbic structures – which has a preference for immediate gratification and leads to quasi-hyperbolic discounting and preference reversals. This theory fits rather well with previous ideas of a cool, rational decision-making

system in the lateral PFC and a hot, emotional one in the OFC/limbic system proposed by Damasio (1994) and Bechara et al. (1999; 2000) (see also Rustichini, 2008 for a discussion of this in relation to other aspects of decision-making behaviour). On the other hand, when considered in relation to animal work which indicates that the integrity of the NAc and OFC (and their modulation by DA) are crucial for self-control and the ability to choose delayed rewards, this study would seem to suggest the opposite, because greater activity in these regions was accompanied by more impulsive choice and the authors propose these regions are only interested in immediate reward. Therefore in their theory, NAc or OFC lesions should promote delayed choice as long as the DLPFC is left intact.

McClure et al. (2007) replicated this paradigm and the major results using primary rewards in the form of fruit juice drinks available to thirsty subjects (time-spans were over a range of minutes), suggesting that similar mechanisms are recruited for intertemporal choice over all time periods and rewards. One interesting difference between primary and secondary rewards was that no differential limbic activity was observed for choices where the smaller-sooner option was delayed more than about 5 or 10 minutes, suggesting that beta activity does not correspond to relative delays but absolute delays and that these are different for primary and secondary reinforcers (see there for elaboration).

A number of criticisms have been raised with regard to these studies. One major concern is that the imaging analyses were completely independent of choice behaviour in the experiment. The authors did not attempt to instantiate the beta-delta model they used in the imaging analyses by using behavioural data and therefore one cannot reliably conclude that the fMRI data validates this model. By extension, the authors did not delineate regions which correlate with discounting or discounted value over time, rather they simply demonstrated that choices with an immediate option induce greater limbic activity. Kable and Glimcher (2007) are

particularly harsh critics of the study – they argue that it provides no evidence at all for the beta-delta model or the dual self model which they espouse. For this to have been achieved, they argue the authors should have provided evidence of activity corresponding to different discount rates in the limbic and DLPFC regions which they failed to do, and specifically that the discount rate in the beta regions was greater than the observed behavioural discount rate of the subjects. Without these demonstrations the results of their arbitrary analysis could simply be explained by proposing that these limbic regions value rewards at all delays and this preferential activity simply reflects the fact that sooner rewards are more valuable.

In their study (Kable and Glimcher, 2007) this point was addressed by scanning subjects who chose between a constant smaller-sooner option and a variable larger later option. In this study (as opposed to McClure et al., 2004) real payment was awarded for a randomly selected choice by way of pre-paid credit cards. The crux of their analysis was to use the hyperbolically discounted values of the larger-later option as a regressor of brain activity. Critically, these values were derived from behavioural estimates of the discount rate parameter, obtained from the choices each subject made (in the context of the Mazur (1987) hyperbolic formula). They found a network of three regions which seemed to track (correlate with) the subjective (discounted) value of the delayed reward – the ventral striatum, medial prefrontal cortex and posterior cingulate cortex. They concluded that these regions – which were also identified as the beta regions by McClure et al. (2004, 2007) – do not exclusively value immediate rewards, as hypothesized by them, rather activity of these regions tracks the subjective value of rewards at all delays, as evidenced from their correlation with the subjective value of the delayed option. Furthermore, these regions do not even primarily value immediate rewards, as the discounting occurring there (implied by the neural activity) was not more

impulsive than the subjects' behaviour, which the beta-delta hypothesis requires. Thus, the finding (McClure et al., 2004) that greater activity was observed in these regions when there was an immediate component was simply because the subjective value was greater in those trials. (See Kable and Glimcher for a discussion of the regions identified in relation to their known roles in valuation).

### **Individual differences in discount rates**

One goal of fMRI studies is the ability to predict individual differences in discounting behaviour based on neural valuation responses. Hariri et al. (2006), based on the ideas of McClure et al. (2004) hypothesized that impulsivity may be determined by the degree of VS (or beta) activation in response to immediate rewards. They first tested subjects behaviourally using a standard discounting procedure to estimate  $K$  values for each subject. Subsequently, subjects performed a reward feedback task in the scanner whereby they had to guess forthcoming cards in order to earn as much money as possible over the task. On each trial they received feedback as to whether their response was correct (i.e. it would earn them money) or not. Feedback stimuli on this task have previously been reported to correlate with VS activity (Delgado et al., 2000). Remarkably, the authors found that individual differences in discount rates predicted the strength of the VS response to feedback cues on the card task (regardless of valence).  $K$  values were also positively correlated with activity in the medial PFC and negatively correlated with activity in the DLPFC. The authors suggested that more impulsive individuals may have a VS circuitry that is relatively indiscriminate and hypersensitive to cues and salient stimuli. However, since the rewards were all instantaneous in this study, the critical test, namely to see if this enhanced VS activity only occurs in response to immediate versus delayed rewards, was not performed. While the conclusion of this study and the link between the two

paradigms involved are rather tenuous, the result is interesting, not least because the two procedures were carried out months apart.

In other correlational studies, Bjork et al. (2009) derived  $K$  values for a number of subjects and correlated them with brain volumes in the frontal cortex using voxel based morphometry (VBM). They found that discount rates were significantly correlated with grey matter volumes in the dorsolateral and inferolateral frontal cortex. Although these regions are not heavily implicated in intertemporal choice, the latter region is interesting because it is thought to be significantly involved in behavioural inhibition (e.g. Chamberlain and Sahakian, 2007; Winstanley et al., 2006a). Discount rates have also been observed to negatively correlate with intelligence and working memory related neural activity in the anterior PFC (Shamosh et al., 2008). Thus no real consensus has yet emerged regarding the neurobiology of individual differences in impulsivity.

### **Dorsal to ventral gradients of discount rates in the striatum**

The striato-cortico basal ganglia loops have also been studied more closely by the Doya group (Schweighofer et al., 2007; Tanaka et al., 2004, 2007) where in two interesting choice paradigms involving both intertemporal choice and reward learning components, they showed that reward prediction errors estimated from subjects' performance data revealed graded maps of time scale within the insula and the striatum. Subjects had to learn to choose between cues that led to small immediate rewards versus cues that led to no rewards (condition 1) or learn to choose between cues leading to small immediate losses but a net positive reward in the long run (condition 2). The duration of this test is in the order of minutes. They observed that areas within the limbic loop, namely the lateral OFC and ventral striatum, were involved in immediate reward prediction (associated with

steeper, behaviourally estimated discount rates). On the other hand, areas within the cognitive and motor loops including the DLPFC and dorsal striatum, were involved in future reward prediction associated with slower discount rates. These topographic maps of the time scales of reward prediction in the insular cortex and striatum, whereby there appears to be a dorsal-ventral gradient of discount rates, were found to be the case independently of whether an exponential or hyperbolic model was used to regress the data. Therefore, these data lend some support to the original dual-system idea of McClure et al. (2004), that the brain does treat short term and long term rewards differently (with differing discount rates). However these paradigms involved a fusion of reward prediction learning and intertemporal choice and so it is difficult to conclude that the results obtain in the valuation of reward options which do not require learning, or in response to the rewards themselves as opposed to predictive cues (e.g. such a difference was observed by Kobayashi and Schultz, 2008). Furthermore, behaviourally estimated discount rates are likely to differ when estimated in these tasks. Note that although this study does give some weight to the idea of separate treatment of immediate and delayed options in the brain, it does not support the neuroanatomical conclusions of McClure et al. (2004) regarding limbic versus cognitive regions.

Ventral striatum activity correlating with hyperbolic discounting of value has also been observed at short time scales (seconds) in response to cues predicting rewards, by another group (Gregorios-Pippas et al., 2009). Furthermore, this activity was greater for cues predicting smaller magnitude rewards, mimicking the magnitude effect.

## **Self control**

Wittmann et al. (2007) analysed regions that were specifically active when subjects chose the delayed (over one year) versus sooner option of a hypothetical choice task. When subjects chose the delayed option, posterior cingulate, insula, and superior temporal regions were more active. Furthermore, caudate was active in trials where the maximum delay was one year versus all other trials (up to 10 years) in an analysis similar to that of McClure et al. (2004). This led the authors to conclude that the insula is critical for delayed gratification and self control. However, these arbitrary analyses suffer from similar problems regarding the assumptions entailed. For example, activity in these ('self-control') regions could simply correlate with value over all timescales as the chosen option is obviously the one with greater subjective value (regardless of timescale) and thus insula activity could simply correlate with subjective value, as indeed is shown in other studies.

## **Probabilistic versus temporal discounting and the nature of discounting**

Luhmann et al. (2008), hypothesized that one could use fMRI to answer the question of whether temporal and probability discounting share the same mechanism or are distinct processes (e.g. Green and Myerson, 2004). In a choice task involving both probabilistic and delayed rewards they found that activity in the posterior cingulate cortex, parahippocampal gyri, and frontal pole was uniquely responsive to the temporal but not probabilistic aspects of reward. They used this evidence to argue that temporal discounting may not simply be explained by the risk associated with waiting for delayed rewards. However, this subtraction analysis is far from conclusive, as it does not prove that the valuation

mechanisms are not shared in both cases, rather that some aspects of the different reward dimensions may invoke differential activity.

This question was addressed in a wider context by Ballard and Knutson (2009) who attempted to look at the effects of increasing delay on blood-oxygen-level dependent (BOLD) activity, independently of reward magnitude. The aim of this study was to test between three possible hypotheses regarding the effects of delay – 1) delay diminishes reward activity classically seen in areas such as the striatum and ventromedial PFC. 2) Increasing delay invokes uncertainty about the likelihood of reward delivery and thus activity should correlate with regions observed in risk studies such as the anterior insula and ACC (e.g. Paulus et al., 2003; Preuschoff et al., 2008). 3) Representation of future reward requires cognitive control and will power, inhibiting pre-potent responses and requiring imagining one's self in the future, activating associated regions such as the DLPFC, inferior frontal gyrus and posterior parietal cortex. To address this question they used a modified adjusting amount task where the information about the amount and delay of the larger-later option was (partially) presented separately to the subjects while being scanned (information about the sooner option was always present on the screen but remained constant throughout). They found that whereas NAc, mPFC and posterior cingulate cortex (PCC) activity correlated with reward magnitude, activity in lateral regions such as DLPFC, temporal-parietal junction and posterior parietal cortex, negatively correlated with reward delay. Looking between subjects, more impulsive individuals showed diminished neural activation to magnitude and also greater deactivations in response to delay. This would seem to concur with many of the previous studies (McClure et al., 2004; Wittman et al. 2007) suggesting decreased activity in lateral regions when selecting smaller-sooner options. The authors concluded by ruling out option 1, as delay information did not affect NAc and mPFC response. Similarly option 2 is ruled out

because of the negative versus positive correlation one would expect if increasing delay is associated with activity of regions encoding uncertainty. This leaves the executive control explanation. However it is not explained why if executive function is required to delay gratification and consider long term rewards, why a negative correlation should have been observed between activity in those regions and increasing delay of the larger option. There are a number of other faults with this study, for example the lack of use of behavioural data in the main analyses to correlate *subjective* value delay parameters with neural activity, inconclusive analyses and unproven assumptions as well as failure to find regions where the subjective value should have been encoded (e.g. as in Kable and Glimcher, 2007). Their conclusion that temporal discounting does not involve the striatum is also surprising given the wealth of evidence that implicates the region in most animal and human studies. Presumably this result is an artefact of the analyses performed.

In summary human neuroimaging studies converge on data from animal lesion and single unit studies, implicating limbic and cognitive cortico-striatal loops comprising ventral and dorsal striatum, insula, medial PFC, lateral OFC, DLPFC inferior frontal regions and posterior cingulate cortex. In addition, a number of posterior regions in the parietal cortex and temporal-parietal junction are also identified in some studies. However, consensus has not been formed on the particular contribution of each region to intertemporal choice and value construction, or the neural basis of individual differences in impulsivity. Moreover, there are some differences with animal studies which will need reconciling. For example, in animal studies, integrity of the NAc is necessary to be able to select larger-later rewards but from imaging studies, NAc seems to be more active in response to sooner rewards and their selection, and in impulsive individuals. This is particularly a problem for dual system models where the NAc is thought to be part of an impulsive decision-making system. Similarly, in many

of the animal DA manipulation studies reviewed above, it was concluded that boosting dopamine activity can decrease discount rates. Presumably however, such enhancement by stimulants would lead to greater ventral striatum activity (e.g. Koob and Bloom, 1988; Robbins et al., 1989; Robinson and Berridge; 2000, 2008). If the ventral striatum is part of an 'impulsive' decision-making system, these results would appear to be contradictory. This issue of a dual-valuation system (deliberative, rational vs. affective, irrational) for long versus short term rewards is one of the most controversial topics currently being debated and highlights the fact that imaging studies can be complicated by the choice of analyses performed and how exactly to interpret them – especially when analyses ignore any behavioural choice data. Of note are the studies by Kable and Glimcher (2007) and Tanaka et al. (2004) where behavioural data were used to correlate subjective values with brain activity and in the former case convincingly demonstrate for the first time a subjective valuation system for delayed rewards, which accords with, and neuronally validates hyperbolic models of temporal discounting and the DU model.

### **Neuropsychiatry of impulsive choice**

We have already seen that a number of psychopathologies and disorders are associated with increased impulsivity, or display it as a core feature. These disorders therefore offer another avenue for gleaning information about the neurobiology and pharmacology of impulsive choice – given what we know about the biological abnormalities in these conditions. Perhaps more significantly, what we know from the studies reviewed above could help gain insight into the underlying biological causes of the abnormal temporal discounting observed as a clinical feature of these disorders, and may better inform its treatment. Some of the

major disorders in this category will be briefly reviewed below and in Chapter 4 will be considered to a greater extent.

### *ADHD*

As discussed in detail above, at least one sub-type of ADHD has been associated with increased rates of discounting (e.g. Sonuga-Barke, 2002, 2003; Winstanley et al., 2006a - see above). It is widely accepted that patients with ADHD have functional and structural abnormalities in the prefrontal and orbitofrontal cortices and possibly also in the striatum and its connectivity with the PFC (e.g. Arnsten, 2006; Castellanos and Tannock, 2002; Reiger et al, 2003; Sergeant, 2000; Solanto, 1998, 2002; Winstanley et al., 2006a). Such observations have led to comparisons of ADHD symptoms with the deficits observed following PFC lesions. Abnormal functioning of the OFC and striatum in ADHD correspond well with the increase in impulsive choice observed following OFC and NAc lesions in rodents, and also with the limbic regions identified in fMRI studies of intertemporal choice. Moreover it has been theorised that ADHD is also caused by a hypofunctional mesolimbic dopamine system (e.g. Johansen et al., 2002; Sagvolden and Sergeant, 1998; Sagvolden et al., 1998) which is normalized by treatment with psychostimulants. This theory also accords well with many of the dopamine manipulation studies in rodents where it is demonstrated that enhanced/reduced dopamine function can lead to reduced/enhanced impulsiveness in choice. Nevertheless, one difficulty in integrating ADHD findings with previous research is that reduced activity (and by extension dopamine function) within the limbic regions should in theory promote choice of the delayed option according to the dual system model (Hariri et al., 2006; McClure et al., 2004) and vice versa when stimulating these regions. We also know that the characterization of a

hypodopaminergic state in ADHD, and the pharmacological basis of treatments with monoaminergic stimulants are very controversial. Some argue that ADHD patients have a hyperfunctioning mesolimbic DA system and a paradoxical reduction in DA activity induced by psychostimulants can treat this deficit (Seeman and Madras, 1998, 2002; Solanto, 1998, 2002; Swanson et al., 1998; Zhuang et al., 2001). Furthermore, we have seen that the effects of dopamine manipulation on intertemporal choice can be very mixed and sometimes show opposing influences on choice. Either way, from a neuroanatomical and pharmacological standpoint, the implicated systems in ADHD have all been identified as critical in intertemporal choice studies.

### *Adolescent behaviour*

Adolescent behaviour – as most parents will confirm – is characterized by impulsive decision-making that is both risky and rewarding in the short-term but poor in the long-term. For example, in a study of over 900 individuals between the ages of 10 and 30, subjects under the age of 16 were observed to have significantly higher discount rates than older subjects and characterized themselves as less concerned about the future and less likely to anticipate the consequences of their decisions (Steinberg et al., 2009). Scheres et al. (2006) also noted greater discounting in children aged 6-11 than those aged 12-17. The adolescent NAc differs in both DA function and synaptic plasticity from that of the adult (e.g. Philpot et al., 2001, see Cardinal et al., 2004) and continues to develop into the 20's (Giedd, 2004). Furthermore, the orbitofrontal cortex is the brain region which both neuroanatomically (Gogtay et al., 2004; Sowell et al., 1999, 2003), and functionally (Brown et al., 2005; Casey et al., 2005, 2008; Durston et al., 2006) develops later than all other brain regions. Galvan et al. (2006) used fMRI while subjects aged between

7 and 29 performed a reward learning task. They found that activity in the NAc in response to reward cues was exaggerated in adolescents, relative to children and adults. Furthermore activity in the OFC of adolescents was not focal, resembling more the activity seen in children and not adults. This led them to speculate that maturing subcortical systems become disproportionately activated relative to later maturing, top-down control systems, biasing the adolescent's action toward immediate over long-term gains. Adolescence is also a time when people are more susceptible to developing addictions (Schramm-Sapyta et al., 2009) which is thought to be linked to ongoing maturation of the PFC (Chambers et al., 2003). Such findings indicate that in adolescence, short-sighted and maladaptive behaviours may stem from an undeveloped OFC, just as damage to the OFC in rodents causes greater temporal discounting. Furthermore, the hypersensitivity of the NAc to rewards chimes with the ideas of Hariri et al. (2006), McClure et al. (2004) and Tanaka et al. (2004) regarding the role of this region in short-term reward selection.

### *Aggression, suicide, depression and mania*

DSM-IV classification (American Psychiatric Association, 1994) states that individuals currently experiencing major depressive episodes often have difficulty making decisions. Manic individuals in particular tend to display excessive involvement in pleasurable and impulsive activities, carrying a high potential for painful consequences. Although impulsivity is a noted feature of depression and mania (e.g. Najt et al., 2007; Swann et al., 2009) especially in those prone to suicide (e.g. Roy and Linnoila, 1988 – see above), as well as certain forms of aggression (see above with regard to serotonin) the specific deficit in impulsivity in these disorders has yet to be addressed. One study has noted that depressive individuals discount

at a greater rate than controls (Takahashi et al., 2008) but they are also more inconsistent in their choices. What is interesting about these disorders from an intertemporal perspective is that there is a vast literature linking depression and other mood disorders including mania and impulsive aggression, to abnormal functioning of certain neurotransmitter systems. It was noted earlier that low serotonin levels have been correlated with greater risk of impulsive aggression and suicide; similarly the monoaminergic hypothesis of depression posits that reduced activity of ascending serotonin and noradrenaline systems are a fundamental etiology of the disease (e.g. Stahl, 2000). This hypothesis is based on the efficacy of selective serotonin/noradrenaline reuptake inhibitors in treating the disorder. Serotonin manipulation studies in intertemporal choice have shown that attenuated 5-HT transmission can also lead to more impulsive choice and therefore may provide a possible basis for some of the impulsive aspects of decision-making observed in these mood disorders. Furthermore, unipolar and bipolar depression have been linked to structural and functional abnormalities in the ventromedial prefrontal cortex, amygdala and striatum (Drevets et al. 1992, 1997) – all of which are identified in intertemporal choice studies. This suggests further research into impulsive choice specifically, is warranted to classify clinical symptoms in these pathologies.

### *Dopamine dysregulation syndrome*

Dopamine dysregulation syndrome (DDS) is a relatively recently described phenomenon whereby certain patients (roughly 4%) suffering from Parkinson's disease (PD) treated with large doses of levodopa (L-Dopa) or dopamine agonists can develop impulsive and compulsive behaviours such as compulsive gambling, hypersexuality, compulsive shopping and eating, as well as other short sighted

behaviours (see Dagher and Robbins, 2009; Merims and Giladi, 2008; O'Sullivan et al., 2009 for reviews). In some aspects, this syndrome is thought to resemble an addiction to the dopamine medication. It has been proposed that these symptoms can arise from a dopamine 'flooding' of the ventral striatum–limbic basal ganglia circuit, which in PD suffers from less DA depletion than the motor loop. Alternatively, neuroadaptations in dopamine projections to accumbens related circuitry is thought to be a cause. Evidence for neuroadaptations and sensitization occurring in DDS include enhanced levodopa-induced ventral striatal dopamine release (see Dagher and Robbins, 2009; O'Sullivan et al., 2009). Although these patients have not been tested on discounting tasks explicitly, one could partially explain the impulsive behaviours in light of studies such as McClure et al. (2004), however the syndrome does not gel as well with the idea that boosting mesolimbic dopamine function can lead to greater self-control (see dopamine manipulation studies above).

### *Addiction*

Impulsivity is a quintessential feature of addiction. Despite intentions to desist from their addictions (in many cases), addicts constantly choose the immediate, small benefit of engaging in their addictions as opposed to the long run but greater reward of abstaining. Moreover, there is awareness that this deleterious course of action is harmful in the long run, yet addicts seem unable to choose otherwise. Aside from these preference reversals which clearly indicate some form of hyperbolic discounting (e.g. Ainslie, 2001; Bickel and Marsch, 2001; Bickel et al., 2007), this behaviour suggests that addicts have abnormally high discount rates, which in turn keeps them chained to immediate gratification.

Over the last few years a large and fruitful literature has emerged on addiction and temporal discounting. In almost every study undertaken, addicts have been shown to have greater discount rates than healthy controls, suggesting a general deficit of impulsive choice occurring in all forms of addiction, which is perhaps necessary for its formation. Greater temporal discount rates relative to controls have been found amongst opioid dependents (Kirby et al., 1999; Madden et al., 1997, 1999; Odum et al. 2000), cocaine dependents (Coffey et al., 2003) problem drinkers (Dom et al., 2006; Petry, 2001a; Richards et al., 1999a; Vuchinich and Simpson, 1998 – though see Kirby and Petry 2004) pathological gamblers (Alessi and Petry, 2003; Petry, 2001b; Petry and Casarella, 1999), and cigarette smokers (Baker et al., 2003; Bickel et al., 1999; Field et al., 2006; Mitchell, 1999; Reynolds, 2004; Reynolds et al., 2003, 2004b – see also Bickel and Marsch, 2001; Bickel et al., 2007; Green and Myerson, 2004; Reynolds, 2006 for reviews). In addition, numerous rodent studies (mostly using cocaine) have shown that rats which have been trained to self-administer drugs and become dependent, or have been chronically exposed to drugs, are more impulsive in intertemporal choice than controls (see Setlow et al., 2009). Dandy and Gatch (2009) for example, showed that chronic exposure to cocaine in rats over a nine day period led to significantly greater discount rates (impulsive choices) than those measured in the same rats pre-exposure as well as a sham control group. Moreover, discount rates increased with each day of exposure to cocaine, and upon cessation of the treatment, rats in a large dose group had continuing elevated levels of impulsive choice.

Interestingly, substance abusers have also been shown to have higher rates of discounting when offered choices between smaller-sooner and larger-later drug rewards (for their drug of choice), than that measured with monetary rewards (which are also abnormally high) (e.g. Madden et al., 1997; Bickel et al., 1999)

suggesting an overall deficit in self-control across reward types, particularly for choices involving the drugs themselves.

A perennial debate in this literature concerns whether excessive discounting/impulsive choice in addicts is a cause or consequence of drug addiction – since greater discounters are presumably more likely to engage and become addicted in the first place (Bickel and Marsch, 2001; Bickel et al., 2007; de Wit, 2009; Reynolds, 2006). Bickel et al. (1999) for example, found that current smokers discounted more than never or ex-smokers. The never and ex-smokers displayed no significant difference in discounting, suggesting that smoking may induce a reversible increase in discount rates. Similarly, Reynolds (2004) demonstrated a correlation between the number of cigarettes smoked and temporal discount rates as well as showing that young-adult smokers discounted more than adolescent smokers – indicating a causative effect of smoking duration on discounting. On the other hand, Perry et al. (2005) trained rats to self-administer cocaine after categorizing them as high or low for impulsiveness, based on intertemporal choice behaviour using food rewards. They observed that cocaine self-administration was acquired by 77% of the rats in the high-impulsivity group, and by only 25% of the rats in the low-impulsivity group - suggesting that the impulsive choice observed in addicts is a trait variable. Of course, it is possible and likely that excessive discounting is both a cause and consequence of drug addiction (de Wit, 2009; Reynolds, 2006).

A number of studies have also demonstrated that during withdrawal addicts are even more impulsive in choice. Field et al. (2006) and Giordino et al. (2002) found that nicotine and heroin addicts were more impulsive (both for money and drugs) and had greater discount rates during withdrawal than when tested just after using the drug (however see Kirby and Petry, 2004). Mitchell (2004) also observed this phenomenon in smokers, but only for drug rewards. This increased discount rate during withdrawal could help to explain why there is such a high relapse rate

amongst addicts. Furthermore, Hoffman et al. (2008) observed differences in cortical and striatal activations in abstinent methamphetamine users and control subjects during intertemporal choice. Control subjects tended to have greater activity in these regions during choice.

There is also limited evidence (Weller et al., 2008; Zhang and Rashad, 2008) that obesity is associated with increased temporal discounting. This finding suggests that impulsive choice is a promising avenue for research into the psychological/neurobiological deficits in obesity. Furthermore, it has been hypothesized that there are strong overlaps between deficits and abnormalities, both behavioural and neurological, in addiction and obesity (Volkow and Wise, 2005; Volkow et al., 2008).

The neurobiology and pharmacology of addiction also go a considerable way to explaining these deficits in self-control, as addiction is heavily linked to alterations in dopamine and limbic function. Drugs of abuse can produce chronic neuroadaptations in brain regions including the NAc (e.g. Koob et al., 1998) and chronic methamphetamine exposure has been shown to increase impulsive responding in rats and induce structural changes in the NAc (e.g. Richards et al., 1999a). Cardinal et al., (2004; Cardinal and Everitt, 2004) therefore argue that one mechanism contributing to addiction may be damage or dysfunction of the NAc which promotes impulsive choice, as observed in their earlier study (Cardinal et al., 2001). Additionally, it has been shown that the brain glucose metabolism of drug addicts is significantly reduced in the OFC (e.g. Volkow and Li, 2004, 2005; Volkow et al., 2004, 2009), and that addicts also show a similar decision-making profile to OFC lesion patients on gambling-tasks (Rogers et al., 1999). Such dysfunctioning of the OFC in addicts could also be a cause of greater impulsiveness since lesions there can induce impulsive choice in rodents. This theory is harder to reconcile with the dual system model (Hariri et al., 2006;

McClure et al., 2004) since in this formulation the OFC is part of an impulsive system. However, impulsivity may also arise due to abnormalities in more cognitive executive regions of the PFC (e.g. Goldstein and Volkow, 2002; Verdejo-Garcia et al., 2004) – the rational long term system in the dual system formulation – which have been theorized to be required to inhibit subcortical responses when selecting long term rewards (e.g. Bickel et al., 2007; Goldstein and Volkow, 2002; Jentsch and Taylor, 1999). The involvement of reduced OFC function is also difficult to reconcile with Roesch et al. (2007a) who argue that post-learning, the OFC is involved in providing discount signals to other brain regions and that damage there could therefore lead to less impulsive choice (see above).

Addiction is also associated with alterations in dopamine function (e.g. Berridge, 2007; Dayan, 2009; Everitt et al., 2001, 2008; Koob, 1992; Koob et al., 1998; le Moal, 2009; Robbins and Everitt, 1999; Robinson and Berridge, 2000, 2008; Volkow & Li, 2004, 2005; Volkow et al., 2004, 2009; Wise, 2008). More specifically, addicts have been shown to have hypofunctioning striatal DA systems, for example, as observed by a reduction in dopamine receptor expression (Koob, 1992; Koob et al., 1998; Volkow & Li, 2004, 2005; Volkow et al., 2004, 2009), especially during a state of withdrawal, when DA levels in the NAc are markedly reduced and susceptibility to relapse is high (Hildebrand et al., 1998; Volkow & Li, 2004, 2005). This reduced mesolimbic DA activity could lead to greater discounting, as shown in some of the pharmacological studies discussed above. However, one of the larger themes in addiction research concerns the chronic changes which occur in the NAc and its connectivity with the VTA, which can lead to sensitization (Berridge, 2007; Everitt et al., 1999, 2001, 2008; Koob, 1992; Koob et al., 1998; Robinson and Berridge, 2000, 2008; Volkow & Li, 2004, 2005; Volkow et al., 2009). Sensitization refers to the phenomenon whereby drugs, or stimuli predicting them, can lead to increased responses of dopamine neurons in the NAc. Such changes

can lead to enhanced motivational salience (or 'wanting') for drugs and potentially other rewards. This enhanced dopamine activity to rewards (especially drugs), and state of wanting could lead to the seeking of immediate rewards, but the theory is more difficult to reconcile with the dominant view of dopamine in intertemporal choice, discussed with respect to the rodent and ADHD studies. However, in the dual system model such changes could promote choice of the sooner option by enhanced activation of regions responsive to short term rewards.

### **Motivational and visceral states: Hedonic impact of rewards**

Although it has not been well studied, an important variable in intertemporal choice is the motivational state of the decision-maker. Ho et al. (1997) (see also Bradshaw and Szabadi, 1992; Wogar et al., 1992) for example, tested for an effect of food deprivation on rats' choices between smaller-sooner and larger-later food rewards. Contrary to what one might have assumed, inferred  $K$  values were actually smaller in rats maintained at 80% versus rats maintained at 90% of their free-feeding body weight (however, Richards et al. (1997a) found no effect of satiety on choice). Other examples of motivational influences include the state of withdrawal, and influences of drug associated cues in addicts, discussed previously.

Another angle on this relates to the sensory information of rewards or cues predicting reward during decision-making. McClure et al. (2004) propose that sensory properties of rewards or cues may act to increase impulsive choice by their propensity to engender activity and dopamine release in the striatum and other limbic reward regions. They conclude:

“Our results help to explain why many factors other than temporal proximity, such as the sight or smell or touch of a desired object, are associated with impulsive behaviour. If

impatient behaviour is driven by limbic activation, it follows that any factor that produces such activation may have effects similar to that of immediacy... Immediacy, it seems, may be only one of many factors that, by producing limbic activation, engenders impatience."

Of course such influences on choice were noted by the earliest thinkers such as Rae and von Bohm-Bawerk (see above). Indeed, anticipation, arousal, motivational and visceral states, and the hedonic impact that can be engendered by spatially and temporally proximate rewards form a major part in modern theories of intertemporal choice (Berns et al., 2007; Loewenstein, 1987, 1996). This is especially the case when temporal or physical proximity can reduce aversive motivational states, leading to a disproportionate but transient increase in the attractiveness of those options. For example, it has been noted that such influences could be responsible for the commonly occurring preference reversals observed in hunger and dieting, addiction, sexual desire and other heat-of-the-moment behaviours (Laibson, 2001; Loewenstein, 1996, 2000 - see Frederick et al., 2002 for further discussion). Although impulsivity arising from visceral states can explain weakness of resolve in the face of temptation, it cannot account for all the findings in intertemporal choice and is not *per se* a theory of discounting or choice. These considerations are discussed further in the final chapter.

## **Real versus hypothetical choices**

An important debate in decision-making studies centres around whether during hypothetical decision tasks, subjects choose as they would in real life situations (e.g. Camerer and Hogarth, 1999). This is particularly relevant in human intertemporal choice tasks where it is often impractical and costly to pay out the kind of sums used for each choice, and over the range of delays tested. Use of hypothetical choice paradigms was very common in the groundbreaking behavioural economic studies of Kahneman and Tversky and rested on the twin

assumptions that subjects know how they would react in a real choice situation and also have no special reason to disguise their preferences (Kahneman and Tversky, 1979). Recently, some economists and psychologists have become more sceptical of this methodology, arguing that hypothetical choices may only reflect people's attitudes or opinions, and not necessarily how they would choose in real life were they to actually endure and experience the delays and rewards. A number of studies have been carried out to test these hypotheses.

Navarick (2004) noted that  $K$  values differed substantially across hypothetical-prospective studies versus short-term real operant studies, where estimates derived from real studies are much larger. That discount rates are higher in real versus hypothetical choice tasks has also been observed by Lane et al. (2003), Coller and Williams (1999) and Kirby and Marakovic (1995). In a review, Kirby (1997) examined the degree to which delayed hypothetical and real rewards were discounted in an across studies comparison. The result indicated that real rewards were discounted more than hypothetical rewards, however it was also pointed out that real reward studies tend to use smaller magnitude rewards which are thought to be discounted at a greater rate due to the magnitude effect. They conclude that although rates may be lower in hypothetical studies, the form (hyperbolic) remains constant so one should not worry too much about such an effect. Interestingly, Scheres et al. (2008) found that ADHD symptom measures in 55 students correlated with delay aversion in intertemporal choice but this relationship was only found when using real rewards, suggesting that real discounting tasks are more sensitive and reliable.

On the other hand, Johnson and Bickel (2002), Madden et al. (2003, 2004) and Lagorio and Madden (2005), all reported no difference when comparing discount rates for real and hypothetical rewards, both within and between subjects. Bickel et al. (2009) even went as far as using fMRI to argue that hypothetical and real

choices were identical. In this study no behavioural differences were found, and moreover, no differences were found in neural signal changes observed in the cingulate, striatum and lateral PFC, which were active during both conditions. However, absence of evidence of BOLD differences is not in itself strong evidence.

A major concern with so called realistic studies is that they employ a system of random selection of one reward post-testing. The idea of these *potentially* realistic studies is that since the subject does not know which choice will be selected for payment, they will treat each choice as if it were for real. To assuage concern that this is not the case, Madden et al. (2004) increased the proportion of potentially rewarded choices from 1 out of 400 to 1 out of 15 choices made and observed no difference in discount rates. However, even if the assumptions of these potential reward paradigms are true, differences still remain between animal operant procedures and human short term discounting experiments, and human realistic but prospective studies. Animals are given forced exposure to the consequences of their choices, experiencing the delay and reward following each trial. By contrast, most human experiments rely on subjects' pre-experiment experience to inform choice, as the delays are only experienced following the completion of all trials, even if payment is carried out realistically. Lagorio and Madden (2005) argue that these differences do not have an effect on measured discount rates. On the other hand, one could argue that most of the important intertemporal choices we face in life are informed by past experience of delay, without repeatedly experiencing each choice – when taking out a mortgage to buy a property, for example. Therefore, as long as the reward is realistic and will be received at a chosen delay, these experiments are, in theory, ecologically valid.

Finally, Gregorias-Pippas et al. (2009) as well as Tanaka et al. (2004) and McClure et al. (2007) have noted that when conducting human intertemporal choice experiments over the range of seconds and minutes, the observed discount

rate would lead to very low subjective values over delays of months, particularly with primary rewards. This suggests that the steepness of discounting appears to be scaled to the predicted range of delays, whereby adaptive brain processes may adjust the discounting factors to the delay range valid in each situation, so as to produce good discrimination among values of delayed rewards within these time ranges. However, investigations comparing different delay ranges in the same participants, or primary versus secondary rewards are still lacking.

### **The problem of non-linear utility and advanced valuation models**

The intertemporal choice experiments reviewed in this introduction have been of great value in understanding temporal discounting and impulsive choice, however, there is potentially a major confound in their interpretation – a confound which a large part of this thesis is devoted to.

The root of this problem lies in the way that the choices differ in both delay and *magnitude*. Take, for example, an abstaining smoker who is offered a cigarette. His choice is between a small, immediate reward (the cigarette) and a large, delayed reward (better health in the future, spend less etc.). If he acts impulsively where another does not, it could be because he is less influenced by outcomes that are delayed considerably (more temporally impulsive), or it could be because he does not perceive the larger reward to be as valuable (in relation to the smaller reward) as his self-controlled counterpart does. In the latter scenario, the smoker acts impulsively because there is not enough utility to be gained in waiting for the larger option, given the *normal* effects of delay.

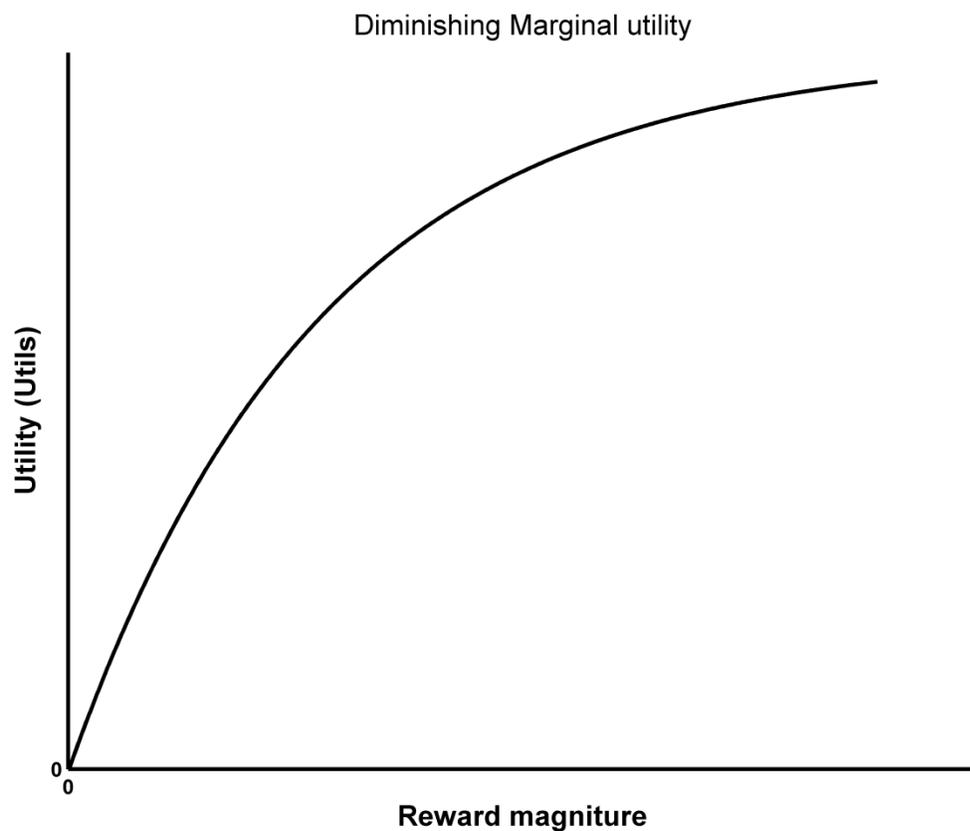
To fully understand this problem, consider the relationship between the size or magnitude of a reward, and its subjective value or utility. This relationship is not a straightforward linear one, but is more likely to be concave (Figure 7). This can be

easily demonstrated by a simple thought experiment – for the average person, winning £2000 in a lottery would make you much happier than winning £1000, but winning £1,002,000 would not really make you much happier than winning £1,001,000. The idea that every unit (marginal) increase in a good brings us successively less and less (marginal) utility has a long history in economic theory and goes to the very heart of value.

Adam Smith (1776) explored the paradox of value when considering the disparity between the ‘value in exchange’ of water, whose ‘value in use’ is fundamental, and diamonds whose value in use is trivial. Whereas Smith was led to the conclusion that value lies in the labor required to extract a good, a subjective theory of value addressed this perplexity by positing that the value of a good is not determined by its maximal utility, rather by the increase in utility obtained by consuming one extra unit of that good, i.e., its marginal utility. A salient feature of marginal utility is that it diminishes as the quantity of a good increases – hence the utility provided by a fixed amount of £10, is greater when added to an option worth £50 than to one worth £500. Since water is so plentiful, its marginal utility (and hence value in exchange) is much smaller than that of scarce diamonds. The concept (often referred to as a law) remains integral to economic theory, most notably in the microeconomic concept of the indifference curve which explains preferences between different bundles of goods, consumer theory and laws of supply and demand (Pindyck and Rubinfeld, 2004), as well as in modern analyses of decision under risk and uncertainty (Kahneman and Tversky, 1979; von Neumann and Morgenstern, 1947). In fact diminishing marginal utility was first proposed by Bernoulli (1738) as a solution to the famous St Petersburg paradox.

It is therefore likely that two features of preference, the discounting of time and also the discounting of magnitude (diminishing marginal utility), contribute to choice outcome in intertemporal choice. This is because the rate at which the

marginal utility of an individual diminishes will determine the perceived increase in (subjective) utility of the larger reward relative to the sooner (independently of temporal discounting). Returning to our smoker, it is now possible to understand why if he had a greater rate of magnitude discounting than his self-controlled counterpart, he could have chosen to smoke – even though they had the same rate of temporal discounting.



**Figure 7. The non-linearity of (instantaneous) utility.** Utility functions describe the relationship between increasing reward magnitudes and subjective value, or utility, derived from them. The most salient feature is that the function is concave for gains – this equates to diminishing *marginal* utility.

Because the majority of discounting experiments rely on the standard hyperbolic model and assume a linear relationship between utility and reward magnitude, choice outcome is deemed to be solely a product of the discount rate – this leads to two potential confounds. The first is that if diminishing marginal utility does play a role in intertemporal choice, it is likely that many studies overestimate the temporal discount rate because diminishing marginal utility has the effect of decreasing the ratio of the (instantaneous) subjective value of the later reward relative to the sooner, and thus shifting preference to the smaller-sooner option. The second and more serious problem is that we now have an interpretational difficulty when comparing differences in intertemporal choice behaviour across experimental groups, be it in lesion, pharmacological manipulation, population comparison or imaging studies. This arises because we cannot determine whether a difference in impulsive choice – arising from for example a lesion, or being a drug addict – is caused by a change in the temporal discount rate or a change in the rate of diminishing marginal utility of the chooser, or both. Since all previous studies assume that the discount rate/temporal discounting is the only determinant of choice outcome, behavioural changes are automatically associated with changes in  $K$  – this casts a shadow of doubt over the conclusions of many of the studies reviewed above.

Moreover, the assumed relationship between  $K$  and impulsivity in choice (e.g. Ainslie, 2001) should break down if  $K$  is not the sole determinant of choice outcome. It would therefore be problematic to equate impulsivity in choice directly with this parameter. Accordingly, studies of temporal discounting are confounded because they assume that behavioural changes reflect a change in the discount rate, and studies of impulsivity are confounded because they assume that impulsivity is a sole product of the temporal discount rate – one needs to know a variable's affect

on both determinants to be able to know how impulsivity will be affected in different choice conditions.

The idea that diminishing marginal utility may play a role in intertemporal choice is rarely discussed although it has been noted by economists (Andersen et al., 2008; Frederick et al., 2002; Kirby and Santiesteban, 2003; Loewenstein and Prelec 1992; Read, 2003), mainly with regard to the possible overestimation of discount rates in economic studies, or in explaining various intertemporal anomalies. Remarkably, no one has empirically tested this idea in humans.

How could we potentially dissociate these two influences on choice and obtain a reliable quantitative measure of each? In original rodent work by the Bradsaw and Szabadi group (see Ho et al., 1999) this has been achieved by way of an integration of temporal discount functions with magnitude discount functions (or utility functions, in economic terms) which mathematically model the relationship between objective and subjective value for magnitude. For example, a common utility function in economic literature – the power law – has the formulation  $U = M^r$  where  $U$  is the utility or subjective value of a reward of magnitude  $M$ . Here  $r$  is a free parameter which determines the rate at which marginal utility diminishes. If  $r$  is less than 1 the utility function will be concave (Figure 7), i.e. exhibiting diminishing marginal utility. The lower the value of  $r$  here, the more concave the utility function and the faster the rate of diminishing marginal utility. If  $r$  is also a determinant of intertemporal choice, the lower the value of  $r$  the more impulsive the individual should be, as the less valuable the larger reward is in relation to the smaller and vice versa.

Ho et al. (1999) have developed a two parameter model and a method for estimation of each parameter individually (described in Chapter 2). This has been successfully used in animal studies and has proved to be an accurate description of rodent intertemporal choice behaviour. In some cases, both parameters have been

observed to change in response to a manipulation, occasionally in opposite directions, exerting opposing influences on impulsive choice, and possibly explaining previous discrepancies in the literature.

There would be numerous advantages to implementing such a model in human studies. First, it would potentially allow for a more accurate and less confounded measure of temporal discount rates, and a better overall description of choice behaviour, revealing fundamental truths about human valuation and decision-making systems. It would also allow us to remove a major confound in empirical experiments of intertemporal choice and determine whether changes in behaviour have as their underlying cause a change in the rate of temporal discounting or magnitude discounting. This would facilitate a better understanding of personality characteristics such as impulsivity.

## **Organization of work in this thesis**

In Chapter 2, human behaviour in intertemporal choice is examined in a hypothetical task, to determine whether complex discounting models which incorporate non-linear utility functions are better at describing subjects' choices than standard models. Specifically, it is hypothesized that that an effect of diminishing marginal utility should be observed to increase impulsive choice in an adjusting delay task – an hypothesis not previously assessed in human studies. This effect is demonstrated and the implications regarding  $K$  parameter estimates are discussed. I start by examining the model of Ho et al. (1999) and go on to develop an alternative model. The new functions, methodology and analyses required to answer these questions are described, and in addition, evidence is debated for the 'size effect'.

Chapter 3 builds on the findings in Chapter 2 and has two major themes. The first theme deals with creating a new and original methodology for both the testing of intertemporal choice tasks in humans, particularly for use in fMRI, as well as for parameter estimation techniques. This new technique avoids indifference point methodology and instead adopts a maximum likelihood approach. This is necessary since the methodology used in Chapter 1 is not suitable for addressing the other goals of this fMRI study. This new method is also devised to be able to compare different models of intertemporal choice which vary in complexity, and to easily estimate individual parameters. Behavioural data are used to show, again, that the integrated model provides a better description of human choice data – this time in a realistic reward task – where the effects of utility concavity are apparent. The second theme revolves around the imaging data gathered, which is analysed to show evidence for the neural implementation of the integrated model. Behavioural data are used to generate valuation regressors with which to analyse the imaging data. These show a network of neural regions correlating with unique sub-components of value based on time and utility (as dictated by the individual components of the model) as well as their integration in the striatum, providing an overall metric of discounted utility. This new description of the value systems relevant to intertemporal choice is discussed in relation to previous dual or single decision-making theories. Furthermore, for the first time, a neural account of the basis of diminishing marginal utility is given. Finally, behavioural and neural data are analysed to look at the effect of choice difficulty/ decision-conflict.

In Chapter 4 the effects of dopaminergic manipulation on intertemporal choice are discussed. Dopamine activity is manipulated using L-Dopa and haloperidol. Analyses of the manipulation on both parameters determining choice, as well as a theory neutral measure of impulsive choice, reveal that L-Dopa causes subject to become more temporally impulsive, a surprising finding in light of the existent

literature. In addition, brain imaging data acquired during task performance is used to a) corroborate the imaging findings discussed in Chapter 3, b) give a neural account of the behavioural effects of dopamine on intertemporal choice, in light of regions previously identified and c) explain inter-subject differences in behavioural effects of the drugs. A pilot study of choice in PD patients tested 'on' and 'off' dopamine drugs is also described.

Finally, Chapter 5, the discussion, provides an integrative summary of all the experimental work carried out and the relevance of the major findings to the existent literature. Suggestions are made for further developments in modelling intertemporal choice, and possible research avenues.

## Chapter 2.

# The effects of diminishing marginal utility for gains on intertemporal choice

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### Introduction

Humans and animals must make important intertemporal choices on a daily basis. To be able to make such choices an agent must discount the value of a reward or punishment in accordance with its delay, to calculate the present value of each option – a process termed temporal discounting. Normative economic theory posits that we should devalue rewards exponentially, as this entails constant percentage devaluation per unit time – engendering rational choice. However a wealth of empirical data has confirmed that humans and animals exhibit temporal discounting which is hyperbolic or quasi-hyperbolic in nature (e.g. Ainslie, 1992, 2001; Frederick et al., 2002; Green and Myerson., 2004; Ho et al., 1999 – see also introduction).

The most common formulation of the hyperbolic discount function was proposed by Mazur (1987), whereby the discounted value ( $V$ ) of a reinforcer of magnitude  $M$ , is related to its time delay ( $d$ ) as follows:

$$V = \frac{M}{1 + K \cdot d} \quad (\text{Eq. 1})$$

The free parameter  $K$  – known as the discount rate – quantifies an individual's tendency to discount future rewards such that a person with a high  $K$  devalues

rewards quickly as they become more distant. This model will be referred to as the simple hyperbolic model (SHM).

Ainslie (1975; 1992) and others (e.g. Evenden, 1999a; Herrnstein, 1981; Ho et al., 1999; Logue, 1988; Mazur, 1987) have applied the term *impulsive choice* to behaviours that favour the selection of small, short-term gains over larger delayed gains in intertemporal choice. As such, the  $K$  parameter is commonly assumed to represent or correspond to an individual's impulsivity in choice – a person with a high  $K$  value can be said to be impulsive and a low  $K$  person can be described as self-controlled.

Much work has been done over the last twenty years, on the behavioural economics, neurobiology and pharmacology of both impulsivity and temporal discounting (Chapter 1), whereby intertemporal choice procedures are used to assess degree of impulsivity in choice, commonly by inferring a value of  $K$  from subjects' choice behaviour. This is most often achieved by employing indifference point methodology using monetary rewards, for example as in the adjusting amount method (e.g. Richards et al., 1997a, 1999a – see Chapter 1). Here the choice is offered between a smaller-sooner amount of money ( $A$ ) and a larger-later option ( $B$ ).  $B$  has a fixed value but is delayed by different amounts across blocks, whereas  $A$  is always immediate but its magnitude varies within blocks until indifference, whereby it is assumed that in terms of the agent,  $V_A = V_B$ . By plotting a curve of the indifference points and inspecting the area underneath it or performing a curve fit using the hyperbolic discount function,  $K$  can be inferred. Using this metric, comparisons can be made across experimental groups, and conclusions drawn about the effects of the independent variable on the discount rate or impulsivity.

However, the fundamental assumption that temporal discounting is the only determinant of intertemporal choice outcome – or impulsivity – implies that most of this work is undermined by a major interpretational problem. This basis of this

problem stems from the fact that intertemporal choices involve choices between rewards of differing magnitude and discrimination of, or sensitivity to increasing magnitudes can be an individually varying factor. The idea that the relationship between the subjective and objective value of a reward is non-linear is a well recognized economic concept and can be represented by a utility function which converts magnitude (e.g. dollars) to utility (in utils). In fact, most individuals discount increasing reward magnitude – or in economic terminology, exhibit diminishing marginal utility. In other words, every unit (marginal) increase in a good brings us successively less and less utility. Thus, the increase in utility or subjective value when obtaining £1000 is significantly greater for someone with £5000 in the bank than someone with £50M. Alternatively, within an individual, the utility provided by a fixed amount of £10 is greater when added to an option worth £50 than to one worth £500. This can be represented by concavity of the utility function (where magnitude is on the  $x$  axis and utility on the  $y$ ). Since most individuals have non-linear or concave utility functions – hence its status as a law in economics – it is likely that intertemporal choice behaviour is also determined by this feature of preference. Specifically, the more concave the utility function of an individual, the greater the rate of diminishing marginal utility and the smaller the increase in subjective value of the larger reward relative to the sooner. Therefore, those with more concave utility functions should be more impulsive relative to those with more linear utility functions – irrespective of the rate of temporal discounting (see Chapter 1 for further elaboration of this problem).

If the rate of diminishing marginal utility is an additional determinant of impulsivity in choice it breaks down the traditional relationship between impulsivity and  $K$ . Furthermore, it implies that the effects of the independent variable on choice – for example, a lesion or pharmacological manipulation – could be explained by a change in utility concavity, as opposed to an effect on the rate

temporal discounting ( $K$ ). Finally, it raises the possibility that discount rates are generally overestimated due to failing to take into account the effects of utility concavity. This possibility has been noted by a number of economists (Andersen et al., 2008; Frederick et al., 2002; Loewenstein and Prelec, 1992; Read, 2003) but has never been empirically tested in humans.

Ho et al. (1999) have attempted to resolve this issue and develop a method to gauge the effects of temporal and magnitude discounting individually, so as to be able to dissociate the two influences on choice. In their multiplicative hyperbolic model (MHM) of choice, this is achieved by integrating the standard temporal discount function with a function that takes into account an increasing hyperbolic discounting of reinforcer magnitude. Essentially, this is achieved by replacing the magnitude numerator in the SHM with a function relating the *instantaneous* value ( $V_i$ ) – or utility – with the physical magnitude ( $q$ ) of a reward accordingly:

$$V_i = \frac{1}{1 + Q/q} \quad (\text{Eq. 2})$$

Here,  $Q$  is the discounting parameter for the reciprocal of reinforcer magnitude, which determines the concavity of the utility function. The greater  $Q$  is, the more linear the utility function and the greater the difference in utility between rewards of differing magnitude. Note that concepts of utility or utility functions do not appear in the language of Ho et al. since their model is rooted in animal literature. In practice, utility concavity/rate of diminishing marginal utility, and magnitude discounting/sensitivity to magnitude of reinforcement (terms used by Ho et al.) amount to the same idea. Strictly speaking, the numerator in Eq. 2 should be  $V_{\max}$  – the theoretical maximum instantaneous value a reward can have for the particular organism, or the value of  $V$  at the asymptote of the function – thereby expressing instantaneous utility as a proportion of its theoretical maximum. Ho et al. (1999)

replace this with 1 since  $V_{\max}$  cancels out of the relevant equations developed. Integrating Equations 1 and 2, by replacing magnitude with the utility function ( $M$  with  $V_i$ ) yields the integrated model for discounted utility:

$$V = \frac{1}{1 + K \cdot d} \cdot \frac{1}{1 + Q/q} \quad (\text{Eq. 3})$$

Since under this framework the valuation of a delayed reward is a function of both discounting processes, it is now possible to appreciate that a change in intertemporal choice outcome can occur as a result of a change in  $K$  or a change in  $Q$ . To solve these parameters, there are a number of methods one could implement. A convenient one is an adjusting delay procedure (Mazur, 1987). In this procedure the size of each reward ( $A$  and  $B$ ) is kept constant throughout the experiment and the delay to the larger reward ( $d_B$ ) is varied until the subject is indifferent (chooses equally) between the two options. On the next block, the delay to the smaller reward ( $d_A$ ) is increased, and the delay to the larger reward is again varied until indifference, and so on. When the indifference points from each block are plotted on a graph of delay to the smaller reward ( $d_A$ ) on the  $x$  axis vs. delay to the larger reward ( $d_B$ ) on the  $y$  axis, the theory predicts a linear relationship (see Chapter 1, Figure 7). This is because at indifference  $V_A = V_B$ . Substituting in the MHM (Eq. 3) and solving for  $d_B$ , Ho et al. (1997, 1999) derive the following linear relationship:

$$d_B = d_A \cdot \left[ \frac{1 + Q/q_A}{1 + Q/q_B} \right] + \left[ \frac{1/(1 + Q/q_B) - 1/(1 + Q/q_A)}{1/(1 + Q/q_A)} \right] \cdot \frac{1}{K} \quad (\text{Eq. 4})$$

$$y = x \cdot \text{gradient} + \text{intercept}$$

As the gradient of the line is a function of the ratio of the two reward utilities, it can be inferred that a change in the gradient of the line from one condition to another (e.g. manipulation) is related to a change in  $Q$ . Conversely, if only the

intercept shifts but not the gradient – that must be caused by a change in  $K$ .  $K$  can also be deduced from the relationship  $K = [\textit{gradient} - 1] / \textit{intercept}$  (see Ho et al., 1997, 1999).

This approach has started to yield very interesting findings in animal studies. Kheramin et al. (2002), for example, resolved a discrepancy in the effects of OFC lesions, where Mobini et al. (2002) observed an increase in impulsive choice and Winstanley et al. (2004b) observed a decrease in impulsive choice. Kheramin et al. found that OFC lesioned rats appeared less impulsive (see Chapter 1). That is on first analysis, their mean indifference delay to the larger reward was longer, indicating more self-control and – according to standard assumptions – shallower discounting. When Kheramin et al. subsequently plotted the indifference points on a  $d_A$  vs.  $d_B$  graph and performed a linear regression, they found that the intercept of the line in the lesioned rats was significantly lower than that of the controls, indicating that they actually had a higher  $K$  value (or were more temporally impulsive). Crucially, they also discovered that the rats had a much larger  $Q$  value – indicating that they were also more sensitive than the sham-lesioned rats to the difference in the size of the two rewards – with the net effect that their higher  $K$  was more than compensated for, enabling them to wait longer for the delayed reward (which post lesion had a greater utility relative to the sooner), and appear more self-controlled. Because Mobini et al. (2002) only used a 1 vs. 2 pellet choice their rats appeared more impulsive, as in this case the enhancing of the difference in utilities of two rewards was not enough to overcome the increased temporal discount rate. In Winstanley et al. (2004b) however, a 1 vs. 4 pellet choice was employed and in this case it is possible that the increase in subjective value of the larger relative to the smaller reward induced by the lesion was significant enough to make the rats appear more self controlled despite the increase in temporal discount rate.

This analysis shows that it does not make sense to talk of OFC lesions as either increasing or decreasing impulsiveness since they exert opposing effects on the two parameters determining choice outcome. One can say the subjects were more temporally impulsive but less impulsive from the perspective of magnitude discounting. Moreover, the effects of this lesion on choice will depend on the particular magnitude and delay ratios used.

However, this approach has yet to be used in human studies of intertemporal choice where longer timeframes and hypothetical choices are typically employed. Furthermore, this type of adjusting delay task has also not typically been used in human studies. The primary purpose of this study was therefore to test whether a two parameter model can account for human data in an adjusting delay task and demonstrate that diminishing marginal utility has an effect on choice. It was predicted according to this hypothesis that the indifference points should be modelled well by a linear fit. It was calculated (see Appendix I for derivation) that according to the standard 1 parameter model (Eq. 1) the relationship between  $d_A$  and  $d_B$  should also be linear, as follows:

$$d_B = d_A \cdot \left(\frac{M_B}{M_A}\right) + \frac{1}{K} \cdot \left(\frac{M_B - M_A}{M_A}\right) \quad (\text{Eq. 5})$$

According to this model, the gradient of the line should simply equal the ratio of the reward magnitudes ( $M_B / M_A$ ) whereas according to the MHM the gradient should equal the ratio of utilities of the two rewards. The latter ratio was predicted to be smaller than the magnitude ratio because of diminishing marginal utility - £100 does not have twice the utility of £50. Interestingly, the normative exponential model of choice predicts that the slope of the line for adjusting delay indifference should equal 1 (see Green et al., 1994; Mazur, 1987; Rodriguez and Logue, 1988).

A further prediction was that estimated  $K$  values should be lower under the MHM than the SHM. This is because diminishing marginal utility has the effect of

making (in particular) the larger-later option less attractive, relative to its value under a linear utility function. Although this has been predicted by economists (see above) MHM proponents have not used the model to demonstrate such an effect.

A potentially fatal flaw in the MHM relates to studies by Green and Myerson (e.g. 2004, see Chapter 1) and others that show a ‘magnitude’ effect in humans, such that  $K$  varies with the size of the reward (large magnitude rewards are discounted less than smaller ones). If  $K$  varies with amount, this creates a problem for the adjusting delay procedure since both  $A$  and  $B$  are delayed, and since they are of different sizes, it would be necessary to factor in a  $K_A$  and a  $K_B$  to the model. This would make the analysis much more complex and unreliable since three parameters would need to be deduced from the line according to the equation (see Appendix I for derivation):

$$d_B = \frac{1}{K_B} \cdot \left[ d_A \cdot K_A \cdot \left( \frac{1+Q/q_B}{1+Q/q_A} \right) \right] + \frac{1}{K_B} \cdot \left[ \frac{1/(1+Q/q_B) - 1/(1+Q/q_A)}{1/(1+Q/q_A)} \right] \quad (\text{Eq. 6})$$

Ho et al. (1999) on the other hand, argue that  $K$  is a stable property of individuals and that the size effect is an artefact of one parameter models that do not take marginal utility into account. Instead, the ability of magnitude to alter choice behaviour is thought by them to arise from modulation of size by  $Q$ . Loewenstein and Prelec (1992) also note that the seeming size effect could be predicted by a non-linear utility function. This may explain why the size effect is reported to disappear at very large reward amounts (Green & Myerson, 2004) – perhaps representing the asymptote of the utility function. Another defence for using a single  $K$  variable comes from the finding that in animal experiments there is no observed magnitude effect (Grace, 1999; Green et al., 2004; Richards et al., 1997a). A possible explanation for this may be that the size effect is a product of human discounting experiments

which involve *hypothetical* choices that are more susceptible to peoples' opinions or attitudes, unlike real life choices (Y. Ho, CM. Bradshaw – personal correspondence). Nevertheless, it has been argued that discounting in humans is no different when comparing real and hypothetical rewards, with both showing a magnitude effect (Johnson and Bickel, 2002; Lagorio & Madden, 2005 – see Chapter 1).

The second purpose of this study was therefore to test whether  $K$  is a stable feature of an individual – and the magnitude effect is accounted for by the effects of non-linear utility – or whether it is amount dependent. This has large ramifications for the theory and practise of discounting research. It was hypothesised that if subjects performed a second session, where the amounts of  $A$  and  $B$  were doubled (i.e. keeping their magnitude ratio the same), the indifference line from the second trial would be expected to have a shallower gradient than the first. Again, this is because the slope is determined by the ratio of reward *utilities* (Eq. 4) which would decrease as magnitude increases – according to the principle of diminishing marginal utility – since the values would come from the more concave part of the curve. The intercept should be correspondingly reduced (Eq. 4) but estimated  $K$  should stay the same if it is stable (according to the MHM function). Furthermore, if the MHM is correct,  $Q$  should remain constant in both trials as it is the scaling parameter for all values and is by definition not amount dependent. According to the standard model (Eq. 5), the slopes should be the same in trial one and two as it is determined by magnitude ratios. According to the exponential model the slope should always equal 1.

Two standard adjusting amount trials were also added for comparison purposes. Here, the values for  $B$  were also doubled across trials. In theory,  $Q$  and  $K$  (if stable) should remain constant irrespective of the task used in measuring discounting and the MHM should provide a good fit to the data. It was also

important to determine whether different methodologies can give rise to different choice outcomes.

## **Methods**

### *Procedure and task design*

Twenty four subjects (10M:14F – mean age 27) were recruited to take part in the study and were screened for a prior history of smoking, drug use, and any mental illness. The participants were paid £5 for their time and were tested individually, in a quiet room. The study was approved by the UCL ethics committee.

The task lasted roughly 35 minutes and was performed on a computer. A pulse occimeter and two electrodes for measuring galvanic skin response were placed on the participants' left hand and they were then read the instructions. The autonomic measures were taken to investigate whether the somatic marker hypothesis (Damasio, 2004) could be applied to intertemporal choice although these data were not analyzed. In addition, subjects were told that by concentrating on the task and making their decisions as realistic as possible, they could win a bonus of between £1 and £3 extra – and that we would be able to assess this based on their skin response and heart rate. All subjects were awarded £2 on this measure (the autonomic data were not used).

The test was run on Matlab (version 7) and consisted of a number of choices between a smaller, sooner reward (*A*) which always appeared on the left side of the screen, and a larger later reward (*B*) which always appeared on the right.

There were two types of trial used – adjusting delay and adjusting amount. In the adjusting delay trials, the choice was always between £300 and £450. There were 7 blocks presented, corresponding to the delay to *A* ( $d_A$ ) used in each block

(today, 1 month, 3 months, 6 months, 9 months, 1 year, 1 year 3 months). Within each block, the delay to  $B$  ( $d_B$ ) was varied until the indifference point was found. This was achieved by using an upper and a lower limit, corresponding to the maximum and minimum delay  $B$  could be set at. These limits started with a maximum  $d_B$  of 4 years and a minimum  $d_B$  set at  $d_A$  for that block. On each trial the delay to  $B$  was randomly selected from between these limits. If the subject chose the larger reward, the lower limit for following trials would be increased to the delay of option  $B$  (on the current trial) whereas if the subject chose  $A$ , the upper limit would be set according to the delay of option  $A$ . These limits got closer as the block progressed, until they were 1 week apart, when the block ended. The indifference point was defined as the mid-point in days of the two limits at this stage. Each block took roughly 8 choices to complete and yielded 1 indifference point (delay to  $B$ ), yielding a total of 7 indifference points from the adjusting delay trials. This method was developed to reduce the time taken to reach indifference and also to eradicate any potential order effects of increasing/decreasing delays. When more traditional procedures are used a predetermined set of choices are presented (i.e. starting  $d_B$  at the same delay as  $d_A$  and increasing it until the subject switches choice). Normally an ascending and a descending block are used to counter order effects (e.g. Rachlin et al, 1991).

The participants were required to complete 2 adjusting delay trials. In the second trial, the amounts of  $A$  and  $B$  were doubled to £600 and £900 respectively and the delays to  $A$  for each block were kept the same.

In addition to these choices, 20 'catch trials' were included and randomly distributed to test whether the subject was concentrating on the task and considering the choices properly. In these choices, the delay to  $B$  was sooner than the delay to  $A$  – engendering a choice between a smaller-later and a larger-sooner reward. The 'correct' choice would be  $B$  in this scenario.

In the adjusting amount trials,  $A$  was always immediate and  $B$  was set at £500. There were 6 blocks, corresponding to the delays to  $B$  in each (1 month, 3 months, 6 months, 9 months, 1 year, 1 year 6 months). Within each block, the magnitude of  $A$  was varied until indifference – using the limiting procedure. The block finished when the limits were within £20 apart and the indifference point (magnitude of  $A$ ) was defined as the midpoint value between the limits. The adjusting amount trials yielded 6 indifference points. Again, the subject was required to do two adjusting amount trials. In the second, the value of  $B$  was increased to £1000.

The participants were required to use their right hand to indicate their choices (left arrow for  $A$ , right arrow for  $B$ ) and the task was self paced. The four trials were mixed in order and counterbalanced across subjects – half the participants did the trials in the order, adjusting amount 1, adjusting delay 2, adjusting amount 2, adjusting delay 1 and the other half did the trials in reverse order. All the values and delays were in the normal range of delays and values used in human discounting experiments.

## Results

Analyses and statistics were carried out using Matlab version 7 and SPSS version 13. Subjects who answered 5 or more catch trials incorrectly (choosing the smaller-later option) were excluded from the analyses. Four subjects fell into this category, leaving data sets from 18 subjects for the analyses.

### *Adjusting delay trials*

For the adjusting delay trials, indifference points were plotted on a graph of  $d_A$  on the  $x$  axis and  $d_B$  on the  $y$  axis for each subject. This was done separately for both

sessions of the adjusting delay task (£300/£450 and £600/£900). A linear least squares regression method was used to fit a line to the indifference points using Matlab curve fitting software. In both trial 1 (£300 vs. £450) and trial 2 (£600 vs. £900) a linear model fit the data with a high degree of accuracy – mean adjusted  $R^2$  values were 0.96 and 0.94 respectively (see Figures 1 and 2).

The linear regression yielded measures of the gradient and intercept of the line for each subject in trials 1 and 2.  $K$  values were estimated from the formula  $K = [\text{gradient} - 1] / \text{intercept}$  (Eq. 7) (Ho et al., 1999). Ho et al. (1999) however do not derive a function for estimating the  $Q$  parameter and instead infer a change in  $Q$  from the slope when comparing two conditions. As a measure of  $Q$  was of interest here, a formula for estimating  $Q$  was derived (see Appendix I) whereby:

$$Q = \frac{q_A \cdot (\text{gradient} - 1)}{1 - (\text{gradient} \cdot q_A / q_B)} \quad (\text{Eq. 8})$$

Note,  $Q$  and  $K$  could also have been directly estimated by applying Equation 4 to fit the data using the curve fitting software.

To assess whether the slope was significantly lower than 1.5 – the ratio of amounts predicted by the SHM (Eq. 5) – and significantly greater than 1 – the slope predicted by exponential discounting (e.g. Green et al., 1994) – gradients for each trial were compared to 1 and 1.5 using one sample t-tests (two-tailed). In accordance with hyperbolic, but not exponential discounting, a unit increase in  $d_A$  resulted in a significantly greater  $d_B$  at indifference. In other words the slope was significantly greater than 1, both in trial 1 ( $p < .001$ ) and trial 2 ( $p < .001$ ) (see Table 1, Figures 1 and 2). Furthermore, the gradient of the line was significantly lower than 1.5 in trial 2 ( $p < .001$ ) and trended towards being significantly lower than 1.5 in trial 1 ( $p = .063$ ) indicating that there was a significant effect of diminishing

marginal utility on subjects' choices (Figures 1 and 2, Table 1). Mean gradients were 1.4 and 1.26 in trials 1 and 2 respectively.

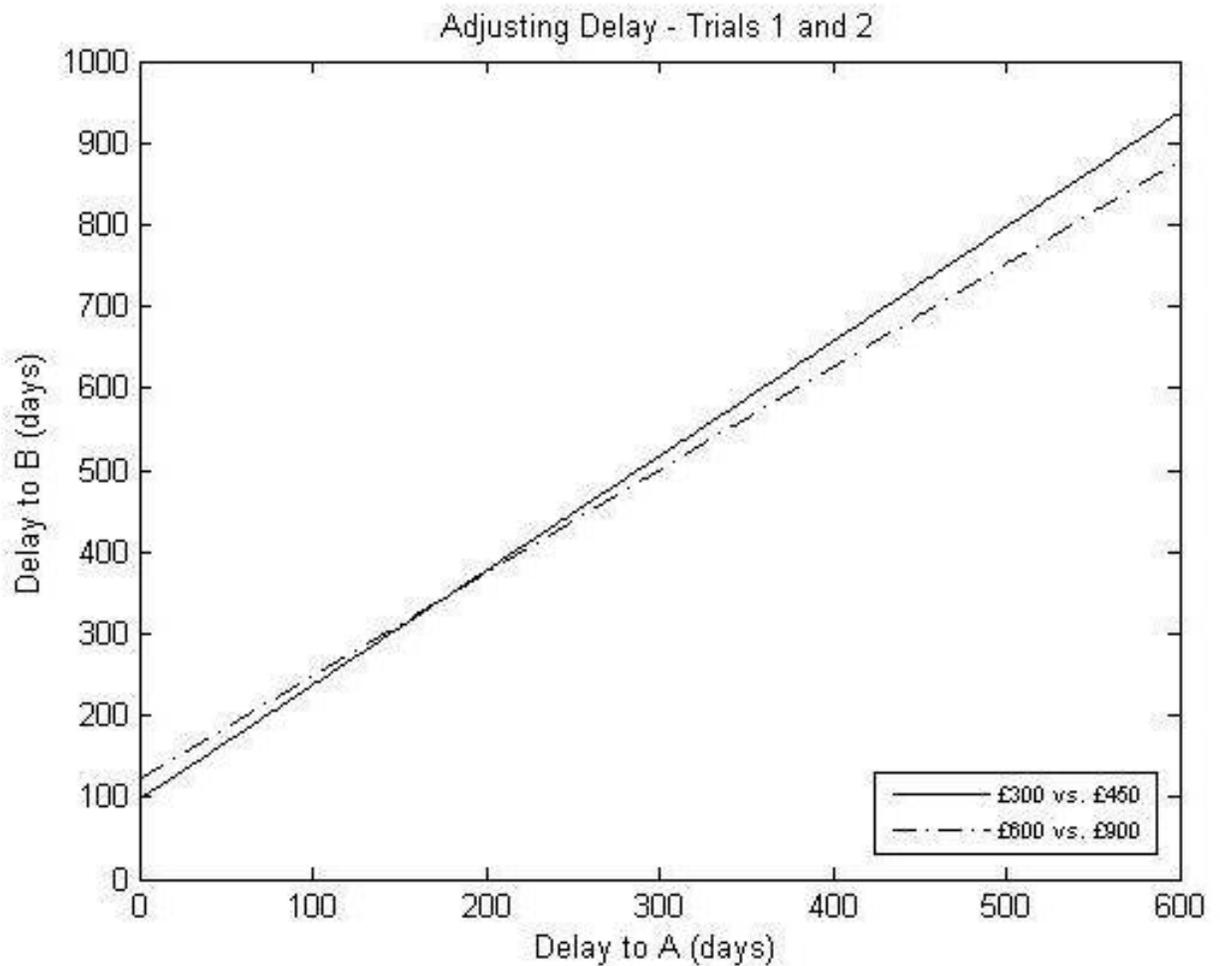
A repeated measures analysis of variance (ANOVA) was performed to compare the gradient and intercept estimates for each subject across trials of the adjusting amount task. This revealed that the gradient of the line was significantly lower in trial 2 than in trial 1 ( $p < .05$ ) and the intercept was significantly greater in trial 2 than trial 1 ( $p < .025$ ) (Table 1). The reduced gradient provided further evidence of the effect of concavity of the utility function on choice, reducing indifference delay to  $B$  as the amounts were doubled (Figures 1 and 2, Table 1).

As parameter estimates for  $K$  were positively skewed – a common finding in previous studies (e.g. Green et al., 2005) – a non-parametric Wilcoxon signed ranks test (two-tailed) was used to compare  $K$  estimates in trials 1 and 2. This revealed that  $K$  was significantly greater in trial 1 than in trial 2 ( $p = .025$ ). This finding is in accordance with greater temporal discounting for smaller rewards (the magnitude effect) and is also indicated by the greater intercept observed in trial 2 (Table 1, Figures 1 and 2).

Unfortunately, the  $Q$  estimates were not suitable for analysis and were not of realistic values in many individuals. This was probably due to inadequacies of the  $Q$  function. Further analysis revealed that if the gradient slightly exceeded 1.5 – indicating convexity of the utility function, or simply due to noise in the data giving rise to such a best fit line – the  $Q$  value became extremely negative very quickly. This had a huge effect on the data (Table 1). Similarly, an estimated gradient of less than 1 led to unrealistic  $Q$  values.

	Trial 1 (£300 vs. £450)	Trial 2 (£600 vs. £900)
<b>Intercept</b>	96.9	121.8
<b>Gradient</b>	1.40	1.26
<b>K</b>	0.013	0.003
<b>Q</b>	-2688	5077

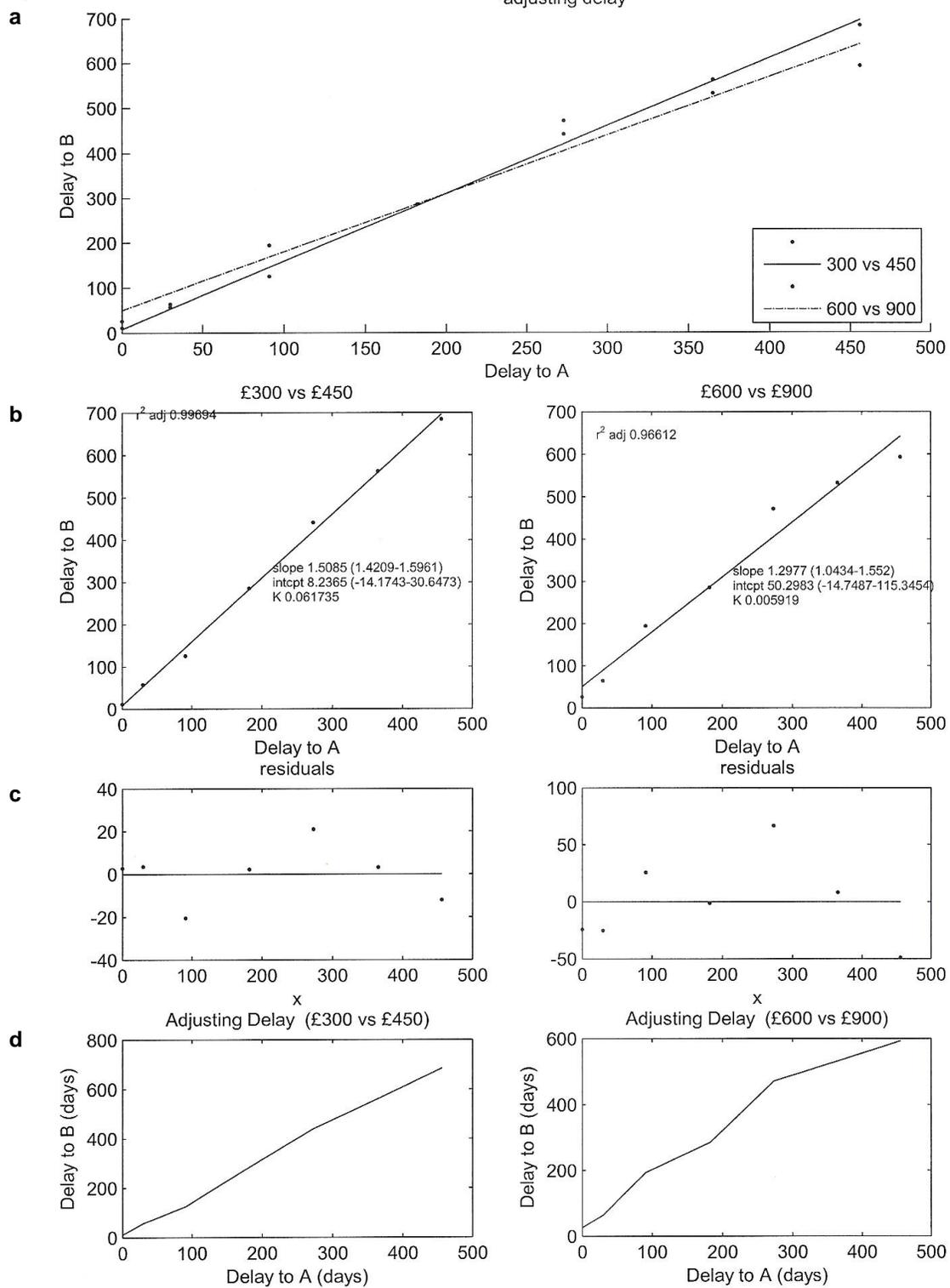
**Table 1. Summary of adjusting delay results (MHM).** Mean gradient and intercept values as well as parameter estimates for trials 1 and 2 of the adjusting delay task. Based on a linear least squares regression of the indifference points for each subject.



**Figure 1. Mean indifference delay to B ( $d_B$ ) for trials 1 and 2.** Gradients were between 1.5 and 1 and were shallower in the larger amounts trial (dashed line) relative to the smaller amounts.

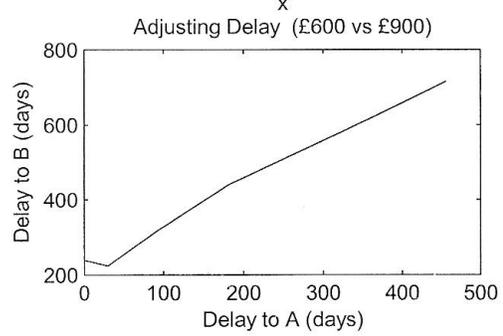
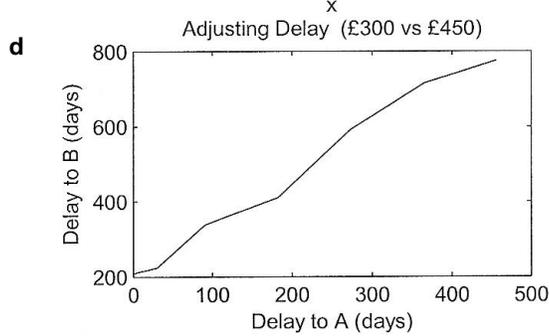
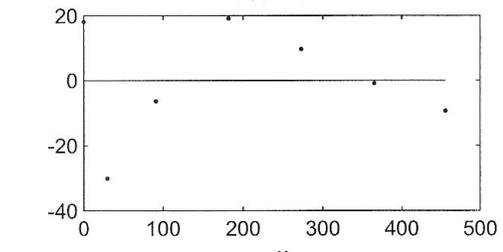
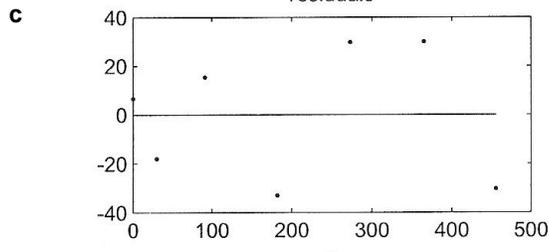
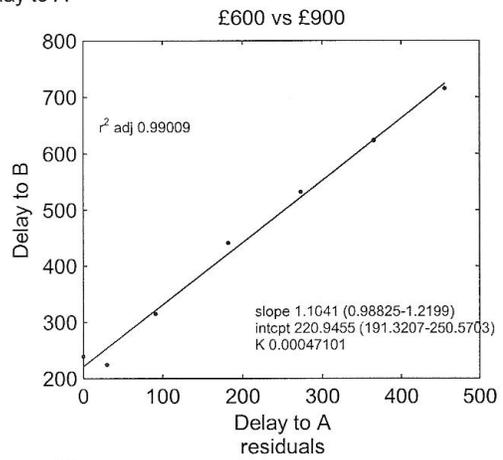
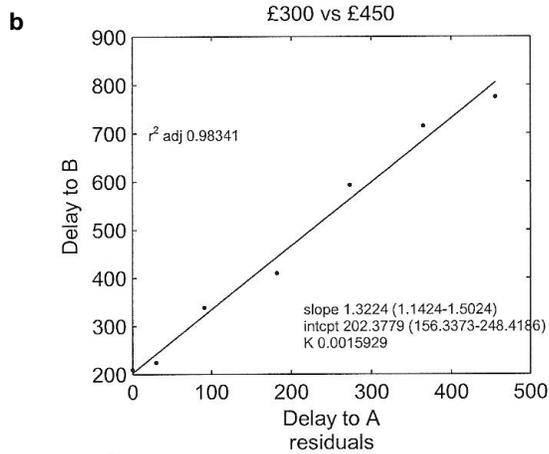
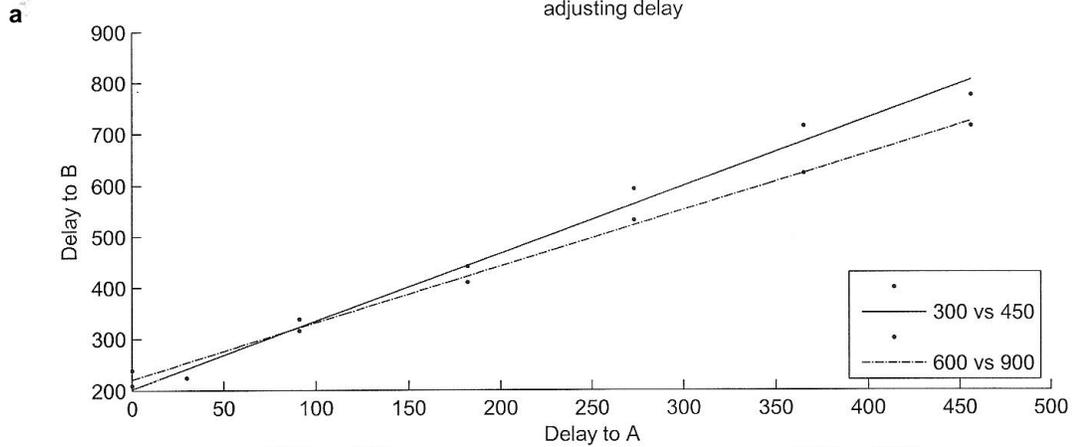
## Subject 4

adjusting delay



Subject 7

adjusting delay



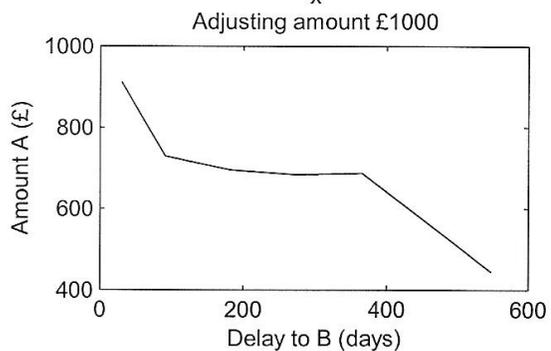
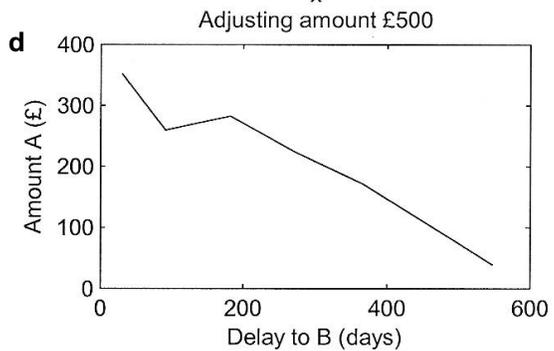
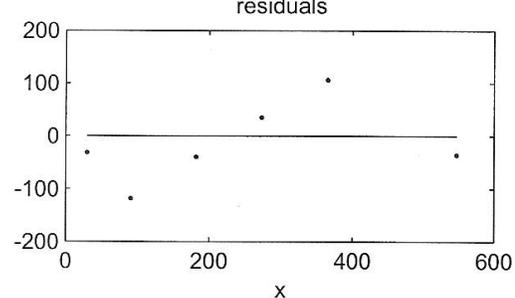
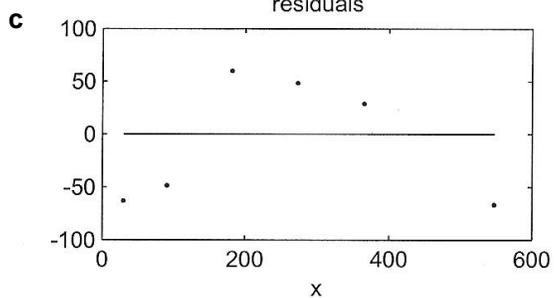
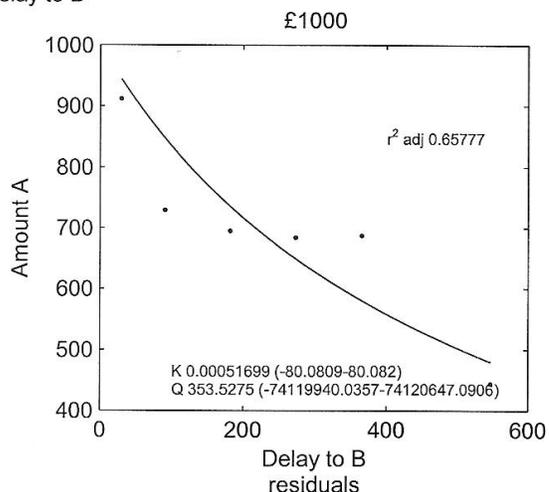
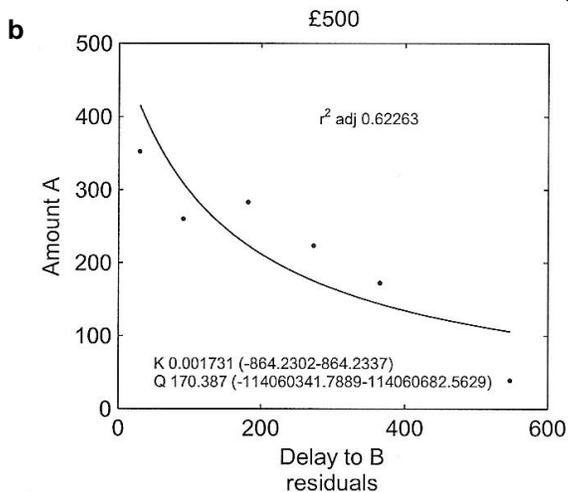
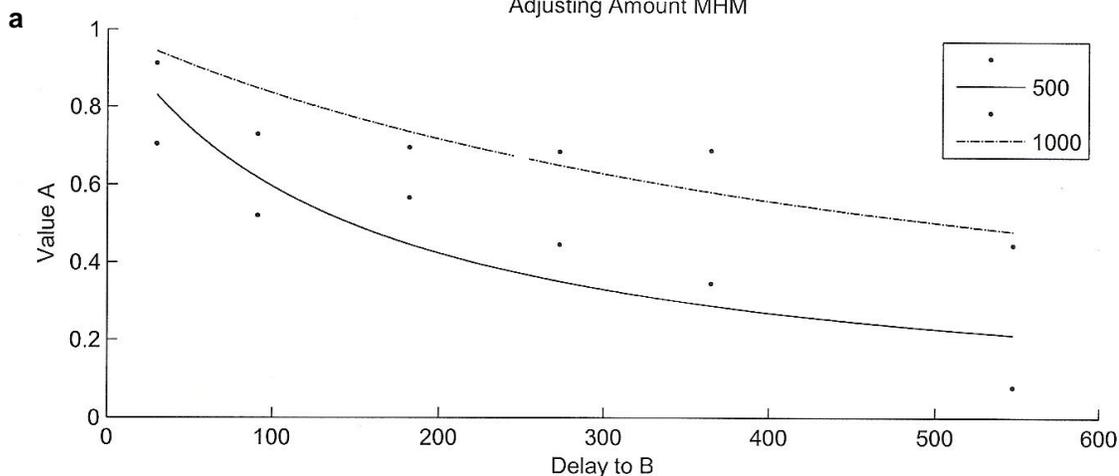
**Figure 2. Single subject adjusting delay data.** Subjects 4 (top) and 7. **a.** Comparison of best fit line in trials one and two. Gradients tended to be shallower in trial 2 (dashed line), the larger amounts trial. **b.** Best fit lines for each trial individually, showing adjusted  $R^2$ , gradient, intercept and estimate of the discount rate parameter ( $K$ ). Note, subject 4 had a gradient above 1.5 in trial one, leading to poor estimation of  $Q$ . **c.** Residuals. **d.** Raw indifference point data.

### *Adjusting amount trials*

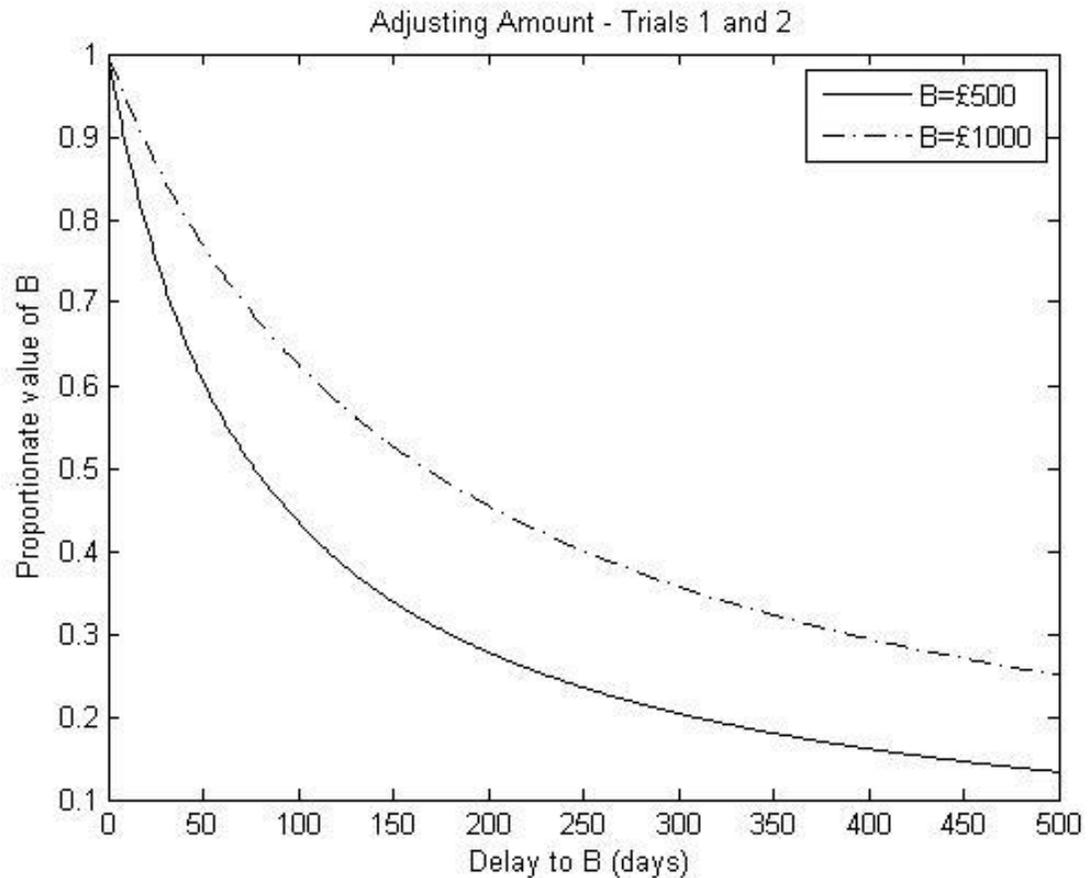
Indifference points from the two adjusting amount trials ( $B = £500$  and  $B = £1000$ ) were plotted on graphs of delay to  $B$  ( $x$ ) vs. magnitude of  $A$  ( $y$ ). These points were then fitted using Matlab curve fitting software according to the standard hyperbolic and MHM models (Equations 1 and 3 respectively) to give estimates of  $K$  and adjusted  $R^2$  for each model, as well as the  $Q$  parameter for the MHM. Note, these models were adjusted to take into account utilities versus magnitudes of  $A$ . Unfortunately, these data were highly noisy and provided a much poorer fit (as measured by  $R^2$  values) than previous experiments report – with the standard model on the adjusting amount procedure usually above 0.8 (e.g. Green and Myerson, 2004). Inspection of individual data sets (Figure 3) revealed that responses to many of the choices were inconsistent with those of other choices in different blocks of the trial – for example, indifference points (magnitude of  $A$ ) to  $B$  at 3 months were sometimes observed to be smaller than the 6 month indifference points. This would indicate that the subject valued the delayed option more when delayed by 6 months than when delayed by 3 months. Given the nature of the data, it was inappropriate to perform any statistical analyses using the parameter estimates; however the mean parameter estimates and  $R^2$  values are presented in Table 2. Figure 4 displays the mean discount functions for trial one and trial two, based on the mean  $K$  values obtained from the standard hyperbolic fit.

Subject 4

Adjusting Amount MHM



**Figure 3. Single subject data (subject 4) on adjusting delay trials.** Fit with the MHM (Eq. 3). **a, b.** Data from both trials were highly noisy and did not provide a good fit to the models, as seen from the adjusted  $R^2$  values.  $Q$  values were also highly inconsistent, as on the adjusting delay trials. **c.** Residuals. **d.** Raw indifference point data show subjects were very inconsistent across blocks of the trials.



**Figure 4. Mean discount functions for discounted value of  $B$  in adjusting amount trials.** Fit using the SHM (Eq. 1) and plotted using mean estimates of  $K$  derived from that model.

	Trial 1 ( $B = \text{£}500$ )	Trial 2 ( $B = \text{£}1000$ )
<b>SHM</b>		
$R^2$ adjusted	0.13	0.25
$K$	0.013	0.006
<b>MHM</b>		
$R^2$ adjusted	-0.09	0.10
$K$	0.002	0.0008
$Q$	203	259

**Table 2. Summary of adjusting amount results.** Mean  $R^2$  and parameter estimates for the SHM and MHM models when fit to the indifference points.

## Interim discussion

The data from the adjusting delay trials were extremely accurate in that they fit the linear model with most of the variance accounted for and, *prima facie*, corroborated the veracity of the two-parameter model on the surface. That is, if the parameters are *inferred* from the line via the gradient and intercept and then these (gradient and intercept) values are compared with those of another condition, the model works well – indeed this is what proponents of the MHM usually do, without actually estimating  $Q$ . However, in this case that method was not sufficient as although it was predicted that the slope should decrease in the second trial – thereby confirming the predicted effect of diminishing marginal utility – estimating the parameter values was necessary to be able to conclude that  $Q$  stayed the same in both trials i.e. that the change in slope was only as predicted by the model, not more or less. When the parameters were actually calculated the model broke down. This was likely due to inadequacy of the  $Q$  function, especially when the best fitting gradient was greater than the ratio of  $B/A$ , where highly negative values were computed for  $Q$ , or when the gradient was less than 1. The former

situation could arise in a subject who had a convex utility function, exhibiting increasing marginal utility (at least over the range of values used in the experiment). This scenario is not permissible under the assumptions of the function used by Ho et al. (1999), based on the Herrnstein (1970) response strength equation (Eq. 2), where instantaneous value is calculated as a proportion of  $V_{\max}$  – an individual's maximum possible value assignment. This is because an individual with a convex utility function would in theory not possess such a maximum value. Such a utility function does not asymptote on the  $y$  axis, instead it increases to infinity.

As well as ensuring that the parameter measuring utility concavity or convexity remained the same across trials – an important assumption for this experiment and a test of the veracity of the integrated model – being able to estimate such a parameter is desirable in research which aims to quantitatively study the basis of the non-linearity of the utility function itself, and factors which may affect it. For example, if a researcher wished to correlate the values of a non-linearity parameter, or a measure of utils based on such a parameter, with BOLD responses in fMRI or with other variables, a reliable estimate of the parameter would be required.

For these reasons, the data were reanalysed using a newly derived model of choice. This model was based on the same principle Ho et al. (1999) and Loewenstein (1992) describe with regard to the possible effect of the non-linearity of the utility function on choice. However, rather than basing the utility function on animal reinforcement literature, a common utility function described in the behavioural economics literature was utilised. This negative exponential formulation was derived from human choices under risk (Holt and Laury, 2002) where according to expected utility theory (von Neumann and Morgenstern, 1947; Kahneman and Tversky, 1979) the non-linearity of the utility function engenders

risk aversion/seeking. In principle, one could adopt any utility function which can tolerate convexity, however this function is thought to provide the best model for risk preferences (Holt and Laury, 2002) and has one free parameter – any more would combine to form a three-parameter discount function which would be overly complex and difficult to determine parameter values for. The chosen function relates the utility ( $U$ ) of a reward to its physical magnitude ( $M$ ) accordingly:

$$U = \frac{1 - e^{(-r \cdot M)}}{r} \quad (\text{Eq. 9})$$

Here,  $r$  is an individual parameter which determines the concavity or convexity of the utility function. The greater the value of  $r$  the more concave the utility function and in theory the more impulsive the individual should be in choice. Negative values of  $r$  imply convexity of the utility function.

Substituting  $U$  for magnitude ( $M$ ), the numerator of the SHM (Eq. 1), the function for the *discounted utility* ( $V$  from here on) can be represented accordingly:

$$V = \frac{1}{1 + K \cdot d} \cdot \frac{1 - e^{(-r \cdot M)}}{r} \quad (\text{Eq. 10})$$

Again, assuming equality of discounted utility at indifference predicts a linear relationship in the adjusting delay paradigm (see Appendix I for derivation) whereby:

$$d_B = d_A \cdot \left[ \frac{1 - e^{(-r \cdot M_B)}}{1 - e^{(-r \cdot M_A)}} \right] + \frac{1}{K} \cdot \left[ \frac{e^{(-r \cdot M_A)} - e^{(-r \cdot M_B)}}{1 - e^{(-r \cdot M_A)}} \right] \quad (11)$$

$$y = x \cdot \textit{gradient} + \textit{intercept}$$

As before, the gradient of the line is a function of the utility ratios and the intercept is determined by both  $K$  and  $r$ .

Another advantage with being able to estimate  $r$  is that it could be used to show that the combined model is superior to the SHM, if on average, subjects'  $r$  is greater than zero, as predicted by diminishing marginal utility. However, Ho et al. (1999) do not demonstrate that this is the case (since concavity is never estimated).

## Results

### *Adjusting delay trials*

A linear regression was performed on the indifference points in the context of the new valuation model (Eq. 11) using Matlab curve fitting software. This yielded parameter estimates of  $K$  and  $r$  for each subject in each trial, as well as a goodness of fit measure. As before  $R^2$  adjusted values were 0.96 for trial 1 and 0.94 for trial 2.

Parameter estimates for  $K$  and  $r$  were positively skewed so a Wilcoxon signed ranks test was used to compare values across the two trials. While there was no significant difference in  $r$  values estimated from the (£300 vs. £450) and (£600 vs. £900) trials there was a significant difference in the  $K$  parameter estimates ( $p < .0025$ ), where  $K$  was observed to be smaller in trial 2 (see Table 3), as found previously. Stability of  $r$  value estimates across trials was consistent with the hypothesis that  $r$  would not be affected by trial type. In addition, one-sample sign tests were used to determine whether  $K$  and  $r$  estimates were significantly greater than zero over all trials. These analyses revealed that  $K$  was significantly greater than zero ( $p < .001$ ), indicating an effect of temporal discounting and that  $r$  was significantly greater than zero ( $p < .025$ ), indicating that subjects exhibited diminishing marginal utility, as represented by concavity of the utility function (Table 3 and Figure 5).

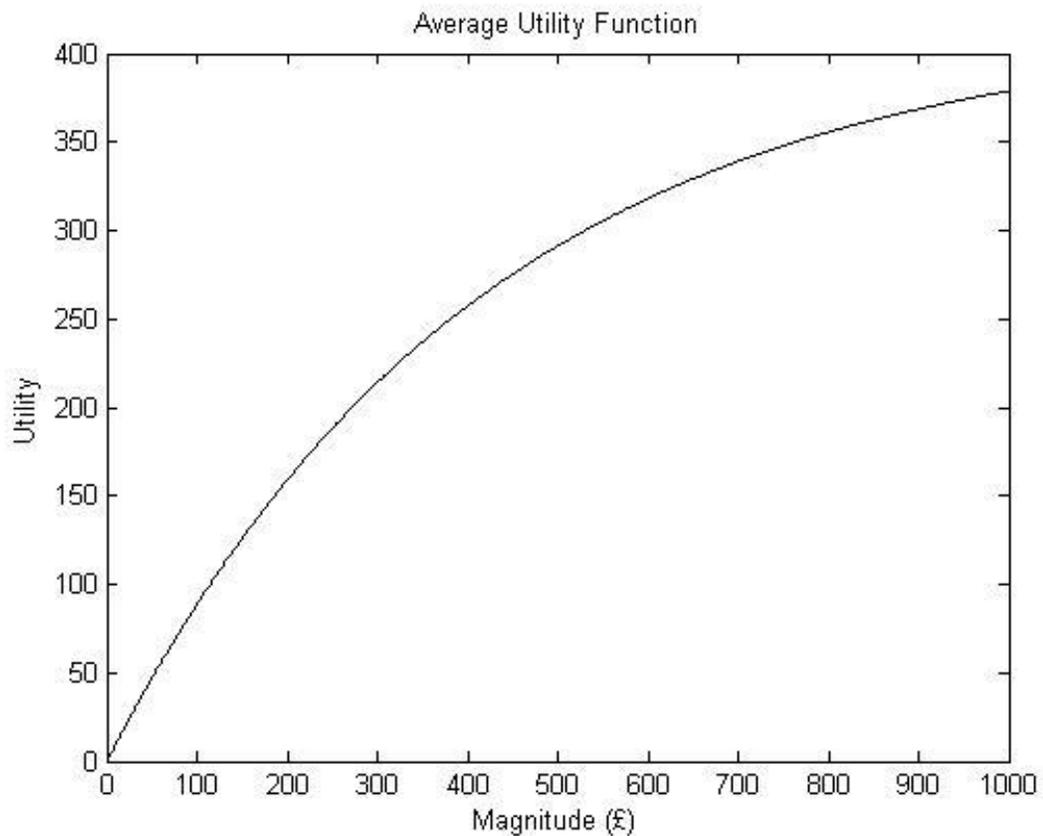
Using the average  $r$  parameter estimate from all trials, in combination with the utility function (Eq. 9), allowed for graphical representation of the average utility function of the subjects (Figure 5) – an advantage over the MHM, which depended on being able to reliably estimate the concavity of the function.

One notable finding was that  $K$  values were much closer in value (across trials 1 and 2) in this analysis than in the preceding analysis, suggesting that some of the magnitude effect could be accounted for by the new model (see Tables 1 and 3). Moreover, one of the subjects had an unusually large  $K$  value in trial 1 which, when removed, caused the average values to narrow and reduce the significance to trend levels ( $p = .059$ ).

Finally, to test the hypothesis that  $K$  is over-estimated in the SHM,  $K$  parameter values were estimated for the SHM by fitting Equation 5 to the data (using the curve fitting software). In theory, this could also be calculated according to the function  $K = [M_B / M_A - 1] / \text{intercept}$ . This formula can be readily derived from Equation 5. These  $K$  parameters were compared to those estimated using the discounted utility, two parameter model using a Wilcoxon signed ranks test.  $K$  values derived from the SHM were significantly greater than those derived from the new discounted utility model for both trials 1 and 2 ( $p < .05$ ) (see Table 3).

	Trial 1 (£300 vs. £450)	Trial 2 (£600 vs. £900)
<b>MHM</b>		
$K$	0.0073	0.0027
$r$	0.0024	0.0024
<b>SHM</b>		
$K$	0.011	0.051

**Table 3. Mean parameter estimates for the adjusting delay trials.** Parameters were estimated using curve fitting in the context of the SHM (Eq. 5) and the new discounted utility model (Eq. 11).



**Figure 5. Mean (instantaneous) utility function.** Plotted with the new utility function (Eq. 9) using the mean concavity ( $r$ ) estimates calculated from the new discounted utility function.

### *Adjusting amount trials*

No statistical analyses were performed on the adjusting amount data as they were highly unreliable (see above) however Table 4 indicates the average parameter estimates and adjusted  $R^2$  values for the two trials fitted according to the new model (Eq. 10, and converted back to magnitudes from utils).

	Trial 1 (£500)	Trial 2 (£1000)
$R^2$ adjusted	0.63	0.55
$K$	0.0067	0.0034
$R$	0.0014	0.005

**Table 4. Summary of parameter values for the adjusting amount trials.** Mean parameter values estimated using the new discounted utility function (Eq. 10).

Interestingly, the new function fit the data with a much greater degree of variance accounted for than either the SHM or the MHM (see Table 2). In the case of the SHM, part of the improvement in fit would have arisen from the additional free parameter.

## **Discussion**

The results from the adjusting delay trials were consistent with the hypothesis that a linear relationship would be found between the delay to  $A$  and the delay to  $B$  at indifference. This was confirmed by the fact that the linear regression accounted

for most of the variance of the data, as shown by the high  $R^2$  values (close to 1). In each case, the gradient was found to be above 1, meaning that a unit increase in the delay to  $A$  produced a greater increase in the delay to  $B$  – consistent with hyperbolic and not exponential discounting.

Additionally, the standard one-parameter hyperbolic model predicted that the gradient of the line would be equivalent to the ratio of the magnitudes of  $B/A$  (1.5) in both trials. The two-parameter model on the other hand, which accounted for the effects of concavity of the utility function, predicted that the gradient should be equivalent to the ratio of the utilities of  $B/A$  (less than 1.5). This is because as size increases, marginal utility gets smaller (that is the utility of  $B$  is less than  $1.5 \cdot A$ ). Additionally, the two-parameter model predicted that the slope would be smaller in the second trial, where the amounts were doubled, because the ratio of the utilities decreases as the utility function becomes more concave, where the magnitudes get bigger. Indeed, it was observed that in the first trial the slope was close to 1.4 and in the second trial 1.26 – clearly supporting the two-parameter approach. This effect of increasing reward magnitudes while keeping ratios constant matches Wogar et al.'s (2002, 2003) observations of a reduction in indifference delays to  $B$  in rodents. The exponential model predicted a slope of 1 in both trials. Further evidence for the involvement of diminishing marginal utility in choice was the finding that the  $r$  parameter estimates from the new model were significantly greater than zero, in accordance with the hypothesis that most individuals have concave utility functions (discount increasing magnitude).

This collective evidence that the rate of diminishing marginal utility is a determinant of intertemporal choice behaviour provides the first demonstration of such an effect in humans and indicates that choice outcome is a product of two features of human preference. This necessitates the use of an integrated model for

discounting to accurately model choice, particularly when assessing the effects of an independent variable.

As predicted, the effect of diminishing marginal utility was to make choice more impulsive (in relation to a linear utility function) because it reduces the instantaneous value of the larger magnitude reward relative to the smaller. Thus, indifference delays to *B* for a given delay to *A* were smaller when the reward magnitudes were doubled but ratios kept constant. A result of this effect is that models which fail to take into account concave utility will overestimate the true discount rate. Thus, *K* parameter estimates were found to be higher when estimated from the SHM than from the new discounted utility model. Although such an effect has been predicted by economists and is evident from the concepts of Ho et al. (1999), proponents of the MHM have never tested this hypothesis by comparing *K* estimates from both models.

The MHM, in addition to predicting a shallower slope in trial 2 of the adjusting delay, predicted that the intercept should be lower if *K* is amount independent. Instead, the intercept was greater in the second trial – consistent with Green & Myerson (2004) that *K* decreases as amount increases (i.e. we temporally devalue larger rewards proportionately less with time). This was confirmed when *K* parameters were estimated, however, how much of an effect there was on *K* (over what the model predicts) is difficult to ascertain. This is because when *Q* values were estimated, it was clear that the *Q* utility function could not properly account for the data. This was especially apparent in a few subjects whose gradient was greater than 1.5, which led to highly negative parameter values affecting the data. Moreover, inability to estimate *Q* meant that the hypothesis that the magnitude discounting parameter (concavity) should remain stable across all trials could not be addressed – nor could it be explicitly shown that the parameter estimates revealed utility concavity.

Stemming from these problems, a new discounted utility model was derived to analyse the data. This model incorporated a utility function that has been found to accurately account for human choice data in behavioural economics experiments of decisions involving risk. When fitted to the adjusting delay data a highly accurate linear fit was found. In addition, all the  $r$  parameter values were within a realistic range ( $r$  being the new parameter that determines the individual's concavity). Remarkably, in line with the hypothesis, estimates of  $r$  were not significantly different across trials, so much so that the mean estimate was identical. This was crucial because  $r$  cannot be size dependent – it is a discounting parameter for magnitude and is thus *a priori* not dependent on it. Estimability of this  $r$  value allowed for plotting the average utility function of the participants according to the new function. Inspection of the function over the range of values used revealed a high degree of concavity. This could be an effect of the hypothetical nature of the task.

In addition to being able to directly estimate concavity values, the new model also had the advantage of being able to directly test for the superiority of the combined model over the SHM, which Ho et al. (1999) have not done. This was achieved (despite the increase in complexity) by showing that  $r$  values were significantly greater than zero, as predicted by concavity (null hypothesis that utility is linear and therefore does not determine choice:  $r = 0$ ) – an approach suggested by Gallant (1987) to compare models with additional parameters.

This study also set out to answer an important question about temporal discounting – is the greater discounting of smaller rewards an effect of an amount dependent  $K$  (Green & Myerson, 2004, see Chapter 1) or can it be explained by the effects of diminishing marginal utility (Ho et al., 1999; Loewenstein and Prelec, 1992)? In the MHM analysis, it would appear that the answer is both – there was an effect of non-linear utility (as shown by the change in slope) but the change in

intercept revealed that there was also an effect of magnitude on  $K$ . Analysis of the  $K$  values estimated from the MHM method revealed that there was quite a large difference in the two trials – with greater temporal discounting for smaller rewards (trial 1). However, these  $K$  value estimates are likely to be affected by the poor  $Q$  function in the MHM. When the data were reanalysed with the new function, the difference in  $K$  across trials was much less marked than that apparent under the MHM and the SHM. Doubling the amounts roughly halved the  $K$  values, as estimated using the new function (as opposed to quartering them according to MHM estimates). From these data it would appear that  $K$  is amount dependent, although the effect is probably smaller than envisaged by Green & Myerson (2004), as the utility concavity (and incorrect estimation of discount rates in standard model experiments) can account for some of the effect. Additionally, it should be noted that the difference in  $K$  in the two trials could be sharply reduced (to trend significance) by the removal of a particularly high  $K$  value from one of the participant's first (low amount) trials.

In conclusion, these results do argue for a smaller than originally thought effect of magnitude on  $K$ , but a further study is required to conclusively resolve this issue. Especially important is the use of realistic as opposed to hypothetical choices employed in this design. One of the main arguments against the existence of the magnitude effect is it that it has not been demonstrated in animals (e.g. Green et al., 2004, see Chapter 1), a finding which could be explained by the hypothetical nature of many of the human studies. In these studies, choices are likely to reflect more abstract attitudes rather than the choices they would make in a real life situation. These attitudes may be more susceptible to manipulations which induce effects such as the magnitude effect. Even human studies which claim to show a magnitude effect in 'realistic' choice situations (e.g. Bickel and Johnson, 2002) are not convincing. For example, in the study cited above, only 6 subjects were tested

and the choices were still only partially realistic. The hypothetical nature of the task here could also have led to the poor performance of some of the subjects who were excluded based on the catch trial threshold. However, if there is an effect of magnitude on  $K$  it may be necessary to alter the discounting function slightly for an adjusting delay (but not adjusting amount) procedure – since both amounts are delayed and will be temporally discounted. Nevertheless, in a comparative study, as long as the two amounts are kept the same one need not worry about this confound unless one assumes that an independent variable can alter the relationship between  $K$  and magnitude. Still, this is a separate consideration to the question of non-linear utility.

Unfortunately, the data from the adjusting amount trials was riddled with inconsistencies (as apparent from the poor  $R^2$  values) which precluded detailed analysis and comparisons. This is surprising given that the adjusting delay data were almost model, and that the adjusting amount procedure is the standard one used in human experiments, where the data is usually very good ( $R^2$  squared typically above 0.8). There were fewer data points (indifference points) used to plot the curve (6 vs. 7 for the adjusting delay trials) but this is unlikely to be the explanation for the poorer data. One possibility is that due to the nature of the programme, if the participant made an error and pressed the wrong key, the limits would be incorrectly set and could not be altered, leading to a potentially highly incorrect indifference point in a particular block of the trial. However, the same limits procedure was used in the adjusting delay trials where data were highly consistent. Furthermore, even where the adjusting amounts trials do provide good data (e.g. Green and Myerson, 2004 – see Chapter 1) the fit is still usually significantly lower than the values of  $R^2$  adjusted reported here. This observation suggests that adjusting delay procedures are more reliable and accurate paradigms to utilise in human studies, although it is not immediately obvious why this should

be the case. This behavioural paradigm effect is another novel finding of the current experiment.

Cursory analysis of the adjusting amount results also indicates a magnitude effect although it is not possible to conclude how much of this is due to  $K$  versus  $r$ , nor is it possible to compare the parameters from this task to those of the adjusting delay. One interesting point to note is that the  $R^2$  adjusted values were dramatically improved compared to the MHM and standard model, when the new model was used to fit the data.

In summary, these results demonstrate that an integrated temporal discounting function, incorporating a utility function, is a more accurate model of delayed reward valuation and correspondingly intertemporal choice in humans. This model has greater accuracy in determining temporal discount rates and also has the novel application of being able to determine the concavity/convexity of an individual's utility function from intertemporal choice paradigms. This allows for neurobiological and pharmacological research into the basis of, and factors affecting magnitude discounting and also addresses an interpretational problem in future temporal discounting and impulsivity research. Using the new model, it is now possible to account for an experimentally induced change in impulsive choice through a change in either of the variable parameters, thus determining whether the independent variable affects temporal discounting, utility concavity or both.

This discounted utility model has particular relevance for the understanding of personality characteristics such as impulsivity. The term 'impulsive' is a general description of a diverse group of behaviours with distinct features (likely dependent on distinct neural processes), which are encompassed by a general theme of behaviour in the absence of adequate foresight (e.g. Evenden, 1999a, see Chapter 1 for further discussion). These include motor/behavioural impulsiveness; the inability to withhold a prepotent behavioural response, and reflection

impulsiveness; a failure to slow down (or 'hold your horses' (Frank et al., 2007)) in response to decision-conflict, to properly consider options. Another feature; choice/temporal impulsiveness, is often defined as the propensity to choose small short-term gains in preference to larger delayed gains (or larger delayed losses in preference to smaller immediate losses) (e.g. Ainslie, 2001; Cardinal et al., 2003; Evenden, 1999a; Herrnstein, 1981; Ho et al., 1999; Logue, 1988; Mazur, 1987). Traditionally, the psychological basis of impulsive choice has rested on the discount rate parameter, such that those with a higher rate are described as impulsive and those with a low rate as self-controlled (e.g. Ainslie, 1992, 2001; Evenden, 1999a; Herrnstein, 1981; Logue, 1988; Mazur, 1987). However, the data presented here illustrate that impulsivity and self-control are also determined by the concavity of an individual's utility function and that these two processes are independent of one another. Specifically, the more concave the function, the faster marginal utility diminishes and the more impulsive is the individual. This is because a concave utility function diminishes the value of the larger reward relative to the smaller reward, making it less attractive. A curious corollary of this is that subjects who are more impulsive (as a result of a more concave utility function) may also be more risk-averse, since the concavity of the utility function is also a key determinant of choice under uncertainty (Kahneman and Tversky, 1979; von Neumann and Morgenstern, 1947; Pindyck and Rubinfeld, 2004 – see Chapter 5 for further discussion). Therefore, one should be extremely cautious when associating impulsivity with temporal discounting, or assuming that differences in impulsive choice are accounted for by greater temporal discounting.

In conclusion, here it was demonstrated that the non-linearity of utility with respect to magnitude can affect intertemporal choice in humans, and that  $K$  parameters are overestimated as a result. Therefore, integrated models of discounting should be used in future intertemporal choice studies. The MHM is

useful in some scenarios in human studies, however to be able to discern parameter estimates for the utility concavity, and demonstrate that integrated models are better than simple hyperbolic ones, the new discounted utility function and estimation procedure is preferable. Finally, impulsivity in choice should be considered by referring to both determinants of choice.

## Chapter 3.

# The encoding and integration of marginal utility with temporal discounting in the human brain

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### Introduction

The behavioural data from the adjusting delay paradigm reviewed in Chapter 2 demonstrated an effect of diminishing marginal utility on intertemporal choice. In light of this data, a new discounted utility function for the valuation of delayed rewards was proposed, the crux of which was an integration of two sub-components of value – the magnitude based utility of the reward and the discounting associated with time. The function was found to provide a good description of behaviour in the adjusting delay paradigm and yield reliable estimates for the free parameters governing the rate of temporal discounting and the rate of diminishing marginal utility (concavity of the utility function).

The purpose of this subsequent study was to demonstrate a neurobiological implementation of the discounted utility function using fMRI. There were a number of compelling reasons to attempt this. First, demonstrating that the brain treats the valuation of delayed rewards in accordance with the new model would provide additional evidence for its veracity, beyond behavioural data. Indeed, the purpose of refining models is to attempt to gain a better description of the ‘reality’ which they attempt to describe. It is logical to assume that if human behaviour in intertemporal choice is accurately described by a valuation process which integrates temporal discounting and magnitude discounting, the same valuation processes should occur at the neuronal level, which leads to the output of such

behaviour. Thus, the second purpose was to give a more sophisticated neurobiological account of intertemporal choice than has previously been described, and in the process, shed new light on the brain's value systems.

More specifically, the experiment was designed with the model in mind, to identify a neural implementation of the two relevant subjective value systems, which individually form sub-components of overall value: a system which relates the objective property of the delay of rewards to their subjective value – in the case of temporal discounting – and a system which relates the objective property of the magnitude of rewards to their subjective value – in the case of marginal utility, or magnitude discounting. To identify these subjective value systems, BOLD responses during valuation were correlated with the sub-components of value, where the values were calculated from parameter estimates derived from the subjects' own behavioural choices, using the model. With the assumption that the brain values distinct properties of rewards separately, it is also necessary to propose that these valuation systems are integrated at some point to provide an overall metric of an option's value, used to guide choice (and in accordance with utility theory). To demonstrate this implementation correlates of overall value were used to analyse BOLD response, calculated from subjects' behaviour, again using the discounted utility model. In effect, studying the neurobiological correlates of dissociable components of value allows one to deconstruct the structure of choice *per se*. Such data go beyond the simple one versus two systems debate which is currently the focus of fMRI intertemporal choice literature.

While previous fMRI studies have made progress in studying the neurobiology temporal discounting (e.g. Kable and Glimcher, 2007; McClure et al., 2004, 2007; Tanaka et al., 2004), none have taken into account the confound of diminishing marginal utility on this measure. Furthermore, no study has identified a unique system which correlates with a hyperbolic discounting of time – as implied by the

new model – which would present an advance in temporal discounting research and provide biological validity to the hyperbolic model.

In contrast to temporal discounting, no study has yet demonstrated a neurobiological basis for diminishing marginal utility, by demonstrating a non-linearity of brain responses to magnitude increases. This concept (often referred to as a law) remains integral to economic theory, most notably in relation to the microeconomic concept of an indifference curve which explains preferences between different bundles of goods, consumer theory and laws of supply and demand (Pindyck and Rubinfeld, 2004), as well as in modern analyses of decision under risk and uncertainty (von Neumann and Morgenstern, 1947; Kahneman and Tversky, 1979). It is taken as a given that utility provided by a fixed amount of £10, is greater when added to an option worth £50 than to one worth £500. Given its central role in economic theory, providing a neurobiological account of diminishing marginal utility would represent a major advance in neuroeconomics and this is a ripe area for research as virtually no studies have explored its biological basis.

In addition, it was hoped that inter-subject variability in temporal and magnitude discount rates could be explained by differences in brain activity of the relevant value systems implicated. A theory of individual differences in discounting has not yet been well-formed (see Chapter 1).

Providing a more complete account of the neural systems involved in intertemporal choice also represents a step forward in impulsivity research since one form of impulsiveness is a propensity to choose smaller-sooner rewards (e.g. Ainslie, 1975, 2002; Evenden, 1999a; Ho et al., 1999; Mazur, 1987). Identifying the relevant systems could help to better understand disorders featuring impulsivity as a symptom, based on the known brain abnormalities in these disorders.

The second major purpose of this study was to give a radical overhaul to the methodology and analyses of intertemporal choice paradigms in human studies. The adjusting delay paradigm, used in Chapter 2, was adequate to demonstrate a behavioural effect of the non-linearity of utility on choice, and will continue to act (along with other indifference point methodologies) as suitable paradigms for behavioural experiments. However, for the purposes of this study it was not sufficient in a number of important ways.

First, in the adjusting delay procedure the magnitudes of the rewards are kept constant throughout, with only delays being varied. The aims of this study required a large degree of variability in both delays and magnitudes – first of all, to be able to identify the neural system implicated in relating magnitude to utility, where it would be necessary to correlate magnitude with BOLD responses, and even further, to assess non-linear responses to increasing magnitudes. This necessitated exposure to a wide array of possible reward magnitudes, to gain more power. Second, intertemporal choice paradigms by their nature consist of smaller-sooner versus larger-later choices. This means that there is an inevitable degree of correlation between delays and magnitudes. As this study aimed to demonstrate value systems responding separately to utility and discounting, as well as to overall value, a high degree of orthogonality was required, involving many different delays and magnitudes, and where large magnitudes could also appear at smaller delays (e.g. £70 in 1 month vs. £85 in 1 month and 2 weeks) and vice versa (e.g. £5 in 11 month vs. £10 in 1 year) in addition to regular choices. Finally, in practice, indifference point methodologies are often confounded by ordering effects. For these reasons indifference point methodology was not employed to estimate individual model parameters, instead, a computational modelling method was devised.

The second major reason for redeveloping the choice paradigm was because another aim of this study was to use behavioural data to evaluate and compare a number of influential valuation models which have been proposed in the literature, and assess which one most accurately described subjects' choices. This has not previously been attempted. One of the features of the adjusting delay procedure is that many models predict a linear relationship at indifference (see Chapter 2). As we saw, this makes it hard to perform goodness of fit comparisons – the fit of the new model was equally as good as the MHM. Furthermore, even where goodness of fit (quantified by adjusted  $R^2$  values, for example) can be applied to evaluate different models, such as in the adjusting amount procedure (e.g. Green and Myerson, 2004; Myerson and Green, 1995), this measure fails to take into account the complexity of each model being compared. As the number of free parameters in a model increases, so does the complexity of the model, and its ability to account for more variance in the data. Therefore, a technique other than goodness of fit must be used when evaluating models of varying complexity. This problem was also addressed using computational model comparison techniques. As in Chapter 2, validity of the new discounted utility model was sought, particularly over the SHM, in addition to a demonstration of the utility concavity.

Another important advance of this study over the design used in Chapter 2 was the use of real versus hypothetical choices. This was implemented using random selection of two of the subject's choices made in the experiment, paid at the specified future date. Considerable amounts of money were offered in many of the choices to ensure subjects were not flippant, and no payment was awarded for mere participation, to impress on the subjects the importance of choosing according to their preferences. It was hoped that the effect of utility concavity on choice would be evident where choices were realistic as well as in the hypothetical domain, as observed in the adjusting delay study.

A related concept to impulsive choice is sometimes referred to as ‘reflection’ impulsiveness (Clark et al., 2006; Kagan, 1966), preparation impulsivity (Evenden, 1998) or the ability to ‘hold your horses’ (Frank et al., 2007) (see Chapter 1). This relates to the speed at which decisions are made, and whether adequate time is given to properly evaluate the options before a behavioural response is elicited. This is particularly relevant when the options in a choice are closely valued, which is known to engender decision-conflict and is accompanied by a slowing down of decision latency (e.g. Botvinick, 2007; Botvinick et al., 2004; Frank et al., 2007). This phenomenon provided another opportunity to assess the utility of the new model since the model could predict which choices were difficult and which were easy, based on the difference in discounted utility of the two options – using the subjects’ estimated parameter values. It was predicted that difficult choices identified by the model should be accompanied by a slowing down of decision latency and also by an increase in the activity of regions such as the ACC which are known to become engaged during conflict and effortful scenarios (e.g. Botvinick et al., 2001, 2004; Botvinick, 2007; Cohen et al., 2005; Kennerly et al., 2006; Pochon et al., 2008). Whilst this phenomenon of decision-conflict is relatively well studied in lower level, perceptual and motor decision-making tasks, it is less well characterized in higher level tasks (Pochon et al., 2008). Such a demonstration would therefore provide valuable evidence that the ACC’s role in conflict monitoring extends to more complex scenarios such as intertemporal choice.

## **Methods**

### *General overview*

fMRI was used while subjects chose between two serially presented options of differing magnitude (from £1 to £100) and delay (from one week to one year)

(Figure 1). These choices were often smaller-sooner versus larger-later in nature and presented serially, to separate decision-making and option valuation processes. Two of each subject's choices were selected at random at the end of the experiment (one from each experimental session) and paid for real, by way of pre-paid credit cards with a timed activation date. Subjects' choices were used to assess a number of models using maximum likelihood estimation (MLE), including the new discounted utility function. This produced estimates of the best fitting parameters for each model which were then used to test the extent of discounting for magnitude (utility concavity) and time (temporal discounting). Model comparison was performed using the Akaike Information Criterion (AIC).

For the purpose of imaging analyses, the model was decomposed into three key terms. In simple terms, the new model states that the function for the discounted utility (subjective value) of a delayed reward ( $V$ ) is equal to  $D \times U$  where  $D$  is a discount factor between 0 and 1 and  $U$  is undiscounted utility.  $D$  is a function of delay to the reward, and includes the individual's discount rate parameter, whereas  $U$  is a function of the magnitude of the reward and includes a subject-specific parameter determining the concavity (or degree of diminishing marginal utility) or convexity of the utility function.

### *Participants*

Twenty-four right-handed, healthy volunteers were included in the experiment (12M:12F, mean age 23, range: 19-28). Subjects were pre-assessed to exclude those with a prior history of neurological or psychiatric illness. All subjects gave informed consent and the study was approved by the UCL ethics committee.

## *Procedure*

Upon arrival, subjects were given an instruction sheet to read (see Appendix II), explaining the task and details of the payment. They were also shown the credit cards and the lottery machine to reassure them that the payment system was genuine (see below). After a short practice of 6 trials, they were taken into the scanner where they performed 2 sessions of 110 trials each.

In order to impose ecological validity, a payment system was designed which ensured that all the choices would be made in a realistic manner, with realistic consequences. The thrust of this design was the random selection of two of the choices that were made during the experiment, with real payment of the option chosen during those two choices. This was achieved by way of two pre-paid credit cards which were loaded with the amounts won and activated at the times associated with the selected options. Each card required a PIN to be activated before any spending could be done with the card. This PIN was emailed to the subject at the specified time. The cards could be used in most retailers or over the internet.

Payment was implemented by way of a manual lottery after completion of all testing. The lottery contained 110 numbered balls, each representing a trial from the first session of testing. The ball which was selected corresponded to the rewarded trial for that testing session. The magnitude and delay of the option which the subject chose in the selected trial was determined and awarded using a pre-paid credit card. The magnitude of the option chosen was loaded onto the card and given to the subject. The activation code on the card was removed and sent by email to the subject at the delay specified by the chosen option. This lottery was then repeated to determine a reward for the second session of testing, and a second card was issued. Both lotteries took place after all testing had been completed.

Thus, the payment each subject received was determined by a combination of the lottery and the choices that they made – a manipulation that ensured subjects treated all choices as real. The payment system was designed so that on average each subject would receive £100. No other payment was awarded for mere participation in the experiment. Since only two choices were paid to the subjects and selected after the testing was completed, one could be confident that any influence of changing reference points (Kahneman and Tversky, 1979) (as a result of increasing wealth) was unlikely to be significant.

In addition, after all testing was complete, subjects were given the Barratt impulsiveness scale (BIS, Patton et al., 1995) to complete. These data did not yield any noteworthy results and are not discussed further.

### ***Task description***

Each trial consisted of a choice between a smaller-sooner reward and a larger-later reward. The choice was presented serially, in three stages (see Figure 1). This serial mode of presentation was a novel aspect of the study in relation to previous designs used in fMRI (e.g. Kable and Glimcher, 2007; McClure et al., 2004) where both options are presented together and the choice can be made from the onset of the presentation (i.e. a single stage). This design was motivated to ensure the separation of the neural valuation signals for each option as well as to separate valuation processes from the actual decision-making processes (thereby providing less ambiguous imaging data).

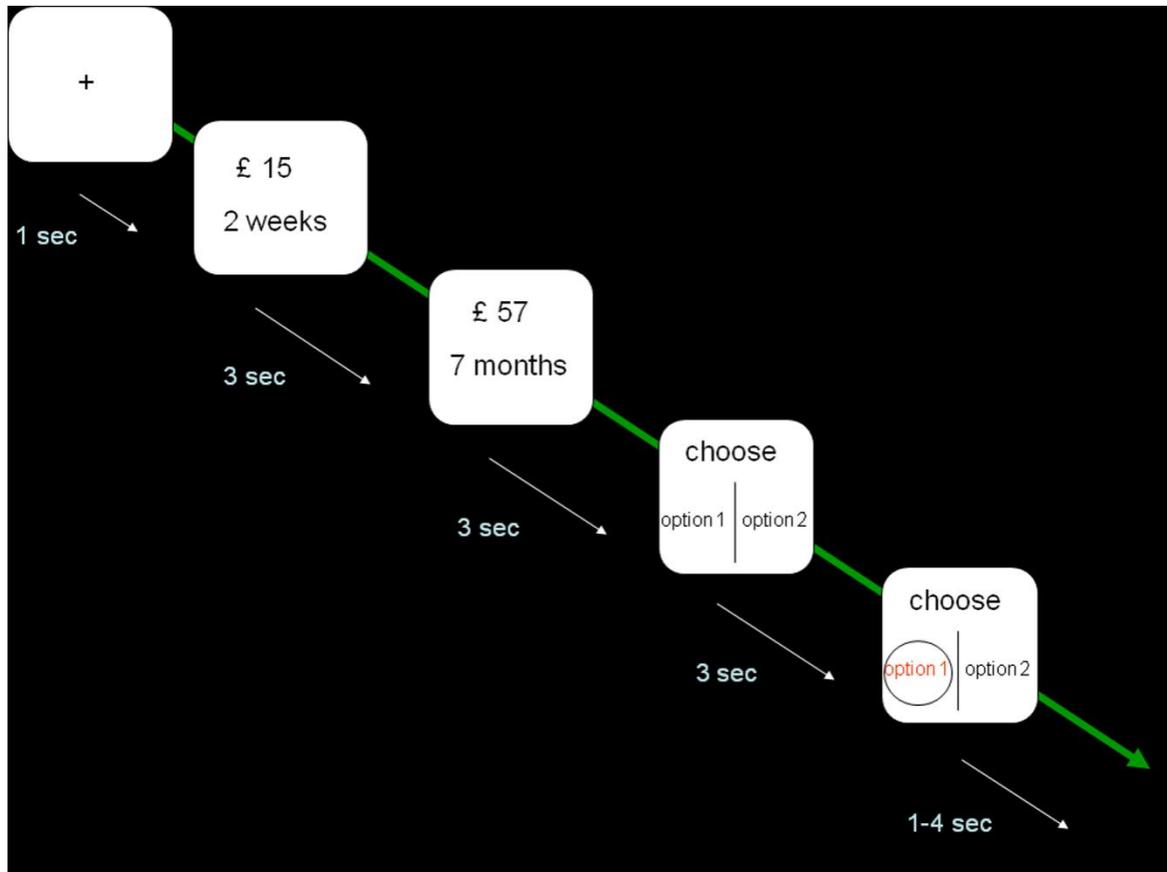
The first two stages consisted of presentation of the details of each option, *i.e.* the value of the reward in pounds and the delay to its receipt in units of weeks and months. After presentation of the options, a third screen prompted the subject to choose between ‘option 1’ (the option which was presented first) or ‘option 2’, by

means of a button-box, using their right hand. A three-second delay ensued each of the three phases. The choice could only be made during the three seconds following presentation of the choice screen. Once a choice had been made, the chosen option was highlighted in blue. Providing there was sufficient time, the subject could change his/her mind. There was a jittered delay of 1-4 secs following the choice phase, followed by presentation of a fixation cross for 1 sec (see Figure 1).

In this design there may be additional processes occurring at the onset of the second option, such as relative comparison, decision-making and prediction error coding – as with previous studies. However, the fMRI analysis is rationalised on the basis that the value should still be encoded at the time of the second stimulus presentation, in addition to these other processes. (Note, the presentation of sooner or later delays, and larger or smaller amounts, was randomized between option 1 and 2).

The experiment consisted of a total of 200 trials. Option 1 was the smaller-sooner reward in 50% of trials. In addition, a further 20 'catch' trials were included, where one of the options was both greater in value and available sooner than the other one. These catch trials occurred approximately every tenth trial and were included to ascertain how well the subjects were concentrating on the task, under the assumption that the norm was to prefer the larger-sooner reward in these choices. Three arrays of choices were created with eight subjects assigned to each. The option values were created using randomly generated magnitudes varying from £1 to £100 in units of £1 and delays ranging from 1 week to 1 year in units of single weeks (but presented as a number of months and weeks), also with a random distribution (using Matlab). This random nature of values and especially the catch trials helped in orthogonalising magnitude and delay. In order to create choices between smaller-sooner and larger-later rewards, a constraint was

introduced to the choice-making program, that the option with greater magnitude should be delayed more than the smaller, and vice versa for the catch trials.



**Figure 1. Experimental task.** The display outlines the sequence of stimuli in a single trial. Subjects are presented with two options – a smaller-sooner and a larger-later amount of money (range £1-100, 1 week – 1 year). Subjects chose the option which they preferred and received their chosen option for two out of the 220 trials; as determined by a lottery and paid using pre-paid credit cards activated at the specified time (see methods).

## *Behavioural analysis*

### **Parameter estimation and model comparison**

The softmax decision rule was utilised to assign a probability ( $P_{O1}$  for option 1;  $P_{O2}$  for option 2) to each option of the choice given the value of the option ( $V_{O1}$  for option 1;  $V_{O2}$  for option 2) whereby

$$P_{O_i} = \frac{e^{(V_{O_i}/\beta)}}{e^{(V_{O_1}/\beta)} + e^{(V_{O_2}/\beta)}} \quad (\text{Eq. 1})$$

$V_{O_i}$  represents the value of an option (i.e. a delayed reward; either 1 or 2) according to a particular model of option valuation (see below). The  $\beta$  parameter represents the degree of stochasticity of the subject's behaviour – in other words how deterministic or rule-based their behaviour is, and their sensitivity to changes in  $V$ .

Seven models of option valuation were compared. The first model was the standard hyperbolic model (Mazur, 1987), which states that the subjective value ( $V$ ) of a reward of magnitude ( $M$ ) and with a delay ( $d$ ) can be expressed as

$$V = D(d) \cdot U(M) = \frac{M}{(1 + K \cdot d)}$$

$$D = \frac{1}{(1 + K \cdot d)} \quad (\text{Eqs. 2})$$

$$U = M$$

$D$  can be thought of as the *discount factor* – the delay-dependent factor (between 0 and 1) by which the utility is discounted. The discount rate parameter  $K$  quantifies an individual's tendency to discount the future such that a person with a high  $K$  devalues rewards quickly as they become more distant.

The second model was the new generalisation of the simple hyperbolic model where magnitude was replaced with undiscounted utility ( $U$ ). As in Chapter 2, the utility function was an exponential function adapted from Holt and Laury (2002). Utility is related to magnitude accordingly:

$$U(M) = \frac{1 - e^{(-r \cdot M)}}{r} \quad (\text{Eq. 3})$$

where  $r$  is a free parameter governing the curvature of the relationship. The greater the value of  $r$  the more concave the utility function, and where  $r$  is negative, the utility function is convex. In both expected utility theory and prospect theory (von Neumann and Morgenstern, 1947; Kahneman and Tversky, 1979)  $r$  also determines an individual's risk aversion (in choices where risk is a factor, such as gambles) such that increasing concavity of the utility function equates to greater risk aversion and increasing convexity to greater risk seeking. Therefore, as described in Chapter 2, according to the new model  $V$  can be expressed as follows:

$$V = D(d) \cdot U(M) = \frac{1}{(1 + K \cdot d)} \cdot \frac{1 - e^{(-r \cdot M)}}{r} \quad (\text{Eq. 4})$$

Value ( $V$ ) here represents discounted utility.

The third model was similar to the second model but incorporated an exponential temporal discounting function instead of a hyperbolic function. The exponential formula is a normative economic model and is deemed to be a 'rational' way to discount future rewards, unlike the hyperbolic model which is 'irrational' as it leads to preference reversals (Ainslie, 2001, see Chapter 1). Most behavioural literature indicates that humans and animals discount hyperbolically (see Chapter 1). Here  $V$  is expressed as follows:

$$V = D(d) \cdot U(M) = e^{(-K \cdot d)} \cdot \frac{1 - e^{(-r \cdot M)}}{r} \quad (\text{Eq. 5})$$

$$D = e^{-K \cdot d}$$

The fourth model was similar to the third model in that it used an exponential discount function but here, undiscounted utility ( $U$ ) was replaced with magnitude ( $M$ ) (i.e. assuming a linear utility function). In this model:

$$V = D(d) \cdot U(M) = e^{(-K \cdot d)} \cdot M \quad (\text{Eq. 6})$$

$$U = M$$

The fifth model was the quasi-hyperbolic beta-delta model (Laibson, 1997; Phelps and Pollack, 1968). According to this model,  $D(d) = \beta \cdot \delta^d$ ; where  $\delta$  represents the discount rate in the standard exponential formula and the  $\beta$  parameter (where  $0 < \beta \leq 1$ ) represents a unique weighting placed on immediate rewards relative to rewards with a more delayed receipt. This parameter therefore devalues future rewards relative to immediate rewards. This model was utilised (McClure et al., 2004) to express the concept of two decision making systems corresponding to the two parameters – one rational and one irrational – devoted to future versus immediate reward evaluation respectively (see Chapter 1). Again, using the utility function above, this can be reformulated as

$$V = D(d) \cdot U(M) = \beta \cdot e^{(-K \cdot d)} \cdot \frac{1 - e^{(-r \cdot M)}}{r} \quad (\text{Eq. 7})$$

$$D = \beta \cdot e^{(-K \cdot d)}$$

The sixth model was similar to the fifth model in implementing the beta delta function except undiscounted utility ( $U$ ) was replaced with magnitude ( $M$ ) (i.e. assuming a linear utility function). In this model

$$V = D(d) \cdot U(M) = \beta \cdot e^{(-K \cdot d)} \cdot M \quad (\text{Eq. 8})$$

$$U = M$$

Finally, the ‘as soon as possible’ model (ASAP) (Glimcher et al., 2007) was also evaluated. This was earlier proposed by Green et al., (2005) as an ‘elimination-by-aspects model’. In this model the delay common to both options is ignored, the sooner option is treated as an immediate one and the later option is hyperbolically discounted (magnitude). This model entails a type of relative valuation rather than a present-value comparison of each option, implied by the other models.

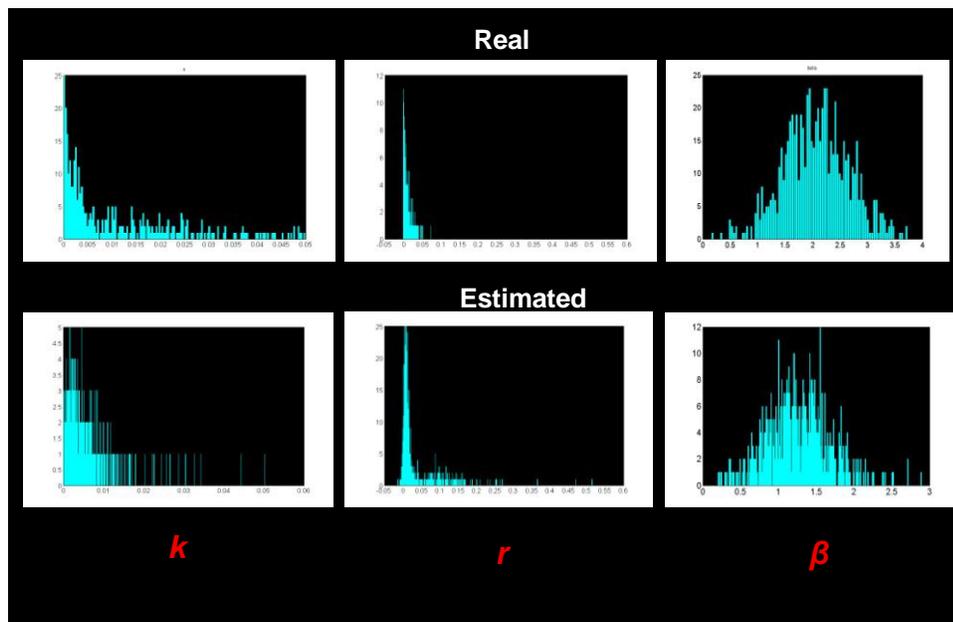
To calculate the maximum likelihood (best fitting) parameters for each model as well as a measure of the fit of the model, maximum likelihood estimation was used. For each subject, the probability was calculated for each of the 220 options chosen from the 220 choices (which included catch trials), using the softmax formula (Eq. 1). The summed log-likelihood was then calculated using the probability of the option chosen at trial  $t$  -  $P_{O(t)}$  - from Eq. 1 such that

$$\ln L = \sum_t \ln P_{O(t)} \quad (\text{Eq. 9})$$

The final stage of the MLE, implemented with optimisation functions in Matlab 7, was to minimize Equation 9 by searching through different parameter values for the free parameters in the softmax function ( $\beta$ ) and the valuation function ( $K$ ,  $r$  etc. See above).

Essentially this tells us how likely the model is given the choices subjects made, and the best fitting parameters given the model. Here, the best fitting parameters are those that lead to the smallest log likelihood values (or greatest probability). The method works by searching for the parameter estimates which lead to the choices most similar to those selected by the subject i.e. the most probable ones.

This method of estimating parameters has been widely used in reward learning experiments (e.g. Daw et al., 2006; Seymour et al., 2004; Pessiglione et al., 2006) however it has not previously been used in intertemporal choice experiments. To informally assess the reliability of this procedure, choice data from the adjusting delay trials in Chapter 2 were fed into the estimation programme. Remarkably, the parameter estimates for  $K$  and  $r$  were very similar to those estimated using linear regression methodology with indifference points in Chapter 2. Additionally, the current experiment was simulated 1000 times using groups of 24 (the number of subjects in the real study) 'agents', simulated using Matlab. These agents were assigned randomly generated parameter values for  $K$ ,  $r$  and  $\beta$  (within the range of values estimated from subjects' choices in Chapter 2). The groups of agents were each assigned to 220 randomly generated intertemporal choices (the number of choices used in this study). The choice data from these agents were then analysed using the maximum likelihood estimation technique described above, to see if the estimated parameter values for each group of agents were similar to the 'real' mean starting values which they were assigned. Although no formal statistics were used, the real and estimated parameter values appeared to be very similar, especially at the group level (see Figure 2).



**Figure 2. Experiment simulation.** The top panel indicates the distribution of starting parameter values for  $K$ ,  $r$ , and  $\beta$ , which were assigned to the agents. Lower panel indicates the distribution of estimated parameter values for the same agents (based on their choices). Analysis of the values for each subject and group indicated that the estimation procedure yielded values close to the starting ones with a high degree of confidence.

To compare the second model (Eq. 4) over the first (Eq. 2), i.e. by demonstrating an effect of concave utility on choice, a one-sample  $t$ -test was also performed, comparing the estimated  $r$  values with zero. It was expected that  $r$  should be greater than zero as most people have marginally decreasing (concave) utility functions (hence the ‘law of diminishing marginal utility’). If there were no effect of diminishing marginal utility on choice behaviour, one would expect  $r$  to vary around zero (null hypothesis). Testing whether parameter estimates differ significantly from the value predicted by the null hypothesis is also a standard approach to addressing the question of whether an additional parameter is necessary (e.g. Gallant, 1987). In addition, a one-sample  $t$ -test comparing the  $K$  values estimated from model 2 to zero was performed, to demonstrate an effect of temporal discounting.

To compare evidence in favour of each model the Akaike Information Criterion (AIC) was calculated for each subject, under each model. AIC is a popular ‘information theoretic’ approach to model comparison and selection (Burnham and Anderson, 2002; Wagenmakers and Farrell, 2004). It is known as information theoretic because it relates to the concept of ‘information’ as defined by Kullback and Leibler (1951; Burnham and Anderson, 2002). Kullback-Leibler information  $I(f,g)$  is the information lost when model  $g$  is used to approximate  $f$  – full reality or truth. Stated more simply, it is the distance between full reality and a model. Clearly, the best model loses the least information relative to other models. Akaike (1973) found an estimator of relative, expected K-L information based on the maximized log-likelihood function.

In model comparison, descriptive accuracy is not the only factor that should be considered – it is generally accepted that parsimony is preferred when selecting models. Under-fitted models can be biased whereas over-fitted models with many parameters may identify spurious effects, thus some balance is required (Burnham and Anderson, 2004). Akaike found that the bias in the maximised log-likelihood estimate is approximately equal to the number of free parameters ( $N$ ) in the model (an asymptotic result) and so incorporated this as an asymptotic bias correction term (see Burnham and Anderson, 2002; Burnham and Anderson, 2004). Equation 10 shows that the AIC rewards descriptive accuracy via the maximum likelihood and penalises lack of parsimony (complexity) according to the number of free parameters:

$$AIC = -2 \ln L + 2N \quad (\text{Eq. 10})$$

Thus, the smaller the AIC, the better/more likely the model is given the evidence. Using an information-theoretic approach, the AIC was summed over all subjects for each model ( $i$ ) separately ( $AIC_i$ ) and the absolute difference between the best model ( $AIC_{\min}$ ) and each of the other models ( $\Delta AIC$ ) was calculated as

$$\Delta AIC = \Delta_i = AIC_i - AIC_{min} \quad (\text{Eq. 11})$$

This reflects our interest in the relative performance of the models as opposed to their absolute AIC values, by telling us how much information is lost by using a particular model relative to the best fitting model (Burnham and Anderson, 2002; Burnham and Anderson, 2004; Wagenmakers and Farrell, 2004). As a rule of thumb, it has been suggested that a  $\Delta AIC$  greater than 2 suggests evidence in favour of the better fitting model and a score of greater than 10 indicates that the worse model has essentially no support (Burnham and Anderson, 2002; Burnham and Anderson, 2004). These guidelines have similar counterparts in the Bayesian literature (Kass and Raftery, 1995, where the AIC is treated as an asymptotic approximation to the log-evidence of the marginal likelihood of a model).

Additionally, Akaike weights ( $W_i$ ) were calculated for each model by normalizing the model likelihoods so that they sum to 1:

$$W_i = \frac{e^{(-\Delta_i/2)}}{\sum_{r=1}^R e^{(-\Delta_r/2)}} \quad (\text{Eq. 12})$$

Therefore, the total sum of the model  $W$ s equals 1. Akaike weights provide another measure of the strength of evidence for each model, and represent the ratio of  $\Delta AIC$  values for each model ( $i$ ) relative to the whole set of  $R$  candidate models (Burnham and Anderson, 2002; Burnham and Anderson, 2004; Wagenmakers and Farrell, 2004). Akaike weights indicate the probability that the model is the K-L best (in the AIC sense, that it minimizes the Kullback–Leibler discrepancy), among the set of candidate models i.e. conditional on the data and set of candidate models. For example, an Akaike weight of 0.8 indicates that given the data, it has an 80% chance of being the best one among those considered. Evidence ratios (the weight of a better over a worse model) can also be calculated to see how many

times more likely the better model is (see Burnham and Anderson, 2004; Wagenmakers and Farrell, 2004).

For the purposes of the imaging and reaction time analyses, a further estimation was performed whereby all the choices from each subject were grouped together (as if made by one subject) and modelled as a canonical subject, to estimate canonical parameter values (using the fitting procedure above, with the second model (Eq. 4)). This was performed to reduce the noise associated with the fitting procedure at the single subject level, to make subjects with greatly differing parameter estimates – over an order of magnitude (see Table 1) – more comparable in the second level analyses and to avoid building individual differences into the model, allowing for a neural analysis of inter-subject variability.

### **Reaction time data**

Reaction time (RT) data were analysed in an analogous manner to the imaging data on choice difficulty (see analysis 3 below). For each subject, three measures of difficulty were calculated for each of the 220 choices (using the canonical parameter estimates and model 2 (Eq. 4)): namely, difference in value ( $\Delta V$ ) (discounted utility), difference in discount factor ( $\Delta D$ ) and difference in undiscounted utility ( $\Delta U$ ) – of the two options. The canonical parameter estimates were the same as those calculated for the other analyses (see above) and were used for a number of reasons – to reduce noise associated with the fitting procedure at the subject level (i.e. of the individual parameter estimates), to make subjects with greatly differing parameter estimates comparable in the second level analyses, and to avoid building individual differences into the model, allowing for a neuronal analysis of inter-subject variability. These three vectors were then de-trended and orthogonalised with respect to each other, in the above-stated order. This final step

was taken to mimic the procedure used in SPM, which is to detrend and orthogonalise regressors by default. Although orthogonalisation can change regressors (the latter two columns in this case), this was necessary in the RT/fMRI analyses as they were significantly correlated. A linear regression was then performed to model the relationship between the reaction time (i.e. decision latency) for each choice and the difficulty measure. The parameter estimates (betas) were then used as a summary statistic and a second level analysis was performed by means of a one-sample t-test comparing the betas against zero (again using the approach implemented by SPM for imaging analysis). This was performed for each difficulty measure -  $\Delta V$ ,  $\Delta D$  and  $\Delta U$  (see below). The sign of the mean of the betas indicated the direction of the correlation (negative for  $\Delta V$  and positive for  $\Delta D$ ). In summary, the imaging and RT analyses both used identical regressors to model the relationship between BOLD response/ decision latency and choice difficulty.

### *Imaging procedure*

Functional imaging was conducted by using a 3 Tesla Siemens Allegra head-only MRI scanner to acquire gradient echo T2\*-weighted echo-planar images (EPI) with blood oxygenation level-dependent (BOLD) contrast. A sequence was utilized which was designed to optimize functional sensitivity in the OFC (Deichmann et al., 2003). This consisted of tilted acquisition in an oblique orientation at 30° to the anterior cingulate - posterior cingulate (AC-PC) line, as well as application of a preparation pulse with a duration of 1 ms and amplitude of -2 mT/m in the slice selection direction. The sequence enabled 36 axial slices of 3 mm thickness and 3 mm in-plane resolution to be acquired with a repetition time (TR) of 2.34 s. Subjects were placed in a light head restraint within the scanner to limit head movement during acquisition. Functional imaging data were acquired in two

separate 610 volume sessions. A T1-weighted structural image and fieldmaps were also acquired for each subject after completion of the testing sessions.

### *Imaging analysis*

Image analysis was performed using SPM5 ([www.fil.ion.ucl.ac.uk/spm](http://www.fil.ion.ucl.ac.uk/spm)). For each session, the first five images were discarded to account for T1 equilibration effects. The remaining images were realigned to the sixth volume (to correct for head movements), unwarped using fieldmaps, spatially normalised to the Montreal Neurological Institute (MNI) standard brain template and smoothed spatially with a three-dimensional Gaussian kernel of 4 mm full-width at half-maximum (FWHM) (and re-sampled, resulting in 3 × 3 × 3 mm voxels). Low-frequency artefacts were removed using a 1/128 Hz high pass filter, and temporal autocorrelation intrinsic to the fMRI time-series was corrected by pre-whitening using an AR(1) process.

Single-subject contrast maps were generated using parametric modulation in the context of the general linear model. Three analyses were performed, examining variance in regional BOLD response attributable to different regressors of interest: absolute  $U$ ,  $D$  and  $V$  for all options (analysis 1); absolute  $M$ ,  $U$  and  $D$  for all options (analysis 2); absolute difference in  $V$ ,  $D$  and  $U$  ( $\Delta V$ ,  $\Delta D$  and  $\Delta U$ ) between the two options on each trial (analysis 3). In these analyses, the interaction term  $V$  was calculated from the mean corrected values of  $D$  and  $U$  (this was not necessary in the non-orthogonalised regression analysis – see below and results). Analysis 1 allowed for the identification of regions implicated in the evaluation and integration of different reward-related information. Analysis 2 allowed for the identification of regions showing response to the (diminishing marginal) utility of rewards, as opposed to their absolute magnitude. Analysis 3 allowed for the

identification of regions where activation correlated with the difficulty of each choice. The 4mm smoothed images were used to perform high resolution single subject analyses (see Figure 4 for examples).

For analysis 1,  $U$ ,  $D$  and  $V$  for each option (two per trial) were calculated using the canonical parameter estimates ( $K$  and  $r$ ) in the context of the second model (discounted utility; Eq. 4), and convolved with the canonical hemodynamic response function (HRF) at the onset of each option. Analysis 2 was performed in a similar manner for  $M$ ,  $U$  and  $D$ . For analysis 3,  $\Delta V$ ,  $\Delta D$  and  $\Delta U$  were convolved with the canonical HRF at the onset of the choice phase. All onsets were modelled as stick functions and all regressors in the same model were detrended and orthogonalised (in the orders stated above) prior to analysis by SPM5. To correct for motion artefacts, the 6 realignment parameters were modelled as regressors of no interest in each analysis.

At the second level (group analysis), regions showing significant modulation by each of the regressors specified at the first level were identified through random effects analysis of the beta images from the single-subject contrast maps. The contrast maps were smoothed prior to analysis with a three-dimensional Gaussian kernel of 7 mm FWHM (this achieved an effective smoothing of 8 mm FWHM at the second level). To look for regions responding to individual differences in the slowing effect of choice difficulty, the betas from the single-subject reaction time analyses (see above) were included as covariates in analysis 3. Another covariate analysis looked for subject-by-subject covariation between regions responding to  $U$  in analysis 2 and the estimated parameter  $r$ , but this did not yield significant results at the required threshold. Results are reported for regions where the peak voxel-level t-value corresponded to  $p < 0.001$  (uncorrected), with a minimum cluster size of 5. Results which were corrected for multiple comparisons (family wise error corrected (FWE)  $p < .05$ ) at the whole brain level, or with small volume

corrections, are indicated in the tables and figures. Additionally, uncorrected results are reported but it is cautioned that these should be considered exploratory findings, which await additional confirmation by further studies. Coordinates were transformed from the MNI array to the stereotaxic array of Talairach and Tournoux (1988) (<http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach>).

To identify regions where modulation by regressors in an analysis overlapped (as in analyses 1 and 3), explicit inclusive masks were constructed using a threshold of  $p < 0.001$  and were used to constrain subsequent analyses. For example, in analysis 1, to observe regions significantly correlating with  $U$ ,  $D$  and  $V$ , regions where  $U$  modulated responses at  $p < 0.001$  were identified, and a mask was created from this image. Regions where  $D$  modulated responses within this mask were then identified at  $p < 0.001$  and a second mask was created from this contrast. Finally, regions where  $V$  modulated responses within this second mask were identified. In analysis 2, a mask was created from regions modulated by presentation of options at  $p < 0.001$ .

The structural T1 images were co-registered to the mean functional EPI images for each subject and normalised using the parameters derived from the EPI images. Anatomical localisation was carried out by overlaying the t-maps on a normalised structural image averaged across subjects, and with reference to the anatomical atlas of Mai et al. (2003).

## Results

### *Behavioural results and model comparison*

As predicted, subjects responded to the 20 catch trials by choosing the larger-sooner reward (mean: 19.5), indicating that they were concentrating well on the task. No subject answered more than 2 catch trials incorrectly.

Maximizing the likelihood of the choices made by the subjects (on a subject-by-subject basis), under the assumptions of the models, enabled the estimation of the individual parameters determining discount rate and utility concavity (Table 1). Analysis of the estimates from model 2 – the hyperbolic discounting of utility model – revealed that subjects discounted the value of future rewards (null hypothesis of no discounting:  $p < .00025$ ) and also that they exhibited diminishing marginal utility for gains (concave, as the mean  $r$  value was greater than zero) (null hypothesis of a linear utility function:  $p < .05$ ). This again proves that the non-linearity of the utility function is a determinant of intertemporal choice.

Comparison of  $K$  values estimated from the SHM and the discounted utility model revealed (using a repeated measures t-test) that  $K$  parameter estimates were significantly greater ( $p < .0025$ ) when estimated using the SHM (mean 0.13 vs. 0.03). This can be attributed to the inherent impulsivity engendered by the concavity of the utility function, which leads to a larger value of  $K$  in the SHM, where temporal discounting is the only determinant of choice (see also Chapter 2) and concavity is not modelled.

Evidence-based model comparison revealed that, in comparison to a number of other influential valuation models, model number 2 (Eq. 4), the hyperbolic discounting of utility model, was the most likely given the data (Akaike weight = .99). This model was significantly better at describing the subjects' choices than a standard hyperbolic model which assumes linear utility (difference in AIC = 34.5),

as well as the other 5 models evaluated (Tables 2 and 3). Paired t-tests were also performed on the individual AIC scores for each model (against all other models) to complement the information-theoretic/Bayesian approach to model comparison, and to ensure group measures were not driven by outliers (Table 4).

Canonical parameter values used in the imaging analysis were  $r = .0089$  and  $K = .0142$ . Note that this value of  $K$  is related to delay in units of weeks and would be equivalent to  $K = .002$  for days. Individual parameter estimates for each subject under each model can be seen in Table 1. The range of estimated parameters was large, as can be seen from the table where, for example, under model 2, the largest estimated  $K$  value was 0.161 and the smallest was 0.0005. However these were outlying values at the extreme tails of the distribution. No significant correlation was found between  $K$  and  $r$  parameters.

Model	1	4	2	2	3	3	6	6	5	5	5
Parameter	$K$	$K$	$K$	$r$	$K$	$R$	$K$	$\beta$	$K$	$R$	$\beta$
Subject											
1	0.0954	0.0379	0.0571	0.0117	0.0322	0.0061	0.0379	0.0001	0.0322	0.0061	0.8182
2	0.0161	0.0122	0.0188	-0.0042	0.0139	-0.0047	0.0122	0.0001	0.0139	-0.0047	0.683
3	0.1358	0.0403	0.0295	0.0328	0.0163	0.0371	0.0403	0.0001	0.0163	0.0371	-0.2897
4	2.326	0.0905	0.161	0.0111	0.0644	0.0165	0.0905	0.0001	0.0644	0.0165	-0.2362
5	0.0233	0.0154	0.0275	-0.004	0.0163	-0.0021	0.0154	0.0001	0.0163	-0.0021	-0.3726
6	0.0232	0.0154	0.0115	0.0152	0.0087	0.0163	0.0154	0.0001	0.0087	0.0163	0.8094
7	0.0023	0.0021	0.0033	-0.0088	0.0031	-0.0088	0.0021	0.0001	0.0031	-0.0088	3.0044
8	0.0005	0.0005	0.0017	0.0097	0.0017	0.0003	0.0005	-7.5916	0.0017	0.0051	1.239
9	0.0124	0.0095	0.0145	-0.0038	0.0105	-0.0029	0.0095	0.0001	0.0105	-0.0029	0.8423
10	0.1946	0.0431	0.1324	0.0056	0.0412	0.0019	0.0431	0.0001	0.0412	0.0019	0.9714
11	0.0402	0.024	0.0256	0.0138	0.0182	0.0118	0.024	0	0.0182	0.0118	0.6969
12	0.0107	0.0082	0.0081	0.0064	0.0065	0.007	0.0082	0.0001	0.0065	0.007	0.8777
13	0.0003	0.0009	0.0012	0.0086	0.0008	0.0088	0.0014	0.0001	0.0002	0.0088	1.1168
14	0.033	0.0196	0.0359	-0.0023	0.0187	0.002	0.0196	0.0001	0.0187	0.002	0.599
15	0.045	0.0255	0.034	0.0102	0.02	0.0129	0.0255	0	0.02	0.0129	0.4518
16	0.0079	0.0064	0.0067	0.004	0.0054	0.0049	0.0064	0.0001	0.0054	0.0049	1.3679
17	0.0431	0.0231	0.0571	-0.0076	0.0233	-0.0004	0.0231	0.0001	0.0233	-0.0004	0.6367
18	0.0013	0.0013	0.001	0.0036	0.0009	0.0036	0.0013	0.0001	0.0009	0.0036	0.8621
19	0.0191	0.013	0.0118	0.0137	0.0087	0.0154	0.013	0.0001	0.0087	0.0154	0.993
20	0.0227	0.0153	0.0385	-0.0133	0.0228	-0.0136	0.0153	0.0001	0.0168	-0.0031	0
21	0.0229	0.0122	0.055	-0.0183	0.014	-0.0057	0.0122	0.0001	0.014	-0.0057	0.6247
22	0.0339	0.0193	0.0265	0.0065	0.0112	0.0211	0.0193	0.0001	0.0112	0.0211	0.3424
23	0.0335	0.0208	0.0328	0.0008	0.0212	-0.0009	0.0208	0.0001	0.0212	-0.0009	0.6767
24	0.0015	0.0015	0.0005	0.016	0.0005	0.0159	0.0015	0.0001	0.0005	0.0159	0.9371
<b>Mean</b>	0.13102	0.01908	0.033	0.00447	0.01585	0.00594	0.01910	-0.3162	0.01558	0.00658	0.7355

**Table 1. Parameter estimates.** The table displays the best fitting parameter estimates for each subject under each model. (Note mean values do not correspond to canonical estimates used in fMRI analyses).

Model number (Eq.)	Sum AIC	Delta AIC	Akaike weight
2,(4) – Hyperbolic discounting of utility	3595	0	1
1,(2) – Hyperbolic discounting of magnitude	3630	35	2.51E-08
4,(6) – Exponential discounting of magnitude	3637	42	7.58E-10
3,(5) – Exponential discounting of utility	3660	65	7.68E-15
6,(8) – Beta delta with magnitude	3685	90	2.86E-20
5,(7) – Beta delta with utility	3709	114	1.76E-25
7 – As soon as possible	4144	549	6.1E-120

**Table 2. Model comparison.** The table displays goodness of fit (summed AIC) and model comparison results for each of the 7 valuation models. (Eq. Refers to the equation numbers listed in the methods).

Model (Eq.)	2 (4)	1 (2)	4 (6)	3 (5)	6 (8)	5 (7)
<b>Subject</b>						
1	96.62	99.58	95.42	95.81	96.92	97.81
2	104.11	103.52	103.52	105.03	105.52	107.03
3	154.74	166.50	167.14	155.22	176.64	157.22
4	186.24	189.76	195.41	199.67	202.41	201.67
5	103.70	105.09	107.59	109.49	109.59	111.49
6	58.11	63.84	65.84	59.52	67.84	61.52
7	45.81	46.52	40.49	45.79	38.49	47.79
8	8.02	10.35	10.35	8.02	12.35	11.06
9	138.25	137.54	136.78	139.96	138.78	141.96
10	94.61	93.98	94.98	96.85	96.98	98.85
11	215.69	215.77	213.55	214.75	212.55	216.75
12	89.97	91.59	91.93	93.17	93.93	95.17
13	69.05	68.68	68.68	69.00	70.68	71.00
14	252.35	250.48	251.69	255.71	253.69	257.71
15	276.14	277.18	272.58	276.48	269.58	278.48
16	133.82	132.57	134.17	135.07	136.17	137.07
17	229.87	228.91	228.07	242.80	230.07	244.80
18	90.03	88.35	88.36	90.03	90.36	92.03
19	231.80	233.64	235.16	233.01	237.16	235.01
20	192.97	197.52	201.10	197.79	203.10	199.79
21	241.90	243.99	246.46	250.98	248.46	252.98
22	238.53	237.55	241.34	242.58	243.34	244.58
23	240.66	238.67	238.71	240.70	240.71	242.70
24	102.36	108.25	108.11	102.36	110.21	104.36
<b>Total</b>	3595.34	3629.80	3637.43	3659.79	3685.53	3708.82

**Table 3. Individual AIC estimates.** The table displays the AIC score for each subject evaluated using each model.

Model (Eq.)	2 (4)	1 (2)	4 (6)	3 (5)	6 (8)	5 (7)
2 (4)	.....	0.037	0.064	0.0032	0.0087	6.05E-06
1 (2)		.....	0.56	0.25	0.019	0.0045
4 (6)			.....	0.37	4.32E-04	0.007
3 (5)				.....	0.41	2.04E-24
6 (8)					.....	0.46
5 (7)						.....

**Table 4. Individual AIC comparisons.** The table displays  $p$  values for t-test comparisons of the individual AIC scores under each model (Table 3). This traditional hypothesis testing of AIC scores was done to complement the Bayesian model comparison techniques.

### *fMRI data*

Brain activity acquired using fMRI during actual task performance was analyzed by constructing parametric regressors to explore the representation of three key quantities during the option valuation phases. The first two quantities were undiscounted utility (which incorporates the non-linear utility function, but ignores time), and the discount factor (the proportion by which utility is reduced in relation to an immediate payoff, i.e. a value between zero and one). The third quantity was discounted utility – the product of the first two, which in statistical terms represents an interaction between utility and discounting. These regressors were generated from the behavioural parameter estimates and orthogonalised with respect to each other. Orthogonalisation was necessary as some regressors were correlated due to the nature of the task where, for the most part, longer delays were associated with larger magnitudes. The discounted utility model (model 2, Eq. 4) was used to create the regressors (see methods).

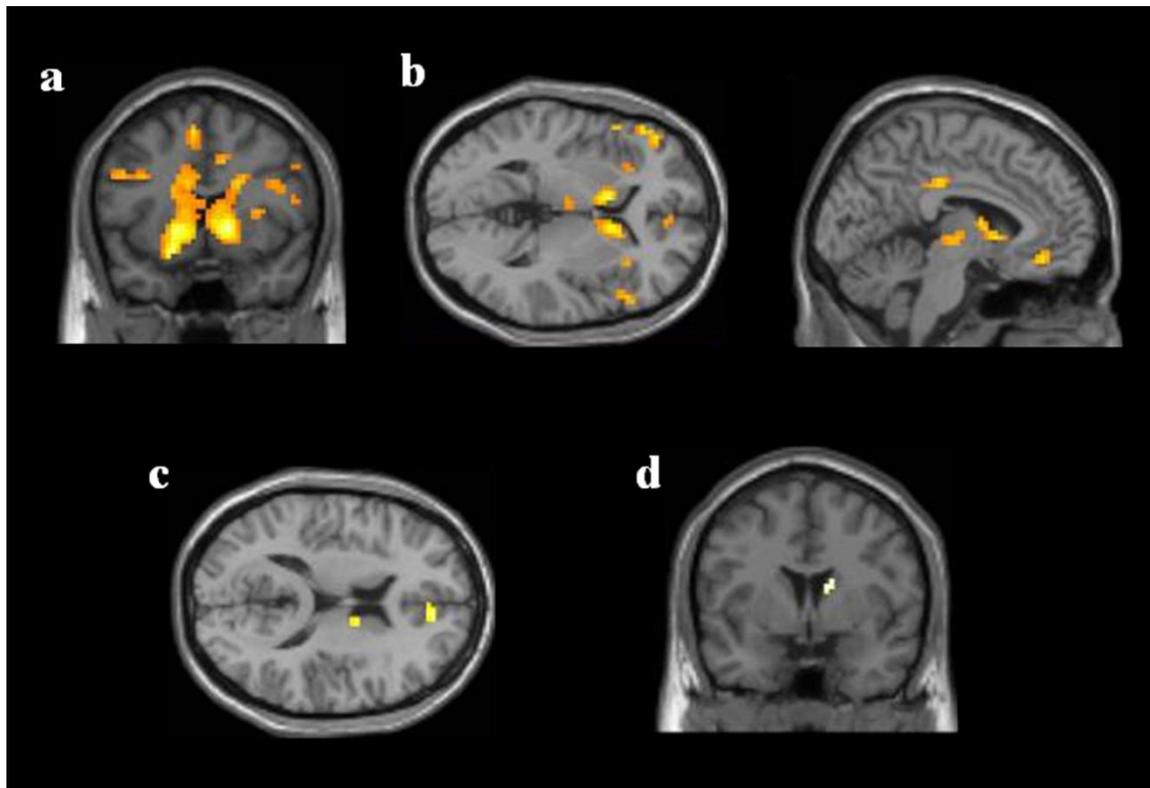
Statistical parametric maps (Figures 3 and 4; Tables 5 and 6) revealed distinct patterns of brain activity associated with each component process aspect of

valuation. Undiscounted utility ( $U$ ) correlated with activity in the striatum, ventral tegmental area (VTA) and anterior cingulate cortex (ACC), consistent with previous findings implicating these regions in the anticipation and receipt of reward (e.g. Breiter et al., 2001; Knutson et al., 2001; Yacubian et al., 2007 – see Chapter 1 discussion on NAc for further references). The discount factor ( $D$ ) correlated with activity in the striatum, insula, posterior and pregenual cingulate cortex, ventromedial orbitofrontal cortex (VMOFC), VTA and inferior frontal gyrus, consistent with, and supplementing previous results from studies of temporal discounting in both animals (e.g. Cardinal et al., 2001, 2004; Kheramin et al., 2002, 2003, 2004; Kim et al., 2008; Kobayashi and Schultz, 2008; Mobini et al., 2002; Roesch et al., 2007b) and humans (e.g. Kable and Glimcher 2007; McClure et al., 2004, 2007; Tanaka et al., 2004 - see also Chapter 1) (see Tables 5 and 6 for comprehensive results).

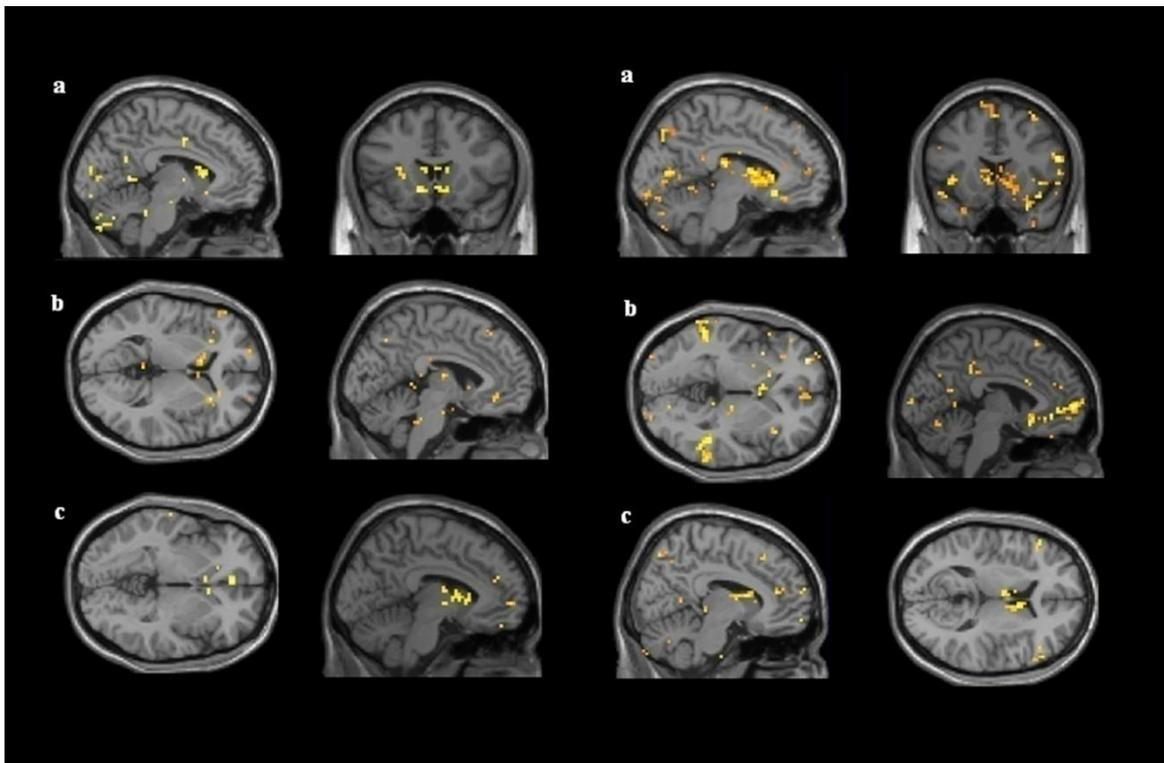
The key analysis, testing for an interaction (i.e. discounted utility,  $V = D \times U$  orthogonalised with respect to  $D$  and  $U$ ), found significant correlates in dorsal striatum and pre-genua cingulate cortex (Figures 3 and 4; Table 7). Critically, this activation in the dorsal striatum incorporated the same anatomical zone that correlated independently with both undiscounted utility and temporal discounting. This is a remarkable finding when one considers the chance probability of getting three significant orthogonal effects in exactly the same brain region is very small. Second, each of these co-localised effects cannot be explained by the other two. This implicates the dorsal striatum in both encoding and possible integration of undiscounted utility and temporal discounting to furnish a discounted utility that plays a critical role in subsequent choice (see Table 7 for comprehensive results).

One potential caveat with respect to these results relates to the orthogonalisation of the regressors. Because  $U$ ,  $D$  and  $V$  have shared variance components,  $V$  was

orthogonalised with respect to  $D$  and  $U$ . This orthogonalisation means we are assigning shared variance to  $U$  (and  $D$ ). This was motivated by the fact that  $V$  is constructed from or depends on  $U$  and  $D$ . However, to ensure that the  $U$  and  $D$  regressors were not modelling any variance attributable to variations in  $V$  (or  $D$ ), the orthogonalisation order was reversed in a second analysis. Importantly, activity in the DS still correlated with all three regressors, though the strength of  $V$  and  $U$  related effects were somewhat swapped when compared to the first analysis ( $V$  activity in striatum resembling the striatal pattern seen for  $U$  in the first regression model). In a further, more conservative analysis, the orthogonalisation step was removed entirely (thus removing any shared variance components) from the regression model. The results of this model revealed that responses in the striatum still correlated with unique components of  $U$ ,  $D$  and  $V$  (Table 8). Thus, these analyses strongly suggest that the striatal responses have three separable variance components that can be predicted by variations that are unique to  $U$ ,  $D$  and their interaction  $V$ . The fact that all three regressors are encoded in the striatum (separately) is consistent with the hypothesis that integration of distinct value components is reflected by activity within the striatum.



**Figure 3. Regions involved in the subjective valuation and integration of objective reward properties (a parametric analysis).** **a.** Correlates of undiscounted utility ( $U$ ) of each option, a concave function of its magnitude **b.** Correlates of the discount factor ( $D$ ) of each option, a hyperbolic function of the delay to receipt of the option. **c.** Interaction of  $U$  and  $D$  affording the (orthogonalised) discounted utility or value ( $V$ ) of the option, used to guide choice. **d.** Dorsal striatum (MNI coordinate and statistical  $z$  score: (15, 3, 18),  $z = 3.26^*$ ) significantly correlated with  $U$ ,  $D$  and  $V$ . These SPMs have been thresholded at  $p < 0.001$  (uncorrected) (for comprehensive results see Tables 5-7). \* Corrected for multiple comparisons (family wise error  $p < .05$ ).



**Figure 4. Single subject SPMs of regions involved in option valuation and integration.** High resolution (4mm smoothed) images of subjects 1 (on the left) and 12. **a.** Regions correlating with the undiscounted utility of each option ( $U$ ) **b.** Regions correlating with the discount factor ( $D$ ) of each option **c.** Regions correlating with the interaction of  $U$  and  $D$  – the discounted utility ( $V$ ) or subjective value of each option.

Comprehensive imaging results for the three analyses depicted in Figure 3 are given in tables 5-7 below. Clusters which were corrected for multiple comparisons (family wise error corrected (FWE)  $p < .05$ ) at the whole brain level, or with small volume corrections are indicated with an asterisk.

REGION	CLUSTER SIZE	MNI COORDINATES	Z VALUE
right occipital cortex / cerebellum	4057* <sup>†</sup>	[15 -78 -12]	5.55
right visual cortex		[12 -96 9]	5.53
left ventral striatum		[-18 9 -15]	5.46
right ventral striatum		[15 12 -3]	5.17
left ventral striatum		[-15 12 -3]	5.04
anterior cingulate cortex		[-6 30 30]	4.4
left putamen / caudate		[-15 9 6]	4.19
ventral tegmental area		[0 -18 -18]	3.91
left occipital cortex	349*	[-30 -96 -9]	5.51
right posterior insula / operculum	30	[30 -24 24]	4.79
left posterior insula / operculum	68	[-30 -30 21]	4.71
left cerebellum	156	[-42 -72 -30]	4.7
right inferior frontal gyrus	75	[45 6 24]	4.63
left postcentral gyrus	199	[-57 -24 48]	4.23
right superior temporal gyrus	41	[-63 -27 6]	4.13
right insula	18	[33 -9 12]	4.02

**Table 5. Regions correlating with undiscounted utility (*U*).** These regions were correlated with the undiscounted utility of each option. These activations correspond to Figure 3a. (<sup>†</sup> This large cluster incorporates all of the regions stated, until left occipital cortex).

REGION	CLUSTER SIZE	MNI COORDINATES	ZVALUE
left inferior temporal cortex	35*	[-57 -51 -15]	5.12
left caudate nucleus	70	[-9 12 0]	4.47
right caudate nucleus	76	[12 12 0]	4.36
left angular gyrus	10	[-42 -60 42]	4.18
right anterior insula	23	[36 27 -3]	4.08
right cerebellum	8	[45 -57 -39]	3.85
right anterior cingulate cortex	22	[9 45 9]	3.85
left subgenual cingulate / medial OFC	20	[-3 42 -12]	3.82
left inferior frontal gyrus orbital part	16	[-42 45 -6]	3.76
left inferior frontal gyrus	24	[-48 42 6]	3.76
left anterior insula	10	[-27 21 -3]	3.73
substantia nigra	9	[3 -18 -18]	3.73
posterior cingulate cortex	13	[-3 -27 33]	3.71
right inferior frontal gyrus	14	[54 24 0]	3.66
right inferior temporal gyrus / sulcus	9	[51 -21 -21]	3.62
right inferior frontal gyrus	21	[-57 21 -3]	3.58
left inferior temporal cortex	13	[-63 -24 -18]	3.52
left inferior frontal gyrus	8	[-51 12 15]	3.5
right laterat orbitofronal cortex	8	[36 36 -12]	3.49
left dorsolateral prefrontal cortex	15	[-54 27 27]	3.47
right dorsolateral prefrontal cortex	6	[54 18 33]	3.42
ventral tegmental area	11	[-6 -15 -3]	3.41

**Table 6. Regions correlating with the temporal discount factor (*D*).** These activations correspond to Figure 3b.

REGION	CLUSTER SIZE	MNI COORDINATES	Z VALUE
left occipital cortex	42	[-21 -99 -9]	4.27
right occipital cortex	30	[15 -81 -9]	4.2
subgenual cingulate cortex	15	[9 45 12]	3.9
right superior temporal / angular gyrus	23	[60 -57 21]	3.58
right caudate nucleus	17	[15 1 15]	3.49
left angular/superior temporal	12	[-57 -54 33]	3.28
left ventral striatum	11	[-9 -3 0]	3.17

**Table 7. Regions correlating with discounted utility (*V*).** These activations correspond to Figure 3c.

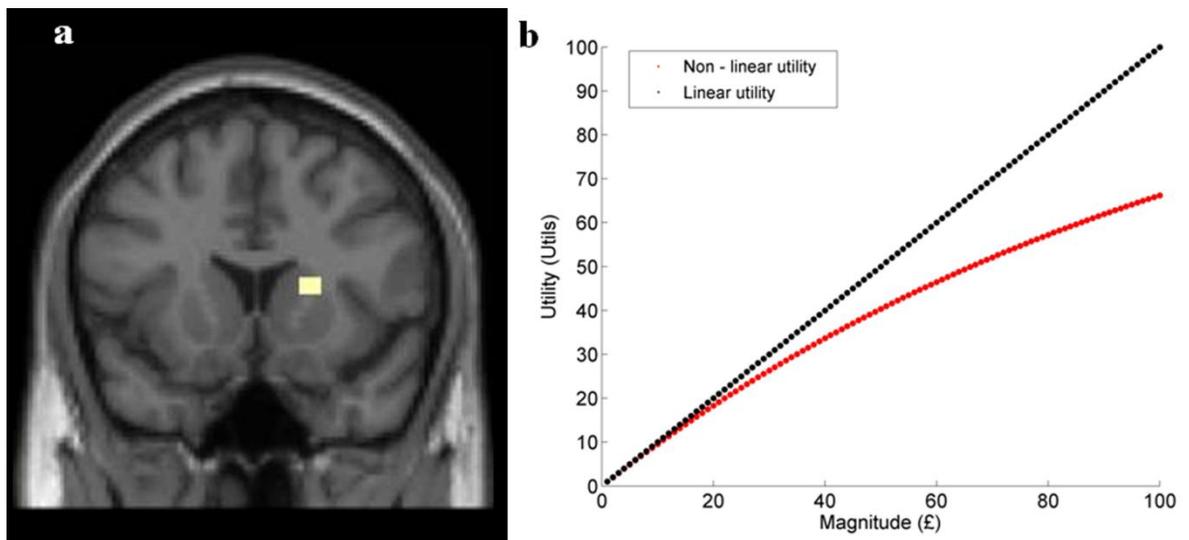
REGRESSOR	CLUSTER SIZE	MNI COORDINATES	Z VALUE
<i>U</i>	5	[18 20 14]	2.58
<i>D</i>	8	[15 24 3]	2.41
<i>V</i>	60	[15 0 15]	3.26

**Table 8. Striatal regions correlating with unique components of *U*, *D* and *V*.** Striatal responses to the regressors in a more conservative regression model where the orthogonalisation step was removed, thus removing any shared variance components from the regressors. (Thresholded at  $p < .01$  due to the strict nature of the model).

In theory, individual differences in utility concavity and temporal discount rates may be seen in the BOLD response of the respective value systems identified, during valuation. To test for this, parametric covariate analyses using the individual  $r$  and  $K$  parameter estimates were performed on the *U* and *D* contrasts; however, no significant correlations were observed, possibly because of the large

range of values (more than an order of magnitude) or noise associated with the single subject parameter estimates from the fitting procedure.

Existing neurobiological evidence of non-linear utility is limited to a previous study (Tobler et al., 2007) which found that learning related neural activity in striatum correlated with subjects' wealth. However, this evidence is based on a fusion of learning theory and marginal utility theory, and leaves open the question as to whether decreasing marginal utility can be detected directly (in response to reward magnitude rather than prediction) on a subject-by-subject basis, and over a range of rewards – as opposed to just observing that wealthier subjects have *generally* lower reward prediction activity. To investigate more directly the representation of basic utility at an individual level, an analysis was performed to assess whether the neural representation of utility in the striatum was better correlated with values generated from the (concave) utility function (Eq. 3), or simply magnitude. Consequently, actual magnitude ( $M$ ), was included as an extra regressor in the original linear model, and the utility regressor ( $U$ ) was orthogonalised with respect to  $M$ . Within this model, the representation of utility ( $U$ ) still correlated with activity in the dorsal striatum (Figure 5). This finding suggests that the dorsal striatum specifically encodes the utility of a good over-and-above that which can be described by its objective value, thereby offering direct neural evidence for the non-linearity (concavity) of subjective instantaneous utility.



**Figure 5. The neural encoding of marginal utility and its diminishing nature (statistical parametric maps and example of regressors).** **a.** Activity in the dorsal striatum correlated with the undiscounted utility of rewards ( $U$ ) over and above its correlation with their objective magnitude ( $M$ ) i.e. a non linear effect of magnitude. A peak was found in the right dorsal caudate (MNI coordinate and statistical  $z$  score: (19, 15, 13),  $z = 3.29$ ).  $U$  was orthogonalised with respect to  $M$  in the regression to isolate the nonlinear or concave aspects of the predictor variable. **b.** Example of regressors used in **a.** Black dots ( $M$ ) show the subjective value of rewards ranging from £1-100 under the assumptions of a linear utility function, while red dots indicate the utility ( $U$ ) of the same magnitudes, calculated using a utility function (Eq. 3) and a canonical estimate of subjects'  $r$  – the concavity (.009).

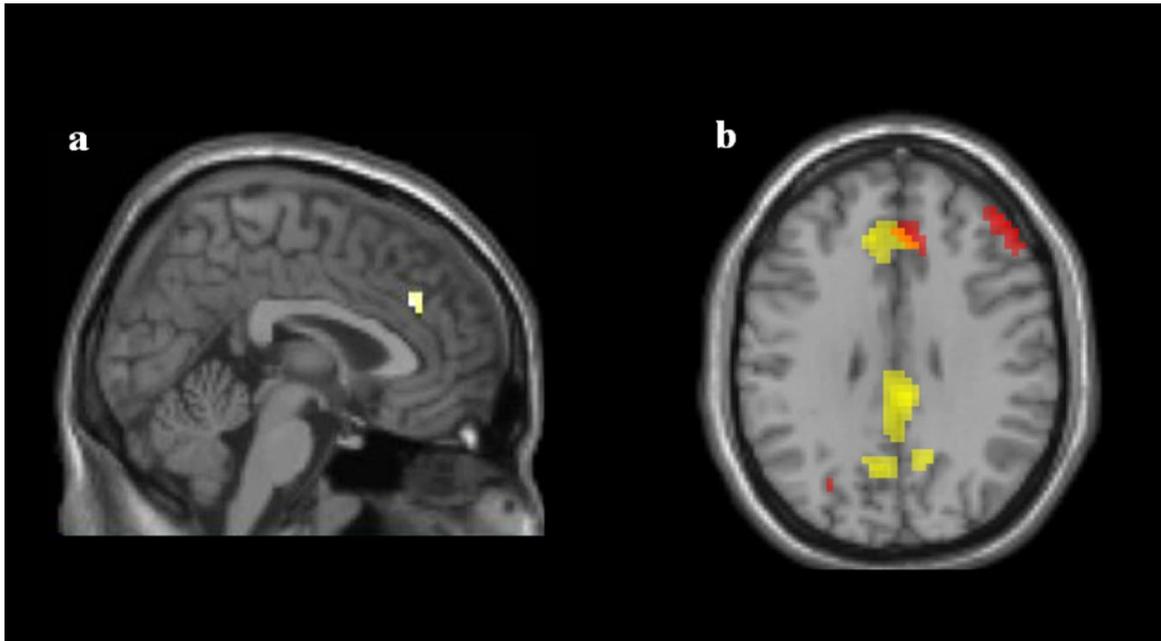
An important aspect of the discounted utility model is that it makes clear predictions regarding choice difficulty. Under the assumption that difficult choices – engendered by a small difference in discounted utility ( $\Delta V$ ) between two options – induce conflict and take longer to make, the model predicts which choices should induce a greater reaction time (decision latency) and more neuronal activity in conflict areas. Consequently, an analysis was performed to test at a behavioural and neural level for these effects. Such an effect was evident from choice latencies, where reaction times were significantly longer in cases where  $\Delta V$  was small ( $p < .00005$ ) i.e. a negative correlation was observed. Furthermore, it was conjectured that in addition to differences in discounted utility ( $\Delta V$ ), greater difficulty would

be incurred by options that were separated more in time. Consistent with such a 'dissonance effect', the analysis revealed that reaction times were also slower when the difference in discount factor ( $\Delta D$ ) was large ( $p < .05$ ), independent of (i.e. orthogonal to)  $\Delta V$  (see methods).

The corresponding fMRI regression tested for brain regions that correlated with both difficulty indices ( $\Delta V$  and orthogonalised  $\Delta D$ ) at the time of choice – that is during the third phase of the trials, where choice was prompted. This revealed correlates in the anterior cingulate cortex (Figure 6; Table 9), suggesting a distinct role for this region in intertemporal choice and response selection. More specifically, a network of conflict and effort related regions including the ACC, insula and DLPFC (see Botvinick, 2007; Botvinick et al., 2004; Pochon et al., 2008) was increasingly activated in response to diminishing difference in overall value, suggesting (alongside the RT data) that choices where options are close in value are more difficult and induce conflict. Furthermore, large differences in delay to each option of a choice also activated some of these conflict areas – irrespective of difference in overall value – in addition to some posterior regions including the PCC and precuneus. This is important in light of a previous finding in which ACC lesions in rodents had no effect on this task (Cardinal et al., 2001). In addition, an inter-subject covariate analysis showed that activity in ACC and DLPFC covaried with the degree to which choice latency was affected by  $\Delta V$ , whereby subjects whose latencies were more affected by difficulty (that is they slowed down more, as measured by the betas from the reaction time regression – see methods) also showed greater activity in ACC in response to increasing difficulty (Table 9).

Drawing on previous insights on the function of this region (e.g. Botvinick, 2007; Botvinick et al., 2004; Bussey et al., 1997; Cohen et al., 2005; Kennerly et al., 2006; Pochon et al., 2008) in decision-making, and on anatomical studies of its connectivity, would suggest that it adopts a regulatory or monitoring role with

respect to the integrative function of the dorsal striatum. It is likely to inhibit behavioural selection and promote continuing effortful evaluation. However, the impact of this function on actual choice behavior (if any) remains to be determined.



**Figure 6. Choice difficulty: The intertemporal dissonance effect.** **a.** Regions that correlated significantly with choice difficulty as measured by closeness in discounted utility between the options ( $\Delta V$ ) and also with difficulty as measured by difference in discount factor (and thus delay) between options ( $\Delta D$ ). Activity here increases as  $\Delta V$  gets smaller and  $\Delta D$  increases. Peak activations (MNI coordinates and statistical  $Z$  scores) are: anterior cingulate cortex (ACC) ((3, 33, 30),  $z = 3.64^*$ ). Activity in the ACC also covaried with the degree to which behaviour (choice latency) was affected by difficulty (as measured by  $\Delta V$ ) across subjects ((12, 39, 33),  $z = 3.64$ ). **b.** Regions correlating with ( $\Delta V$ ) alone (in red) and ( $\Delta D$ ) alone (in yellow). Orange (overlap) area correlated with both and corresponds to the region in **a.** (See Table 9 for comprehensive results). \*Corrected for multiple comparisons (family wise error  $p < .05$ ).

REGION	CLUSTER SIZE	MNI COORDINATES	Z VALUE
<b>A</b>			
motor / anterior cingulate cortex	108	[6 21 51]	4.88
right dorsolateral prefrontal cortex	101	[51 42 18]	4.86
right frontal pole	40	[30 60 9]	3.97
right anterior insula	34	[33 21 -9]	3.80
right anterior cingulate cortex	32	[6 36 27]	3.78
right supramarginal gyrus	7	[48 -36 45]	3.44
left anterior cingulate cortex	6	[-9 33 21]	3.44
<b>B</b>			
right dorsolateral prefrontal cortex	9	[54 15 12]	3.75
right anterior cingulate cortex	10	[12 39 33]	3.64
<b>C</b>			
posterior cingulate cortex	205	[0 -30 36]	5.07
anterior cingulate cortex	90	[-9 33 30]	4.4
left precuneus	31	[-6 -63 30]	4.15
left cerebellum	52	[-36 -69 -39]	4.09
right cerebellum	65	[39 -78 -36]	4.04
superior temporal gyrus	30	[-60 -27 -18]	3.93
right precuneus	17	[15 -60 30]	3.88
left anterior insula	21	[-39 18 -12]	3.79
right frontal pole	5	[33 57 -3]	3.49
right motor cingulate	13	[6 45 36]	3.39

**Table 9. Regions correlating with choice difficulty.** **A.** Regions correlating with difference in discounted utility  $\Delta V$  (red areas). **B.** Regions correlating with  $\Delta V$  which covaried with reaction time (decision latency) parameters on a subject-by-subject basis. **C.** Regions correlating with  $\Delta D$  (yellow areas). These activations relate to the data presented in Figure 6.

## Discussion

In summary, these data provide both direct behavioural and neurobiological support for marginal utility theory in the context of a choice model that incorporates temporal discounting. Furthermore, the results suggest that the dorsal striatum may act as a site of convergence of these two systems – so as to construct the discounted utility that plays an important role in guiding subsequent choice.

### *Behavioural data*

Results from the behavioural data indicated again that most subjects have concave utility functions, exhibiting diminishing marginal utility, and that this concavity is therefore a determinant of choice. Furthermore, the SHM once again misattributed this effect, resulting in much greater estimates of the discount rate. As realistic choices were used in this study, it also extends the findings from the adjusting delay task where the effect was observed in the hypothetical domain. The realistic nature of the task was likely responsible for superior performance as measured by correct responses on catch trials (subjects were not paid for mere participation). This suggests realistic task designs are preferable and lead to more accurate data.

The maximum likelihood estimation procedure was successful in allowing for a new methodology to estimate  $K$  and  $r$  parameters in intertemporal choice, and validating the discounted utility model. In addition, this fitting procedure gives estimates of fit in the form of likelihoods. The model comparison techniques showed that irrespective of model complexity, the discounted utility model was better in accounting for subjects' choice behaviour than the SHM. Furthermore, it was superior to a number of other influential models which have been proposed in the literature, such as the beta-delta (Laibson, 1997; McClure et al., 2004) and the as-soon-as-possible model (Kable and Glimcher, 2007; Myerson and Green, 2005) –

even when modifying those models to factor in the non-linearity of utility. This suggests that the hyperbolic form for temporal discounting is still the most accurate description and better than the two-parameter or quasi-hyperbolic models such as the beta-delta.

While the adjusting delays procedure excels in some respects, here a new paradigm for intertemporal choice was designed, where reliance on indifference points was not necessary. This paradigm allows for greater control over the amounts and delays used in the choices, which is important to consider in fMRI designs. Additionally, the random nature of the sampling rules out any confounds from order effects which one must normally account for in indifference point tasks. Finally, the model comparison technique (AIC) based on likelihoods conveniently solves the problem of model complexity. This remains a problem for indifference paradigms, where  $R^2$  values are typically used to compare models (e.g. Bickel et al., 2007; Green and Myerson, 2004).

Additionally, by calculating the difference in discounted utility of the two options (using subjects' parameter estimates) the model proved accurate in being able to predict which choices the subjects would have found to be more difficult. As predicted, closeness in option value engendered decision-conflict as measured by a slowing down in decision latency. This is consistent with the idea that decision-conflict arises from closely valued options (e.g. Botvinick, 2007; Pochon et al., 2008). Surprisingly, irrespective of this measure of difficulty, analysis of the latencies also revealed that difference in delay of the options engendered conflict, whereby choices whose options were far apart in time further slowed down decision-making latency. Note, these results do not add further proof for the veracity of the model over the SHM. The SHM would likely predict choice difficulty as measured by difference in discounted magnitude, which would be fairly similar. However, the discounted utility model is presumably more accurate

in estimating difficulty because it also factors in non-linear utility which will contribute to differences in value of the two options.

### *Imaging data*

One of the main purposes of this study was to attempt to corroborate the new intertemporal choice model using brain imaging data. If a model accurately describes behaviour it should also describe the neural processes underlying it. Consistent with the model, BOLD responses measured during option valuation demonstrated that the brain evaluates delayed rewards in an integrative fashion; first estimating the instantaneous or undiscounted utility of rewards with a system which relates subjective value to the magnitude dimension, and separately, with a system which evaluates the subjective, present value of rewards based on their delay, to calculate a discount factor. This is consistent with the separation of  $D$  and  $U$  in the model. Finally, to estimate the overall value ( $V$ ), a further network of regions encodes the integrated value of these sub-components. This value is then used to guide decisions. Critically, it was demonstrated that the dorsal striatum is the site where information from the individual value systems is integrated and represented. This is a novel idea since it assumes a much more complex role for the striatum than has been previously assumed. Previously, such complex calculations would have been thought to take place in higher centres such as the orbitofrontal cortex (Kalenscher et al., 2005, who propose based on pigeon neurophysiological studies that integration takes place in OFC, however see Roesch et al., 2007a and Chapter 1).

Although OFC has been implicated in intertemporal choice, both in animals (e.g. Kalenscher et al., 2005; Kehramin et al., 2002, 2003, 2004; Mobini et al., 2002; Roesch et al., 2007a; Rudebeck et al., 2006; Winstanley et al., 2004b) and in some human

studies (e.g. McClure et al., 2004, 2007; Tanaka et al., 2004 see also Chapter 1 review of fMRI studies) but not all (Fellows and Farah 2005; Kable and Glimcher, 2007), relatively little activity was observed there in this study, in relation to other regions. Instead, more medial regions of the PFC were found to correlate with overall value, and lateral regions of the OFC with the discount factor. This could be due to differences in what is considered to be the rat and human OFC, parametric versus non parametric analyses, difficulty in detecting BOLD response in the region due to signal dropout, or a role for the OFC in *learning* as opposed to valuation of delayed rewards (e.g. Roesch et al., 2007a). However, in Chapter 4 activity was observed more ventrally, in the OFC proper.

The striatum has been identified in previous studies of temporal discounting in both animals (Cardinal and Cheung, 2005; Cardinal et al., 2001; Kobayashi and Schultz, 2008; Roesch et al., 2007b – see Ch. 1), and humans (Ballard and Knutson, 2009; Kable and Glimcher 2007; Luhmann et al., 2008; McClure et al., 2004, 2007; Tanaka et al., 2004, 2007; Wittmann et al., 2008) and less directly, in marginal utility (Tobler et al., 2007). In humans, activity has been shown to correlate with preferences for immediate options (McClure et al., 2004), and for discounted magnitude across both immediate and delayed options, over short (Tanaka et al., 2004) and long timescales (Kable and Glimcher, 2007). However, the exact nature of this signal has been unclear, including whether it merely reports on value calculations, or their prediction errors, performed elsewhere (Luhmann et al., 2008; Tanaka et al., 2004, 2007). For instance, the well-recognised role of this region in reinforcement learning (Haruno and Kawato, 2006; O'Doherty et al., 2004; Robbins et al., 1989; Seymour et al., 2004) does not necessarily speak to a role in constructing value and choice. The data presented here advance these insights and support a broader and more sophisticated role for this region than previously

thought, wherein choices are determined by an integration of distinct determinants of value.

These imaging data results are significant in being the first to delineate distinct neural systems for the valuation of different reward dimensions. Temporal discounting has been relatively well studied in fMRI. The main debate here is whether separate systems value immediate versus delayed options. Many imaging studies have employed such an analysis, without reference to behavioural data. McClure et al. (2004, 2007) were the first to demonstrate that limbic areas were preferentially active in response to rewards with an immediate component. This observation was proposed to corroborate a dual-self type model of choice where a deliberative (exponential) discount system is instantiated in cortical cognitive areas such as DLPFC and is activated in evaluating all reward types, in addition to an irrational, affective system instantiated in limbic areas such as the striatum and OFC, becoming active in response to immediate rewards and placing a special value on them (the  $\beta$  in the beta-delta model). This notion came under heavy criticism from Kable and Glimcher (2007), who argued that their conclusions were not valid because of the way they chose to model their data. To demonstrate this, they correlated brain responses with the actual discounted magnitude of rewards. Critically, these estimates were derived from subjects' behaviourally derived discount functions, using the standard hyperbolic model. They found that activity in the striatum, PCC and medial PFC tracked the discounted magnitude of all rewards, regardless of delay. McClure et al. simply found greater activity in those regions in response to immediate rewards because those rewards would have had greater discounted magnitude values. In their study, Kable and Glimcher provided the first demonstration of hyperbolic-like discounting in the brain.

The results described here go a stage further. Kable and Glimcher argue for a single subjective valuation process subserved by a single neural value system

whereas these results reveal a hierarchical integrative process. The results here are consistent with Kable and Glimcher, in that the striatum and medial PFC (subgenual cingulate) track the overall value of rewards (discounted utility in this case), however, they also demonstrate a discrete and expanded network of regions that specifically encode the discount factor, comprising additional regions such as the insula, ACC, inferior frontal gyrus and superior temporal cortex, in addition to the striatum, PCC and mPFC. Thus, these results demonstrate (hyperbolic) temporal discounting at the most fundamental level in the brain, not just correlates of overall value which of course are related. These regions form a system specifically engaged by delay. To illustrate the difference, one could argue, for example, that the posterior cingulate cortex activity reported by Kable and Glimcher, was actually related to a discount system rather than an overall value system – as is apparent from this study where it only correlated with  $D$  and not  $V$ . Furthermore, this is demonstrated without the confound of non-linear utility, which Kable and Glimcher did not take into account. Additionally, the serial design of the task ensured that no relative valuation processes or decision-making processes were being engaged (at least for the first option) which was a possibility in the simultaneous presentation design of previous studies.

Activity of the ACC, insula and inferior frontal regions in response to reward proximity is notable as it may underlie self-control or effort required to hold back from making responses to nearer options (Ballard and Knutson, 2009; Wittmann et al., 2007). The inferior frontal gyrus is also implicated in behavioural response inhibition (e.g. Aron and Poldrack, 2005; Aron et al., 2004; Chamberlain and Sahakian, 2007) and grey matter volumes there have been found to inversely correlate with discount rates (Bjork et al., 2009). One surprising finding was that activity in regions of the superior and inferior temporal gyrus and the angular gyrus correlated markedly with  $U$ ,  $D$  and  $V$ . There is no a priori reason which

explains these findings however the angular gyrus, particularly on the left has been associated with mathematical calculation (Grabner et al., 2007, 2009). Such activity (which has previously been observed in intertemporal choice – see Chapter 1) could represent the conscious calculations made by subjects during the task; the role of this region should be further explored.

The exact nature of the representation of temporal discounting remains unclear (Ballard and Knutson, 2009; Wittmann and Paulus, 2008). Superficially, the diminished utility associated with increasing time has strong parallels to probability discounting, and indeed some theoretical accounts of temporal discounting propose just this: that uncertainty, for instance through unexpected occurrences that might interfere with reward delivery, accumulates with time (Stevenson, 1986; see also Chapter 1). However, recent neurophysiological evidence suggests that uncertainty and temporal discount factors may be, at least in part, distinct (Luhmann et al., 2008). Furthermore, that the BOLD activity correlates with a single parametric regressor does not in itself imply that it is driven by a single neural determinant, since distinct psychological processes (such as the utility of anticipation or anxiety, Lowenstein, 1987; Wu, 1999) and neurochemical processes (such as 5HT and DA; Roesch et al., 2007b; Tanaka, 2007) may make independent contributions. One factor arguing against a shared mechanism for probability and temporal discounting is the observed correlation between insula activity and reward proximity ( $D$ ). Increased activity in the insula has also been frequently observed in response to increasing risk (Kuhnen and Knutson, 2005; Singer et al., 2009; Preuschoff et al., 2008). However, if the increase in risk associated with delay is a cause of temporal discounting, the expected correlation between the discount factor and insula activity should manifest inversely, with greater activity for delayed as opposed to proximate rewards. Indeed, Ballard and Knutson (2009) came to the same conclusion regarding their

observed insula activity to increasing temporal proximity. This separation of delay and probability discounting also accords with evidence from behavioural studies (Green and Myerson, 2004).

The analysis here supports Kable and Glimcher (2007), that there is no separate treatment/valuation of near and far rewards, although it also differs in that it supports individual systems for the evaluation of delay and magnitude, as well as a separate representation of overall value. This distinction is an important one, as noted by Roesch et al. (2007a) who came to similar conclusions based on single unit recordings in rats. They observed neurons whose activity decreased as rats waited for reward over a delay, but crucially, although they encoded this temporal discounting, they were not sensitive to the reward magnitude. Therefore, they argue that overall value must be encoded by an integration of discounting and magnitude in some other region (see Chapter 1). Further, the delay and overall value systems identified here differ somewhat from the single-value system identified by Kable and Glimcher, as mentioned above. The analyses carried out did not test the idea of Tanaka et al. (2004) that different loops (dorsal-ventral) within the striatum are involved in valuing sooner versus later rewards, so this remains a possibility. Again, the results here support Kable and Glimcher (2007) and not McClure et al. (2004) in that there are no impulsive versus patient decision-making systems and therefore activity in limbic regions is not related to more impulsive choice in this regard. Choice, according to this thesis, is based on the discounted utility of each option, which corresponds to activity in the *V* regions.

The second system identified, for evaluating the (marginal) utility of rewards, is a major finding – given the importance of this economic concept and that no neurological basis has previously been described for the law of diminishing marginal utility. A previous study has shown that the strength of reward prediction error signals in the striatum correlate inversely with the wealth of

subjects (Tobler et al., 2007), but this is indirect evidence which depends on the complexities of learning theory and is far removed from the original concept. Here, it was shown that an area of the dorsal striatum correlated with the utility of rewards ( $U$ ) (as calculated using Eq. 3), even when any variance attributable to the (linear) magnitude of those rewards was factored out using orthogonalisation. It is likely that other regions may also encode marginal utility but were 'lost' by the strict orthogonalisation process which was necessary to demonstrate that the regions were not simply encoding magnitude (which was obviously highly correlated with utility). Figure 3a demonstrates the much larger activations which correlate with ( $U$ ) when magnitude was not orthogonalised.

This comprehensive account of the systems involved in intertemporal choice also helps to clarify which regions are important for the understanding of impulsivity, from the perspective of both its possible determinants. This could help to better understand disorders featuring impulsivity as a symptom, based on the known brain abnormalities in these disorders (Chapter 1). Unfortunately, none of the activations observed during valuation were found to covary with subject-by-subject estimates of the discount rate or utility concavity, so the basis for individual differences in both types of discounting remains to be determined. Activity in the OFC was observed to correlate with subject scores on a relevant subscale of the BIS (data not presented), however BIS scores did not correlate with discount rates (for time or magnitude).

When comparing different valuation models, hyperbolic discounting of utility was found to be the best model for describing the behavioural data. However, due to constraints in the design of the study, fMRI data were not able to make such inferences regarding the likelihood of the different models (although they do demonstrate that models incorporating non-linear utility have more validity – based on the DS utility observation). The regressors used to analyse the imaging

data were created only from the new model proposed, which was also selected by the AIC analysis; and so these fMRI results may not be independent of the model used (e.g. exponential vs. hyperbolic). Further studies are anticipated which aim to assess the validity of these models using fMRI data, although this is challenging.

From a behavioural and economic perspective, neglecting non-linear utility has the potential to confound inferences about discounting since any model could over-estimate the discount rate to account for marginal utility effects. Indeed, discount rates were higher when estimated by the SHM than by the discounted utility model, confirming a similar finding in the adjusting delay task, and in a study where gambles were used to elicit utility functions which were then applied to temporal discounting data (Andersen et al., 2008). A similar argument could apply to the neurophysiological data. Future fMRI studies should take this into account.

As discussed in Chapter 2, choice outcome has previously been thought only to be determined by temporal discounting – as axiomatized in the standard hyperbolic model – leading to the view that impulsivity in choice and temporal discounting are one and the same process (e.g. Ainslie, 1992, 2001). Taking into account the effects of the non-linearity of utility adds another dimension and determinant of impulsivity in choice whereby individuals with more concave functions are more impulsive, as well as those with high discount rates. Therefore, impulsivity in choice should not solely be defined by  $K$ . Moreover,  $K$  and  $r$  should be kept separate as there is no theoretical reason why the discounting of time and of magnitude (two different features of preferences) should influence each other. Although it has been suggested that such a correlation may exist (Anderhub et al., 2001), it was not observed in these data, and previous attempts to find a correlation by simultaneously administering risk preference (to estimate  $r$ ) and intertemporal choice (to estimate  $K$ ) tasks have been mixed (Ahlbrecht and Weber, 1997;

Anderhub et al., 2001). According to the integrated model presented here, it is perfectly possible that a person with a high discount rate but a close to linear utility function is as behaviourally impulsive as a counterpart with a low discount rate but a more concave function – although both parameters will correlate with impulsiveness, individually. Future studies of impulsive choice should therefore consider these determinants when hypothesizing about the underlying cause of a change in intertemporal choice behaviour across experimental conditions. These considerations have an important bearing on studies of psychopathologies where impulsive choice is a central clinical feature, such as drug addiction (e.g. Bickel and Marsch, 2001; Bickel et al., 2007; Cardinal et al., 2003, 2004) and attention-deficit hyperactivity disorder (Sagvolden and Segeant, 1998; Winstanley et al., 2006a), particularly since dysfunction of the striatum is implicated in both conditions (Chapter 1).

One of the useful aspects of the model is the ability to calculate utility functions from intertemporal choices. Previous methods to construct utility functions have mostly used risk preference tasks such as simple gambles. Some of these studies suggest that the average utility function derived from risk-preference tasks is (in the context of a power law utility function) magnitude to the power of 0.88 (Tversky and Kahneman, 1992). This value leads to a slightly more concave utility function than that observed in this task. This discrepancy may have arisen from natural variance of the population, or the range of magnitudes used to characterise the function (£1-£100) in this study vs. a larger hypothetical or smaller real range of amounts, used in other studies. It is also likely that the realistic nature of the study (real amounts paid with real delays) leads to differences from previous estimates, where, for the most part, hypothetical choices were made. Alternatively, utility concavity estimates derived from intertemporal choices may differ from those derived from gambles (see Ch. 5).

Finally, the results bear relevance to a related, but distinct personality trait – that of decisiveness. When people have to make choices between similarly valued options, decision-conflict can occur. Decision-conflict often leads to a slowing down of responses and an increase in activity of conflict areas such as the ACC (e.g. Botvinick et al., 2004; Botvinick, 2007; Cohen et al., 2005; Kennerly et al., 2006; Pochon et al., 2008). Whilst this phenomenon is relatively well studied in lower level, perceptual and motor decision-making tasks, it is less well characterized in higher level tasks (Pochon et al., 2008). Here, it was shown that decision-conflict occurs in intertemporal choice, and that it can be engendered by choosing between similarly valued options but also options that are far apart in time (independent of difference in value). Furthermore, conflict regions including ACC were activated in response to decision conflict and this activity correlated with the degree to which individual subjects were slowed down by choice difficulty. This suggests that the psychological trait of decisiveness may be predicted by or relate to an individual's degree of ACC activity. One possible function of the ACC could therefore be to inhibit choice so as to be able to give proper and effortful consideration to each option. Such an account accords with previous reports of motor impulsivity or disinhibited responding in ACC lesioned rats, which have been found to over-respond to unrewarded stimuli and to respond prematurely in situations where they are required to wait (Bussey et al., 1997; Parkinson et al., 2000).

Interestingly, when looking at neural responses to difficulty as measured by difference in delay alone; strong activity was observed bilaterally in the precuneus and posterior cingulate. This area of the posteromedial parietal cortex has been identified in another intertemporal imaging study (Bickel et al., 2009) and has been identified in tasks requiring imagery, first person perspective taking, episodic memory retrieval and agency (Cavanna and Trimble, 2006). One speculative conclusion regarding this activation is that deciding between sooner and later

rewards requires the decision-maker to imagine his/her future self and how that self would perceive the receipt of the reward, requiring a change of perspective. This idea chimes with some of the original thoughts about time preference of von Böhm-Bawerk (1889) (see Chapter 1) who argued that humans suffer from a systematic tendency to underestimate or an inability to imagine future wants – “we limn a more or less incomplete picture of our future wants and especially of the remote distant ones”. Viewing the problem of discounting as being one of how we represent and think about future outcomes has wide currency. Becker and Mulligan (1997), for example, argue that the discount rate is a function of the resources invested in imagining the future. In their model, decision makers maximize lifetime utility subject to difficulties in envisioning exactly how rewarding the future will be. Hence, they will expend resources to make their image of the future vivid and clear. Basing this particular imaging result on these theories is of course rather speculative.

## Chapter 4.

# The involvement of dopamine in intertemporal choice and impulsivity

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### Introduction

The previous studies established the veracity and importance of using the integrated model of intertemporal choice, as well as its neural implementation. The purpose of this study was to demonstrate its practical uses in experiments where a manipulation is carried out – specifically, to determine the role of the neurotransmitter dopamine in intertemporal choice behaviour. There have only been a handful of studies using pharmacological manipulation in human intertemporal choice experiments – none have attempted this technique in combination with fMRI. This study took advantage of the fMRI methodology and results discussed in Chapter 3, to assess not only dopamine's effect on behaviour, but also on brain activity during choice. It was hypothesized that any effect of dopamine manipulation on choice should also be observed in the brain, and that the two forms of independent evidence should support each other. Additionally, a small pilot study was carried out along-side, using data from a relevant patient group.

Disordered dopamine neurotransmission is implicated in a range of disorders that have impulsivity and lack of self-control as core features, such as substance addiction and pathological gambling (e.g. Berridge, 2007; Dagher and Robbins, 2009; Dayan, 2009; Everitt et al., 2001, 2008; Hildebrand et al., 1998; Koob, 1992; Koob et al., 1998; le Moal, 2009; Robinson and Berridge, 2000, 2008; Volkow and Li,

2004, 2005; Volkow et al., 2008, 2009; Wise, 2008), mania (e.g. Gerner et al., 1976; Stahl, 2002), attention-deficit/hyperactivity disorder (e.g. Arnsten, 2006; Pattij and Vanderschuren, 2008; Sagvolden and Sergeant, 1998; Solanto, 1998, 2002; Sonuga-Barke, 2002, 2003; Swanson and Volkow, 2009; Winstanley et al., 2006a), and the dopamine dysregulation syndrome (DDS) seen in Parkinson's disease (Dagher and Robbins, 2009; Evans and Lees, 2004; Merims and Giladi, 2008; O'Sullivan et al., 2009). In the latter instance, dopamine agonist therapy in PD renders some patients (4%) prone to compulsive gambling, compulsive shopping and eating, hypersexuality and other short-sighted behaviours (e.g. Cools et al., 2003; Dagher and Robbins, 2009; Giladi et al., 2007; Ondo and Lai 2008; O'sullivan et al., 2009; Weintraub et al., 2006). However, the broad phenotype of impulsivity which characterizes these behaviours, subsumes a diversity of distinct decision-making processes (Evenden, 1999a; Ho et al., 1999; Moeller et al., 2001, see Chapter 1) including lack of inhibition of prepotent motor responses, overweighting of rewards relative to losses, a propensity to choose smaller-sooner over larger-later rewards (e.g. Ainslie, 1992, 2001; Cardinal et al., 2004; Evenden, 1999a; Herrnstein, 1981; Ho et al., 1999; Logue, 1988; Mazur, 1987) and a failure to slow down in the face of decision-conflict so as to adequately consider available options when faced with a difficult choice (Clark et al., 2006; Evenden, 1998, 1999a; Frank et al., 2007; Kagan, 1966). In principle, some of these deficits can be related to a dopaminergic effect by way of its well established role in reward learning (see Dagher and Robbins, 2009; Frank et al., 2007; Redish, 2004). However, temporal impulsivity (the preference for smaller-sooner rewards, due to excessive discounting of future rewards) is much harder to account for in these terms, although it remains an important feature of putative dopaminergic impulsivity. Indeed, laboratory tests of intertemporal choice reveal that addicts (e.g. Bickel and Marsch, 2001; Bickel et al., 2007; Madden et al. 1997, 1999 – see Chapter 1) and a sub-group of ADHD patients (e.g. Sagvolden and Sergeant, 1998; Sonuga-Barke, 2002, 2003; Winstanley et al.

2006a – see Chapter 1) are more impulsive in choice and have abnormally high discount rates. This poses the question of whether dopamine has a specific role in computing how the temporal proximity of a reward relates to its subjective value (i.e. temporal discounting), independent of an established contribution to reward learning.

A consensus has started to emerge in the literature that reduced dopamine function can lead to greater impulsivity (e.g. Cardinal et al., 2004; Dagher and Robbins, 2009; de Wit et al., 2002; Pattij and Vanderschuren, 2008; van Gaalen et al., 2006; Wade et al., 2000; Winstanley et al., 2006a). This view initially stemmed from the finding that psychostimulants such as methylphenidate and amphetamine, which act to boost activity of monoaminergic neurotransmitter systems including dopamine (e.g. Feldman et al., 1997; Koob and Bloom, 1988; Kuczenski and Segal, 1997; Ritz and Kuhar, 1989; Rothman et al., 2001; Seiden et al., 1993; Sulzer et al., 1995), are effective treatments for ADHD (Bradley, 1937; Porrino et al., 1983; Solanto, 1988; Spencer et al., 2001). This led to the proposal that certain forms of ADHD are characterized by extreme discounting which is in turn caused by a hypofunctioning mesolimbic DA system and which can be ‘normalized’ by psychostimulants (Sagvolden and Sergeant, 1998; Sagvolden et al., 1998; Johansen et al., 2002). However, this view is not without controversy; whether ADHD is characterized by a hyper or a hypodopaminergic state is strongly debated (Seeman and Madras, 1998, 2002; Solanto, 1998, 2002; Swanson et al., 1998; Zhuang et al., 2001), furthermore, the actions of amphetamine and methylphenidate in relation to dopamine function in this disorder are extremely complex, with some arguing that these medications could actually reduce DA function (Seeman and Madras, 1998, 2002; Solanto, 1998, 2002). Indeed, the paradox of using psychostimulants to treat ADHD has often been noted (e.g. Dagher and Robbins, 2009; Seeman and Madras, 1998, 2002). In addition, many of the observations leading to the hypothesis were

based on the spontaneously hypertensive rat model of ADHD or dopamine transporter knockout mice, which exhibit a number of complex neuroanatomical and neurochemical abnormalities, and where the status of dopamine function is also debated (see Chapter 1 for a comprehensive discussion).

Laboratory tests of intertemporal choice, particularly in rodents, have indeed shown – using an array of different drugs or methods which augment or attenuate dopamine transmission – that increasing dopamine activity can enhance self-control and reducing it can lead to greater impulsiveness (see Chapter 1). However, in some cases the reverse relationship or no effect has been observed. Furthermore, a closer look at the literature reveals that often, the effect is only apparent at certain doses and delays, appears only transiently, could depend on the presence of a cue, or is dependent on whether the manipulation occurs pre or post learning (Chapter 1). In the four human experiments carried out to date, de Wit et al. (2002), found that moderate but not low doses of amphetamine increased self-control (*decreased K*), Acheson and de Wit (2008) observed no effect of amphetamine on impulsivity, Hamidovic et al. (2008) found no effect using the D2/D3 receptor agonist pramipexole, and Pietras et al. (2003) found that adults with a history of criminal behaviour seemed to be less impulsive after taking methylphenidate (although the results were not entirely clear). Therefore, the consensus view mentioned above, regarding the role of dopamine in modulating intertemporal choice, is in fact not very as well supported as it first appears, particularly with respect to human evidence. Moreover, this view does not fit well with DDS symptoms, where overdosing of dopamine medication causes extreme impulsive behaviour.

One possible explanation for these inconsistent effects of dopamine manipulation could be that dopamine modulates both the discount rate and the utility concavity. If it were to have opposing effects on these parameters – for

example, increasing the discount rate but decreasing the utility function concavity – it is possible that in some cases behaviour would be observed to be more impulsive and vice versa, depending on the particular amounts and delays used in the experiment. This is what Kheramin et al. (2002) observed when investigating OFC lesions. This theory is quite plausible given dopamine's widespread influences over brain regions including the striatum and PFC (e.g. Robbins and Everitt, 1996; Robbins et al., 1989) and its ubiquitous role in mediating incentive salience (e.g. Berridge, 2007; Robbins and Everitt, 1996; Robinson and Berridge, 2000, 2008) and reward learning (Dayan, 2009; Dayan and Balleine, 2002; Doya, 2008; Iversen and Iversen, 2007; Robbins and Everitt, 1996; Robbins et al., 1989; Schultz, 2002, 2004, 2007; Spanagel and Weiss, 1999; Wise, 2004). Previous dopamine manipulation studies always assume a change in behaviour occurs as a result of a change in the discount rate.

To investigate whether dopamine modulates impulsive choice behaviour, how it affects brain function during option valuation, and whether it differentially affects  $K$  and  $r$ , the dopamine precursor L-Dopa, the dopamine antagonist Haloperidol, and placebo, were administered to healthy volunteers whilst they performed the choice task developed in Chapter 3. The hypothesis was probed at both behavioural and neurophysiological levels, using fMRI to determine which brain regions correlated with a change in behaviour across drug conditions and whether they related to specific influences on components of the model. That is, if the manipulation caused any changes in either of the two estimated parameters, it was expected that this change should also be reflected in the relevant neuronal value systems for  $D$  and  $U$  identified in Chapter 3. Furthermore, if an overall change in impulsive behaviour was observed, it was expected that this should be reflected in the regions identified with discounted utility ( $V$ ). It was also proposed that fMRI analyses of the placebo condition alone would replicate and confirm the results

found in Chapter 3, and that the general results could give an account of the various dopamine related disorders associated with impulsive choice. This is the first combined fMRI and pharmacological manipulation study in intertemporal choice.

To distinguish global from discrete influences on impulsivity, the decision latencies were also analyzed and compared across condition to assess whether dopamine had any effect on the rate of slowing down in response to decision-conflict. No previous study has tested whether dopamine modulates reflection impulsiveness and decision-conflict, so such a finding would also broaden its role in the impulsive phenotype.

The choices of L-Dopa and haloperidol were motivated by a number of considerations. First, no previous human study has assessed whether these drugs can influence impulsiveness in intertemporal choice. Previous studies in animals and humans most often use monoaminergic stimulants; however, drugs such as amphetamine and methylphenidate have wide ranging effects and enhance activity of multiple neurotransmitter systems including serotonin and noradrenaline (Balcioglu et al., 2003; Kuczenski et al., 1987; Kuczenski and Segal, 1989, 1997). Enhancing serotonin function has been observed to alter preference in intertemporal choice (e.g. Bizot et al., 1988; Poulous et al., 1996 - see Chapter 1 for review) and the 5-HT system is critical for the self-control enhancing effects of amphetamine (Winstanley et al., 2003, 2005). Thus, to rule out any influences on serotonin, L-Dopa was used as its effects are much 'cleaner' than those of psychostimulants - in theory not significantly affecting 5-HT function. Furthermore, as L-Dopa is a DA precursor, it was thought that some of the complications regarding pre versus post synaptic effects of psychostimulants would be avoided (Seeman and Madras, 1998, 2002; Solanto, 1998, 2002 - see Chapter 1). Additionally, stimulants are known to cause physiological and visceral

states which can impact on choice and confound effects (Loewenstein, 1987, 1996, see Chapter 1). The final motivation for using L-Dopa was to be able to potentially give a direct account of the impulsivity that can occur in PD when patients are given or self-administer high doses of dopaminergic medication including L-Dopa (dopamine dysregulation syndrome) (e.g. Cools et al., 2003, see above).

Concurrently, a pilot study was carried out<sup>1</sup> to test the choice behavior of PD patients whilst 'on' and 'off' L-Dopa and dopamine agonist medication. There were a number of hypotheses to motivate this pilot. First, no previous study has assessed PD subjects using intertemporal choice – the question here was whether impulsivity is only observed in those patients who develop DDS, or whether 'normal' PD patients on dopamine medication would also show subtle signs of impulsiveness, which may be picked up by specific and sensitive tasks. Second, DDS is associated with impulsive behaviours such as gambling, excessive shopping and hypersexuality, some aspects of which are consistent with temporal impulsiveness. However, unlike in addiction and ADHD, no study has yet shown a specific deficit in impulsive choice, or excessive discounting in this condition by testing patients on intertemporal choice tasks. If the first hypothesis was shown to be true, it could answer this question. Third, by testing patients on and off their dopaminergic medication, it was proposed that a similar behavioural effect would be observed to that observed in the pharmacological manipulation of the healthy subjects i.e. one of augmented versus attenuated dopamine function.

To improve power, these studies employed a within-subjects design whereby in each condition the subject was given the exact same array of choices. This was also done to ensure that parameter estimates for single subjects – which are noisy to an extent – were as close as possible, and that any changes would accurately reflect associated changes in discounting behaviour. In addition, using the same choice

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<sup>1</sup> This pilot study was done in collaboration with Tamara Shiner who collected the data.

arrays across conditions allowed for a theory-neutral measure of impulsivity which was not model dependent. This measure was simply the proportion of smaller-sooner versus larger-later options chosen in each condition. Thus, an overall picture of behaviour could be assessed across conditions, to show that any changes in parameter estimates actually accorded with a change in behaviour.

To control for any subjective effects of the drugs on choice, visual analogue scales (Bond and Lader, 1974) were completed by subjects before and after each testing session (see Appendix IV).

## **Methods**

### *Participants*

Fourteen right-handed, healthy volunteers were included in the experiment (6M:8F, mean age 21, range: 18-30). Subjects were pre-assessed to exclude those with a prior history of neurological or psychiatric illness as well as excessive drug use and smoking. All subjects gave informed consent and the study was approved by the UCL ethics committee. One subject dropped out of the study after the first session and was not included in the results. Another did not complete the final (placebo) session in the scanner but her data were used in the analyses.

In the PD pilot study, 6 PD patients were recruited from a local PD clinic (5M:1F, mean age, 61, range: 47-81). The patients were being treated with L-Dopa (Sinemet) and dopamine agonists (ronipirole, parimpexole, or mirapexin) at standard clinical doses.

### *Procedure and task description*

Each subject was tested on three separate occasions. Upon arrival on each occasion subjects were given an instruction sheet to read explaining how the drug blinding would be implemented. They then completed a visual analogue scale (Bond and Lader, 1974) which measured subjective states such as alertness etc., and were subsequently given an envelope containing 2 pills which were either 1.5mg Haloperidol, or placebo. One and a half hours after taking the first set of pills subjects were given another envelope containing 2 pills which were either Madopar, containing 150mg of L-Dopa, or placebo. The placebo tablets (vitamin c or multivitamins) were indistinguishable from the drugs. In all, each subject received one dose of Madopar on one session, one dose of Haloperidol on another, and on one session both sets of tablets were placebo. The order of each drug condition in relation to the testing session was counterbalanced across subjects and was unknown to the experimenter, to achieve a double-blind design. Testing commenced 30 minutes after ingestion of the second set of tablets. The timings were aimed to achieve a peak plasma concentration of the drug, roughly half way through the testing. After testing, subjects completed another (identical) visual analogue scale. No two testing sessions occurred within one week of each other.

Before subjects were taken into the scanner, they were shown the lottery machine and given an explanation as to how the bank transfer would be implemented to reassure them that the payment and selection system was genuine. After reading an instruction sheet explaining the task (Appendix III) and a short practice of 6 trials, they were taken into the scanner where they performed 2 sessions of 110 trials each, lasting in total around 50 minutes.

The task itself was mostly as described in Chapter 3. As before, the experiment consisted of a total of 200 trials. Option 1 was the smaller-sooner reward in 50% of

trials. In addition a further 20 'catch' trials were included where one of the options was both greater in value and available sooner than the other one. These catch trials occurred approximately every tenth trial and were included to gauge performance and orthogonalize the design. Each subject was given the same array of choices in each testing session (i.e. each drug condition) with the exception of the first 2 subjects who were given a different set of choices on their first testing session. This time, the option values were created using randomly generated magnitudes varying from £1 to £150 in units of £1 and delays ranging from 1 week to 1 year in units of single weeks (but presented as a number of months and weeks), again with a random distribution. The range of magnitudes was increased in order to gain more power in estimating the utility concavity and any potential changes in this measure across conditions.

As before, to impose ecological validity a payment system was utilized which ensured that all the choices would be made in a realistic manner, with realistic consequences. In this case, due to the larger range of magnitudes used, only one of the choices made during the experiment was selected. This was achieved by way of a bank transfer made at the time associated with, and consisting of the amount of the selected option. Payment selection was implemented using a manual lottery after completion of all testing. The lottery contained 220 numbered balls, each representing a single trial from the task. The ball which was selected corresponded to the rewarded trial for that testing session. The magnitude and delay of the option which the subject chose in the selected trial was determined and awarded using a bank transfer. Thus, the payment each subject received was determined by a combination of the lottery and the choices that they made – a manipulation that ensured subjects treated all choices as real. The payment system was designed so that on average each subject would receive £75 per session (£225 for the 3 sessions). No other payment was awarded for mere participation in the experiment.

In the pilot PD patient study there were a number of differences. First, only behavioural data was collected. The task was therefore not presented serially, rather the options were presented side by side and choice was prompted on the same screen. The task was also self-paced so as to make sure that a large number of trials were not missed due to slow responding of the patients. No catch trials were included as the patients took a substantial amount of time to complete all the trials and became tired. Rather than reduce the number of experimental trials (which would have resulted in a reduction of parameter estimate accuracy) the catch trials were excluded. Finally, in the patient study the choices were hypothetical with no payment awarded. All other details of the task were as described above.

In the 'off' condition, the patients were tested after an overnight washout of PD medication (i.e. they took their last dose the night before and missed the morning dose). If they were on long acting levodopa preparations they were asked not to take them the night before as well. In the 'on' condition, they took their PD medication as usual. Testing was carried out at the same time of day in both conditions and the order of testing was counterbalanced across patients.

### *Imaging procedure*

Functional imaging was conducted by using a 3 Tesla Siemens Allegra head-only MRI scanner to acquire gradient echo T2\*-weighted echo-planar images (EPI) with blood oxygenation level-dependent (BOLD) contrast. A sequence designed to optimize functional sensitivity in the OFC (Deichmann et al., 2003) was used. This consisted of tilted acquisition in an oblique orientation at 30° to the AC-PC line, as well as application of a preparation pulse with a duration of 1 ms and amplitude of -2 mT/m in the slice selection direction. The sequence enabled 36 axial slices of 3

mm thickness and 3 mm in-plane resolution to be acquired with a TR of 2.34 s. Subjects were placed in a light head restraint within the scanner to limit head movement during acquisition. Functional imaging data were acquired in two separate 610 volume sessions. A T1-weighted structural image and fieldmaps were also acquired for each subject following the functional testing sessions.

### *Behavioural analysis*

To obtain an overall (theory neutral) measure of impulsive choice, the number of sooner options chosen out of the 220 trials (200 in the PD study), was calculated under each drug condition, for each subject. Trials where a response was not made were excluded from this sum in all three drug conditions. For example, if one subject did not respond in time for trial number 35 in the placebo condition, this trial was excluded from the count in the other two conditions, for that subject. This ensured that the comparisons were made on a trial by trial basis (as the same array of trials was given in each testing session) and any effect of drug on this measure was not related to the *number* of choices made. A paired samples t-test was used to look for any differences in this overall measure across drug conditions.

### *Parameter estimation*

Parameter estimation was performed by the same technique described in Chapter 3, using maximum likelihood estimation of the softmax rule in the context of the new discounted utility mode (model 2, Eq. 4 in Chapter 3). This produced parameter estimates for  $K$  and  $r$  for each subject in each condition (as well as the  $\beta$  parameter in the softmax function).

A paired samples t-test was used to test for any differences in the discount rate ( $K$ ) and the utility concavity ( $r$ ) across drug conditions. In addition, subjects' estimates were compared to zero to test for a main effect of temporal discounting and an effect of diminishing marginal utility on choice.

For the purposes of the imaging and reaction time analyses, a further estimation was performed whereby all the choices from each subject in each condition were grouped together (as if made by one subject) and modelled as a canonical subject to estimate canonical parameter values (using the fitting procedure – see also Chapter 3). This was performed to reduce the noise associated with the fitting procedure at the single subject level and to make subjects (with greatly differing parameter estimates, over an order of magnitude - see Table 1) more comparable in the second level analyses. In addition, it was important not to build the behavioural differences into the regression models when analysing the fMRI data, as independent evidence for the behavioural findings was sought.

### *Imaging analysis*

Image analysis was performed using SPM5 ([www.fil.ion.ucl.ac.uk/spm](http://www.fil.ion.ucl.ac.uk/spm)). For each session, the first five images were discarded to account for T1 equilibration effects. The remaining images were realigned to the sixth volume (to correct for head movements), unwarped using fieldmaps, spatially normalised to the Montreal Neurological Institute (MNI) standard brain template and smoothed spatially with a three-dimensional Gaussian kernel of 8 mm full-width at half-maximum (FWHM) (and re-sampled, resulting in 3 × 3 × 3 mm voxels). Low-frequency artefacts were removed using a 1/128 Hz high pass filter and temporal autocorrelation intrinsic to the fMRI time-series was corrected by pre-whitening using an AR(1) process.

Single-subject contrast maps were generated using parametric modulation in the context of the general linear model. An analysis examining variance in regional BOLD response attributable to different regressors of interest:  $U$ ,  $D$  and  $V$ , was performed for all options over all drug conditions. This allowed identification of regions implicated in the evaluation and integration of different components of value (in the placebo condition) and to look for any differences in these activations across drug conditions using subtraction analyses.

$U$ ,  $D$  and  $V$  for each option (two per trial) were calculated using the canonical parameter estimates ( $K$  and  $r$ ) in the context of the discounted utility model (Chapter 3, Eq. 4), and convolved with the canonical hemodynamic response function (HRF) at the onset of each option. All onsets were modelled as stick functions and all regressors in the same model were orthogonalised (in the orders stated above) prior to analysis by SPM5. To correct for motion artefacts, the 6 realignment parameters were modelled as regressors of no interest in each analysis. In an additional analysis, a potential confound relating to the orthogonalisation of the regressors in the fMRI analysis was removed by implementing another regression model but now removing the orthogonalisation step. Here, regressors were allowed to compete for variance such that in this more conservative model any shared variance components were removed, revealing only unique components of  $U$ ,  $D$  and  $V$ . Under this model, the same differences in  $D$  and  $V$  were observed across drug conditions and no difference in  $U$ , although the magnitude of the differences was reduced.

At the second level (group analysis), regions showing significant modulation by each of the regressors specified at the first level were identified through random effects analysis of the beta images from the single-subject contrast maps. A change in impulsivity measure (difference in number of sooner options chosen, between two drug conditions), was included as a covariate when performing the contrast

relating to differences in L-Dopa and placebo trials. Results are reported for regions where the peak voxel-level t-value corresponded to  $p < 0.005$  (uncorrected), with a minimum cluster size of 5. Coordinates were transformed from the MNI array to the stereotaxic array of Talairach and Tournoux (1988) (<http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach>).

The structural T1 images were co-registered to the mean functional EPI images for each subject and normalised using the parameters derived from the EPI images. Anatomical localisation was carried out by overlaying the t-maps on a normalised structural image averaged across subjects, and with reference to the anatomical atlas of Mai et al. (2003).

### *Decision latency data*

To examine the effect of decision conflict (choice difficulty) on decision latency, a measure of difficulty was estimated for each of the 220 choices by calculating the difference in discounted utility ( $\Delta V$ ) of the two options. This measure was calculated using the discounted utility model and the canonical parameter estimates (for the same reason they were used in the fMRI analyses). A linear regression was then performed to model the relationship between the decision latency for each choice and the difficulty measure (separately for each drug condition). The parameter estimates (betas) were then used as a summary statistic and a second level analysis was performed by means of a one-sample t-test comparing the betas against zero. This was performed separately for the group in each drug condition to test for an effect of slowing decision latencies in response to conflict. To test for any differences in the relationship between conflict and decision latency across drug conditions, paired samples t-tests were used,

comparing the betas in each drug condition (see also Chapter 3 for more detail on modelling decision latencies and choice conflict).

## Results

### *Behavioural data*

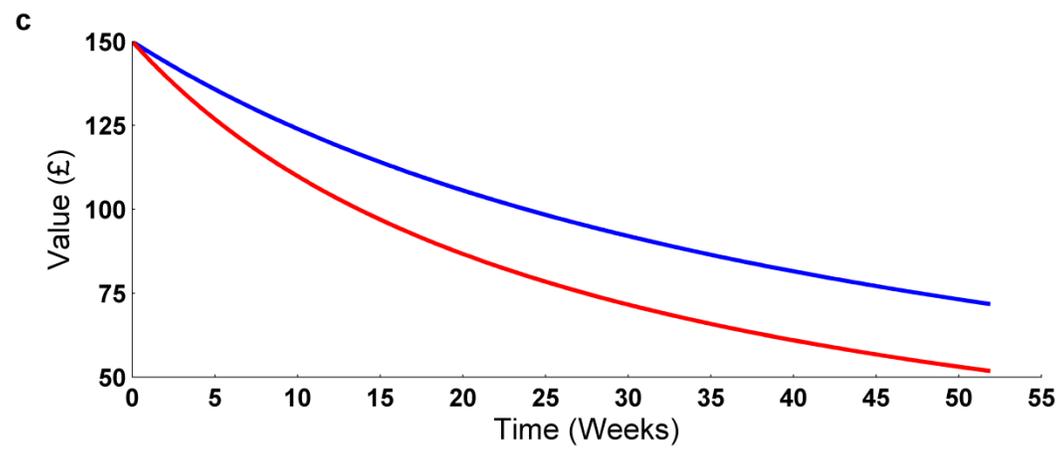
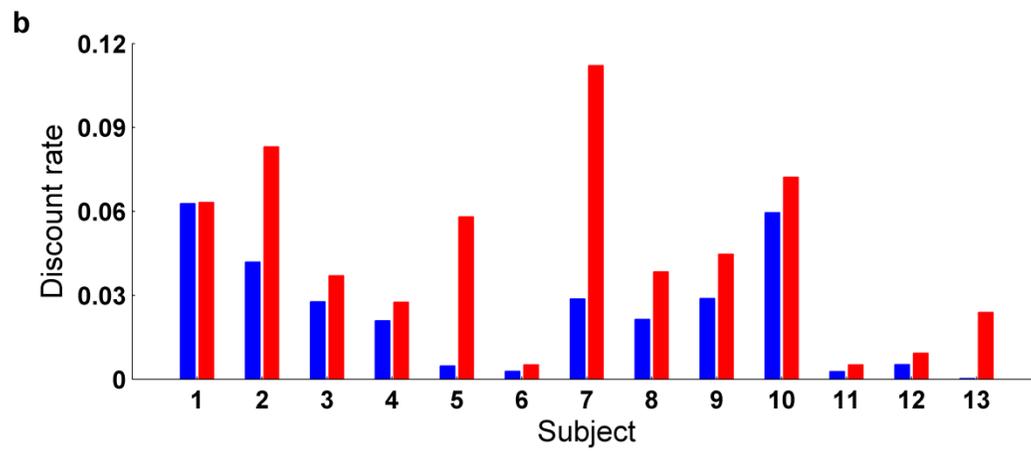
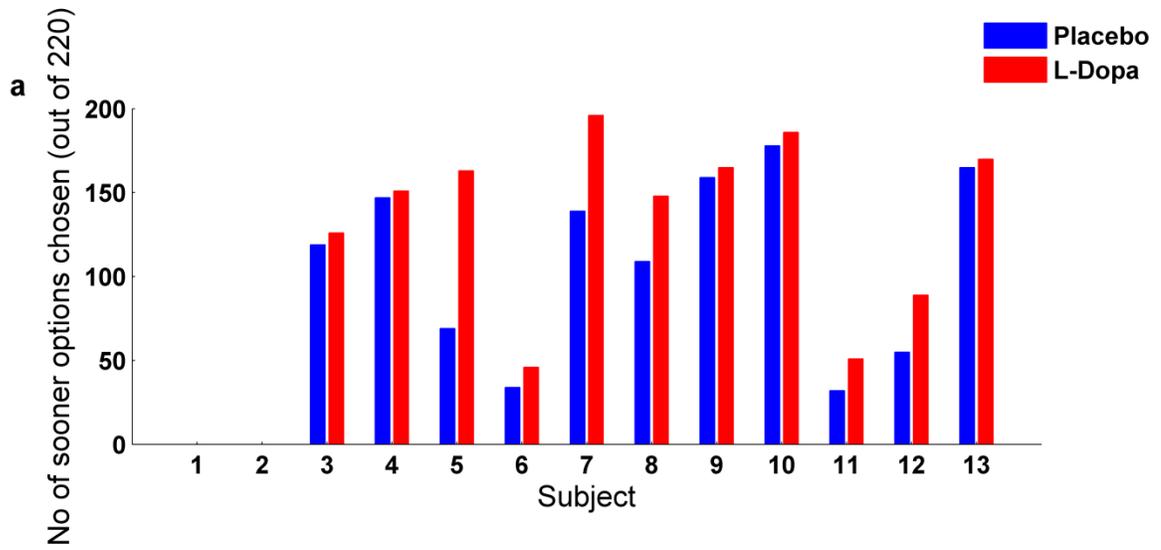
Subjects performed well on the task, answering on average over 19 of the 20 catch trials correctly (Table 1).

The effects of the drug manipulation on behaviour were analyzed by considering the proportion of smaller-sooner relative to larger-later options chosen, out of a total of two hundred and twenty choices made in each condition. These data revealed a marked increase in the number of sooner options chosen in the L-Dopa condition relative to the placebo condition ( $p = 0.013$ ) (Table 1 and Figure 1). On average, subjects chose 110 of the sooner options under placebo and 136 under L-Dopa (Table 1). Strikingly, this pattern was observed in all subjects where this comparison could be made (2 subjects performed different choice arrays in two of the conditions) (Table 1). There was no significant difference between haloperidol and placebo conditions on this disposition. Note, the task consisted of the same choice array in each condition. This effect could not be accounted for by the number of missed trials since these were subtracted from all conditions (see methods).

Maximum likelihood estimation was used to find the best fitting parameters ( $K$  and  $r$ ) for the discounted utility model, for each subject in each condition, to determine whether a specific effect on either of these parameters mediated the observed increase in behavioural impulsivity. By comparing the estimated parameters controlling the discount rate and utility concavity across conditions, a

specific effect of L-Dopa on the discount rate was found, with no effect on utility concavity (Figure 1 and Table 1). Thus, under L-dopa, a higher discount rate was observed relative to placebo ( $p = 0.01$ ) leading to a greater devaluation of future rewards. By way of illustration, using a group canonical parameter estimate to plot a discount function for each drug condition, it can be seen that under placebo it required a delay of around 35 weeks for a £150 reward to have a present (subjective) value of £100, however, under L-Dopa the same devaluation took place with a delay of just 15 weeks (Figure 1). Canonical parameter estimates used for the imaging analyses were 0.0293 for  $K$  and 0.0019 for  $r$ .

As in the previous study, one sample t-tests were used to compare the  $K$  and  $r$  value for each subject (an average of the parameters estimated in the three conditions for each subject) against zero. This revealed both a significant effect of temporal discounting ( $p < .001$ ) and non-linearity (concave as the  $r$  estimates were above zero) of utility ( $p < .05$ ).



**Figure 1. Behavioural comparisons and parameter estimates in placebo and L-Dopa conditions.** **a** Subjects performed exactly the same set of (220) choices under all 3 treatment conditions but more often chose the smaller-sooner than larger-later option after taking L-Dopa. For clarity of presentation, data for Haloperidol is not shown as these data did not differ from placebo. (Note, subjects 1 and 2 performed a different set of choices under each condition and so cannot be compared in this way). **b** Maximum likelihood estimation of the individual parameters revealed that subjects had a higher discount rate under L-Dopa than placebo. **c** The estimated discount function for a £150 reward over the course of a 52 week delay, using the group parameter estimate, reveals a much steeper devaluation of future rewards under L-Dopa relative to placebo.

Subject	PLACEBO			L-DOPA			HALOPERIDOL		
	Catch trials	No sooner chosen	<i>K</i> value	Catch trials	No sooner chosen	<i>K</i> value	Catch trials	No sooner chosen	<i>K</i> value
1	20		0.0628	20		0.0632	20		0.0225
2	20		0.0419	19		0.0831	19		0.0039
3	20	119	0.0277	20	126	0.037	19	133	0.0364
4	20	147	0.0209	20	151	0.0276	20	119	0.0175
5	20	69	0.0048	20	163	0.0581	20	59	0.0036
6	20	34	0.0029	20	46	0.0052	20	43	0.0023
7	20	139	0.0287	20	196	0.1122	20	174	0.0679
8	19	109	0.0214	20	148	0.0384	20	160	0.0452
9	18	159	0.0289	20	165	0.0447	18	170	0.1298
10	20	178	0.0596	20	186	0.0723	20	174	0.0758
11	20	32	0.0028	20	51	0.0052	20	43	0.0024
12	20	55	0.0053	20	89	0.0093	20	31	0.0014
13	20	165	0.0003	20	170	0.0239	19	165	0.0477
<b>Mean</b>	19.769	109.636	0.024	19.923	135.545	0.045	19.615	115.545	0.035

**Table 1. Summary of behavioural findings.** Subjects more often chose the smaller-sooner reward in L-Dopa versus placebo conditions (note that subjects 1 and 2 performed different choice arrays across conditions so cannot be meaningfully compared in this way). Discount rate parameter (*K*) was greater under L-Dopa than placebo conditions. Subjects nearly always answered catch trials (out of 20) correctly i.e. choosing the larger-sooner option.

A subsequent analysis examined whether a slowing down in decision latencies was apparent as choices became increasingly difficult – consequent upon increasing closeness in option values – and whether any group differences (e.g. drug versus placebo) were apparent on this measure. A regression was performed to assess the relationship between decision latency and choice conflict as measured by the difference in discounted utility ( $\Delta V$ ) of the two choice options, calculated using the estimated parameter values. In placebo ( $p < 0.001$ ), L-Dopa ( $p < 0.001$ ) and haloperidol ( $p < 0.001$ ) conditions, subjects' decision latencies increased as  $\Delta V$  decreased, that is, as the difference in subjective value between the options got smaller (and conflict increased). However, no overall difference was observed in this measure across drug conditions. This indicates that unlike the choice outcome, dopamine manipulation did not influence the amount of time given to weigh-up a decision, i.e. an individual's decisiveness (preparation impulsivity - Evenden, 1998, 1999a) or ability to 'hold your horses' (Frank et al. 2007). This observation accords with a previous finding that DA medication status in PD patients was not associated with change in decision latencies in a different choice task (Frank et al., 2007).

Subjective drug effects were assessed using results from the visual analogue scales (see Appendix IV). The scales comprised a total of 16 100mm lines anchored at either end by antonyms. Subjects marked their current subjective state between the antonyms on the line. Each line was scored as millimeters to the mark from the negative antonym. The 16 scales were combined, as recommended by the authors (Bond and Lader, 1974) to form 3 mood factors (derived using factor analysis): 'alertness', 'calmness' and 'contentedness'. Scores for each factor represent the weighted average number of millimeters from the negative antonym for the individual scales contributing to the factor. The results were analysed by

subtracting the scores before testing from those after testing, to generate a single change-from-baseline score. A repeated measures ANOVA was then employed to look for any differences in this measure between the placebo and drug conditions. A significant difference was found ( $p < .025$ ) in the haloperidol condition, which indicated that subjects became significantly less alert following haloperidol, relative to the change in this factor incurred by placebo (see Table 2).

	Placebo		L-Dopa		Haloperidol	
	Baseline	Post-dose	Baseline	Post-dose	Baseline	Post-dose
<b>Alertness</b>	63.54	54.37	61.28	53.84	61.09	47.46
<b>Contentedness</b>	56.14	56.80	58.72	55.93	54.38	49.81
<b>Calmness</b>	54.07	58.71	56.90	60.13	60.22	59.56

**Table 2. Subjective drug effects.** Mean raw scores of the three factors of the Bond and Lader (1974) visual analogue scales, assessed pre and post testing in each drug condition. Subjects became significantly less alert in the haloperidol condition relative to placebo.

### *Patient data*

An analysis of the number of smaller-sooner options chosen out of 200 choices revealed that 5 of the 6 patients were more impulsive when tested on their medication than when off their medication (Table 3). However, this effect was not significant at the group level, presumably due to the small sample size and the 6<sup>th</sup> subject who displayed the opposite pattern to an extreme extent. Unfortunately, due to the time constraints no catch trials were included, so how consistently each subject performed cannot be ascertained. Parameter estimates also revealed an increase in  $K$  in four of the patients.

Subject	ON MEDICATION	OFF MEDICATION
	No smaller-sooner chosen	
1	17	5
2	168	105
3	119	109
4	49	48
5	101	94
6	6	74
<b>Mean</b>	76.7	72.5

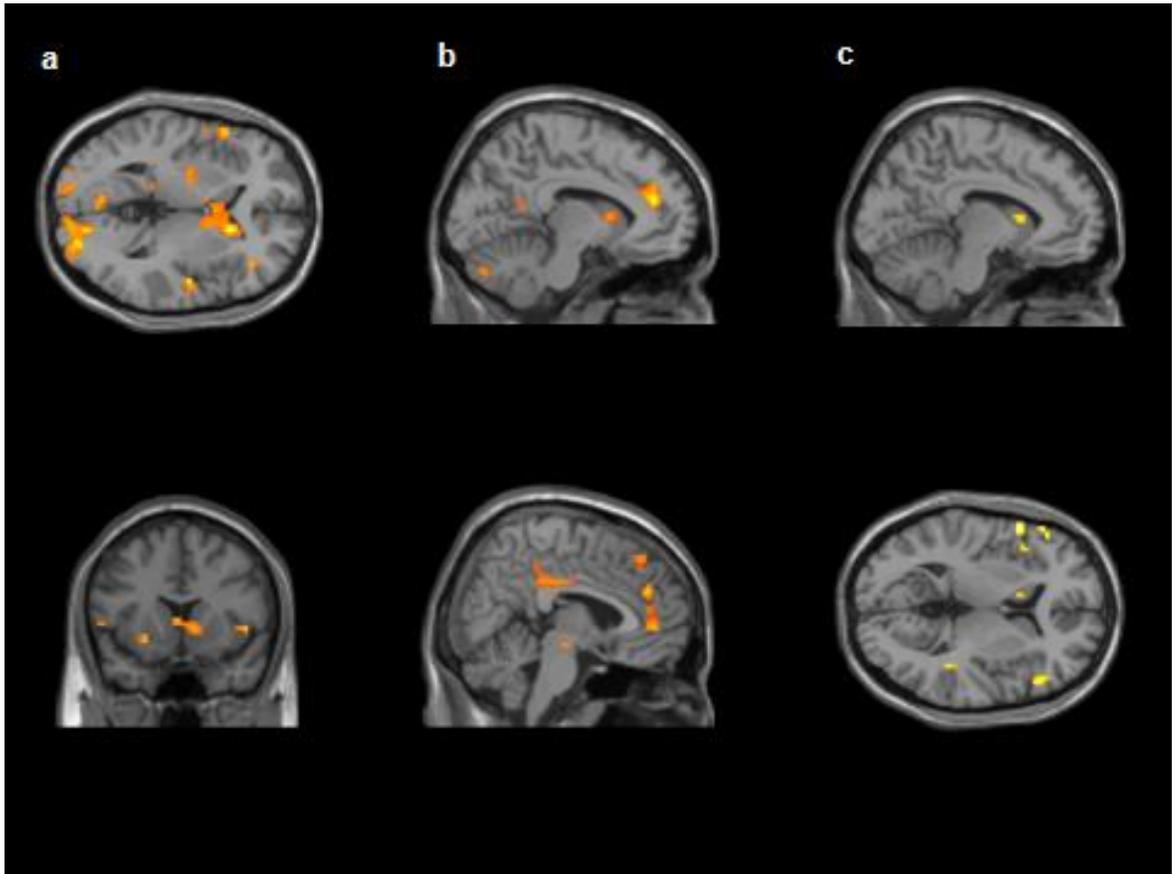
**Table 3. Impulsive choice in PD patients.** Patients more often chose the smaller-sooner reward when on versus off medication in 5 out of 6 cases. Difference was not significant at the group level.

### *Imaging data*

To establish how enhanced impulsivity under L-Dopa was represented at a neural level, a general linear model applied three (orthogonalized) parametric regressors,  $U$ ,  $D$  and  $V$  associated with the presentation of each option, as dictated by the model, to the brain imaging data acquired whilst subjects performed the task. The regressors were created for each subject, in each condition, using canonical parameter values estimated from all subjects' choices over all sessions – in a test of the null hypothesis that brain activity does not differ between conditions.

In a preliminary analysis, correlations for these 3 regressors in the placebo condition were examined to replicate previous findings. The results (Figure 2, Tables 4-6) were consistent with those shown previously (Chapter 3), in that  $D$ ,  $U$ ,

and  $V$  all independently correlated with activity in the caudate nucleus (amongst other regions). There were however some differences in the exact network of regions correlating with each regressor (see Tables 4-6).



**Figure 2. Neural correlates of discounted utility model in the placebo condition.** **a** Regions correlating with the utility ( $U$ ) of each option in the placebo condition. **b** Regions correlating with the discount factor ( $D$ ) of each option in the placebo condition. **c** Regions correlating with the discounted utility ( $V$ ) of each option in the placebo condition.

REGION	CLUSTER SIZE	MNI COORDINATES	Z VALUE
Region bordering putamen and amygdala (right)	22	[30 -3 -12]	4.45
Visual cortex	673	[12 -90 -9]	4.43
		[27 -48 -27]	3.91
		[-9 -99 -6]	3.86
Cerebellum	19	[-30 -75 -21]	4.04
Right superior temporal cortex	45	[63 -24 12]	3.93
Right caudate	114	[15 21 3]	3.80
		[21 24 -3]	3.30
		[9 6 -3]	3.23
Precentral gyrus	26	[51 -9 3]	3.63
Separans gyrus/ frontal operculum	27	[45 9 0]	3.52
Left inferior frontal gyrus	11	[-54 15 3]	3.37
Left thalamus / tail of caudate	30	[-13 -36 0]	3.33
		[-18 -30 6]	3.05
		[-15 -24 18]	3.05
Posterior cingulate / occipital gyrus	34	[12 -54 0]	3.32
		[-6 -72 3]	3.14
Left putamen	23	[-24 12 -9]	3.23
		[-24 6 -3]	3.17
Left putamen	28	[-27 -6 6]	3.23
Occipital gyrus	9	[15 -48 -3]	3.17
Dorsolateral PFC	5	[39 36 3]	3.23
Left superior temporal gyrus	14	[-57 -3 -6]	3.07
Ventral tegmental area	6	[15 -15 -27]	3.07
Internal capsule	12	[21 -18 9]	2.94

**Table 4.** Regions correlating with the utility ( $U$ ) of each option in the placebo condition alone (Fig. 2a).

REGION	CLUSTER SIZE	MNI COORDINATES	Z VALUE
Dorsolateral PFC	139	[48 27 18]	4.75
		[45 33 6]	3.39
		[54 42 6]	3.16
Superior temporal gyrus	160	[63 -36 -15]	4.74
		[57 -45 -15]	4.17
		[57 -45 -18]	3.91
Dorsolateral PFC	97	[51 24 30]	4.70
		[42 18 27]	4.16
		[51 15 30]	4.00
Anterior cingulate cortex	169	[-9 42 18]	3.91
		[6 42 27]	3.59
		[9 45 0]	3.56
Orbitofrontal cortex	11	[-24 39 -18]	3.87
Thalamus	21	[21 -36 6]	3.72
Rostral ACC / cingulate gyrus	27	[12 -51 18]	3.70
Superior temporal gyrus	92	[-51 -51 -21]	3.68
		[-48 -54 -6]	3.13
		[-60 -39 -18]	3.09
Posterior cingulate cortex	86	[-3 -9 33]	3.58
		[9 -24 33]	3.23
		[6 -33 33]	3.11
Dorsolateral PFC	35	[-39 18 24]	3.56
Frontomarginal Gyrus	35	[39 54 3]	3.54
Orbitofrontal cortex	11	[-24 39 -21]	3.41
Orbitofrontal cortex	10	[27 39 -6]	3.30
Caudate	12	[-9 9 6]	3.26
Inferior frontal gyrus (orbital)	11	[-39 36 3]	3.23
Ventral tegmental area / SN	8	[6 -18 -12]	3.15

**Table 5.** Regions correlating with the discount factor ( $D$ ) of each option in the placebo condition alone (Fig. 2b).

REGION	CLUSTER SIZE	MNI COORDINATES	Z VALUE
Inferior frontal gyrus (orbital)	21	[-57 12 6]	3.92
Dorsolateral PFC	37	[-45 33 18]	3.64
		[-51 33 6]	3.32
Lateral orbital gyrus / inferior frontal	22	[39 21 -15]	3.47
Dorsolateral PFC	23	[54 24 9]	3.38
Inferior frontal / lateral orbital gyrus	10	[-39 21 -6]	3.28
Lateral OFC	7	[45 39 -6]	3.10
Dorsolateral PFC	15	[45 36 18]	3.02
Caudate	6	[-9 12 9]	3.01

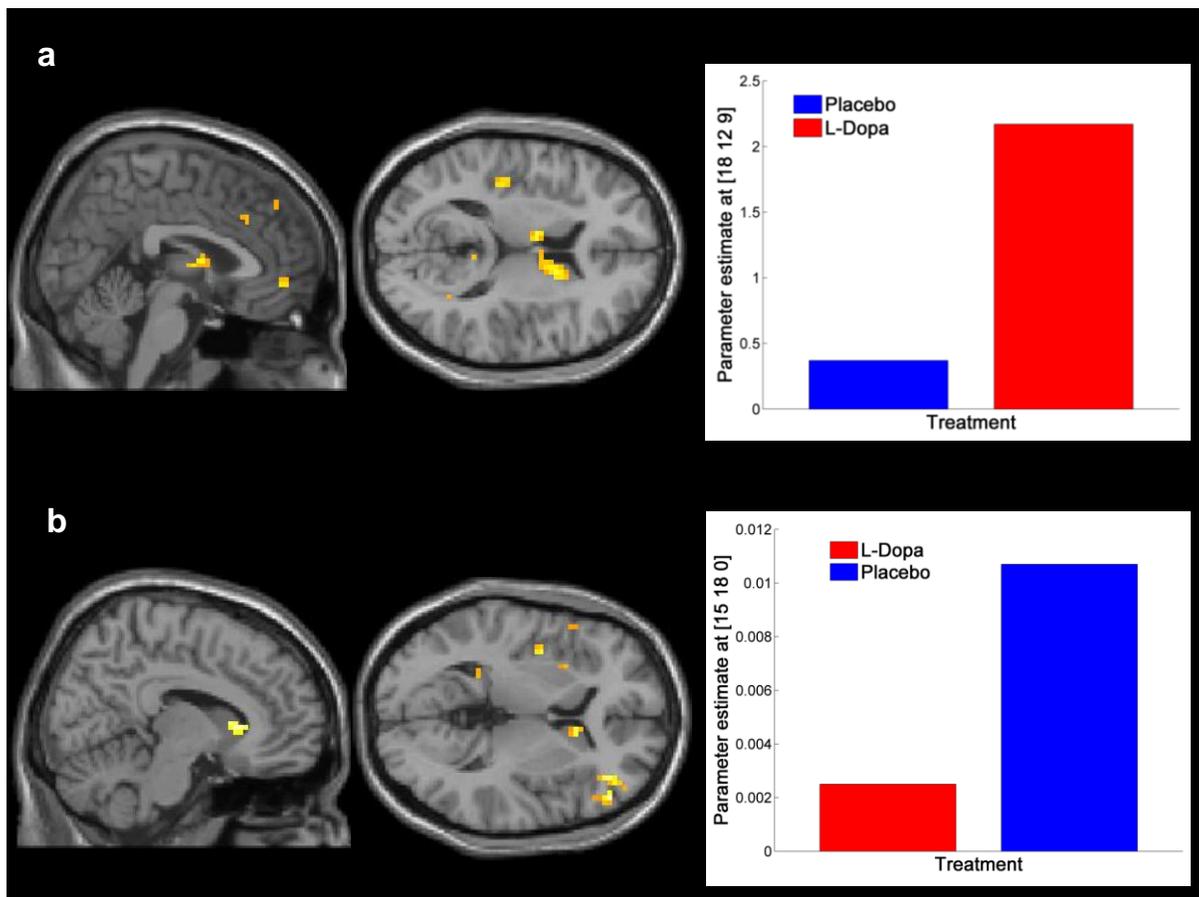
**Table 6.** Regions correlating with the discounted utility ( $V$ ) of each option in the placebo group alone (Fig. 2c).

The critical fMRI analyses focused on the key behavioural difference in option valuation under L-Dopa compared to placebo conditions. When comparing neural activity for  $U$ ,  $D$  and  $V$  significant differences were found for both  $D$  and  $V$  (Figure 3), a finding that exactly matched the behavioural results. Specifically, enhanced activity was observed in the dorsal striatum, subgenual cingulate cortex and insula in relation to the discount factor  $D$ , under L-Dopa relative to placebo conditions (Figure 3a, see Table 7 for comprehensive results). Activity in these areas was previously shown (Chapter 3) to correlate with the discount factor, an effect also highlighted in this study in the analysis of the placebo group alone (Figure 2, Table 5). These data, and those of previous studies (e.g. Kable and Glimcher, 2007; McClure et al., 2004) point to an increase in activity in the striatal, insular and subgenual cingulate regions as rewards become available sooner (i.e. as  $D$  gets bigger). The drug versus placebo contrasts show that this increase in activity is more marked in the L-Dopa relative to placebo conditions in a manner that parallels the behavioural finding where L-Dopa increased preference for sooner rewards by increasing the discount rate, thereby rendering them more

attractive/valuable relative to later rewards. In other words, the neural activity in the L-Dopa group reveals a greater preference for sooner versus later options, in relation to the placebo group.

Previous studies (Kable and Glimcher, 2007; Chapter 3), as well as an analysis of the current placebo group alone (Figure 2, Table 6) implicate striatal regions, amongst others, in encoding discounted utility ( $V$ ). When comparing regions correlating with  $V$ , enhanced activity was observed in caudate, insula, and lateral inferior frontal regions, in the placebo compared to the L-Dopa condition (Figure 3b – see Table 8 for comprehensive results). Thus, greater activity in regions that encode subjective value indicates that for a reward of a given magnitude and delay, greater activity was evoked under placebo, compared to L-Dopa conditions, corresponding to a greater discounted utility of the option under placebo relative to L-Dopa – again matching the behavioural results. This led to an increase in the selection of the larger-later option in placebo relative to L-Dopa conditions.

Because the fMRI data were modelled using the same single set of canonical parameters (the group estimate of  $r$  and  $K$  across all conditions, testing the null hypothesis that brain activity did not differ), they accord with and add independent evidence for the behavioural results (Figure 1, Table 1) where it was shown that by increasing the discount rate under L-Dopa, there is a reduction in  $D$  (especially in more delayed relative to sooner options), leading to a corresponding reduction in  $V$  and, hence, an increased *relative* preference for sooner rewards. Note that if dopamine encoded discounted utility alone, one would predict the opposite result, with greater activity in the L-dopa condition.



**Figure 3. Differences in neural activity between L-Dopa and placebo conditions, in response to subjective value and the discount factor (statistical parametric maps and parameter estimates).** **a** Regions which correlated with the discount factor  $D$  (i.e. reward proximity) and were significantly more active in L-Dopa compared with placebo trials. **b** Regions which correlated with the discounted utility ( $V$ ) or subjective value of the options and were significantly more active in placebo relative to L-Dopa trials. Bar charts indicate the mean parameter estimates at the peak striatal voxel relating to  $D$  (in a) and  $V$  (in b) activity.

REGION	CLUSTER SIZE	MNI COORDINATES	ZVALUE
Right caudate	114	[18 12 9]	3.88
Left caudate		[-3 -6 6]	3.60
Thalamus		[6 0 9]	3.20
Right putamen / insula	9	[30 -24 6]	3.70
Left putamen / insula	10	[-30 -15 -3]	3.47
Right striatum	5	[24 -9 6]	3.25
Left superior temporal gyrus	12	[-48 9 -9]	3.20
Left insula	6	[-39 -24 12]	3.03
Subgenual cingulate cortex	6	[3 48 -6]	2.97
Inferior frontal gyrus / lateral orbital	7	[-39 21 -15]	2.97

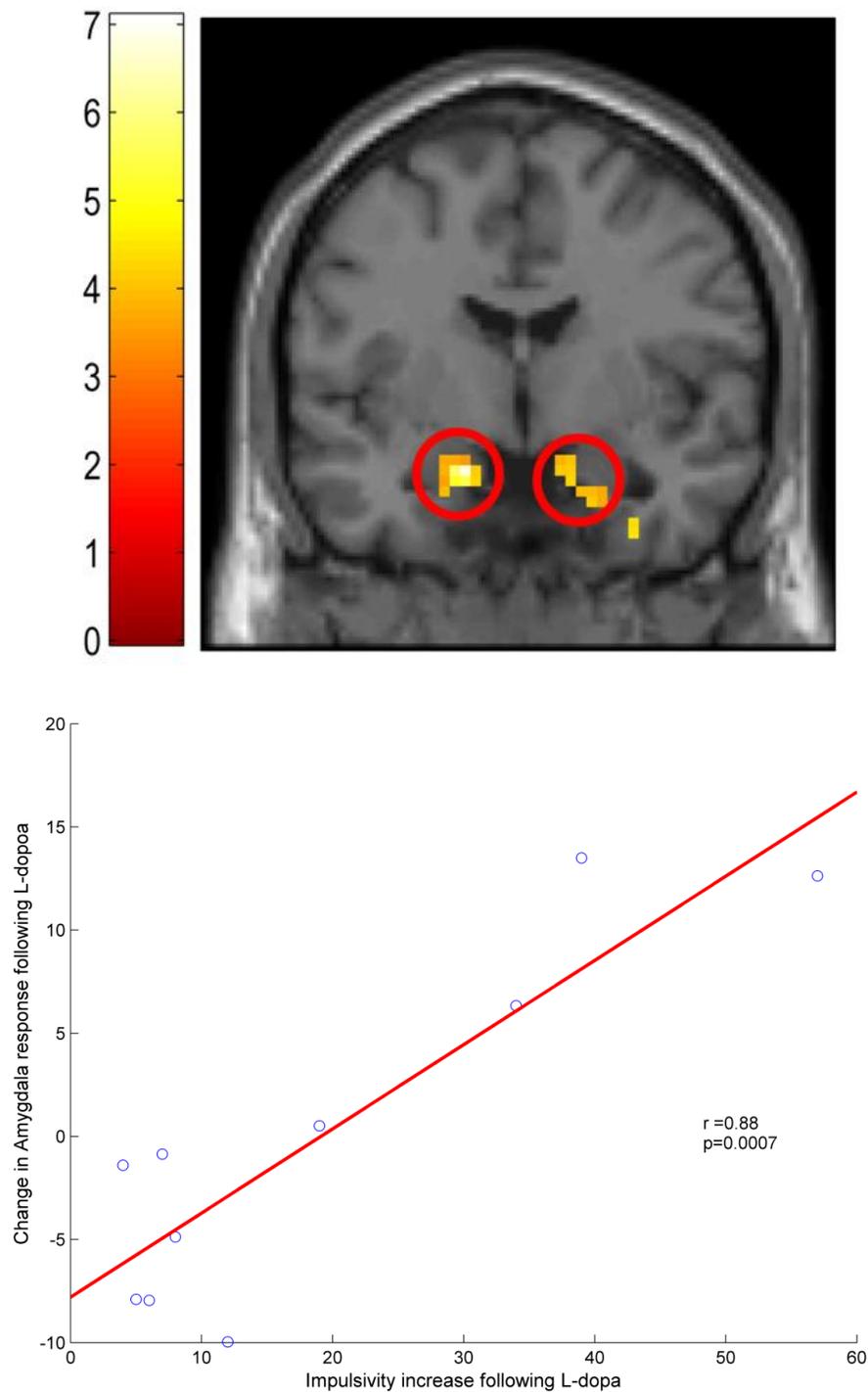
**Table 7.** Discount (*D*) regions which were more active in L-Dopa than placebo conditions (Fig. 3a).

REGION	CLUSTER SIZE	MNI COORDINATES	Z VALUE
Occipital gyrus	28	[-15 -51 9]	4.13
Cingulate gyrus		[-9 -54 3]	3.49
Precuneus / striate cortex	88	[3 -81 21]	4.04
Left insula	28	[-42 -6 0]	4.00
Right parietal operculum	34	[66 -18 15]	4.00
Right caudate	32	[24 7 -3]	3.50
		[15 18 0]	3.44
Inferior frontal gyrus (lateral)	13	[-60 9 9]	3.38
Occipital gyrus	8	[21 -75 18]	3.37
Medial temporal gyrus	9	[-54 3 -15]	3.35
Occipital gyrus	11	[36 -45 -12]	3.26
Superior temporal gyrus	9	[54 -6 -3]	3.23
Occipital gyrus	18	[12 -57 9]	3.17
Insula	9	[-30 -30 21]	3.14
Putamen	21	[-24 -12 6]	3.13
Putamen/insula		[-33 -18 6]	3.03
Insula	9	[36 -9 -6]	3.04
Superior temporal gyrus	7	[48 3 -12]	3.02
Superior temporal gyrus	7	[-57 -27 6]	3.00
Insula	9	[45 9 -3]	2.95

**Table 8.** Discounted utility ( $V$ ) regions which were more active in Placebo than L-Dopa conditions (Fig. 3b).

Inspection of the behavioural results (Figure 1, Table 1) revealed that an increase in impulsivity following L-Dopa was expressed to a greater extent in some subjects than in others. On this basis, a covariate analysis was performed on the previous contrasts by calculating a difference score of the number of sooner options chosen in the placebo and L-Dopa trials for each subject. The larger this metric, the greater the increase in impulsivity (discount rate) induced by L-Dopa. By regressing this quantity as a covariate in the contrast comparing  $D$  in L-dopa minus placebo conditions (Figure 3a), a marked and significant correlation was found with activity in the amygdala (bilaterally, Figure 4), suggesting that individual subject

susceptibility to impulsivity under the influence of L-Dopa, is modulated by the degree of amygdala response to the temporal proximity of reward (see Table 9 for comprehensive results).



**Figure 4. Inter-subject variability in increase in impulsivity following L-Dopa.** **a** statistical parametric map showing areas expressing an overall sensitivity to the discount factor (in L-Dopa minus placebo conditions) and which covaried with the degree to which choices became more impulsive following L-Dopa, relative to placebo, on a subject-by-subject basis. A significant correlation was observed bilaterally in the amygdala (see Table 9). **b** Change in BOLD response in the amygdala (peak voxel) as reward proximity increased, in relation to the degree to which each subject became more impulsive under L-Dopa.

REGION	CLUSTER SIZE	MNI COORDINATES	Z VALUE
Cerebellum	12	[33 -78 -33]	4.09
Cerebellum	39	[9 -66 -30]	3.88
Left amygdala	38	[-24 3 -21]	3.83
		[-15 -3 -21]	3.80
Right inferior temporal cortex / amygdala	61	[33 -6 -36]	3.78
		[24 -6 -30]	3.33
		[39 -27 -24]	3.24
Right inferior temporal gyrus	18	[39 12 -33]	3.60
Brainstem	9	[-6 -24 30]	3.50
Left inferior temporal gyrus	10	[-30 -9 -33]	3.50
Occipital gyrus	13	[-3 -57 6]	3.27
Medial temporal gyrus	12	[-57 -3 -21]	3.20

**Table 9.** Discount (*D*) regions which covaried with the degree to which choice became more impulsive on a subject by subject basis, in L-Dopa minus placebo conditions (Figure 4a).

## Discussion

Existing theories of dopamine focus on its role in reward learning, where dopamine is thought (on the basis of extensive evidence) to mediate a prediction error signal used to update the values of states and actions that allow prediction and control, respectively, during decision-making (e.g. Dayan, 2009; Dayan and Balleine, 2002; Doya, 2008; Iversen and Iversen, 2007; Schultz, 2002, 2004, 2007). Indeed, these models have been used to illustrate how abnormal dopamine processing might lead to impulsive and addictive behaviours, on the basis of experience (i.e. through learning) (Dagher and Robbins, 2009; Dayan, 2009; Dayan and Balleine, 2002; Everitt et al., 2001, 2008; Frank et al., 2006, 2007; Redish, 2004; Robbins et al., 1989, 1996), and specifically, failing to learn from actions with aversive outcomes. Here, a distinct aspect of impulsivity was explicitly probed, based on the relationship of the timing of rewards and their utility, independently of feedback and learning. Within this framework, dopamine could potentially

increase impulsivity in two distinct ways – as a result of an increased rate of diminishing marginal utility for gains (which would decrease the subjective instantaneous value of larger magnitude relative to smaller magnitude rewards), or through enhanced temporal discounting of future rewards. However, the results suggest that dopamine selectively impacts on the discount rate, without any significant effect on the utility function. Moreover, these behavioural results were independently supported by the fMRI data in that the key difference engendered by L-Dopa was a modulation of neural responses in regions associated with the discounting of rewards and, consequently, their overall subjective value – with no effects evident for the actual utility of rewards. These results are significant in showing for the first time that enhanced dopamine activity can lead to greater temporal impulsiveness in humans and in providing a neuronal account of this effect.

### ***Behavioural results***

Once again, the behavioural paradigm, valuation model and parameter estimation technique proved successful. As was discussed in the previous studies, parameter estimates revealed both an effect of temporal discounting and non-linearity of the utility function. Specifically, the group exhibited diminishing marginal utility. Taking into consideration the non-linearity of the utility function was extremely important in being able to determine how exactly dopamine exerted its effects on choice – in this case by increasing the discount rate. Furthermore, although estimation was not performed with the simple hyperbolic model, it is likely that discount rates would have been higher, due to misattributing the concavity of utility. This again underlines the importance of modelling both determinants of

choice when analyzing intertemporal data – both behavioural and neurophysiological.

The behavioural effects of L-Dopa were striking in that they were consistent across all subjects. This was observed both in a theory neutral measure of impulsive choice – based on the number of smaller-sooner options chosen, in identical choice arrays – and was consistent with the observed increase in  $K$  estimated by the model. Moreover 5 of the 6 patients in the PD group followed a similar pattern of behaviour – more often choosing the smaller-sooner reward when taking their dopamine agonists and L-Dopa, than when not. The 6<sup>th</sup> subject's results were questionable in that there was such a large discrepancy across conditions (6 versus 74 sooner choices). Unfortunately there was no easy way of determining how consistently the subject was performing given the lack of implementation of catch trials in the patient group. Therefore, although as a group there was no significant difference across conditions, this pilot strongly warrants further studies. If the effects were found to be significant in a larger group, a number of important conclusions would be drawn. First, they would support the evidence here from healthy subjects that boosting dopamine function can lead to increased impulsivity in choice. Second, that dopamine replacement and agonist therapy can lead to enhanced impulsiveness even in patients who do not go on to develop dopamine dysregulation syndrome and show overt signs of impulsive behaviour. Finally it would demonstrate a specific deficit of temporal impulsiveness in these patients, which has not yet been shown, as it has in other disorders associated with altered dopamine function and impulsivity (see introduction above).

Importantly, these results add weight to the suggestion that impulsivity is not a unitary construct (e.g. Evenden, 1999a; Ho et al., 1999; Moeller et al. 2001; Winstanley et al. 2004a, 2006a, see Chapter 1) and moreover that different sub-

types of impulsiveness can be dissociated pharmacologically and neurophysiologically. The effects of dopamine were only observable in impulsive choice as measured by choice outcome/preference but did not impact on deliberation – ‘holding your horses’ (Frank et al., 2007) – that occurs when options are closely valued, engendering decision-conflict (Botvinick, 2007; Botvinick et al, 2004), also termed reflection or preparation impulsiveness (Clark et al., 2006; Evenden, 1999a, 1998; Kagan, 1966).

### *Imaging results*

The imaging results provided additional support and a neural account of the behavioural findings. Here, an increase in activity of discount ( $D$ ) regions was observed in L-Dopa relative to placebo conditions. Thus as rewards became more temporally proximate, these regions were active to a greater extent in the L-Dopa condition, indicating that there was a *relative* increase in the valuation of sooner versus later rewards under L-Dopa. This is consistent with a greater rate of temporal discounting in this condition. The model predicts that a greater rate of temporal discounting would lead to a reduction in the discounted utility ( $V$ ). This was observed in the imaging data where some  $V$  regions were significantly more active in placebo relative to L-Dopa conditions. Thus for a reward of a given delay and magnitude,  $V$  was greater under placebo than L-Dopa both behaviourally and neurophysiologically. Since choice is ultimately guided by  $V$ , these findings explain the increase in choice of the sooner option under L-Dopa. Notably, the fMRI differences were observed without building the behavioural differences into the regression model. By using single canonical parameter estimates for  $K$  and  $r$  to create the regressors in each condition, the imaging results independently supported the behavioural findings. Imaging analyses were not performed on the

haloperidol data as no significant differences were found across this condition and the other conditions in the behavioural data (which were noisy under haloperidol).

These results highlight why it is important both behaviourally and neurophysiologically to analyze data with reference to an integrated model. For example, in the Kable and Glimcher (2007) method, by assuming a single valuation system and only correlating discounted value regressors, only the  $V$  effect would have been observable. This would have indicated that delayed options have greater value in placebo relative to L-Dopa but it would not have provided an explanation as to why this is the case and would have not been sensitive to changes in discount region activity. One could have proposed that DA simply enhanced the instantaneous utility of the smaller relative to the larger reward. In the McClure et al. (2004) dual system framework, the results would have been interpreted by assuming that dopamine enhances activity of the 'impulsive', limbic decision-making system relative to the DLPFC, deliberative one, however this is not the case. Dopamine impacts on one value system which is sensitive to rewards at *all* delays and it does so by increasing the discount rate of that value system, as reflected by greater activity there in proximate *relative* to distal rewards.

### **Relationship of imaging results to systems described in Chapter 3**

As well as providing support and a neurobiological basis for the behavioural findings, the imaging analyses from the placebo condition corroborated the neurophysiological results in Chapter 3. The analyses again supported a hierarchical model of choice whereby independent valuation systems for magnitude and delay were integrated in the striatum to furnish a representation of overall value used to guide choice. There were some differences in activations observed across the two studies. Some regions such as the insula, were not

observed in the *D* regions – this could be due to the smaller number of subjects taking part and a consequent reduction in power. However activity in the insula was observed in the L-Dopa-placebo *D* contrast. Also, whereas in Chapter 3, medial PFC (subgenual cingulate) activity correlated with *D* and *V*, activations were instead observed more ventrally, in the OFC (both regions have previously been highlighted in imaging studies, e.g. Kable and Glimcher, 2007; McClure et al., 2004, 2007, and in animal studies, see Chapter 1). Interestingly, there were a number of additional regions highlighted in this study. The DLPFC and inferior frontal gyri for example were particularly active in the *D* and *V* contrasts. DLPFC has previously been shown to correlate with subjective value in intertemporal choice in single unit monkey recordings (Kim et al., 2008) and to be generally active in intertemporal choice in humans (McClure et al., 2004). As with the previous study, posterior regions of the temporal cortex (inferior and superior) were markedly active in the contrasts, including the L-dopa-placebo difference contrasts. Although the role of this region is unclear in intertemporal choice, one could speculate it is involved in conscious mathematical calculations made by subjects, based on some of its known functions in this domain (Grabner et al., 2007, 2009).

### *Relationship of the results to previous dopamine manipulation studies*

Single cell studies in animals (Kobayashi and Schultz, 2008; Roesch et al., 2007b), and previous imaging studies (Chapter 3; Kable and Glimcher, 2007; McClure et al., 2004, 2007; Schweighoffer et al., 2007; Tanaka et al., 2004) have implicated VTA and its efferent regions such as striatum in intertemporal choice (e.g. in the observation that striatal responses increase in response to temporal proximity of reward, and that the firing of VTA neurons encodes certain reward properties

including delay), however no human study has as yet demonstrated dopamine's propensity to enhance impulsivity in choice. Notably, dopamine manipulations in rodents have shown inconsistent effects in intertemporal choice, with some showing that dopamine enhancement leads to a decrease in impulsive choice, or that dopamine attenuation leads to an increase (Bizot et al., 2007; Cardinal et al., 2000; Denk et al., 2005; Floresco et al., 2008; Isles et al., 2003; Richards et al., 1999a; Sagvolden et al., 1992; van Gaalen et al., 2006; Wade et al., 2000; Winstanley et al., 2003, 2007) whilst others demonstrate the opposite, dose dependent, or no effect (Bizot et al., 2007; Cardinal et al., 2000; Charrier and Thiébot, 1996; Evenden & Ryan, 1996; Floresco et al., 2008; Helms et al., 2006; Isles et al., 2003; Logue et al., 1992; Richards et al., 1997b, 1999a). A number of factors may contribute to these discrepancies, namely, whether the manipulation occurs pre or post learning, whether a cue is present during the delay, pre vs. post synaptic drug effects; the paradigm used, the drug used, the involvement of serotonin and particularly the drug dosage. Chapter 1 reviews these studies in depth and elaborates on these explanations. Human studies have observed an increase in self control (de Wit et al., 2002; Pietras et al., 2003) or no effect (Acheson and de Wit, 2008; Hamidovic et al., 2008). The original hypothesis – that dopamine may modulate both  $K$  and  $r$ , with opposing influences on choice – was not supported by this study and can therefore be ruled out as a possible explanation of some of these discrepancies. Nevertheless, the results observed here were marked and clearly demonstrated that augmenting DA function leads to an increase in impulsivity.

L-Dopa has not previously been demonstrated to affect impulsive choice, and perhaps offers more compelling and direct evidence for dopamine's role than studies employing monoaminergic stimulants, which are indirect dopamine agonists and mainly exert their effects via blocking of the DA transporter (Bannon et al., 1995; Feldman et al., 1997; Groves and Tepper, 1983; Sonders et al., 1997). Of

particular concern in studies using these drugs, is that they are known to be powerful releasers of serotonin (Balcioglu et al., 2003; Kuczenski et al., 1987; Kuczenski and Segal, 1989, 1997). This is problematic and makes inferences from their dopaminergic effects difficult since 5-HT is also known to influence intertemporal choice. Specifically, a number of studies (Al-Ruwaitea et al., 1999; Bizo et al., 1988; Denk et al., 2005; Mobini et al., 2000a, 2000b; Poulos et al., 1996; Richards and Seiden, 1995; Thiébot, 1992; Wogar et al., 1993) have demonstrated that enhancing 5-HT function can lead to greater self control or vice versa. Indeed Winstanley et al., (2003) explicitly demonstrated that a decrease in impulsive choice engendered by amphetamine, in rats, is abolished by destruction of 5-HT neurons. This represents a major confound to the human and animal manipulation studies carried out to date – most of which have employed psychostimulants.

Effects of stimulants are also complicated by dosage. For example, while low doses of amphetamine induce a slowing of locomotor activity, high doses increase such activity and induce stereotypy (Solanto, 1984; Solanto and Wender, 1989). On the basis of this and other extensive evidence it has been proposed that low doses of amphetamine paradoxically reduce DA neurotransmission. According to one theory, low doses of stimulant reduce dopaminergic transmission because the raised synaptic concentration of DA activates autoreceptors on the pre-synaptic terminal which inhibit transmission. A related suggestion is that in low doses there is a significant increase in the resting or basal extracellular concentration of DA; however the raised baseline causes a relative reduction in the impulse associated release of DA expressed as a percentage increase from baseline. This may also occur as a result of presynaptic autoreceptor activation. The reduction in amplitude of pulsatile DA release results in less activation of the post-synaptic receptors. At high doses however, both basal and pulsatile DA release markedly increase, causing widespread activation of post-synaptic receptors whilst

overcoming any inhibition from the autoreceptors (see Seeman and Madras, 1998, 2002; Solanto, 1998, 2002; Solanto et al., 2001).

Indeed de Wit et al. (2002) who showed an increase in self-control using mild doses of amphetamine in humans, speculate that this could have been caused by such a mechanism. Many of the rodent manipulation studies reviewed in Chapter 1 have also shown that low doses of amphetamine decrease choice of the smaller-sooner option while high doses increase such choice (e.g. Isles et al., 2003; Richards et al., 1999a, see Chapter 1).

Finally, another confound to consider when relating the current results to animal studies is the involvement of reward learning, which necessarily takes place in animal studies. Some studies apply manipulations before learning has taken place so it is possible that dopamine affects this process; particularly given its known role in reward learning (see references above). In fact Cardinal et al. (2000) have shown this to be the case.

Therefore in light of these confounds in animal and stimulant manipulation studies, the results here should challenge the consensus assumed by some authors that dopamine function and impulsivity have an inverse relationship (e.g. Dagher and Robbins, 2009; van Gaalen et al., 2006; Pattij and Vanderschuren, 2008; Winstanley et al., 2006a).

The failure to find a corresponding reduction in impulsivity relative to placebo, with administration of the putative dopaminergic antagonist haloperidol, is likely to reflect a number of factors. These include haloperidol's non-specific and widespread pharmacological and cognitive effects (Hardman et al., 2001; Woodward et al., 2007), lack of specificity for the DA receptor (Hardman et al., 2001), dosage – some studies indicate haloperidol may paradoxically boost DA in small doses, due to pre-synaptic effects (e.g. Frank and O'Reilly, 2006, where it is used by this group

as an indirect agonist). Additionally, the subjective effects caused by the drug, including an increase in sedation and a reduction in alertness and attentiveness, may have made the data more noisy. Further studies should use more specific dopamine antagonists to assess whether a reduction in DA function can decrease impulsivity.

An alternative hypothesis is that the relationship between DA function and impulsivity in choice may resemble an inverted U shaped function where an hypo or hyperfunctioning of the DA system may result in greater impulsivity (see Williams and Dayan (2005) for a computational account), although it is not immediately obvious why this should be the case and no mechanism has been proposed for such a relationship in this case. Such a relationship has been observed with DA function in the DLPFC and working memory (e.g. Goldman-Rakic et al., 2000).

### *Mechanisms of dopamine's modulation of K and the role of the amygdala*

Dopamine is known to have a dominant effect on primitive reward behaviours such as approach and consummation (Dayan et al., 2006; Dayan, 2009; Parkinson et al., 2000, 2002). Such effects are consistent with a broad role in the construction of incentive salience (Berridge, 2007; Berridge and Robinson, 1998; Everitt et al., 2001, 2008; Robbins et al., 1996; Robinson and Berridge, 2000, 2008), and are more difficult to account for in terms of learning, per se. The mediation of unconditioned and conditioned responses by dopamine relates to the concept of Pavlovian impulsivity, where responses associated with primary, innate values form a simple, evolutionarily specified action set operating alongside, and sometimes in competition with other control mechanisms, such as habit-based and goal-directed action (Dayan, 2009; Dayan et al., 2006; Seymour and Dolan, 2008; Seymour et al.,

2009) and are modulated by DA. Importantly, these 'Pavlovian values and actions' are characteristically dependent on spatial and temporal proximity to rewards and, as such, provide a mechanism via which dopamine could control the apparent rate of temporal discounting. For example, proximity to a food is associated with these innate values which guide behaviour or lead to fixed responses. Since such values are under the influence of dopamine, it could be that enhancing dopamine activity, leads to an increase of the 'Pavlovian' values placed on spatially and temporally proximate rewards, resulting in greater reward activity to sooner options, as reflected in the  $D$  activations and increased  $K$ . If such a process underlay dopamine induced impulsivity in this task, then it would suggest that intrinsic/Pavlovian response systems operate in a much broader context than currently appreciated, since the rewards in this task are secondary rewards occurring at a minimum of 1 week.

Such an account potentially offers insight into the amygdala dependent susceptibility to dopamine-induced impulsivity that was observed. Here, amygdala activity in response to  $D$  covaried with the degree to which behaviour became more impulsive following L-Dopa. In Pavlovian-instrumental transfer (PIT), a phenomenon dependent on connectivity between amygdala and striatum (Cardinal et al., 2002; Dayan, 2009; Parkinson et al., 2000; Seymour and Dolan, 2008) which is also modulated by dopamine (Dickinson et al., 2000; Lex and Hauber, 2008; Smith and Dickinson, 1998), Pavlovian values associated with a predictor increase responding for rewards. Notably, individual susceptibility to this influence correlates with amygdala activity (Talmi et al., 2008), suggesting that the amygdala might modulate the extent to which primary conditioned and unconditioned reward values are permitted to influence instrumental (habit and goal-directed) choice. If this is the case then it predicts that concurrent and independent presentation of reward-cues during inter-temporal choice, should

elicit temporal impulsivity via an amygdala-dependent mechanism. This mechanism may depend on reciprocal VTA-amygdala-striatum connectivity, the amygdala's ability to control dopaminergic input from the VTA to the striatum and the responsiveness of striatal neurons to such input (Cardinal et al., 2002). Such an account may explain the strong influence of drug related cues in causing addicts to relapse, which is related to a strong firing of DA neurons in response to cues (e.g. Goldstein et al., 2009; Volkow and Li, 2004, 2005; Volkow et al., 2008, 2009).

Lesions of the basolateral amygdala have been shown to increase impulsivity in choice in rodents (Winstanley et al., 2004b) and more recently Hoffman et al. (2008) have shown that amygdala activity correlated with the rate of discounting in abstinent methamphetamine individuals. The current results suggest that the amygdala has a critical role in regulating impulsive choice via its ability to control dopaminergic input from the VTA to the striatum (e.g. Cardinal et al., 2002) possibly regulating the degree to which primary conditioned and unconditioned reward values are permitted to influence reward valuations and instrumental choice, as discussed above.

Alternative approaches to the Pavlovian explanation are that DA either has a direct role in modulating/encoding the discount rate (see for example Kobayashi and Schultz (2008) for some evidence), or that enhanced DA activity in the mesolimbic pathway leads to a greater influence of the 'irrational' short-term value system, in the terminology of the dual-system proponents (McClure et al., 2004, 2007; Hariri et al., 2006). Although the results presented here, in Chapter 3 and in Kable and Glimcher (2007) argue against striatum activity as an 'impulsivity signal'.

### *Implications for the understanding of dopamine related disorders of impulsiveness*

These results also speak to a wider clinical context and offer an explanation as to why an increase in impulsive and risky behaviours is often observed (Dagher and Robbins, 2009; Evans, 2004; Merims and Giladi, 2008; O'Sullivan et al., 2009) as a feature of treatment for PD using high doses of dopamine agonists and L-Dopa. Prevalence of this syndrome is estimated at 3-4% of PD patients (O'Sullivan et al., 2009) and occurs most often when patients are exposed to larger doses than required to treat their motor problems. Often this can occur from self-administration, in a manner similar to addiction. The results here suggest that such impulsive behaviour can be accounted for by a DA related increase in the discount rate. More specifically, it has been proposed that DDS can result from a flooding if the more ventral, limbic cortico-striatal loops of the basal ganglia, which, unlike the motor loop suffer relatively less DA depletion in PD (Dagher and Robbins, 2009; Swainson et al., 2000). Other putative mechanisms are suggested by evidence for neuroadaptations and sensitization occurring in DDS which include enhanced levodopa-induced ventral striatal dopamine release (see Dagher and Robbins, 2009; O'Sullivan et al., 2009) (levodopa is still considered the most potent trigger for DDS in Parkinson's disease). These theories also accord with the results of this study.

The concept of sensitization is also a prevalent theory in drug addiction (e.g. Robinson and Berridge, 1998, 2000, 2008; Volkow and Li, 2004, 2005; Volkow et al., 2008, 2009, see also above and Chapter 1) where an increased effect of stimulant drugs occurs with repeated administration (Paulson et al., 1995) and has been demonstrated in human responses to amphetamine using positron emission tomography (PET) (Boileau et al., 2006). According to the incentive sensitization theory of addiction (Robinson and Berridge, 1998, 2000, 2008) repeated exposure to

drugs of abuse can lead to sensitization of the circuits (VTA-NAc) responsible for attributing incentive salience (or 'wanting') to rewards, such that a pathological level of salience/wanting is attributed to drugs and stimuli which are predictive of them. This incentive sensitization is a direct function of increasing magnitude of ventral-striatal DA release over time. Thus, although addiction is generally associated with reduced DA function throughout the brain (Volkow and Li, 2004, 2005; Volkow et al., 2008, 2009) – which in turn is associated with a reduction in pre-frontal circuits which exert top-down inhibitory control mechanisms – it is also associated with increasing VS DA release in response to drugs and their associated cues.

Significantly, by spreading beyond the associative focus of wanting on drug targets, incentive sensitization can also sometimes spill over in animals or humans to other targets, such as food, sex and money (Robinson and Berridge, 2008). For example repeated treatment with amphetamine in rats can later facilitate the appetitive or anticipatory phase of a sexual encounter (see Robinson and Berridge, 2000). This sensitization-related facilitation of sexual motivation is accompanied by augmented dopamine efflux in the nucleus accumbens in response to presentation of a receptive female. Therefore the increase in VS dopamine release to rewards engendered by sensitization accords well with the findings here that increased DA release can cause a transient increase in temporal discount rates/ impulsive choice. This could explain why addicts have been shown to have abnormally high discount rates, which increase over increasing time of drug use (e.g. Bickel and Marsch, 2001; Bickel et al., 2007 – see Chapter 1). Moreover, substance abusers have also been shown to have higher rates of discounting when offered choices between smaller-sooner and larger-later drug rewards (for the drug of choice), than that measured with monetary rewards (which are also abnormally high) (e.g. Madden, 1997; Bickel et al., 1999). Since incentive sensitization occurs to the greatest extent

in response to the drug itself, and to a lesser extent other rewards (Robinson and Berridge, 2008) an enhanced DA release in relation to non-drug rewards could explain this effect. Interestingly, Robinson and Berridge (2008) argue that sensitization can facilitate the acquisition of Pavlovian associations and that this ability is related to enhanced DA efflux in the striatum and amygdala.

In summary, just as enhanced DA activity led to an increase in impulsive choice in this task, enhanced DA efflux in the striatum in both DDS and in addiction (as a result of dopaminergic drugs and rewards) could similarly lead to an increase in impulsive choice. In fact any rewarding stimulus (such as a drug associated cue) which leads to a release of DA in the striatum (Vanderschuren and Everitt, 2005) will cause a transient increase in impulsivity in these conditions. According to the theory that enhancing DA function can lead to greater self-control, these findings from addiction and DDS would be very difficult to explain. As mentioned above one could suggest 3 mechanisms of dopamine-mediate impulsiveness. First, DA acts as a direct modulator/ encoder of the discount rate. Second, DA release in the VS acts to enhance the output of an immediate, irrational and short-sighted reward system, relative to a longer-term and less impulsive one. Most likely, DA release in the striatum and its control by the amygdala acts to enhance the influence of innate values which are dependent on spatial and temporal proximity to rewards.

Prima facie these results are difficult to integrate with the effective use of psychostimulants such as methylphenidate and amphetamine in the treatment of ADHD. Specifically, that the underlying deficit in a subtype of ADHD is an increased preference for sooner rewards, whose pharmacological basis is a hypoactive mesolimbic DA system, which is then normalized by dopaminergic medication (Johansen et al., 2002; Sagvolden and Sergeant, 1998; Sagvolden, et al., 1992; Winstanley et al., 2006a, see above). However, as discussed above whether ADHD is characterized by a hyper or hypo DA state and how this may be

'normalized' by psychomotor-stimulants is controversial, indeed, the very idea that stimulants can treat ADHD has been deemed paradoxical. The results presented here support theories of ADHD which highlight a *hyperactive* mesolimbic DA system, and a treatment by low doses of stimulant medication which *reduce* dopamine neurotransmission (Seeman and Madras, 1998, 2002; Solanto, 1998, 2002; Solanto et al., 2001; Swanson et al., 1998; Zhuang et al., 2001). The biphasic action of stimulants proposed by these authors is also evident in human responses to stimulant medication, explaining why low doses are most effective in ADHD treatment (Seeman and Madras, 1998, 2002; Solanto, 1998, 2002; Solanto et al., 2001; Swanson et al., 1998). This view that effective pharmacological treatments for ADHD reduce DA transmission accords with the finding that small doses of amphetamine given to a group of hyperactive children significantly lowered CSF levels of homovanillic acid, the major metabolite of DA, in relation to their clinical improvement (Shetty and Chase, 1976). See Solanto et al. (2001) for further evidence of this theory.

Another possibility is that the effects of methylphenidate and amphetamine are mediated by their effects on serotonin and noradrenaline, which are also thought to be involved in impulsive choice (see above).

In summary, this study provides evidence that dopamine controls how the timing of a reward is incorporated into the construction of its ultimate value, independently of the magnitude of the reward itself. This effect is manifest in an enhanced representation of temporal discounting, observed in the striatum, and possibly modulated by connectivity with the amygdala. These data provide a novel mechanism through which dopamine controls human choice and, correspondingly, traits such as impulsiveness, and offers a powerful explanation for the enhanced impulsivity seen in disorders associated with abnormal DA efflux.

## Chapter 5.

### General discussion

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#### Introduction

The experiments described in this thesis addressed the evaluation, neural instantiation and ramifications of a new model of intertemporal choice, the crux of which was an integration of non-linear utility functions into existing models of temporal discounting. The role of dopamine in modulating aspects of this model and neural function in intertemporal choice was also assessed. In this concluding Chapter, the findings from these experiments will first be summarized briefly. The results have already been discussed in Chapters 2 – 4. Here their implications will be discussed in a wider and integrative context. Finally future research directions which are warranted from the work carried out here will be suggested.

#### Summary of results

##### *Study 1: The effects of diminishing marginal utility for gains on intertemporal choice*

Widely used, standard models of discounting (Mazur, 1987) assert that intertemporal choice outcome is only a determinant of one valuation process, namely, temporal discounting. As such choice outcome can only vary as a result of a change in the discount rate,  $K$ . The aim of this study was to determine whether diminishing marginal utility, the discounting of magnitude (or concavity of the

utility function) is also determinant of choice outcome. This idea has been proposed by economists (Frederick et al., 2002; Loewenstein and Prelec, 1992; Read, 2003) but has not been empirically tested in human studies of intertemporal choice. The study aimed to assess the Multiplicative Hyperbolic Model of choice (Ho et al., 1999) which has been able to dissociate these separate influences in animal manipulation studies. Based on the model, a prediction was formed whereby in an adjusting delays task – which has not been extensively used in human studies – indifference points of the delay to  $B$  (larger-later) for a given delay to  $A$  (smaller-sooner), would be described by a linear function. The gradient of this function was determined to be a function of the reward utilities, whereas the intercept of the function was influenced by the discount rate and the reward utilities. Specifically, the gradient was hypothesized to equal the ratio of instantaneous utilities  $[U(B) / U(A)]$ . One trial of adjusting delays used a £450 vs. £300 choice, for  $B$  and  $A$  respectively, over varying delays to each. Derivation of a function for a standard hyperbolic model also predicted a linear relationship where the gradient should equal the ratio of reward *magnitudes* – in this case 1.5. Derivation of a function for exponential discounting, predicted a linear relationship where the gradient should always equal 1. The MHM predicted a gradient of more than 1 but less than 1.5, since a concave utility function would imply that the utility of £450 is slightly less than 1.5 times the utility of £300. A linear utility function would imply a utility ratio of 1.5. Additionally, a second trial of adjusting delays was added, this time doubling the values of  $A$  and  $B$ , thereby keeping their magnitude ratios constant. The model predictions in this trial were for a gradient of 1 and 1.5 according to the exponential and SHM models. According to the MHM the gradient was expected to be between 1 and 1.5 but less than the gradient observed in the first trial, as the effects of concavity would be more apparent in this trial where the magnitudes were bigger. This would lead to a reduction in instantaneous utility ratios  $[U(B) / U(A)]$ . The additional utility gained

in waiting for  $B$  would be less than in trial one, leading to a reduction in indifference delay to  $B$  and hence the gradient, as predicted by the MHM.

For comparison purposes, two trials of the adjusting amounts (e.g. Richards et al., 1997a) procedure were also performed by subjects, where the amount of  $B$  was doubled. Here, curve fitting procedures were used to estimate the parameters for both the SHM and MHM as well as to give a measure of the goodness of fit using adjusted  $R^2$ .

Three additional hypotheses were tested. It was proposed that the magnitude effect (e.g. Green and Myerson, 2004) whereby discount rates appear to differ according to reward size, could be explained by the non-linearity of the utility function. It was also proposed that the parameter determining utility concavity ( $Q$  in the MHM) would remain constant as it applies to all magnitudes. Therefore parameter estimates were determined for both trials in the adjusting amounts and delays trials to see if they remained stable. The MHM predicted a reduction in intercept due when amounts were doubled, whereas the intercept would be expected to rise if the magnitude effect were true. Finally, it was hypothesized that the discount rate would be higher when estimated by the SHM than the integrated model, due to a misattribution of impulsivity engendered by utility function concavity. These hypotheses had not been tested by Ho et al. (1999) in use of their model which is primarily for comparative studies.

Results of the adjusting delay trials showed that indifference points fit a linear regression with a high degree of accuracy, as predicted by all models. Analysis of the gradients indicated that the MHM predictions were correct. The gradient was less than 1.5 in the low magnitudes trial and was further reduced in the high magnitudes trial. In other words, indifference delays to  $B$  were reduced in the second trial, demonstrating that diminishing marginal utility can cause an increase

in preference of the sooner option. Furthermore the gradients were above 1, which ruled out exponential discounting.

The data from the adjusting amount trials were very noisy and were not suitable for statistical analyses. This suggested that adjusting delays may be a preferable paradigm to use in human studies.

Analysis of the parameter estimates  $K$  and  $Q$  for each subject in the adjusting delay trials indicated that  $K$ , the discount rate, was reduced in the larger magnitude trials, confirming a magnitude effect. Further evidence of this was a reduction in the intercept, in the larger magnitudes trial.  $Q$  parameter estimates were of unrealistic values. This was partially a problem of the  $Q$  function which did not allow for a convex (marginally increasing) utility function, observed in some subjects.

To better model human choice, and estimate parameters a new function was proposed whereby the  $Q$  function was replaced with a utility function which has described risk preference choices in humans (Holt and Laury, 2002). When the data were reanalyzed (using linear regression) with this discounted utility model, sensible values for  $r$ , the parameter determining the utility concavity, were estimated. These values were stable across the two trials and were greater than zero, indicating along with evidence from the gradients, that the group exhibited diminishing marginal utility. This conclusively showed that the integrated model is better at describing human choice than the standard hyperbolic model, and for the first time demonstrated the effects of diminishing marginal utility on choice. This result justifies the use of the new model of intertemporal choice and allows for estimation of concavity parameters in future studies wishing to explore this feature of preference.  $K$  value estimates were still judged to be smaller in the larger magnitudes trial, indicating a magnitude effect was present, however the difference was reduced in comparison to the difference observed under the MHM.

Furthermore,  $K$  estimates under the new model were smaller than those estimated by the SHM, confirming that the simple model misattributed impulsivity arising from utility concavity, to a greater temporal discount rate, another novel finding. It was concluded that impulsivity in choice is both determined by  $K$  and  $r$  and that the simple relationship between  $K$  and impulsivity is not accurate.

***Study 2: The encoding and integration of temporal discounting with marginal utility in the human brain***

There were a number of major aims in this study. By using fMRI during intertemporal choice, it was hoped that neurophysiological as well as behavioural data would corroborate the veracity of the new discounted utility model. The model predicted the existence of value systems responding individually to the temporal discount weightings and utility of rewards, as well as a representation of discounted utility which is furnished by an integration of these two systems. Demonstration of these separable systems for different reward components would be a novel finding and demonstrate a true temporal discounting network, free from the confound of utility. It would also be the first neurobiological account of the non-linearity of utility, or specifically the law of diminishing marginal utility.

To test these hypotheses, behavioural data collected during scanning were used to estimate model parameters for the subjects. These model parameters were then used to calculate parametric regressors corresponding to the three components of the model ( $D$ ,  $U$ , and  $V$ ), to apply to the brain imaging data during the option valuation stages. The task used a novel imaging design whereby the options were presented serially, and prior to the decision phase. To look for brain regions correlating with utility of rewards, as opposed to their magnitude, the magnitude was included as a parametric regressor and utility was orthogonalised with respect

to magnitude. This highlighted regions where activity could only be explained by the encoding of non-linear utility.

The second major focus of the experiment was to develop a new parameter and model estimation technique. This was necessary to be able to expose the subjects to a varying magnitudes and delays in order to increase the power of the imaging analyses. Indifference point methodology was therefore abandoned in favour of a sampling method involving maximum likelihood estimation of the softmax decision rule, in the context of the discounted utility model, to estimate the most likely parameters of the model given the subjects choices. It was hypothesized that the  $K$  and  $r$  estimates should be greater than zero, to indicate temporal and magnitude discounting. This technique also allowed for a measure of the model fit based on the likelihoods. Using this measure of model likelihood given the data, a number of other influential valuation models were compared, to the new hyperbolic discounting of utility model. These other models were also tested both with a linear and a non-linear utility function. The advantage of this comparison technique over a comparison of  $R^2$  values was that it could also overcome the problem of comparing models with different complexities, caused by varying numbers of free parameters. This was achieved by use of the Akaike information criterion which penalized the likelihood scores of models based on their number of free parameters. Thus, the discounted utility model could be shown to be better than the SHM by both a lower AIC score and also by showing that the  $r$  estimates were greater than zero. As in the first study, it was also expected that  $K$  parameter values would be greater when estimated using the SHM than the new model. In this study, payment was awarded from two randomly selected choices made by the subject, using pre-paid credit cards, to ensure the effect was apparent in real choice scenarios.

A final hypothesis of the study was that the model and parameter estimates could be used to predict which choices the subjects would have found difficult, based on the degree to which the choice options were similar in value (engendering decision-conflict - Botvinick, 2007). Choices involving greater decision-conflict were predicted to be associated with an increase in decision latency and an increase in activity of conflict areas in the brain such as the ACC and DLPFC, during the decision phase.

Results of the model estimation technique revealed both an effect of temporal discounting on choice and of utility concavity ( $r$  estimates were significantly greater than zero). Additionally, AIC scores revealed that the hyperbolic discounting of utility was the most likely in the set of candidate models compared, even when other models were modified to incorporate non-linearity of utility.  $K$  values estimated by the SHM were greater than those estimated by the discounted utility model, resulting from a misattribution of utility effects which bias choice to the smaller-sooner option. Additionally, there was no correlation observed between  $K$  and  $r$  estimates. This suggested the two processes should be kept separate.

fMRI analyses revealed three distinct networks of regions associated with the three components of the valuation model. This demonstrated that the brain values different reward dimensions individually, and revealed a distinct network of discount regions whose activity constituted a hyperbolic discounting of time. Moreover regions comprising medial PFC / subgenual cingulate, and caudate were found to correlate with overall value used to guide choice. Critically, a region of overlap was found where activity correlated with all three regressors. This region in the dorsal striatum was therefore implicated in the integration of different sub-components of value to guide choice. Additionally, a region in the dorsal striatum was also found to correlate with the utility of rewards, even when factoring out

any activity that could have been explained by reward magnitude. This demonstrated the first evidence that the brain values instantaneous rewards in a non-linear (concave) fashion, and so giving a neural account of diminishing marginal utility.

Finally, decision latencies were observed to slow in response to increasing choice difficulty, as measured by smaller differences in overall value of the two options. Surprisingly, decision-conflict was also induced by a large difference in delays, irrespective of difference in overall value. Imaging results confirmed the decision latency findings, showing a network of conflict areas including ACC and DLPFC which correlated with increasing difficulty as measured by both small differences in overall value and large differences in delay to each option. The strength of ACC and DLPFC activation in response to decision-conflict also covaried with intersubject variability in the rate of conflict-induced slowing down. These results demonstrated that decision-conflict under the control of the ACC, can occur in higher level decisions as well as perceptual and motor tasks where it has previously been observed (Pochon et al., 2008).

The imaging and behavioural analyses showed that neither a dual decision-making system account (Berns et al., 2007; McClure et al., 2004) nor a single valuation system account (Kable and Glimcher, 2007) were an accurate portrayal of the neuronal valuation processes in intertemporal choice. Instead an integrated hierarchical account was offered.

### *Study 3: The involvement of dopamine in intertemporal choice and impulsivity*

The aim of this study was to use the modelling and brain imaging techniques described in the previous study to determine the exact role of dopamine in

intertemporal choice. One purpose was to try to explain previous discrepancies in the literature on dopamine and intertemporal choice by looking at its effects on both  $K$  and  $r$ . Another purpose was to try and give an account of the impulsive behaviours observed in disorders associated with altered dopamine function, such as ADHD, DDS and addiction.

These aims were achieved by manipulating dopamine function of healthy volunteers in a within subjects design. In one condition subjects received a dose of the dopamine precursor L-Dopa, in another they received a dose of the dopamine antagonist Haloperidol, and in a control condition subjects received placebo. fMRI was used while subjects performed the task, to be able to link any behavioural changes across conditions with changes in neuronal activity of regions associated with the various model components, and to provide additional and independent evidence. A regression of the model components  $D$ ,  $U$ , and  $V$  was also performed on imaging data from the placebo condition, to corroborate the results found in the previous study. To enhance sensitivity, subjects performed the same set of choices in each condition.

To distinguish global from discrete influences on impulsivity, and perhaps discover novel roles for dopamine, the degree of slowing down of decision latency in response to conflict was compared across conditions.

The use of L-Dopa was based on a number of factors. 1) It has not yet been shown to affect intertemporal choice, as other dopaminergic drugs have. 2) Using L-Dopa is a 'cleaner' and direct way of augmenting dopamine function. Previous studies (e.g. de Wit et al., 2002) have focused on psychostimulants such as amphetamine, which have widespread effects, including enhanced 5-HT efflux. Serotonin has also been shown to modulate intertemporal choice (e.g. Winstanley et al., 2003, 2005). Additionally, stimulants have complicated dose related effects (Solanto, 1998). Here it was hoped that DA would be shown to modulate impulsive

choice without these confounds. 3) To give an account of DDS, where Parkinson's disease patients on high doses of L-Dopa (and also dopamine agonist therapy) can develop extremely impulsive behaviours (O'Sullivan, 2009).

In addition a behavioural pilot study was carried out on 6 Parkinson's patients who were being treated with L-Dopa and dopamine agonists. They were tested in an 'on' condition and an 'off' condition. In the latter condition they did not take their usual medication prior to testing. It was hypothesized that choice behaviour of these subjects should mimic any behavioural effect of augmented vs. attenuated dopamine function in the healthy volunteer group. This pilot was also performed to see whether impulsivity is enhanced in all patients on dopamine replacement therapy, not just those who develop DDS, and if so to demonstrate for the first time a specific deficit in impulsive choice in these conditions.

As well as assessing behavioural changes using parameter estimates, subject's performed the same set of choices in each condition so a clear, theory neutral demonstration of any change in impulsive choice could be observed across conditions.

The behavioural results demonstrated a marked increase in impulsive choice under L-Dopa relative to the placebo condition, as measured by a significantly greater choice of the sooner option in that condition. There was no significant difference observed in the Haloperidol condition, relative to placebo. Analysis of the parameter estimates revealed that this effect was mediated by an increase in the discount rate in all subjects, under L-Dopa with no effect on utility concavity.  $K$  and  $r$  were significantly greater than zero in both cases, showing an effect of time and magnitude discounting. Although subjects' decision latencies were increased as choices became more difficult (i.e. as option values got closer), in each condition, there was no difference in the degree of slowing down across conditions, indicating a discrete effect of dopamine on impulsive choice. A similar pattern of

behaviour was observed in the patient group, where 5 of the 6 subjects chose more impulsively in the 'on' medication condition versus the 'off' condition. These differences were not significant at the group level, presumably due to the small sample size and outlying values of the 6<sup>th</sup> subject who showed an extreme opposite pattern.

Analysis of the fMRI data in the placebo condition corroborated and extended the results observed in Experiment 2. Again, a distinct pattern of activations was associated with each regressor and activity in more dorsal regions of the caudate was observed in all cases, indicating its integrative function. Imaging results across conditions accorded with the behavioural results. Activity in *D* regions was greater in L-Dopa than placebo conditions. This demonstrated that there was an increase in the value weighting of sooner relative to later options in this condition, consistent with the finding that the discount rate was increased. Furthermore, activity in *V* regions was reduced in L-Dopa relative to the placebo condition, consistent with a reduction in overall value of delayed options in the L-Dopa condition, caused by the increased discount rate, and leading to the increased selection of the sooner option. Finally, by covarying inter-subject differences in the number of sooner options chosen in L-Dopa vs. placebo conditions, with the difference in *D* activations across these conditions, significant activity was observed in the amygdala. This demonstrated that the degree of enhanced impulsiveness caused by L-Dopa (on a subject by subject basis), was associated with degree to which the amygdala was active in response to reward proximity. These analyses used regressors that were created from canonical parameter estimates for *K* and *r* across all trials and therefore independently corroborate the behavioural findings.

Three putative mechanisms were offered for enhanced impulsiveness under L-Dopa. 1) Dopamine neurons directly modulate / encode the discount rate. 2)

Increased DA activity in the mesolimbic pathway and its associated basal ganglia circuit enhances the influence of a short-term impulsive decision making system relative to a more rational, long-term system located in the DLPFC. 3) Dopamine potentiates the control of 'Pavlovian' innate values and evolutionary action sets over behaviour. Such values are engaged by reinforcers which are spatially proximate, and perhaps also temporally proximate.

The results were used to give an account of enhanced impulsivity observed in addiction and DDS, and were used to support a model of ADHD (Solanto, 1998, 2002) which proposes a hyperactive DA system as the cause of the disorder, where psychostimulants in low doses act to reduce DA function. It was suggested that the consensus view that dopamine augmentation leads to greater self control was unlikely to be true.

## **Wider implications and directions for future research**

### *The ramifications of models in intertemporal choice: possible extensions*

One could ask why it is so important to determine the exact form of the function for valuation of delayed rewards? After all, standard models of discounting fit data rather well – is the extra effort in developing and proving a new model really worth the extra few log likelihood, or R squared points? The simple answer here would be that this endeavor is not just about improving the fit of the model. In this case, the integrated valuation model was developed to be able to properly estimate discount rates, which in most experiments will have been grossly overvalued (Andersen et al., 2008; Frederick et al., 2002; Loewenstein and Prelec, 1992). And it was developed to remove a major confound of interpretation in studies which attempt to relate changes in intertemporal choice behaviour to economic, biological or psychological variables. This confound was applicable to those studying the

basis of temporal discounting or those studying the basis of impulsive choice (using temporal discounting as a proxy). Developing a new model was also valuable because in the process of trying to solve confounds in traditional models, a new way and method of studying the confound itself, namely, the non-linearity of utility, was developed – potentially leading to new research avenues.

A more ontological view would be to say that different models instantiate different assumptions regarding fundamental aspects of the processes described by them. This can be related to the concept discussed in Chapter 3, of Kullback-Leibler information  $I(f,g)$ , which is the information lost when model  $g$  is used to approximate  $f$  – full reality or truth (Burnham and Anderson, 2002). Stated more simply it is the distance between full reality and a model. By reducing KL-divergence, one gains a clearer picture of fundamental truths, an ability to make new and more accurate predictions, and one leaves less room for surprises which reality has up its sleeve. For example, if an exponential model of discounting was found to provide the best description, this could be consistent with the assumption that temporal discounting is based on the risk associated with waiting for a reward, or an opportunity cost (Frederick et al., 2002; Kacelnik, 1997; Kagel et al., 1986). Hyperbolic discounting would be consistent with other assumptions regarding the nature of time preference (e.g. Ainslie, 1975; 1992; Frederick et al., 2002; Berns et al., 2007). In our case, the model significantly changes the assumptions about the basis and determinants of intertemporal choice, as well as how reward valuation and choice are implemented neuronally. Whereas the beta-delta model of choice (Laibson, 1997; Phelps and Pollak, 1968) has been used to propose a dual system neuronal decision-making process (McClure et al., 2004), and the standard hyperbolic model for a single neural valuation process (Kable and Glimcher, 2007), the model presented here assumes an integrative, hierarchical value system in the brain. Importantly, this system was implicated and

demonstrated by use of the model, and would not have been discovered by analyses using the above mentioned models.

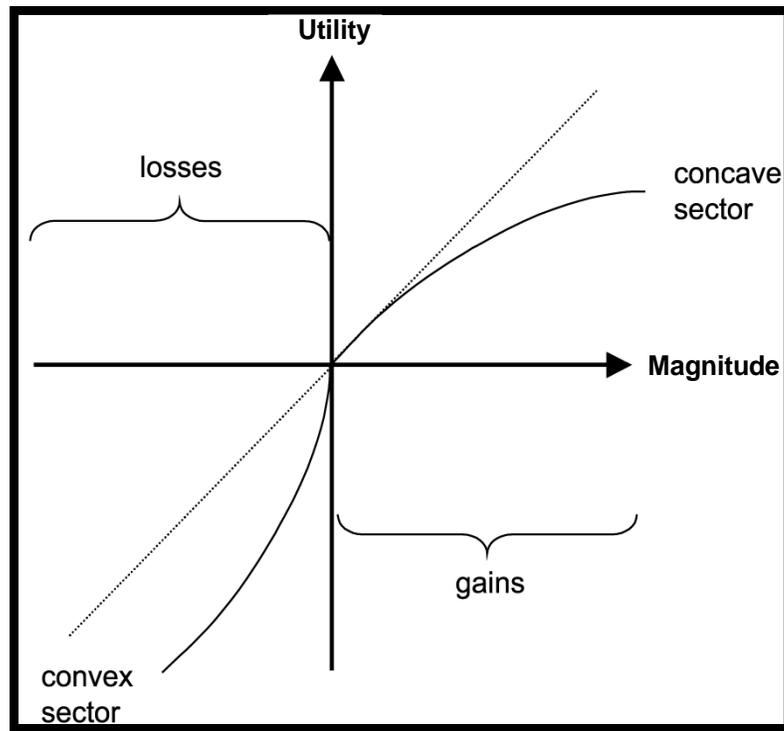
### **Intertemporal choice in the loss domain**

One simple and useful way the model could be extended is to apply it to the valuation of delayed punishment (losses) as well as rewards. Intertemporal choice in the loss domain has attracted relatively little attention although many features are similar, such as the hyperbolic-like form of temporal discounting (Baker et al., 2003; Estle et al., 2006; Green and Estle, 2003; Green and Myerson, 2004; Loewenstein, 1987; Mackeigan et al., 1993; Murphy et al., 2001; Thaler, 1981 - see also Chapter 1) as well as preference reversals (Holt et al., 2008). Most of these studies have observed a phenomenon known as the 'sign effect', whereby equivalent losses are discounted less steeply than gains – or less willingness to trade larger-later for smaller-sooner losses (see Chapter 1). As with the magnitude effect, it has been noted that this anomaly could be explained by the utility function (Frederick et al., 2002; Loewenstein and Prelec, 1992; Prelec and Loewenstein, 1991). Specifically, it could be explained by an (instantaneous) utility function envisaged by prospect theory (Kahneman and Tversky, 1979), where there is a 'kink' in the function at the  $x$  axis (Figure 1). This kink is produced by the gradient of the function becoming steeper as one moves from gains to losses, meaning that losses loom larger than gains [ $U(-M) / -U(M) > 1$ ]. In fact experimental evidence from risk preference tasks indicates that the negative utility of a loss is roughly twice that of an equivalent gain (Tversky and Kahneman, 1992). Interestingly, Estle et al. (2006) found that the sign effect decreases with larger amounts. Perhaps this could be explained by the convexity of the function as the magnitude of losses increases. These observations suggest that the model used for gains in this thesis could easily be extended to give an accurate account of

intertemporal choice in all domains, by replacing the utility function with a function based on the one envisaged by prospect theory. Tversky and Kahneman (1992) suggest the following functional form for the instantaneous utility function:

$$U(M) = \begin{cases} M^r & \text{if } M \geq 0 \\ -\gamma(-M)^s & \text{if } M \leq 0 \end{cases}$$

Here,  $s$  is the convexity of the function in the loss domain and  $r$  is the concavity in the gain domain. In the loss domain gamma ( $\gamma$ ) is known as the loss aversion coefficient and is thought to roughly equal 2.25 as mentioned above (Tversky and Kahneman, 1992), although this differs across individuals and studies. Note, this scheme suggested by Tversky and Kahneman uses a power function to describe the concavity and convexity and could be easily adapted for the exponential form of the utility function used in this thesis, which is thought to be more accurate (Holt and Laury, 2002).



**Figure 1. Utility function for losses and gains.** As envisaged by Kahneman and Tversky (1979). Main features are concavity for gains, convexity for losses, and a kink in the function as it crosses the x axis as a result of a steeper curve, indicating loss aversion. Dotted line represents a linear utility function.

Applying the integrated model to the loss domain using this scheme would also engender a novel application for intertemporal choice tasks in being able to estimate loss aversion coefficients, something never previously attempted. One could then test to see whether this accorded with loss aversion coefficients derived from the same subjects using traditional methods such as risk preference / gamble tasks. Of course the additional free parameter in the loss domain would reduce the power of the maximum likelihood estimation procedure, potentially giving less reliable estimates, so a greater number of choices may need to be employed. In addition one could test for an effect of independent variables (pharmacological manipulation, brain lesion etc.) on this measure. Using the integrated model would

then address a double-confound in intertemporal loss studies which rely on the standard hyperbolic model.

It has been proposed that discounting of losses may involve different processes to discounting of gains (Estle et al., 2006). In theory this extended model would not predict this is the case, however one could assess this by using a similar fMRI design employed in Chapter 3, but including choices with losses. Estimating the parameters from behavioural data, one could perform a regression of the three value components ( $U$ ,  $D$  and  $V$ ) to model BOLD responses during the valuation stage, and look for differences in loss versus gain trials. Xu et al. (2009) and Bickel et al. (2009) have used imaging to show that a single system is involved discounting gains and losses however their designs are limited by the models used and by not using regressors estimated from behaviour to delineate the relevant neural value systems. Finally, by comparing utility activations across trials one could obtain a neural basis for gamma. It would be interesting to see whether this accorded with the neural basis for loss aversion reported by Tom et al (2007) using gambles.

### **Intertemporal choice with probabilistic outcomes**

Another way in which the model could be extended is to incorporate the third major reward dimension – probability. Ho et al. (1999) in their Multiplicative Hyperbolic Model of choice have provided a template for this by simply proposing that overall value is a product of the three sub-components of value. Using the terminology developed in this thesis this can mathematically described as follows:

$$V = D \cdot U \cdot P$$

where,

$$P = \frac{1}{1 + H \cdot \theta}$$

Here,  $P$  is also a discount factor between zero and one, by which the value is discounted in accordance with the probability ( $p$ ) of not receiving the reward, or odds against ( $\theta$ ). Theta, the 'odds-against' ratio =  $[1/p]-1$ .  $H$  is the discounting parameter for the odds against occurrence. An  $H$  greater than 1 leads to risk aversion, and less than 1, to risk seeking. As can be seen from the formula, discounting of risky options (decreasing probability) is also hyperbolic in nature. This form has been experimentally determined both in animal and human choice studies (e.g. Estle et al., 2006, 2009; Green and Myerson, 1996; Green et al., 1997; Ho et al., 1999; Ostaszewski et al., 1998; Rachlin et al., 1986, 1991; Rachlin and Siegel, 1994; Rachlin and Raineri, 1992).

There are a number of potentially interesting ways in which one could apply this function (see Ho et al., 1999 for examples). The most interesting, from the perspective of this thesis would be to perform an imaging study similar to the one in Chapter 3, but adding in a probability dimension to the choices. Assuming one could reliably estimate all three free parameters (perhaps a larger number of trials would be required) a regression of the three components of value ( $D$ ,  $U$  and  $P$ ) as well as the overall value could be performed. In theory, according to the ideas presented earlier, this should yield a fascinating result whereby all three sub-components of value correlate with unique valuation networks for each dimension of the reward. Furthermore, one could speculate that the dorsal striatum would be the site of integration of the three value systems, to encode the overall value used to guide choice. Such a finding would be remarkable. This study could also corroborate the hypothesis that magnitude and probability discounting do not engage a single process (e.g. Green and Myerson, 2004). Such an idea was also advanced here based on the insula activations observed in response to reward proximity (see Chapter 3) and in studies by Luhmann et al. (2008) and Ballard and

Knutson (2009). Imaging analyses in the latter studies were not model based and independent of behaviour, so a formal test of the hypothesis that temporal discounting is not (solely) based on risk incurred with waiting is warranted.

### **The magnitude effect**

Finally, in order to clarify whether potential adjustments to the model are required, more work should be carried out to assess whether the magnitude effect is based on amount dependent discount rates, i.e. is real, or is simply a function of the utility concavity (Ho et al., 1999; Loewenstein and Prelec, 1992). If it were a reliable and real effect one would need to factor in an extra  $K$  parameter, and so parameter estimation as well as interpretation of independent variable effects would get more complicated. Although a magnitude effect was observed in Chapter 2 here, the study involved hypothetical choices which may be more susceptible to such effects. As mentioned in Chapter 1, the magnitude effect has not been observed in animals (Grace, 1999; Green et al., 2004; Richards et al., 1997a), or in human studies of discounting for losses (Estle et al., 2006). A magnitude effect would not be too problematic for the maximum likelihood estimation technique developed here (again, it would weaken power slightly), however it would be potentially more problematic for inferences made on the basis of the gradient and intercept of the linear function in the adjusting delays procedure. More specifically, it could be argued that a change in slope across conditions could arise from a change in the ratios of the two  $K$  parameters (see Green et al., 1994).

### *The methodology of intertemporal choice*

This thesis has described two useful methods for determining the joint influences of temporal discounting and utility concavity on choice, in humans. One motivation to develop these methods was that previous studies were confounded by the problem of assuming that temporal discounting was the only factor in determining choice. As this hypothesis was corroborated by the experiments carried out here, showing that choice outcome is also determined by the rate at which the marginal utility of the chooser diminishes, future studies should implement this model and these methodologies. In addition, when comparing different models of choice which have varying numbers of free parameters, the AIC evidence based method should be used, rather than an  $R^2$  measure.

Further studies may wish to assess the confidence of parameter estimation using the maximum likelihood estimation (MLE) procedure described in Chapter 3. While analysis of the data from Chapter 2, using this procedure, yielded similar results to parameters estimated from indifference points, no statistical tests or formal assessments of accuracy were carried out here. Nevertheless such techniques are standard procedures in studies which model reward learning (e.g. e.g. Daw et al., 2006; Seymour et al., 2004; Pessiglione et al., 2006). Of particular concern is how independent the parameter estimates are from each other. For example, the behavioural effect of L-Dopa on impulsive choice (Chapter 4) was ascribed to a change in  $K$ . Perhaps the likelihood estimation technique is always more likely to ascribe changes in impulsive choice to  $K$  rather than  $r$ ?

In answer to this, crucial factors in the MLE method are the choice arrays and the number of choices used. As many choices will be of no value to the fitting procedure in estimating parameters (i.e. obvious choices such as £10 today vs. £12 in 1 year – where all subjects are likely to choose the former option) it is essential to

use as many choices as possible. The essential choices for the fitting procedure are those identified as difficult choices (Chapter 3) where the difference in overall value between the two options is small and the subject will be close to indifference. Here a constraint was imposed by the limited time subjects could spend in the scanner and the serial presentation (allowing only 2200 choices), however in behavioural studies a larger number of choices should be used to improve estimability. Alternatively, specific choice arrays could be designed for subjects with different degrees of impulsivity. Subjects could first be pre-assessed on a quick and dirty questionnaire task such as the Kirby method (Kirby and Marakovic, 1996, see Chapter 1). They could then be assigned to a choice array designed to include many difficult (near indifference) choices for a subject whose parameters are in the region of that assessed by the pre-screening. The best method one could employ to accurately estimate parameters is a task where the choice arrays are not predetermined but are based on previous choices of the subject in the trial. Here, one would need to implement a live fitting procedure where based on previous choices, the programme would determine the next choice – to be able to zoom in on the parameter estimates – until a confidence level is achieved, or subsequent choices no longer improve the fit. Note that indifference point methodology (such as employed in Chapter 2) avoids some of these problems by using this zooming in technique.

In the imaging studies in this thesis, task design (as well as analysis – see below) was an important and novel feature. Since valuation was the crucial phase, it was important to separate this phase from the decision-making itself. Furthermore, to avoid conflicting or relative value signals, the options were presented serially. This is the first time that such a procedure has been used and most likely engenders less ambiguous data and improved power. Potentially, some of these processes may have occurred from the presentation of option 2 onwards, so perhaps an analysis

focused solely on the valuation stage of option 1 may be warranted. Nevertheless, in this regard the design is an improvement over previous paradigms (e.g. McClure, 2004; Kable and Glimcher, 2007). Ideally, a task could be designed to completely remove choice and only involve valuation. Perhaps this could be achieved by first estimating parameters with choices outside the scanner. Subsequently fMRI could be applied to a task where options (delayed rewards) are presented and some response is required based on these options (such an approach has been developed by Luo et al. (in review)).

### *Diminishing marginal utility, risk aversion and $r$*

It has been noted that one of the benefits of the model is that it provides a novel way of studying the non-linearity of utility functions (or magnitude discounting), using intertemporal choice. This is based on the fact that if most people have concave utility functions (i.e. exhibit diminishing marginal utility for gains), choice should be biased towards the sooner option as the option magnitudes are increased. This is because the utility of the larger relative to the sooner option decreases as magnitudes get bigger, where the curve approaches its asymptote. Indeed, this was found to be the case in all the studies in this thesis, moreover, on average, estimates of subjects'  $r$  parameter were significantly greater than zero, indicating utility concavity.

Interestingly, there is very little in the way of biological and psychological research directed at this phenomenon. This is particularly surprising given that the law of diminishing marginal utility has been hailed as "not only the key-stone of the theory of value, but, as affording the explanation of all economic transactions, it is the key-stone of all economical theory" (von Böhm-Bawerk, 1888). Indeed this simple theory which relates subjective to objective value goes to the heart of the

theories about value which economists such as Adam Smith (1776) explored. It remains integral to economic theory, most notably in the microeconomic concept of the indifference curve which explains preferences between different bundles of goods, consumer theory and laws of supply and demand (Pindyck and Rubinfeld, 2004), as well as in modern analyses of decision under risk and uncertainty (Kahneman and Tversky, 1979; von Neumann and Morgenstern, 1947). Here, for the first time a neurobiological basis has been given for this theory. The results presented in Chapter 3 show that there are brain regions, particularly the striatum, which encode the value of increasing reward magnitudes in a concave fashion – consistent with the theory. Behaviourally, some subjects actually showed the reverse pattern, increasing choice of the later option as reward magnitudes increased, consistent with a convex utility function. Observations of convex utility functions are common in economic literature, however one would assume that such subjects have ‘s’ shaped functions, where eventually, as magnitudes get extremely large, the curve becomes concave.

Further studies should therefore determine psychological, pharmacological and neurobiological variables which may affect or modulate the rate of diminishing marginal utility, just as previous studies have attempted for temporal discounting. In this regard two studies are noteworthy. Ho et al. (1997) showed that food deprived rats have more concave utility functions (lower  $Q$ ) as indicated by a reduction in the indifference gradient in an adjusting delay procedure. Replicating such a finding in humans would be interesting, especially if motivational/physiological states such as hunger could impact on the utility of rewards in other domains such as money. Such a finding would also shed light on the role of these variables in influencing risk preferences (see below). The other study where a manipulation was found to influence magnitude discounting was Kheramin et al. (2002), where OFC lesions led to decreasing concavity of the utility

function, i.e. a reduction in magnitude discounting and increased sensitivity to increasing magnitude.

As mentioned above, diminishing marginal utility is invoked by expected utility theory and prospect theory to explain risk preference (Kahneman and Tversky, 1979, von Neumann and Morgenstern, 1947). In these theories, risk preference is explained as follows: The expected value of a gamble is simply a product of the probability of the payoff and the utility. Under the assumptions of a linear utility function (also known as expected value theory) an individual should be indifferent between an option which has a 50% chance of paying out £100 and a 50% chance of paying out £0, and another option of a guaranteed £50. The expected value of the former option is 0.5 multiplied by 100. In fact most people are risk averse in such choices, preferring the certain option, and not switching preference until the value of the certain option is reduced substantially. In EU theory, risk aversion follows if one were to calculate the expected *utilities* rather than the expected magnitudes. The certain option may be worth say, 45 utils but since the utility function is concave and  $B$  is not worth twice  $A$ , the risky option may only be worth  $0.5 \times 80$  utils. Thus the certain option is valued more than the risky option. According to these theories, it follows that the greater  $r$  (more concave) the greater the risk aversion of an individual. Conversely, risk seeking can be explained by a convex utility function ( $r > 1$ ).

These theories about risk preference lead to a rather paradoxical prediction, that people who are *more* risk averse should be *more* impulsive in choice, and vice-versa, since the concavity of the utility function determines both behaviours (partially in the case of intertemporal choice). Such a finding would not fit with the usual stereotype of the 'impulsive personality', where risk seeking and impulsive choice are often grouped together (e.g. Bechara et al., 2000; Damasio, 1994; Daruna and Barnes, 1993). Indeed, Rogers et al. (1999) found that while OFC lesion patients

are more risk seeking, they are also slower in making choices, often deliberating for long periods of time. This may suggest, at least in terms of preparation or reflection (Evenden, 1998, 1999a; Clarke et al., 2006; Frank et al., 2007) that they are less impulsive. Interestingly, OFC lesions in humans are known to induce risk seeking (Bechara et al., 1994, 2000; Damasio, 1994; Lishman, 1998; Rogers et al., 1999), and using the adjusting delays procedure, Kheramin et al. (2002) found that OFC lesions can cause a linearization of the utility function (less concave), which according to EU theory would equate to reduced risk aversion. This observation explains why risk seeking is observed in OFC patients and also why in some cases (*some* because it also increases  $K$ ) OFC lesions cause a reduction in impulsive choice in rodents (Winstanley et al., 2004b see also introduction to Chapter 2). Such observations suggest intertemporal choice paradigms which implement the integrated valuation function should be able to make predictions about the risk preferences (and change in those preferences with experimental manipulations) of humans and animals.

The preceding observation is an important one. There is actually less direct behavioural evidence for decreasing marginal utility than is commonly assumed. The fact that humans tend to be risk averse (primarily for gains) does not provide incontrovertible evidence for decreasing marginal utility, because the link between risk aversion and decreasing marginal utility exists only in theory. In other words the concavity of the utility function does not itself model anything to do with risk preference. There are a number of other plausible factors that may explain risk aversion besides the way humans discount magnitude, for example, aversive states, non-rational probability discounting and so on. Furthermore, empirical testing of decreasing marginal utility is hampered by the fact that the most straightforward experiment, namely, to record subjects' willingness to pay as they become richer, is flawed because preferences are known to be set with respect to a

reference point that moves as subjects acquire more wealth – a central tenet of prospect theory (Kahneman and Tversky, 1979). Therefore one could argue that the evidence for utility concavity derived from intertemporal choice is actually extremely significant. This is because the utility concavity evidence derived from intertemporal choice is directly based on how people value a reward of one magnitude relative to another and how this changes with increasing magnitude – which is what the utility function fundamentally describes. There is no alternative explanation for a change in preference to the sooner option as magnitudes increase but ratios remain constant. However, the fact that people are risk averse may have no bearing on the way they value a reward of one magnitude relative to another. Therefore a simple way of empirically verifying expected utility theory – one of the most fundamental theorems in decision theory – would be to test a group of subjects using both an intertemporal choice task and a risk preference task. In theory, the parameter estimate derived for the utility concavity in intertemporal choice should match the risk aversion parameter estimate derived from the same subject. If this is found to be the case, one could really prove that risk aversion is solely explained by diminishing marginal utility for gains.

### *Neuroimaging in intertemporal choice*

Recent debate in the neuroimaging of intertemporal choice has focused on whether behaviour can best be described by the interaction of multiple brain systems or by a single system (Kable and Glimcher, 2007; Loewenstein et al., 2008; Rustichini, 2008). The motivation in this debate is to explain the cause of dynamically inconsistent choices, and the nature of the temporal discount function. On one side of this debate are those who argue that preference reversals and other such behaviours arise from a conflict between two decision making systems – a

deliberative and rational (exponential) decision making system which has both long term and short term goals and is located in the DLPFC, and an affective system which only has short term interests and is located in the limbic system (Berns et al., 2007; Hariri et al., 2006; Loewenstein and O'Donoghue, 2005; McClure et al., 2004). This is very much reminiscent of the idea of a conflict between a future and a present self (Ainslie, 1992, see Chapter 1) and is motivated by a quasi hyperbolic temporal discount function which comprises an exponential discount function with an extra parameter that places an additional value weighting on sooner relative to later rewards (beta-delta model). On the other side of the debate is Kable and Glimcher (2007) who argue that behaviour is a product of a single system (standard hyperbolic) of reward valuation which responds to rewards at all delays, and that the evidence of McClure et al. (2004) is simply an artifact of a poorly conceived task design and analysis.

The results presented here are more in line with the ideas of a single system. The discount and overall value systems observed here indicate that activity in these regions correlates with reward values at all delays. This implies that the limbic/cognitive distinction is incorrect. Indeed the behavioural model comparison results in Chapter 3 also revealed that the hyperbolic temporal discount model was superior to the beta-delta model. These results do not however preclude differential activity *within* these regions (e.g. dorsal versus ventral striatum) for short versus long delays (Tanaka et al., 2004) and a further study should use the same method but perform an additional analysis of immediate versus delayed rewards to test the idea – however such a hypothesis is not implied by the valuation model. The results presented here also differ from the idea of Kable and Glimcher (2007) who argue for a single valuation system which responds to the subjective value of rewards at all delays. Here it was shown that there are multiple unique systems for first valuing the delay and magnitude aspects of a reward (and

presumably the probability too) – and these sub-components of value are integrated by a further system which represents overall subjective value and is used to guide choice between options. Therefore, decision-making in this framework arises from a single process of option valuation, whereby choice follows from activity of the overall value system – not from a struggle between two conflicting decision-making systems which have independent and conflicting goals. Therefore, contrary to McClure et al. (2004) impulsive choice cannot be engendered by boosting activity of the limbic system. Interestingly, the regions observed in the overall value system were remarkably similar to those observed by Kable and Glimcher (2007), which implies that they did indeed observe a single valuation system but by using the standard model, their analysis missed out on the individual value systems which report to it.

The results presented here and by Kable and Glimcher suggest that when trying to make inferences about subjective value systems in the brain it is crucial to actually regress behaviourally determined subjective values with BOLD responses. Most imaging studies have relied on analyses such as activity in immediate versus delayed conditions, with no reference to behaviour at all – making assessments about value systems without correlating the value they entail. Such analyses lead to poor inferences about how brain activity relates to behaviour and the neuronal instantiation of subjective value systems.

The model presented in this thesis implies that preference reversals simply arise from hyperbolic temporal discounting in keeping with Ainslie (1975, 1992, 2001) and other theorists (Chapter 1). However, the model is agnostic with regards to the underlying causes of this functional form, and indeed the underlying causes of temporal discounting itself, which is most likely a number of factors (Frederick et al., 2002 - Chapter1). The imaging data did give some clues, for example the ruling out of risk as a sole reason for temporal discounting (Chapter 3) and with regards

to hyperbolic discounting, possible involvement of an innate value system responsive to proximity (Chapter 4, see below).

Hyperbolic temporal discounting was shown from behaviour to be more likely than exponential and other forms of discounting, and although neural activity in the *D* regions was consistent with hyperbolically derived parametric regressors, it is difficult to prove from the neuroimaging data itself that hyperbolic and not exponential discounting is encoded. This is because any regions correlating with hyperbolically derived discount factors will likely correlate with exponentially derived ones. However, one could in theory use the technique devised here for demonstrating a concave versus a linear utility function. By orthogonalizing hyperbolically derived discount factors with respect to exponentially derived ones, one could demonstrate regions where activity could *only* be explained by hyperbolic or similar discounting, where any activity that could be explained by exponential discounting is removed. This would be a noteworthy finding.

When evaluating models with different value components which are likely to be correlated, it is necessary to use orthogonalization in fMRI, to ensure neuronal activity really does correlate with a given regressor (e.g. *V*) and not its closely related counterpart (e.g. *U*). Using orthogonalization is undesirable because many results are dependent on the order of orthogonalization – with most variance being attributed to those in the first positions and the least to those in the last. Unfortunately there is no simple solution to this but one can improve things by increasing the orthogonality of the design, for example by including catch trials (Chapter 3). To avoid order effects, the gold standard is to remove orthogonalization and let the regressors compete for variance, however this is very strict as it effectively amounts to a situation where all regressors are orthogonalized with respect to each other. Therefore one should bear in mind that the precise regions delineated here with respect to each value component are not

strictly fixed and are impossible to fully discern in the paradigms used here. The orthogonalizations were ordered in a naturally strict and theoretically derived way, for example  $V$  was put in the last position since it contained components of  $U$  and  $D$ . The reverse order was also tested. The take home message was therefore more about the structure of value, in terms of the hierarchical integrated systems, which was strictly proven by the analyses.

Finally, future imaging and neurobiological studies should explore and address some of the findings presented. The precise role of each region identified in each valuation network is unclear. For example, why do both the mPFC/subgenual cingulate and the dorsal striatum encode overall value? No neurobiological account was found to explain inter-subject differences in discount rates or utility concavity, perhaps due to lack of accuracy of parameter estimates at the single subject level. One could potentially overcome this problem by asking subjects to perform more choices outside the scanner, to be able to obtain more accurate estimates. Further studies should also seek to understand and explain the marked activations observed here and in other studies (see Chapter 1) in the posterior temporal cortex – a region one would not a priori associate with valuation of delayed rewards. As discussed in Chapter 3, these activations may be related to conscious mathematical calculations being performed. The model could also be used to give an account of instrumental learning of delayed rewards – in combination with learning models – as how actions may become associated with delayed outcomes was not addressed by this thesis. It would also be interesting to learn how motivational and physiological states as well as conditioned cues, impact on behaviour and how this occurs from a neurobiological standpoint (see below).

### *Impulsivity, disorders and dopamine*

In this thesis, the new model was used to demonstrate and predict that enhanced impulsive choice can be engendered by one of two mechanisms – an increase in the discount rate and an increase in utility concavity. Therefore in research, the terms more or less impulsive should be qualified with reference to these two processes, especially if a variable changes both parameters in opposite directions. Consequently  $K$  should not be used as a proxy for impulsivity, which most previous studies tend to do (e.g. Ainslie, 1992, Bickel et al., 2007, deWit et al., 2002, see Chapter 1)

Data from laboratory experiments indicates that dopamine manipulations – particularly using amphetamines and other monoaminergic stimulants – have mixed effects on impulsive choice (see Chapters 1 and 4). However, the data presented here indicates for the first time that enhancing dopamine function in humans leads to increased impulsive choice in humans, without various confounds present in previous studies. This demonstration could provide a convincing mechanism for the enhanced impulsivity observed in addiction and DDS which are known to be associated with dopamine flooding (in the case of DDS) and sensitization of the mesolimbic dopamine neurons (Dagher and Robbins, 2009; O’Sullivan et al., 2009 - see Chapter 4). While impulsive choice and greater temporal discounting has been explicitly observed in addiction, the pilot study also demonstrated that this specific deficit could also be observed in PD patients treated with dopamine who do not even show overt signs of impulsivity. Further studies using a larger number of patients should confirm that this is a reliable finding. Perhaps the most interesting clinical ramification of the dopamine result relates to ADHD where enhanced impulsive choice has also been observed. As discussed in Chapter 4, this finding supports a less orthodox view of ADHD as a disorder associated with a *hyper*-functioning DA system (Seeman and Madras,

1998, 2002; Solanto, 1998, 2002; Solanto et al., 2001). The result also supports the idea that monoaminergic stimulants in low doses can actually reduce DA function and serve to normalize behaviour in ADHD (Seeman and Madras, 1998, 2002; Solanto, 1998, 2002; Solanto et al., 2001) or that the effects of these stimulants may be mediated by serotonin. In any case, future research directed at dopamine may wish to use L-Dopa or other more specific drugs, rather than stimulants which are neither specific for dopamine nor have simple dose-response effects.

There are two ways within the framework of utility theory to produce 'pathological' choice. One way is to alter the agent's preferences. For example, a drug addict may assign an abnormally large utility to consuming drugs, despite the long term detrimental consequences (see Becker and Murphy, 1988). Alternatively, they may abnormally discount the value of future rewards and losses. While the underlying choice remains rational as it maximizes utility, the agent's preferences generate abnormal behaviour. Indeed some theories assume that addiction is rational (Becker and Murphy, 1988). A mechanism considered less often is that the agent's preferences are normal, but the decision process itself is flawed. Thus, a smoker who intends to abstain, but lights a cigarette, may have a flawed decision-making system, or the actual utility of smoking is higher than he thought. This distinction is difficult. Some theorists (Williams, 1994) see it as axiomatic that agents make rational or optimal decisions, so the experimenter's job is to uncover the value system of the subject.

The dopamine study results indicated that under L-Dopa subjects had greater temporal discount rates and that this was reflected in enhanced activity of the discount regions. This suggests that the impulsivity arising in dopamine related disorders stems from an abnormal alteration of the patients' preferences rather than a deficit in the decision-process. In fact, *prima facie*, the discounted utility model would be hard to reconcile with the latter view which would require

invoking competing systems or selves, such as the one proposed by McClure et al. (2004) or other theorists (Ainslie, 1992; Berns et al., 2007; Loewenstein, 1996; Metcalfe and Mischel, 1999; Shefrin and Thaler, 1988, see also Frederick et al., 2002), whereby some top-down mechanism is required to arbitrate between the competing desires of these systems. Such a function has been proposed to be mediated by the ACC in dual system accounts, and where self-control, or will exerts its influences through suppressing the activity of the more short-sighted system – a role thought to be mediated by the inferior frontal cortex (e.g. Berns et al., 2007).

*The nature of time preference: the role of visceral states, self-control, will and other influences on choice*

The preceding point raises some broader issues which require clarification in terms of the behavioural and neurobiological model for intertemporal choice delineated here.

The discounted utility model of intertemporal choice sets out a simple, deterministic process whereby choice is the behavioural selection of one of a set of options whose consequences lead to utility maximization. Here, it is assumed that choice is an optimization problem and will always be determined by the principle of utility maximization (Williams, 1994), where the utility of an option is subjective in the sense that it is partially determined by the agent. Option valuation is therefore the key. The process described here proposes that delayed rewards are valued by an integration of two subjective value systems. One of these systems relates the subjective value of a given reward to its delay, such that delayed rewards are valued less than sooner ones. This devaluation is of a hyperbolic form – where a greater proportion is lost in the initial phases of the delay than later

phases – and the rate of discounting is determined by the individual's time preferences. This process of assigning a weighting to a reward based on its delay and an individual time preference is also accounted for neuronally, by a network of regions whose activity determines this weighting in a manner consistent with the temporal discount function. The second system relates the subjective value of a reward to its magnitude in a concave manner (for most individuals), whereby successive (marginal) increases in magnitude lead to diminishing marginal increases in utility. The rate at which marginal utility decreases is also determined by an individual preference for increasing magnitudes. This system is also accounted for neuronally by a number of regions whose activity determines the utility of the reward in a manner consistent with the utility function. Finally the discount weighting is applied to the utility (or integrated with it), possibly by the dorsal striatum, to produce a discounted utility value represented in another network of regions. This approach of reducing choice alternatives to a single value and then comparing them in order to select the option with the greatest value, corresponds directly with utility theory (Chapter 1).

The question is where does this model leave room for other factors which are known to influence intertemporal choice? These include visceral and motivational influences engendered by sensory aspects of rewards, anticipation of their impending receipt, and cues associated with them as well as physiological states such as craving and hunger – which are known to enhance preference for the sooner option (e.g. Berns et al., 2007; Frederick et al., 2002; Loewenstein, 1987, 1996). They also include self-control, will and representation, which can enhance preference for the later option (e.g. Ainslie, 1992, 2001; Becker and Mulligan, 1997; Berns et al., 2007; Frederick et al., 2002, Thaler and Shefrin, 1981). Do these influences not need to be formally taken into account by the model, or require an account of choice which envisions a conflict between a short-sighted affective

decision making system and a long-sighted deliberative system? Potentially not. One could envisage a system as follows. Rewards lose value over time, or we have positive time preference, because of a number of combined factors that include opportunity cost, risk associated with waiting and so on (Frederick et al., 2002 – see Chapter 1). These factors remain constant over time, that is to say they will cause a unit decrease in the rewards value as time goes on, in a manner consistent with exponential discounting. Presumably, these factors will be related to activations in the *D* system identified here which assigns a weighting to rewards based on delay, whereby in the normal course *D* activity will also decrease in a constant manner per unit time. However, as Frederick et al., (2002) point out, we also have a *pure time preference* for sooner utility. Perhaps one cause of this is that in the initial phases of the delay, as rewards are relatively near (spatially and temporally), other factors, namely sensory (sights, smells etc.), cue and anticipation induced reward activity will act to enhance activity in the *D* system, presumably by boosting dopamine activity in the striatum and the activity of other *D* regions. Such reward activity may occur because of learned or innate Pavlovian values associated with the sensory and anticipatory information detected during situations where the reward is either spatially or temporally proximate (Cardinal et al., 2002; Dayan et al., 2006; Seymour et al., 2009), and serve to initiate responses to those stimuli. These sensory and anticipatory induced responses boost reward activity in the initial phase relative to the later phases of the delay where they are no longer present, accounting for the hyperbolic nature of *D* related activity, and consequently behaviour. Moreover these learned and innate values associated with (internal and external sensory information associated with) proximate rewards can be potentiated by dopamine, via amygdala dependent mechanisms (Cardinal et al., 2002; Dayan, 2009; Everitt et al., 2003; Parkinson et al., 2000; Seymour and Dolan, 2008), as was observed in Chapter 4, where *D* activity increased in sooner relative to later options under L-Dopa. They may also be influenced by physiological states

such as craving. These ideas go back to the earliest notions of time preference mooted by Rae:

Such pleasures as may now be enjoyed generally awaken a passion strongly prompting to the partaking of them. The actual presence of the immediate object of desire in the mind by exciting the attention, seems to rouse all the faculties, as it were to fix their view on it, and leads them to a very lively conception of the enjoyments which it offers to their instant possession. (Rae, 1834; p. 120).

These extra influences which can bias choice to the sooner option are therefore compatible with, accounted for, and in fact offer an explanation for the mathematical (hyperbolic) models of temporal discounting but interpret the discount function as the sum of the contributions of several factors and motives operating in any one situation – in line with the ideas of Frederick et al. (2002) and Cardinal (2006). Therefore in a situation where these influences are increased, for example if one were making a choice between one piece of cake today and 2 pieces of cake tomorrow, but in one condition the sooner option was visible to the subject, the enhanced preference for the sooner option in the visible condition would simply be caused by increase in  $D$  related activity in the second condition relative to the first, *reflected* by an increase in the discount rate implied from behaviour. Alternatively, one could also envisage a situation whereby these influences act to boost the instantaneous utility of the sooner option, relative to the later one, reflecting an effective increase in utility concavity, by similar neurobiological mechanisms. In this framework, all one need assume is that the parameters determining the preferences and values of the individual are susceptible to manipulation by those Pavlovian, visceral, anticipatory and other influences, just as they are to pharmacological manipulation. These hypotheses could be empirically tested by performing an imaging experiment whereby the sensory properties of the rewards are enhanced or reduced, in one condition, or by presenting Pavlovian conditioned stimuli, to determine how these influences exert

their effects. This stands in contrast to the dual model systems whereby these factors enhance the influence of an impulsive, affective decision making system, which is in competition for behavioural output with a deliberative, rational one (McClure et al., 2004). In the model advanced here, choice still follows from selection of the option with the greatest utility; it is the subjective utility which changes. Therefore, in this model one may need to relax the assumption that parameter values which contribute to the determination of preference are stable within the individual, as assumed by some theorists (Herrnstein, 1981; Herrnstein and Prelec, 1992; Ho et al., 1999).

Within this framework one could also explain self-control and 'will' as factors which will influence the valuation systems described. One could imagine that self-control arises from a powerful re-evaluation of the larger-later option and the long term goals of an individual, bringing new information to light which will act to boost the utility of that option relative to the smaller-sooner one (effectively decreasing utility concavity). This also brings us back to the early ideas of discounting of von Böhm-Bawerk:

It may be that we possess inadequate power to imagine and to abstract, or that we are not willing to put forth the necessary effort, but in any event we limn a more or less incomplete picture of our future wants and especially of the remotely distant ones. And then there are all those wants that never come to mind at all. (Böhm-Bawerk, 1889; pp. 268–69).

It was mentioned in Chapter 3 that viewing the problem of discounting as being due to how we represent and think about future outcomes has been taken on by Becker and Mulligan (1997) amongst others, who argue that the discount rate is a function of the resources invested in imagining the future. In their model, decision makers maximize lifetime utility subject to difficulties in envisioning exactly how rewarding the future will be. Hence, they will expend resources to make their

image of the future vivid and clear. Therefore re-evaluation will act to boost the value of the larger-later relative to the smaller sooner and will be reflected by changes in activity of the relevant neural  $U$  system and  $r$  parameter. Change in the utility related neural activity of options, engendered by extra consideration, has been observed in an fMRI study by Sharot et al. (2009).

Alternatively self-control could involve the recruitment of some prefrontal mechanism (as Berns et al., 2007 envisage) which serves to dampen the salience of those sensory values and mechanisms which boost reward activity to nearer options – manifest in brain and behaviour as a decrease in the discount rate. This might be reflected in the increased lateral inferior frontal cortex activity in response to increasing proximity of rewards observed in Chapter 3 and 4.

In this view, the will or self-control is not seen as something that intervenes to select the desires of a deliberative versus an impulsive decision-making system, rather it acts to change values and preferences of options under a single decision-making system which acts to maximize (subjectively determined) utility.

Dual system and current versus future self models are partially invoked to explain the inner tension or fight that we often feel when making an intertemporal choice – between wanting that piece of cake and knowing that it is bad for you (e.g. Ainslie, 1992; McClure et al., 2004). More realistically this tension is not a struggle between two systems or a current and future self, but simply represents the difficulty in choice when options are closely valued, engendering decision-conflict. In conflict scenarios more consideration needs to be given to each option to adequately determine its true value. Repeated consideration of each option could lead to the inner conflict we feel. This effort and struggle to maximize utility could be represented and mediated by the anterior cingulate cortex and DLPFC activity observed in Chapter 3 (see also Botvinick, 2007), when options were closely valued and decision-latencies slowed down.

## Appendix I

### Mathematical derivations – Chapter 2

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#### Relationship between $d_B$ and $d_A$ at indifference in the adjusting delay procedure – standard hyperbolic model (Eq. 5)

Starting from Equation 1, the Mazur (1987) model:

$$V = \frac{M}{1 + K \cdot d}$$

At indifference  $V_A = V_B$

Substituting in:

$$\frac{M_A}{1 + K \cdot d_A} = \frac{M_B}{1 + K \cdot d_B}$$

therefore,

$$\frac{M_B}{M_A} = \frac{1 + K \cdot d_B}{1 + K \cdot d_A}$$

hence,

$$1 + K \cdot d_B = K \cdot d_A \left( \frac{M_B}{M_A} \right) + \left( \frac{M_B}{M_A} \right)$$

rearranging for  $d_B$ ,

$$d_B = d_A \left( \frac{M_B}{M_A} \right) + \frac{1}{K} \cdot \left( \frac{M_B - M_A}{M_A} \right) \quad (\text{Eq. 5})$$

$$y = x \cdot \text{gradient} + \text{intercept}$$

**Multiplicative hyperbolic model if  $K$  is amount dependent – adjusting delay (Eq. 6)**

At indifference:

$$\frac{V_A}{1 + K_A \cdot d_A} = \frac{V_B}{1 + K_B \cdot d_B}$$

Therefore,

$$V_B(1 + K_A \cdot d_A) = V_A + (V_A \cdot K_B \cdot d_B)$$

rearranging for  $d_B$ ,

$$d_B = \frac{V_B}{V_A} \left( \frac{1 + K_A \cdot D_A}{K_B} \right) - \frac{1}{K_B}$$

hence,

$$d_B = \frac{1}{K_B} \cdot \left[ d_A \cdot K_A \left( \frac{V_B}{V_A} \right) \right] + \left[ \frac{1}{K_B} \cdot \left( \frac{V_B - V_A}{V_A} \right) \right]$$

From Ho et al. (1999) (Eq. 2)

$$V = \frac{1}{1 + Q/q}$$

Substituting in:

$$d_B = \frac{1}{K_B} \cdot \left[ d_A \cdot K_A \cdot \left( \frac{1+Q/q_B}{1+Q/q_A} \right) \right] + \frac{1}{K_B} \cdot \left[ \frac{1/(1+Q/q_B) - 1/(1+Q/q_A)}{1/(1+Q/q_A)} \right] \quad (\text{Eq. 6})$$

$$y = x \cdot \text{gradient} + \text{intercept}$$

**Derivation of  $Q$  in the MHM adjusting delay task (Eq. 8)**

From Ho et al. (1999) at indifference:

$$d_B = d_A \cdot \left[ \frac{1+Q/q_A}{1+Q/q_B} \right] + \left[ \frac{1/(1+Q/q_B) - 1/(1+Q/q_A)}{1/(1+Q/q_A)} \right] \cdot \frac{1}{K} \quad (\text{Eq. 4})$$

$$y = x \cdot \text{gradient} + \text{intercept}$$

$$\text{gradient} = \frac{1+Q/q_A}{1+Q/q_B}$$

therefore,

$$\text{gradient} \cdot \left( 1 + Q/q_B \right) = 1 + Q/q_A$$

Multiplying by  $q_A$ ,

$$Q = q_A \cdot \text{gradient} \cdot \left( 1 + Q/q_B \right) - q_A$$

and,

$$Q = q_A \cdot \text{gradient} + Q/q_B \cdot q_A \cdot \text{gradient} - q_A$$

hence,

$$Q - Q/q_B \cdot q_A \cdot \text{gradient} = q_A \cdot \text{gradient} - q_A$$

and,

$$Q(1 - \text{gradient} \cdot q_A/q_B) = q_A(\text{gradient} - 1)$$

solving for  $Q$ ,

$$Q = \frac{q_A \cdot (\text{gradient} - 1)}{1 - (\text{gradient} \cdot q_A/q_B)} \quad (\text{Eq. 8})$$

### Derivation of new discounted utility model for adjusting delay task (Eq. 11)

Starting from Eq. 5, hyperbolic discounting of magnitude, see above for derivation:

$$d_B = d_A \left( \frac{M_B}{M_A} \right) + \frac{1}{K} \cdot \left( \frac{M_B - M_A}{M_A} \right)$$

Replacing  $M$  with  $U$  from new utility function (Eq. 9):

$$U = \frac{1 - e^{(-r \cdot M)}}{r}$$

Substituting in:

$$d_B = d_A \cdot \left[ \frac{1 - e^{(-r \cdot M_B)/r}}{1 - e^{(-r \cdot M_A)/r}} \right] + \frac{1}{K} \cdot \frac{[1 - e^{(-r \cdot M_B)/r}] - [1 - e^{(-r \cdot M_A)/r}]}{[1 - e^{(-r \cdot M_A)/r}]}$$

therefore,

$$d_B = d_A \cdot \left[ \frac{1 - e^{(-r \cdot M_B)}}{1 - e^{(-r \cdot M_A)}} \right] + \frac{1}{K} \cdot \left[ \frac{e^{(-r \cdot M_A)} - e^{(-r \cdot M_B)}}{1 - e^{(-r \cdot M_A)}} \right] \quad (11)$$

$$y = x \cdot \textit{gradient} + \textit{intercept}$$

## Appendix II

### Participant instruction sheet – Chapter 3

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In this task, you have to make choices between two financial options. Each option consists of an amount of money between £1 and £100, available at some point in the future, between 1 week and 1 year. You have to choose the option you would prefer, and two of your choices will be selected randomly at the end of the experiment and paid to you in full, and at the specified time in the future.

You will first see 'option 1' which will remain on the screen for 3 seconds, after which you will then see 'option 2', for a further 3 seconds. After option 2, you will be asked to choose which one you prefer, by selecting either one on the 'choice' screen, during which you have roughly 3 seconds to indicate your preference using a keypad. On the choice screen, the words 'option 1' will appear on the left and 'option 2' on the right. In the practice version that you will do in a minute, if you prefer option 1 press the left shift key, if you prefer option 2, press the right shift key. In the scanner, you will get a proper left-right keypad to make your choices. Remember, option 1 refers to the option that was presented first, not the option which is paid first. Once you have chosen one of the options, your choice will be highlighted. You can change your mind for as long as the choice screen is present, but please try to choose correctly first time since you don't have too much time.

Please remember that when you come out of the scanner, 2 choices will be randomly selected – one from each session, and you will receive the option that you chose, for each of those 2 choices. It is therefore very important that you select the option which you really prefer. To do the random selection, you will then spin a genuine lottery machine, which contains numbered balls corresponding to each

of the trials. The ball that comes out will be looked up from all the choices you made and it will be the choice you get (one for each session). We do it in this way so that you appreciate that it is a real gamble, and we will genuinely pay you the correct amount, so it is important you make your decisions understanding that they might be selected for real.

Of course, we have no control over the two options that are selected at the end, so there is quite a variation in the amount you could get, because some of the options are for small, and some large, amounts of money. In agreeing to take part in the experiment, you have to accept that this is a real gamble, and you might be unlucky and only get a few pounds, whereas other subjects might get lots. We cannot change the two selected options afterwards, and we are ethically obliged to give you no more or no less.

The way we pay you is with commercial pre-paid credit cards, which are activated at the time specified by the option. We arrange this after the experiment, and we have funded pot of money to cover the winnings for all our subjects. We will send you the cards (or you can pick it up if you prefer) after the experiment, and it will be activated automatically at the future date specified (we will keep all records here as well).

Please try and concentrate well for the whole experiment. You will do two sessions, each lasting 20mins. Please try to stay as still as possible throughout the task, and good luck!!!!

## Appendix III

### Participant instruction sheet – Chapter 4

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In this task, you have to make choices between two financial options. Each option consists of an amount of money between £1 and £150, available at some point in the future, between 1 week and 1 year. You have to choose the option you would prefer, and one of your choices will be selected randomly at the end of the experiment and paid to you in full, and at the specified time in the future.

You will first see 'option 1' which will remain on the screen for 3 seconds, after which you will then see 'option 2', for a further 3 seconds. After option 2, you will be asked to choose which one you prefer, by selecting either one on the 'choice' screen, during which you have roughly 3 seconds to indicate your preference using a keypad. On the choice screen, the words 'option 1' will appear on the left and 'option 2' on the right. In the practice version that you will do in a minute, if you prefer option 1 press the left shift key, if you prefer option 2, press the right shift key. In the scanner, you will get a proper left-right keypad to make your choices. Remember, option 1 refers to the option that was presented first, not the option which is paid first. Once you have chosen one of the options, your choice will be highlighted. You can change your mind for as long as the choice screen is present, but please try to choose correctly first time since you don't have too much time. Sometimes, due to the speed, or lack of concentration, you might find you can't remember one or both of the options when you get to the choice phase. If this occurs don't just randomly choose anything, as it will negatively impact our results. Instead just do nothing and wait for the next trial. (If a choice you missed is selected for payment we will choose a different one).

Please remember that when you come out of the scanner, 1 trial of all the ones you made will be randomly selected by you, and you will receive the option that you chose, within that choice. It is therefore very important that you select the option which you really prefer. To do the random selection, you will spin a genuine lottery machine, which contains numbered balls corresponding to each of the trials. The ball that comes out will be looked up from all the choices you made and it will be the choice you receive. We do it in this way so that you appreciate that it is a real gamble, and we will genuinely pay you the correct amount, so it is important you make your decisions understanding that they might be selected for real.

Of course, we have no control over the two options that are selected at the end, so there is quite a variation in the amount you could get, because some of the options are for small, and some large amounts of money. In agreeing to take part in the experiment, you have to accept that this is a real gamble, and you might be unlucky and only get a few pounds, whereas other subjects might get lots. We cannot change the two selected options afterwards, and we are ethically obliged to give you no more or no less. However you will be doing this experiment on 3 occasions and will have an option chosen on each occasion.

The way we pay you is either with a direct bank transfer, or a cheque sent to you, at the time specified by the option. We arrange this after the experiment, and we have funded pot of money to cover the winnings for all our subjects. We will keep records of your winnings and their time to delivery here at the centre as well as give you a receipt for you to keep. I will enter the rewards into my diary to remind me to send them to you at the correct time. The reason we go through all this trouble is because the choices you make must be realistic and not hypothetical – this leads to better results.

Please try and concentrate well for the whole experiment. You will do two sessions, each lasting 20mins. Please try to stay as still as possible throughout the task, and good luck!!!!

## Appendix IV

### Visual analogue scales – Chapter 4

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ALERT	—————	DROWSY
CALM	—————	EXCITED
STRONG	—————	FEEBLE
MUZZY	—————	CLEAR HEADED
WELL COORDINATED	—————	CLUMSY
LETHARGIC	—————	ENERGETIC
CONTENTED	—————	DISCONTENTED
TROUBLED	—————	TRANQUIL
MENTALLY SLOW	—————	QUICK WITTED
TENSE	—————	RELAXED
ATTENTIVE	—————	DREAMY
INCOMPETENT	—————	PROFICIENT
HAPPY	—————	SAD
ANTAGONISTIC	—————	FRIENDLY
INTERESTED	—————	BORED
WITHDRAWN	—————	SOCIABLE

Subjects were required to bisect the line in the position where they estimated they currently felt between the two extremes. One was completed before the drugs were ingested and one after testing, to control for subjective drug effects. From Bond and Lader (1974).

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