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EMOTION-BASED LEARNING: AN EXPERIMENTAL AND CLINICAL INVESTIGATION

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Submitted: July 2009

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ABSTRACT

Emotion-based learning has emerged as a concept referring to a specific class of learning in uncertain situations that is facilitated by a substantial input from the emotion system. The precise nature of this input, however, remains a controversial and well-studied topic. The present thesis builds on existing emotion-based learning research and investigates several understudied and novel research questions in both experimental and clinical domains. In Chapter 1, a literature review outlines the evolution of research on emotion-based learning, its neuropsychological correlates and focuses on one of the most popular tasks used to measure the concept: the Iowa Gambling Task (IGT). The IGT is an experimental task developed in order to simulate real world complex decision-making. In it, participants make choices from decks of cards that vary in both frequency and magnitude of reward (gain) and punishment (loss). Advantageous decision-making involves foregoing immediate gains with higher long-term losses for lower immediate gains and lower long-term losses. Research has indicated considerable variability in the extent to which healthy controls produce evidence of advantageous learning on the IGT. Chapter 2 showed that placing time constraints on the critical decision-making period in the IGT systematically disrupted the performance of healthy participants. Chapters 3 and 4 introduced a novel variant contingency shifting IGT in which the reward and punishment contingencies were systematically altered following initial exposure to the task. Research was undertaken with a large sample, using a repeated exposure design and by measuring the autonomic skin conductance correlates of contingency shifting IGT performance. Chapter 5 extended the investigation to the dimensional spectrum of

depression and schizophrenia by applying the task to participants scoring high and low on measures of psychosis proneness and depression. Results showed that individuals with high psychotic and depressive features displayed poor flexible emotion-based learning performance. Chapter 6 showed that patients with schizophrenia exhibit impaired performance compared to controls, while Chapter 7 showed that depressed patients also underperformed compared to controls, in both the initial and contingency shifting phase of the variant IGT. Overall, the findings of the present thesis offer insights into the nature of flexible emotion-based learning, as measured with the contingency shifting IGT, and its impairment, across healthy volunteers, individuals at higher risk of developing psychosis or depression and patients with schizophrenia and depression.

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Chapter 2

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Chapter 1

Introduction

Over the past 30 years, research interest in the topic of emotion has increased considerably (LeDoux, 1996; Rolls, 2005). One of the main reasons behind this scholarly growth is the acknowledgment that emotion plays a central role in our lives and that our behaviour is controlled, to a large extent, by affect (Damasio, 1994). Of the different accounts proposed to study emotion, neuroscience has been one of the most fruitful (Panksepp, 1998). Neuroscience research has been mainly concerned with the identification of different emotional systems, at the neural level, in the attempt to identify the structures involved in eliciting and controlling emotional responses (Calder, Lawrence & Young, 2001).

In the early 1990's it was proposed that emotion might play an important role in underpinning complex human behaviours and support complex cognitive functions (Damasio, 1994). The research regarding the influence of emotion over complex behaviour started with clinical observations conducted with brain injury patients with orbitofrontal damage; these patients often showed a picture of preserved intelligence paired with a considerable difficulty in making advantageous choices in personal- and social-life settings (Elsinger & Damasio, 1985).

Similar to people with orbitofrontal injury, people with mental illness show difficulties in real life decision-making often leading to social and occupational dysfunction. Neuropsychiatric investigations have suggested that frontal lobe abnormalities are implicated in many psychiatric conditions especially in enduring or recurrent mental health problems such as schizophrenia and depression (Antonova,

Sharma, Morris & Kumari, 2004; Brunet-Gouet & Decety, 2006; Fitzgerald, Oxley, Laird, Kulkarni, Egan & Daskalakis, 2006).

The research presented in this thesis seeks to investigate the role of emotion in decision-making by considering several under-developed research questions. In its six experimental chapters, this work will investigate emotion-based learning and the relevance of this concept for experimental and clinical research. The first empirical chapter will examine the effects of time constraints on the emotion-based learning. The following chapter will introduce a paradigm to measure emotion-based learning flexibility. The third experimental chapter will investigate the physiological correlates of flexible emotion-based learning. Finally, the last three chapters will examine flexible emotion-based learning in depression and schizophrenia from a sub-clinical and clinical perspective. The series of investigations proposed will measure emotion-based learning with behavioural, subjective and physiological methods. Before moving to the experimental chapters, the following sections will outline the concept of emotion-based learning and review the relevant research conducted around the research questions addressed by this thesis.

Emotion-based learning

Emotion-based learning is a term that refers to a specific class of learning in which learning in uncertain situations is achieved via a substantial contribution of the emotion system (Damasio, 1996; LeDoux, 1996, 2000; Turnbull, Berry & Bowman, 2003). The system appears to provide knowledge about the outcome of decisions on the basis of previous experience of the emotional consequences of interaction with particular stimuli (Damasio, 1996; Tranel & Damasio, 1994; Turnbull, Evans, Kemish, Park &

Bowman 2006). Bowman and Turnbull (2004) suggested the emotion-learning system to be an aggregate of learning principles, such that they provide information about the often long and complex reinforcement history with which the individual has had with an object. The addition of emotion is claimed to be particularly helpful in uncertain conditions where individuals are required to make rapid decisions in the absence of a clear understanding of the situation, or when advantageous outcomes of a decision do not result in an immediate gain (Damasio, 1996; LeDoux, 1996). Emotion-based support for decision-making can be crucial in many real life situations such as choosing a career, deciding whether to stop or continue at the yellow traffic light, invest savings, start a new business and select a friend or a partner. In uncertain scenarios, the emotion-based learning system can provide a shorter path, compared to traditional strategies relying on cost and benefit, and individuals can reach a decision by considering the emotional correlates attached to the situation. In other words, emotion-based learning processes achieve quick and efficient decisions using emotion-based heuristics.

Interest in the relationship between emotion-based learning and decision-making began with some challenging cases of brain injury that, despite showing intact intellect, presented marked inability to make beneficial choices in social and personal context. The formulation of the Somatic Marker Hypothesis (SMH; Damasio, 1994) and the more general concept of emotion-based learning (EBL) have deep roots in the clinical presentation of the first neurological patients with orbitofrontal damage. For this reason it appears important to take a retrospective look to how the study of the 'emotional brain' began (MacLean, 1949).

Chapter 1

Neurological Investigation of Emotion-based Learning

On the 13th of September 1848, Phineas Gage, a railway worker, inadvertently blew a iron bar through the left side of his frontal skull presenting neuropsychology with a timeless case of intriguing neurological deficit; that of impaired social cognition (Adolphs, 1999; Goldberg, 2001). Despite the severity of the prefrontal cortex injury, Gage had a quick recovery and in less the two months he was well enough to leave the hospital (Macmillan, 2000).

The first clinical records of Gage after his discharge from the hospital were remarkable; the patient did not show any loss in crucial functions such as language, memory, attention or reasoning. However, it soon become evident that Gage had lost his original personality and with it the ability to interact purposefully with the environment. Formerly a responsible and reliable person in both personal and professional life, Gage become, after the injury, incapable of considering consequences of his actions as well as little concern about the consequences of his behaviour. An account of his physician described Gage as: "a fitful and irreverent man, indulging in the grossest profanity, manifesting little deference for his fellows, obstinate, impatient, irreverent devising many plans for future operation quickly dismissed..." (Damasio, 1994, p.8).

More than a century after Gage's death, Damasio and colleagues reconstructed the site of the brain damage from the fractures found in the skull and showed that Gage's brain would have sustained a substantial damage in the ventral part of the orbitofrontal cortex (Damasio, Grabowski, Frank, Galaburda & Damasio, 1994). Phineas Gage's case suggested a substantial contribution of the prefrontal cortex to personality and emotional

processing and also indicates that these functions are dissociated from general intellect (Rolls, 2005).

In the years following Gage's accident, frontal lobes incision, also called lobotomy, were initially performed across the world in order to treat severe and enduring mental illness (Macmillan, 1996; Tierney, 2000). Frontal neurosurgery involved drilling a hole in the skull and inserting a wire knife into the brain in order to sever the matter connecting the frontal lobes with the rest of the brain (Sabbatini, 1997). According to Hoffman (1949), "these patients are not only no longer distressed by their mental conflicts but also seem to have little capacity for any emotional experiences pleasurable or otherwise" (p.238).

By the late 20th century a contribution of the frontal lobes to social cognition and emotion processing was widely acknowledged by the scientific community although exact localization of the function was yet to be achieved (Rankin, 2006). The improvement in neuroscience scanning techniques in conjunction with the development of research interest in this area produced outstanding advancement in the understanding of the neurological substrate of emotion and social cognition. Before reviewing the studies that paved the way for the formulation of the SMH, it is appropriate to provide an anatomical account of the frontal lobes.

The prefrontal cortex

Frontal lobes constitute the third of the human cortex located in front of the central fissure, separating it from the parietal lobes, and above the lateral fissure, separating the frontal cortex from the temporal lobes (Luria, 1966). Three different regions, subserving different functions, can be distinguished within the frontal lobes: the

motor cortex which encompass most of the precentral gyrus located immediately in front of the central sulcus; the *premotor cortex* extending in front of the motor cortex including parts of the precentral, middle frontal and superior gyiri; and the *prefrontal region* constituting the anterior part of the frontal lobes (Damasio, 1995).The prefrontal cortex is the critical region implicated in processing environmental stimulation in order to achieve complex behaviour. For its relevance to the studies presented in this thesis the current section will concentrate on the prefrontal regions implicated in decision-making.

According to Krawczyk (2002), there are four main regions contributing to the decision-making process at the cortical level: the orbitofrontal (OFC) and ventromedial (VMPFC) areas, the dorsolateral prefrontal cortex (DLPFC) and the anterior and ventral cingulate. The OFC can be described as the part of the prefrontal region that is located on the roof of the orbit and covers the ventral surface of the frontal lobes (Ongur & Price, 2000). A further distinction within the OFC is also often made when referring to the ventromedial prefrontal cortex (VMPFC), defined as the inner-most medial areas of the ventral frontal lobes. This distinction is supported by an increasing number of studies that find functional dissociation between the ventromedial and ventrolateral areas (see Elliott, Dolan and Frith, 2000, for a review). Functionally, the OFC and the ventromedial prefrontal regions can be viewed as an integration centre for emotional content, an area involved in processing the reward value of environmental stimuli, a central area in the decision-making process, as well as an area processing peripheral signals from the body (Damasio, 1994). Moreover, this area seems to be involved in adapting to rapid changes in reward contingencies and suppressing responses to stimuli that are no longer rewarding. This function of the OFC appears to be critical especially in unclear

situations, while deciding under time pressure or when different options need to be evaluated (Krawczyk, 2002). The OFC, through its connection with sub-cortical regions, is also responsible for inhibiting motor responses and adjusting behaviour when social contingencies change (Cummings, 1995).

Most of the knowledge about impaired decision-making process comes from research conducted with OFC brain injured populations. Orbitofrontal patients, unlike DLPFC patients, demonstrate an important social impairment in every day life although they preserve verbal memory of social and moral principles (Saver & Damasio, 1991). The pioneering work of Damasio and colleagues shows how debilitating and profound is the disability that is incurred with such damage and highlights the selective nature of the deficit caused (Bechara, Damasio, Damasio & Anderson, 1994; Damasio, 1995; Eslinger & Damasio, 1985). Selective OFC damage can affect different functions ranging from social behaviour in everyday context to the ability to predict reward and punishment. A study from Goel, Grafman, Tajik, Gana and Danto (1998) found that, in a financial planning task, OFC patients spent an abnormally long time deliberating and not enough time generating solutions and future plans. Patients with OFC damage seem also to have problems in reward processing; several neuroimaging studies have shown activation in the orbitofrontal cortex, caudate and insula during steaks of wins and losses, suggesting the importance of these regions for reward sensitivity (e.g., Elliott, Friston, & Dolan, 2000).

In a study strongly related to non-human primate work (see Cavada, Company, Tejedor, Cruz-Rizzolo & Reinoso-Suarez, 2000 for a review), Drewe (1975) investigated binary choice behaviour in frontal lobe patients; results indicate that damage to the OFC

caused difficulties in withholding responses. A similar finding has been achieved in a study aiming to investigate the role of the ventromedial prefrontal cortex in learning. Rolls and colleagues found patients with VMPFC lesions to be impaired in performing a binary reward reversal choice task, displaying a particular insensibility to shifting and modification of the reward schedules (Rolls, Hornak, Wade & McGrath, 1994).

The role of risk taking behaviour and impulsivity of OFC patients has been extensively investigated in a series of studies by Miller (e.g. Miller, 1985; 1992). Results indicated that patients with frontal lobe excision made more predictions based on insufficient information than patients with temporal lobe excision and normal controls. Given the difficulties in understanding risk probability and reward schedules that OFC patients showed, Rogers et al. (1999) investigated several classifications of brain damage employing a decision-making task in which participants were required to gamble on a task with known reward chances. In this task, participants were asked to find a token hidden in one coloured box among many of different colours. Each coloured box was presented with a probability of finding the token (e.g., 25%). The task required to select a box and bet some virtual points on the choice. Patients were therefore explicitly presented with the possibility to obtain higher reward by selecting from the more rewarding gambling options. OFC patients, compared to other prefrontal patients, performed worst (Rogers,et al., 1999). This study provided evidence that OFC damage leads to disadvantageous choices even under circumstances where the probabilities of success are explicitly available.

Like the OFC, the DLPFC appears to sub-serve unique functions relevant to decision-making. The DLPFC occupies the upper and side regions of the frontal lobes,

roughly corresponding to Brodmann areas 9 and 46. Most of the studies have investigated the DLPFC area in relation to the functionality of the working memory (Goldman-Rakic, 1992). Functions related to the working memory are of obvious contribution to decision-making as they are essential for maintaining a focus on goal hierarchies, monitoring and assess the status of competing options and possibly storing affective information relevant to attributes. The DLPFC is also supporting the decision-making by disambiguating similar choices and evaluate the overall value of an option by estimating the summary of its attributes (Mellers & Biagini, 1994). Also, it seems that the DLPFC plays a crucial role in the integration process of information; such processes would include developing overall impressions of options based on the comparisons of various attributes, as well as evaluating the overall goodness. An example of such process could be a situation involving the purchase of a bike. The choice will be possibly addressed by considering the physical proprieties of the vehicles, memories of past experience with the similar objects, emotionally driven subjective impression, as well as knowledge of costs and future financial implications of the purchase. When deliberating about that an integration process is required in order to make the final choice, this process has high implication for the working memory and relies, in the final stage, on the integration functions of the DLPFC (Waltz et al., 1999).

Last of the three main areas thought to be mostly implicated in the decision-making process is the anterior cingulate (AC). The AC is situated in the frontal part of the cingulated cortex, extending as a collar around the corpus callosum. The AC appears to be involved in decisions that are highly ambiguous, in mental situations proposing a conflicting options and high likelihood of making an error (Botvinick, Nystom, Fissell,

Carter & Cohen, 1999; Carter, Braver, Barch, Botvinick, Noll & Cohen, 1998). AC has also been found to be implicated in anticipatory activation in gambling related decision-making (Critchley, Mathias & Dolan, 2001). Overall, the AC appears to be involved in a number of relevant decision-making processes, providing monitoring and mediation functions to conflictual or multiple choice situations. Krawczyk (2002) has suggested that AC functions are similar to a signal amplifier; the AC can top strength in case certain features of an option are not taken in account properly during the early stages of the decision processes. AC, also, seems to be involved in monitoring the outcome information and detecting the possible need for a behavioural adjustment.

Emotion and Decision-making: The Somatic Marker Hypothesis

Evidence from the clinical presentation of individuals with OFC damage has produced a consensus around the debilitating aspect of damage to this area with particular emphasis on poor decision-making ability. In order to explain the reason for decision-making deficits following OFC damage, Damasio proposed the Somatic Marker Hypothesis (SMH) (Bechara, 2004; Damasio, 1994; Dunn, Dalgleish, Lawrence et al., 2006). Through a series of experiments conducted at Iowa University, Damasio and co-workers identified a crucial area responsible of effective decision-making: namely the ventromedial prefrontal cortex (VMPFC). The SMH postulates that "somatic marker" biasing signals from the body are represented and regulated in the emotion circuitry of the brain, specifically in the VMPFC, to help regulate decision-making in situations of complexity and uncertainty (e.g., Bechara, Tranel & Damasio, 2000; Damasio, 1994; 1996). In other words, visceral responses to events in the environment are processed by the brain and used to "mark" (positively or negatively) the consequence of actions. In this

frame the VMPFC functions to elicit visceral responses that reflect the anticipated value of the choices (Naqui, Tranel & Bechara, 2006). The contribution of somatic markers, as advanced in the formulation of the SMH, applies only to specific types of decision-making, in particular those situations where the meaning of the event is indeterminate and the consequences of the behaviour uncertain. Examples of situations where somatic markers might aid the decision-making process are, according to Damasio, social interactions, decision about personal and financial life and all those situations in which the consequence of the behaviour have emotional value (Damasio, 1994). Such situations are those where rules that govern the behaviour are not explicit, but yet require some form of on-line deliberation. In order to be efficient an organism is required to understand the environment contingencies using a particular form of reasoning that does not rationally weight positive and negative consequences but intuitively select the most appropriate behaviour upon the emotional consequences attached to early events (Naqui et al., 2006).

According to the formulation of the SMH, the re-occurrence of previously experienced situations does not require a novel association between bodily states and class of stimuli. It is claimed that when a situation re-occurs the VMPFC can reactivate the already generated association. This process can be elicited in two ways: via the *body loop,* which regenerate the original somatic signal thus sending information to the somatosensory cortex or alternatively via the as *as-if body loop*, which rather that re-creating the signal in the body sends the appropriate triggers from the VMPFC to the somatosensory cortex (Tranel, Bechara & Damasio, 1999) (see Figure 1). In order to maintain the association between somatic markers and stimuli, it is proposed that the

VMPFC is able to store the associations formed and then reactivate them in case the same situation is presented or generalise the association to similar situations (Tranel et al., 1994).

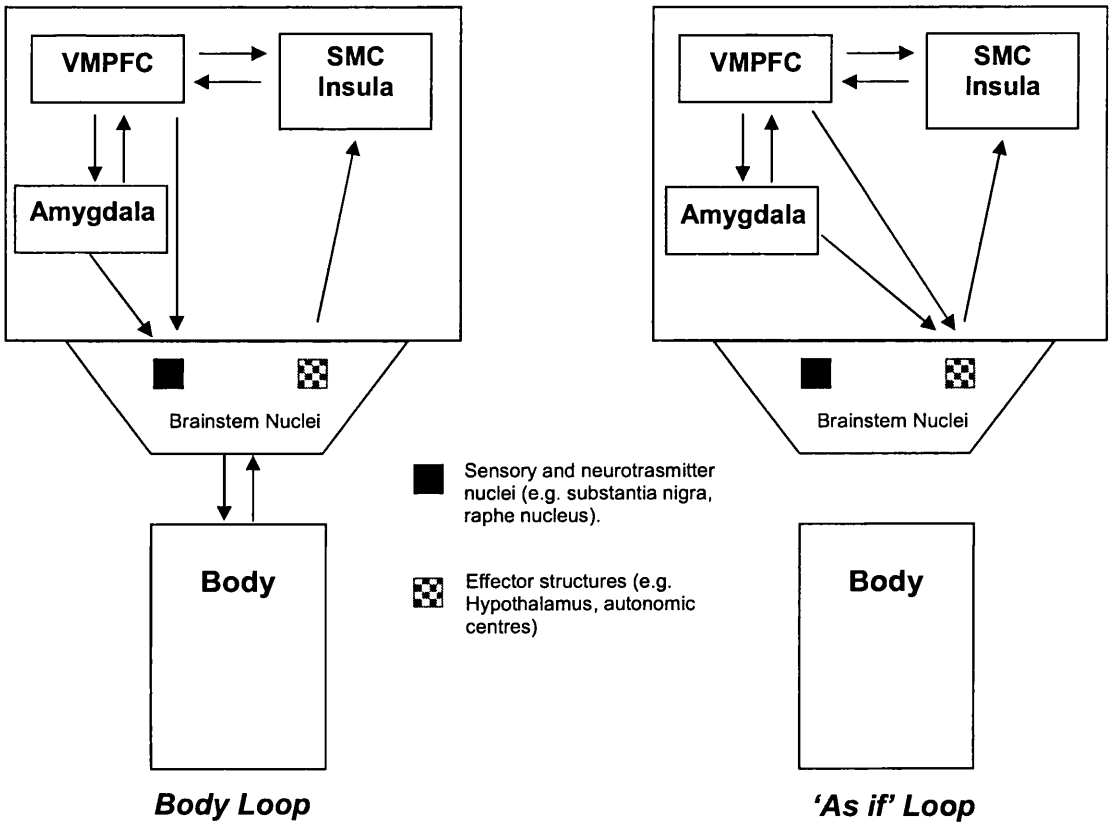

Figure 1: Neural architecture implicated in the SMH. A schematic representation of the body loop is presented on the left hand side while the 'as if' body loop is illustrated on the right. VMPFC: Ventromedial Prefrontal Cortex, SMC: Somatosensory Cortex.

According to Tranel, somatic markers can operate either consciously or unconsciously. Overt or conscious somatic markers provide the organism with an

incentive or deterrent, while covert or unconscious somatic markers facilitate appetitive or avoidance behaviour (Tranel et al., 2000).

The influence of somatic markers on the quality of decision-making might not always be a determinant to successfully accomplish a task. It has been proposed that somatic markers are particularly important in the early stages of decision-making whereas later stages can be more dependent on overt reasoning and executive function (Bechara, Damasio, Tranel & Anderson, 1998; Brand, Recknor, Grabenhorst & Bechara, 2007). It is likely that overt reasoning using explicit memory is mediated by the dorsolateral prefrontal cortex (DLPFC). The interplay between VMPFC and DLPFC would allow consolidating memory and guiding long term decision-making performance (Bechara et al., 1998).

Criticisms of the Somatic Marker Hypothesis

Despite being almost 20 years since it was originally formulated, and having accumulated a large volume of research support, the SMH still attracts criticism (e.g., Heims et al., 2004; Maia & McClelland, 2004; Öngur & Price, 2000; Tomb, Hauser, Deldin & Caramazza, 2002). While the deficit noted in people with OFC lesions is not under debate, the theory formulated by Damasio and co-workers does not provide a problem-free account on why VM damage might lead to such catastrophic decision-making outcome (Dunn et al., 2006). Perhaps the strongest problem to the theory is the fact that other explanations are possible for the decision-making deficit in people with VM damage.

The claim that peripheral feedback is necessary for advantageous decision-making has been partially disconfirmed by several research accounts. As for the James-

Lange theory, the SMH could be criticised in the same way as all theories of peripheral feedback. The James-Lange theory holds the view that bodily states, such as changes in heart rate or in the skeletal muscles, generate the feeling of the emotion (Lang, 1994). According to this view an emotion is experienced as a result of three consecutive processes: a physical reaction to a stimulus, sensing the physical reaction and finally the elicitation of a congruent emotion in response to the peripheral feedback. Such a theory was difficult to investigate and as it is based on "introspection". Also it was unspecified why particular events (e.g., see a tiger) are specifically associated with certain action (e.g., run away).

The relationship between emotion and peripheral activity has been investigated, since the first formulation of the theory, in a variety of studies all concluding that emotions can be generated in the absence of peripheral activity (Chwalisz, Diener & Gallagher, 1988; Ferguson & Katkin, 1996). The parallelism between theories of peripheral activity and the SMH is clear and indeed research evidence able to describe the decision-making deficit in VM patients using different account creates partial falsification argument. For example, North and O'Carroll (2001) compared decision-making performance in people with and without spinal injury. The rationale of the study was to compare two populations with a different physiological means of conveying body signals. In patients with spinal cord damage, the emotional signal could not travel on the fast route, the spinal cord, but had to reach the brain via the endocrine system. The authors found that there was no difference in decision-making performance, as measured by the Iowa Gambling Task, between the two groups. In a similar study conducted with patients with pure autonomic failure (a degenerative disease of the peripheral nervous

system), it was found that decision-making performance was also not impaired (Heims, Critchley, Dolan, Mathias & Cipolotti, 2004). Bechara (2004) explained these findings suggesting that emotional learning is not critically tied to on-going experience of autonomic arousal state and that acquisition of autonomic failure later in life may protect against maladaptive behaviour.

Another potential problematic account for the SMH arose from a theory of emotion advanced by Rolls (1999, 2000, 2005). This theory proposed that the OFC can predict the rewarding and punishing values of environmental stimuli based on the emotion association experienced in similar situation. According to this theory, emotion-based learning is achieved via a learnt history of exposure to reward and punishing stimuli in the environment associated with emotions. In this way, emotions become "states elicited by rewards and punishers" (Rolls, 2005, p.11). The link between decision-making performance, the association stimulus valence and emotions, and OFC proposed by Rolls is supported by several research investigations (Fellows & Farah, 2003; Rolls, Hornak, Wade & McGrath, 1994; Rolls, 2005).

Another criticism of the neural underpinnings of the SMH is the lack of consensus in relation to the brain location proposed as the centre of emotional decision-making, namely the VMPFC. More lateralized OFC lesions than the ones proposed by Damasio and colleagues have been associated with similar decision-making deficits (Rolls et al., 1994).

A further criticism is that the SMH proposes a decision-making strategy that is inefficient. It requires a vast amount of processing in order to be learnt at the cortical

level; it might be that other, simpler functions, could account for the deficit demonstrated by VM patients (Rolls, 2000).

Finally, almost all the research accumulated to investigate emotion-based decision-making has used a single task, the Iowa Gambling Task (IGT). Although this is not a criticism per se, due to the value of consistency in measurement, support for the SMH currently lacks concurrent validity with other tasks. Also, a range of different methodological issues have been proposed as important elements affecting the measurement of the concept of emotion-based learning as described by Damasio. Due to the vastness of the topic and the centrality of the issue to the current work, the following section will be dedicated to reviewing the studies employing the IGT.

The Iowa Gambling Task

The IGT is an experimental paradigm developed in order to simulate real world complex decision-making situations. Its use has been mainly related to the development and consolidation of the SMH, although recently it has become an accepted means to measure complex decision-making. Bechara et al. (1994) devised the task to measure decision-making ability in people with acquired OFC brain injury. The overall format of the experiment resembles a real gambling situation where the experimental participant is required to gamble virtual money on a card game. The key feature of the task is that participants have to forego short-term benefit for long-term profit.

In the standard version of the IGT, participants sit in front of four real decks of card labelled A, B, C, and D. The player is initially given a loan of facsimile play money ($2000 in Bechara et al.'s 1994 original version). The participant is also instructed that the goal of the game is to win as much money as possible or, if impossible, to avoid

losing money. Play consists in turning cards, one at time, from any of the four decks, until the experimenter says stop. Participants are told that every card choice will result in a gain of a certain amount of money and, every so often, a card choice will result in a gain and a loss. All wins and losses are summed or detracted from the initial loan amount and, in the original version using play money, the participant complete the transaction. No other instructions concerning the value of the wins and losses in any deck or about the reward/punishment schedule embedded in the decks are given at the outset. Participants are only provided with a hint concerning the nature of the decks making them aware of the fact that some decks are worst than others and in order to do well they might need to stay away from the worst decks (See Appendix 1 for full Bechara et al.1999 instructions).

The IGT requires participants to select from one of the four concurrently available decks of identical physical appearance for 100 trials. As specified in the instruction to the participants, each card selection leads to a variable financial reward that sometimes is combined with a financial penalty. Schedules of monetary gain and loss are pre-fixed in the task and are not performance dependent. In this respect, all participants are exposed to the same environmental contingencies.

In the original version of the task (Bechara et al., 1994) each selection from decks A and B resulted in a $100 gain, while each selection from decks C and D resulted in a $50 gain. According to the schedule of monetary losses, every so often a penalty is also given. Deck A delivers a loss in five out of ten trials ranging from $150 to $350. On deck B a loss of $1250 is given once every ten trials. On deck C, five out of ten trials are involving a loss ranging from $25 to $75. On deck D, one choice out of ten delivers a loss of $250. According to the monetary reward and punishment schedule of the task the high

immediate reward decks (A and B) give greater punishments, leading to a net loss of $250 every ten trials, whereas the low immediate reward decks (C and D) give smaller punishments, leading to a net gain of $250 in every ten trials (see Table 1). Given that participants will incur in frequent punishments and a net loss if they choose more often from decks A and B while a more frequent selections of decks C and D will lead to a financial gain.

Deck	Reward	Punishment	Net Profit (over 10 trials)
A	$100 (10/10 trials)	$150 to $350 (5/10 trials)	- $250
B	$100 (10/10 trials)	$1250 (1/10 trials)	- $250
C	$50 (10/10 trials)	$25 to $75 (5/10 trials)	+ $250
D	$50 (10/10 trials)	$250 (1/10 trials)	+ $250

Table 1: Schedules of rewards, punishment and net balance for bad (A and B) and good (C and D) decks from a representative Iowa Gambling Task (Bechara et al., 1994).

Learning profiles on the IGT

Participants' selections during the 100 IGT trials are conventionally plotted in learning profile graphs. For every 20 selections the mean net score is calculated by subtracting disadvantageous from advantageous selections [(C+D)-(A+B)]. A net score above zero is indicative of advantageous selections, while a net score below zero implies disadvantageous selections.

Over the course of the 100 card choices, neurologically normal participants tend to select more cards from the advantageous decks (C and D) than from the disadvantageous decks (A and B), compared to patients with VM lesions (Bechara et al., 1994; Bechara, Tranel, Damasio & Damasio, 1996; Bechara et al., 1999). Neurologically unimpaired participants, typically, start sampling more cards from the bad decks, due to their immediate higher reward, but as the game progress this preference tends to reverse in favour of the good decks. Neurologically unimpaired participants tend to have a shift in the deck's preference relatively early in the game (typically around the 30^{th} trial) and maintain this preference until the end. As a result of this shift in preference the plot of neurologically unimpaired participants is similar to a learning curve growing from negative to positive (Figure 2).

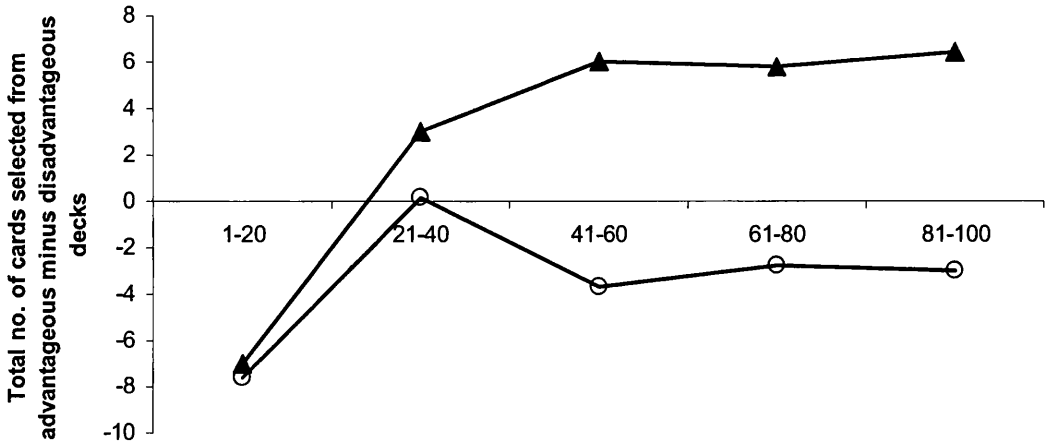

*Figure 2: L*earning profiles across each of the five, twenty trial-blocks of the IGT for VM patients (empty circles) and normal controls (filled triangles) (Reproduced from Bechara, Tranel and Damasio, 2000b).

In contrast, the performance of VMPFC patients plotted with the same method shows significant preference for disadvantageous decks compared to neurologically unimpaired group with no evidence of learning during the task (see Figure 2). Several investigations confirmed the specific deficit in this task for people with VMPFC lesion even when re-exposed to the IGT after a month (e.g., Bechara et al., 1994; 2000b).

Physiological correlates of IGT performance

Physiological studies on VMPFC patients playing the IGT have provided key support for the influence of somatic markers on decision-making. In the early nineties, Damasio, Damasio and Tranel (1990) analysed the autonomic arousal of several OFC patients by measuring skin conductance responses (SCRs) during the presentation of emotional (e.g., injuries) and neutral pictures (e.g., flowers). It was found that medial

OFC damaged patients showed depressed SCRs to emotional pictures compared to other brain injury populations and to normal controls.

Few years after, Bechara et al. (1996) measured autonomic activity in seven patients with VMPFC damage and twelve controls while playing the IGT. The authors measured 'anticipatory' (described as the electrodermal response in the time period prior to making a card selection from any given deck) and 'consequence' responses (described as the electrodermal response in the time period following the choice) (Bechara et al., 1996, p. 221). It was found that both groups initially showed autonomic activation as a consequence of wins and losses, although after a short period of time the control group started to develop anticipatory SCRs before choosing from bad decks. The authors noted that the lack of anticipatory autonomic activation in VM patients was correlating with impaired IGT performance. The interpretation given by the authors was that the lack of anticipatory SCRs production in VM patients was evidence that physiological correlates of insensitivity to future outcomes are responsible of the decision-making deficits (Tranel et al., 2000). Although various studies seem to suggest the existence of a link between advantageous performance on the IGT and anticipatory marker signals the interpretation of *why* this is happening is still largely speculative.

The IGT has been used in a number of experimental investigations nevertheless only a small sub-set has recorded physiological activation associated with the task. Most studies, as noted by Dunn et al. (2006), measuring SCR did replicate the finding of greater anticipatory SCR to disadvantageous decks, relative to advantageous (e.g., Bechara & Damasio, 2002; Campbell, Stout & Finn, 2004; Crone, Somsen, van Beek & van der Molen, 2004; Hinson, Jameson & Whitney, 2002; Suzuki, Hirota, Takasawa &

Shigemasu, 2003; Tomb et al., 2002). Further, some studies did slightly alter the original task or the recording methodology but nevertheless found comparable results suggesting that modification of the task might not impact largely on findings. Crone et al. (2004a), for example, used a children adapted version of the IGT with adults (collect apples to feed a hungry donkey). Suzuki et al. (2003) employed a shorter, 80-trial version of the IGT that required verbal feedback. In this study the anticipatory recording window was of 10 s, compared to the 5 s duration chosen by Bechara et al. (1999). Regardless of the methodological differences both Crone et al (2004a) and Suzuki et al (2003) showed that a proportion of the controls participants did not show the claimed higher level of arousal prior to the selection of disadvantageous decks in the early phases of the IGT. The lack of consistent performance both at the behavioural and at the physiological level in some control participants suggests the existence of a level of variability in healthy individuals.

Variability in 'normal group' IGT performance

While subsequent investigations with the IGT have considerably improved the understanding of neuropsychological correlates of decision-making, it has become increasingly evident that a high percentage of control participants underperforms on the task. Bechara and Damasio (2002) first noted that not all control participants performed advantageously on the IGT. As for other neuropsychological tests, a degree of variability between control participants is expected (Strauss, Sherman & Spreen, 2006); in the case of the IGT, Bechara and Damasio (2002) found that as much as a third of the control participants had a similar, impaired, performance to VM patients. Although the underperforming third of the control group had a performance similar to VM patients, it was noted that they still generated appropriate anticipatory SCRs (Bechara, Damasio &

Damasio, 2000). Bechara et al. (2000b) suggested that the underperforming control participants might be thrill seekers or potential gamblers. This consideration implicitly suggested that individual differences may play a role in influencing IGT performance. As noticed by Dunn et al. (2006) the variability in IGT control participants is not a direct problem for the SMH but there might be a need to develop independent and objective performance criteria so that studies can be directly compared (for example, having a number of good decks selections higher than chance).

Sample composition and demographic variables, like gender and age, have also been proposed to influence IGT performance. Reavis and Overman (2001) found a superiority of males on the IGT compared to females. More recently, Glicksohn, Naor-Ziv and Leshem (2007) reported a percentage equal to 46% of a student sample (age range 19-26) performing under chance levels (i.e., mean net score below 0) on the IGT. In attempting to explain the finding, the authors proposed that the role of impulsivity could affect performance. Finding showed that impulsivity, as assessed by two independent measures, the Barratt impulsiveness scale (Barratt, Stanford, Kent & Felthous, 1997) and the Impulsiveness Questionnaire (Eysenck, Pearson, Easting & Allsopp, 1985), did not correlate with IGT performance. In discussing the results the authors suggested that the decisive role of other factors might have influenced the low performance of such a large proportion of the sample and invited future studies to draw attention to the decisive role of individual differences (Glicksohn et al., 2007; p. 203).

Davis, Patte, Tweed and Curtis (2007) in a similar study found similar percentage of non-learner on the IGT (in this case defined as the participants with a learning profile visually similar to VM patients leaning profiles as in Bechara et al. (1999)). Differently

from Glicksohn et al. (2007), the authors of this study found that impulsivity predicted the IGT performance of the non-learners. In another recent study Caroselli et al. (2006) investigated IGT performance in a large sample of university students (mean age 21.7 (4.6).These authors found that, unlike the controls used by Bechara et al. (1994; 1996; 1999; 2000a), a substantial proportion of young adult participants tended to display a learning profile similar to those of VM patients. Analysis conducted on the participants' pattern of selection across the 100 trials indicated that IGT performance is primarily governed by the frequency of positive outcomes on a trial-by-trial basis rather than by a longer term prospect of winning accumulation.

Taken together, the studies reviewed in this section suggest a high degree of variability in IGT control participants' performance with sometimes as many as two thirds of the sample displaying preference for the disadvantageous decks. Results from clinical populations presenting impaired performance compared to control participants have been used to support various claims regarding the nature of different deficits (Bechara et al., 1996; Cavedini, Riboldi, D'Annucci, Belotti, Cisma & Bellodi, 2002; Clark et al., 2001; Sevy et al., 2007). Although studies showing variability in control participants' performance do not per se contradict the clinical findings, they might recommend caution in the interpretation of the data. Future studies should take the variation in participants' performance in more serious account and study what might influence it. Several factors have been advanced to have an influence on the IGT performance and potentially be able to contribute to the explanation of variability. Of those the cognitive penetrability of the IGT schedule have been largely debated.

Cognitive penetrability and subjective experience

Awareness about the schedule of wins and losses embedded in the IGT decks is central to the claim that the task can only be successfully completed through recourse to emotion-based learning process mediated by somatic marker signals. Empirical support for this claim was sought in an experiment by Bechara et al. (1997) in which VM patients and controls were asked a verbal question about the nature of the decks (i.e., "Tell me all you know about what is going on in the game").

It was found that neurologically normal participants indicated a preference for disadvantageous decks in the first few trials without showing any anticipatory autonomic response. After experiencing few losses, control participants started to develop anticipatory SCRs for disadvantageous decks but they were still unable to describe the schedule of reward and punishment. This stage was described few years later by Bechara et al. as the 'pre-hunch phase' (2000a, p.300). After having accomplished roughly two thirds of the 100 trials, control participants begun to be able to identify disadvantageous decks as the more risky and advantageous decks as the most safe and long term winning. This stage, called the 'hunch phase', was markedly associated with behavioural preference for good decks (i.e. average mean net score above zero) and steady anticipatory SCRs activation in case of disadvantageous selections. Finally, Bechara et al. described the last quarter of the game as the 'conceptual' phase where neurologically normal participants were able to describe accurately which deck was good and which one was bad (Bechara et al., 2000a, p.300). Participants who reached the conceptual phase where able to describe A and B as bad decks resulting in net money loss and C and D as the decks that should be preferred in order to do well at the task. On the contrary, VM

patients failed to achieve the hunch phase, although around half of the patients could produce statement similar to the one of control participant who reached the conceptual phase. Despite some awareness on the nature of the decks was reached by VM patients this knowledge did not impact on their performance or elicited anticipatory SCRs prior disadvantageous selections.

According to Damasio, the IGT is a very distinctive paradigm by which participants discriminate choice by feeling; in healthy individuals, it is claimed, non-conscious somatic biases guide reasoning and decision-making behaviour before conscious knowledge does, and without the help of such biases, overt knowledge may be insufficient to ensure advantageous behaviour (Tranel et al., 1999). In this respect the task should not be intended as a probabilistic reasoning task but as a task aimed to test learning assisted by unconscious emotional signal.

In order to support the claim that emotion biasing signals aiding learning are not conscious, is essential that the task does not allow penetrability of the schedules of reward and punishment by the participants. Bechara et al. based the assumption of the impenetrability of the task on a simple broad question asked at the end of the task (Bechara et al., 1997). Maia and McClelland (2004) challenged the validity of the method used by Bechara et al. (1997) arguing that a post-experiment single broad, open-ended question, such as "Tell me all you know about what is going on in this game", is not a rigorous method to assess conscious awareness of the task contingencies and this should not be considered as a sufficiently sensitive method to exclude participants' awareness during the task (Lovibond & Shanks, 2002).

In order to investigate the role of awareness in the task, Maia and McClelland (2004) presented healthy participants playing the Bechara et al. (2000a) version of IGT with a specific set of questions after the first 20 trials and subsequently after every 10. The methodology employed required participants to rate on a slider scale the goodness or badness of each deck, tentatively evaluate the net profit or loss of ten consecutive selections for each deck, rate on a slider scale how much they felt in control of the game and indicate the most advantageous deck (Maia & McClelland, 2004, p.16076). Maia and McClelland (2004) concluded that advantageous selections on IGT are guided by conscious knowledge given that participants' rating of goodness and badness of the decks was directly related to the performance on the task.

The latter finding implies the possibility that performance on the IGT could be guided by conscious knowledge of the reward/punishment schedule and that SCRs are the consequences of this knowledge. If the IGT can be performed through access to conscious knowledge about the schedules embedded in the decks, it is therefore not possible to claim that successful completion of the task is entirely dependent of the generation on non-conscious somatic marker signals (Maia & McClelland, 2005).

The criticism expressed by Maia and McClelland (2004) was addressed by Bechara et al. (Bechara et al., 2005). Firstly, it was specified that "the central feature of the SMH hypothesis is not that non-conscious biases accomplish decisions in the absence of conscious knowledge, but rather that emotion-related signals assist cognitive process even when they are non-conscious" (p.159). Second, anticipatory SCR responses began, in the original Bechara study (Bechara et al., 1997), in a phase in which Maia and McClelland called 'minimal knowledge'. Therefore, the claim that anticipatory SCRs

developed after conscious knowledge was acquired by participants was not shown. Finally, and most importantly for present purposes, the issue of reversal learning deficit was suggested by Maia and McClelland as a possible alternative explanation for the poor performance of VM patients. The issue of reversal learning revolves around the preference shift that advantageously performing participants typically undergo in the first third of the task where preference for the disadvantageous decks is progressively replaced by a marked preference for the advantageous. This account was countered by Bechara et al. (2005) who argued that a reversal learning deficit is not incompatible with the SMH. The emotional activation claimed by the SMH to assist learning in uncertain situations it is not hypothesised to be disentangled to other cognitive processes but rather have a biasing influence. In other words the lack of somatic marker would negatively influenced reversal learning, among other cognitive functions, as the emotion would not help to discontinue a behavioural pattern (i.e. selection of disadvantageous decks).

In a reply to Bechara et al. (2005), Maia and McClelland (2005) further stressed the argument of reversal learning providing support from other studies (e.g. Clark & Manes, 2004; Fellows & Farah 2005; Fellows & Farah 2003; Rolls, 1999) that have identified the VM cortex as a crucial area to performing reversal learning tasks. Maia and McClelland concluded that their findings, together with the neuropsychological evidence gathered with lesion studies, do not prove that the SMH is wrong but some of the results are at odds with its predictions (2005, p.164).

In a related investigation on the role of subjective awareness in IGT performance, Bowman, Evans and Turnbull (2005) measured the subjective experience of healthy participants every 20 trials. Participants were asked to provide a rating for each deck of

card in term of how good or bad they felt each deck was on a scale from zero (very bad) to 10 (very good) (Bowman et al., 2005, p.23). Results showed a substantial rise in the level of awareness (i.e., ratings of relative goodness/badness) between the first and the second block of 20 trials; the level of awareness remained stable for the remaining three blocks until the end of the task. As advanced from Maia and McClelland (2004), the findings of Bowman et al. (2005) seem to suggest that participants have greater awareness about the nature of the decks than proposed by Bechara et al. (1997; 2000a). In particular the pre-hunch phase, as described in Bechara et al. (2000a), appears, in the Bowman et al. (2005) study, to be confined at a very early stage of the game and the hunch phase occurring in the first rather than in the second third of the task.

Aside of the penetrability of the schedule of reinforcement being initially challenged by Maia and McClelland (2004) other alternative hypotheses were advanced in order to explain the VM patients poor performance on the IGT. The theory that reversal learning deficit in VM patient may be responsible of disadvantageous performance on the IGT gathered substantial interest in the research community. The following section will introduce the already-mentioned concept of reversal learning and review the research conducted on this topic in relation to the IGT and the SMH.

The IGT, reversal learning and set-shifting ability

The importance of being able to learn arbitrary relations is as crucial for humans as the ability to break those arbitrary rules in order to learn more advantageous ones. Reversal learning is the ability to shift from a contingency previously associated with reward but now associated with punishment, to a new contingency associated with reward (Robbins, 2007). In a changing environment the ability to perform quickly and

efficiently reversal learning task can provide help to various fields such as economical decision (e.g., buying and selling shares), social interaction (e.g., being collaborative or conflictual) and health (e.g., smoking cessation).

Neuropsychological and lesion evidence suggest that one of the functions implemented in the OFC is stimulus-reinforcement association learning and the correction of these associations when environmental contingencies change (Rolls, 2005). Reversal and shift learning are two functions heavily involved in the so called executive functions that have been shown to have strong reliance of OFC structures (Fellow & Farah, 2003; Hornak, O'Doherty, Bramham, Rolls, Morris & Bullock, 2004; Iversen & Mishkin, 1970; Rolls et al., 1994). As previously seen in this chapter the ability to perform advantageously on the IGT seems to be strongly associated with structures of the OFC, in particular the VMPFC.

Early critics of the task were advanced on the basis that the IGT failure in patients with VM lesions could have been due to lack of reward sensitivity (O'Doherty, Kringelbach, Rolls, Hornak & Andrews, 2001; Rolls et al., 1994). In order to dismiss this claim, Bechara et al. (2000a) exposed VMPFC patients and controls to the original and a variant form (called EFGH) of the IGT. In the EFGH variant task every E and G selection corresponded to $100 loss while every selection from deck F and H corresponded to a $50 loss. Every so often, using a similar schedule to the original IGT, money rewards were given in addition to the penalties. Deck E delivered a win of $1250 once every ten trials; deck F delivered wins ranging from $25 to $75 in five out of ten trials; deck G delivered wins in five out of ten trials ranging from $150 to $350; deck H delivered once every ten trials a win of $250. Over ten selections decks E and G yielded a net profit of

$250 while F and H yielded a net loss of $250. In the EFGH version advantageous decks delivered immediate higher punishment but long term higher rewards. Even in this version of the task VMPFC patients showed marked disadvantageous performance demonstrating that impairment on IGT is unlikely to be dependent reward sensitivity.

Reversal learning has more recently been re-advanced as an alternative mechanism to explain impaired performance in the IGT due to overlapping of the OFC areas described as necessary to perform both reversal learning and IGT (Fellows, 2007). A crucial aspect of the IGT is that participants have to perform a response reversal, shifting their preference from decks that are initially rewarding but long term disadvantageous, to decks that are immediately less rewarding but long term advantageous.

A number of studies have shown that patients with ventral prefrontal cortex damage have a substantial difficulty in reversal learning task (Fellows & Farah, 2003; Rolls et al., 1994). In order to test whether the impairment in IGT was directly dependent on reversal learning Fellows and Farah (2005) re-arranged the schedule of reinforcement of the first trials of the IGT such that there was no perceived advantage in selecting from the bad decks at the beginning of the game. When patients with VMPFC were exposed to this shuffled variant of the IGT they performed at comparable levels to controls.

This finding, although partially at odds with the SMH, did not provide an alternative account of what the signal is that triggers the change in the learning strategy (Bechara et al., 2005). The SMH claims that the "stop signal" that would trigger the shift from one contingency to another is an emotional signal: in other words the somatic marker (Damasio, 1994; 1996).

The use of IGT has been administered often with the Wisconsin Card Sorting Task (WCST; Grant & Berg, 1948). The main reason for the combined use of the two tasks in neuropsychological investigations was to provide an understanding of how complex decision-making, as measured by the IGT, correlates with more classic measures of executive function and set-shifting (i.e., the ability to display flexibility in the face of changing schedules of reinforcement). Brand, Lubudda and Markowitsch (2006) proposed the existence of an asymmetric relationship between IGT performance and standard executive function tests such as the WCST, Behavioural Assessment of the Dysexecutive Syndrome (BADS) and Brixton Test (Brand et al., 2007; Burgess & Shallice, 1997; Milner, 1963; Rabbitt, 1997). Neuropsychological and neurolesion evidence suggested that damage or dysfunctions to ventromedial and anterior prefrontal regions is associated with impaired IGT but not WCST (Bechara et al., 1998; Bechara et al. 2001). Differently, focal damage or dysfunction to the dorsolateral prefrontal cortex has been associated with impaired performance on WCST and IGT (Bechara et al., 1998; Bersani, Clemente, Gherardelli & Pancheri, 2004; Stratta, Arduini, Daneluzzo, Rinaldi, Genova & Rossi, 2004).

The existence of dissociation between the two tasks might suggest that the decision-making, as measured by the IGT, does not overlap completely with executive function and therefore the task is a specific measure of emotion-based learning. In an attempt to investigate this claim, Brand et al. (2007) studied IGT and executive function in a large sample of healthy subjects showing that the fist and the last part of IGT require participants to deploy different resources. Where the first part of the task requires a decision under ambiguity (i.e., where outcomes are not associated with a probability

distribution), minimally dependent on executive function, the second part of the IGT requires a decision under risk (i.e., where likelihood of outcomes respond to a probability) known to draw more heavily on neural systems concerned with the processing of executive information (Brand, Fujiwara, Borsutzky, Kalbe, Kessler & Markowitsch, 2005; Brand, Kalbe, Labudda, Fujiwara, Kessler, & Markowitsch, 2005).

Although the latter part of the task seems to have a more pronounced influence on executive function, the IGT, as originally designed, does not require further shift or change in preferences. In fact when preference for the advantageous decks is established participants are not required to further adjust to other more advantageous contingencies. The IGT does not present, per se, a changing environment but an opaque and misleading set of contingencies. Executive function tests usually present marked components of shift and/or reversal learning. In the attempt to include those components in an emotion-based learning context, Turnbull et al. (2006) developed a modified version of the IGT that adds to the standard 100 trials (Phase 1), 3 signalled contingency shifts of 40 trials each, in which schedule of reinforcement are systematically modified (Phase 2). During the contingency modification phase formerly advantageous decks (C and D) become progressively disadvantageous, with deck C returning advantageous in the last shift. Similarly, formerly disadvantageous decks (A and B) become progressively advantageous with deck A returning disadvantageous in the last shift (see Figure 3).

Deck	Phase 1	Phase 2		
		1	2	3
A	-	+	+	-
B	-	-	+	+
C	+	-	-	+
D	+	+	-	-

Figure 3: Advantageous (+) and disadvantageous (-) decks during Phase 1 and each of the three shift phases of Phase 2 (adapted form Turnbull et al., 2006).

The rationale for the modification of the original task was to investigate how emotion-based learning history would impact on a changing environment and whether or not this form of learning would bias adaptation in patients with schizophrenia (Turnbull, Evans, Bunce, Carzolio & O'Connor, 2005). Results showed dissociation between the performance in Phase1 and Phase 2, suggesting that some aspects of decision-making, as measured by IGT, are dissociate from simple reversal learning. Shift, reversal learning investigations and modification of the task have been warranted by Dunn et al. (2006) as a valuable tool to further understand components involved in the IGT. Modification of the task and of the experimental environment can indeed shed some light on the factors that may influence decision-making. The following sections will review how this approach has been embraced by different researchers to study determinants of IGT performance.

Task design issues and instructions

The large number of research papers featuring the IGT (over 200 papers on the topic, as retrieved by Web of Science on the 20th of November 2008) is in itself an acknowledgement of the capacity of the task to measure specific decision-making

components. Despite its widespread use, the IGT is not immune to design problems. Over the years the computerised version of the IGT (Bechara et al., 1998) attempted successfully to eliminate experimenter bias (i.e., prompting or cueing selection of particular decks) but even in its computerised form, the task still presents several potentially biasing features.

First, deck position is rarely counterbalanced meaning that selections from the participants could simply reflect position biases. In the Bechara computerized version of the task (Bechara et al., 1998) decks are presented form left-to-right labelled with the letters A, B, C and D with A and B being always the bad decks and C and D being always the good decks. Second, the schedule of rewards in the original version of the task (e.g., Bechara et al., 1994) is easily predictable, meaning that participants in order to do well have to attend only to the punishment component (Maia & McClelland, 2005). Third, the classification of advantageous and disadvantageous decks is questionable because participants are judging without previous experience of the decks' relative goodness or badness. In the first few trials, in fact, the so-called disadvantageous decks appear to be rewarding by delivering higher immediate payoffs. The IGT classifies advantageous and disadvantageous decks a-priori without considering at what stage of learning the participant is. Fourth, in the Bechara et al. (1994) original task participants can only select 80 times from each deck raising the possibility that options available in the last 20 trials might be reduced. This feature could eventually provide inaccurate evidence of learning by the fact that choosing from a particular deck is not possible in the remaining trials.

Notwithstanding these critical task design issues, the provision of different task instructions could affect the comparability across IGT studies. It was Schmitt et al. (1999) that first considered the issue of lack of consistency in IGT participants' performance by advancing the potential confounding role of task instructions. Schmitt et al. (1999) evaluated IGT performance in a group of psychopathic individuals in order to assess whether this group would fail to become risk aversive. Finding showed that IGT performance was poor in male offenders and correlate highly with anxiety. In discussing the findings, the authors advanced that the original instruction, as given in Bechara et al. (1994), could be a potential source of bias for the performance. In fact, the detailed instruction, as provided in Bechara et al. (1994,1999 and 2000a) can provide participants with hints about the nature of the task. Participants were told:

> "The computer does not make you lose money at random. However, there is no way for you to figure out when the computer will make you lose. All I can say is that you may find yourself losing money on all of the decks, but some decks will make you lose more than others. You can win if you stay away from the worst decks" (Bechara et al., 1999, p.5474).

Fernie and Tunney (2005) argued that including this "hint" in the instructions gave participants a considerable advantage on task performance if compared to the instruction without hint. To test this hypothesis, Fernie and Tunney (2005) exposed control participants to two experimental conditions with and without the hint sentence included in Bechara et al.'s (1999; 2000a) original instructions. The experimental manipulation consisted of excluding the following sentence from the original set of instructions for the "no hint" experimental group:

> "All I can say is that some decks are worse than others. You may find all of them bad, but some are worse than others. No matter how much you find yourself losing you can still win if you stay away from the worst decks".

Results showed how the presence of this hint in the instructions positively influenced subsequent performance on the IGT (Fernie & Tunney, 2005, p.100).

The quality and detail of the instructions given is widely known to influence performance in experimental tasks. For instance, causal learning can be influenced by subtle instructions changes (Buehner & May, 2004) and detailed instruction improves performance above the level of contingency-governed behaviour in self-control tasks (e.g., Kudadjie-Gyamfi & Rachlin, 2002). The fact that differences in instructions could influence IGT performance is particularly controversial in light of the claim made by the SMH that learning is driven by somatic markers and not by explicit knowledge participants' hold concerning the nature of the task.

In the experiments presented in this thesis, a novel computerized version of the IGT is used. Instructions presented are minimal in order to avoid the confounding aspect of providing knowledge about the nature of the decks prior to the beginning of the task. For this reason the hint statement was not used throughout all the experiments.

Emotion-based learning and mental health

Psychiatric disorders present a wide range of difficulties in social cognition often associated with marked decision-making problems (Aleman, David & Medford 2006; Yudofsky & Hales, 1997). In the last ten years research has developed a pronounced interest in the investigation of the neural substrate of the decision-making deficit in psychiatric patients (Cavedini et al., 2002a; Clark, Iversen & Goodwin, 2001; Martino,

Bucay, Butman & Allegri, 2007; Must, Szabó, Bódi, Szász, Janka & Kéri, 2006). Prefrontal cortex functional and structural abnormalities have increasingly gathered evidence as primary candidate to explain the decision-making behaviour in psychiatric patients. The interest in this area arose following a number of studies identifying an association between VMPFC brain injury patients and impairment in emotion-based decision-making as measured by the IGT (Bechara et al., 1996; Bechara et al., 2000a,b).

The clinical applications of the IGT with psychiatric populations have received considerable interest lately and seem to point in the direction of a generalized impairment across different disorders. Although findings are far from consistent, with some psychiatric conditions yielding particularly inconclusive results with specific groups of participants (e.g., individuals with schizophrenia), investigations in this area seem important for understanding the contribution of emotions over cognitive processes. The latter part of this chapter will review findings in relation to clinical applications of the IGT to mental health disorders with a particular stress on schizophrenia and depression.

IGT and psychopathology

To some extent, almost all of the spectrums of psychiatric disorders present a deficiency in decision-making ability (Ovsiew, 1999; Yudofsky & Hales, 1997). The similarities between the clinical presentation of VM patients and several psychiatric disorders initiated the interest for emotion-based learning in psychopathology. Up until now, the IGT has been widely used to assess decision-making in psychiatric conditions such as obsessive compulsive disorder (OCD) (e.g., Nielen, Veltman, de Jong, Mulder, den Boer & Nielen, 2002), eating disorder (e.g., Cavedini, Bassi, Ubbiali, Casolari, Giordani & Zorzi, 2004), substance abuse (e.g., Bechara & Damasio, 2002), pathological

gambling (e.g. Cavedini, Riboldi, Keller, D'Annucci & Bellodi, 2002b), personality disorders (e.g., Haaland & Landrø, 2007), mania (e.g., Clark et al., 2001), schizophrenia (e.g., Beringer, Wasserman, Zanibbi, Charbonneau, Mangels & Beninger, 2003) and depression (e.g,. Must et al., 2006).

Of the clinical groups studied, schizophrenia is certainly the disorder that presents the highest and the most controversial number of studies (Sevy et al., 2007). Depression, despite a high incidence in the general population and its known relation to poor decision-making and insensitivity to reward, is one of the least researched mental health problems in the frame of emotion-based learning. For this reason the current work proposes to explore flexible emotion-based learning in depression and schizophrenia. The following two sections will review research conducted on depression and schizophrenia using the IGT.

Schizophrenia. Schizophrenia is a mental illness with substantial short and long-term consequences for individuals, their families, the health service and society. The incidence is estimated around 1% during the life course although the highest incidence is in people in their early twenty (National Institute for Clinical Excellence, 2002, p.1). Symptoms of schizophrenia are usually divided into positive, including hallucinations and delusions, and negative symptoms, such as social withdrawal, lack of drive, emotional apathy, self-neglect and poverty of speech. Frith (2004) suggested that difficulties in social cognition should be considered a core deficit of psychosis; patients affected by schizophrenia present, in fact, wide difficulties in emotional processing, social interaction and decision-making (Green, Penn, Bentall, Carpenter, Gaebel, Gur et al., 2008).

The interest on emotion-based learning in schizophrenia has been driven by neuropsychological studies showing OFC patients presenting deficit in social cognition (Bechara et al., 1996; Damasio, 1994). Abnormalities in the dorsolateral prefrontal cortex (DLPFC) and in the OFC have already been extensively documented in schizophrenia (Bertollo, Cowen & Levy, 1996; Convit, Wolf, de Leon, Patalinjug, Kandil, Caraos, Scherer, Saint Louis & Cancro, 2001; Crespo-Facorro, Kim, Andreasen, O'Leary & Magnotta, 2000; Weinberger & Berman, 1996). Neurofunctional and neuroanatomical evidence taken together with the social cognition deficit seen in OFC and in schizophrenic patients suggested that psychotic symptomatology could be related to a deficit in emotion-based learning. Due to its extensive neuropsychological background the IGT became the most used task to investigate emotion-based learning in schizophrenia. Although some research evidence seems to point in the direction of an impairment of emotion-based learning in schizophrenia, findings gathered with the IGT have been largely controversial and inconclusive.

Several studies showed people with schizophrenia performing poorly on IGT compared to healthy individuals. One of the first studies in this respect was conducted by Beninger et al. (2003) in the attempt to characterise the effect of typical and atypical antipsychotic medications on emotion-based decision-making. Results showed that patients on atypical (e.g., Risperidone), but not on typical antipsychotic (e.g., Chlopromazine) performed worse than healthy controls on the IGT. Ritter et al., (2004) compared the IGT performance of a mixed group of schizophrenic and schizoaffective disorder with a group of age, gender and education matched healthy controls and found that patients were selecting more cards from the disadvantageous decks than healthy

controls. In a pilot study designed to explore the decision-making ability in different subtypes of schizophrenia, Bark et al., (2005) compared the IGT performance of a group of catatonic patients with a paranoid group and a healthy control group. Impaired IGT performance (i.e. total mean net score below zero) was found only in the catatonic group with the paranoia group performing at controls level. In order to clarify the relationship between schizophrenic symptomatology and frontal areas, such as VMPFC, DLPFC and OFC, Shurman et al. (2005) assessed, with a battery of neuropsychological tests, a group of stabilized schizophrenic outpatients. Results showed patients with schizophrenia having a poorer performance on the IGT compared to controls. The authors noted that while the performance of schizophrenic patients on the IGT appears similar to that of patients with OFC lesions in several respects, some features of schizophrenia patients' performance on this task might not wholly resemble the OFC pattern (Shurman et al., 2005, p. 221). This finding led the authors to hypothesise that the specificity of the decision-making impairment in schizophrenia could be due to specific psychotic symptoms. In support of a decision-making deficit in schizophrenia, Kester et al., (2006) found adolescent with an early onset of schizophrenia performing worst at the IGT than age and education matched controls. More recently, in two similar studies Martino et al (2007) and Lee et al (2007) found that patients with schizophrenia displayed a preference towards disadvantageous decks with a marked low profile in learning accentuated in the last two blocks.

Despite the above evidence seeming to suggest an impairing role of schizophrenic symptomatology on IGT performance, several similar studies yielded contrasting results. Wilder et al. (1998) found a similar learning profile, in term of number of advantageous

and disadvantageous cards chosen, between control participants and schizophrenics. In a study designed to compare frontal cortex dysfunctions in OCD and schizophrenia, Cavallaro et al. (2003) found OCD patients' performance on the IGT to be significantly worse than the performance of controls and schizophrenic patients. No difference was found between control participants' performance and schizophrenia patients. Evans et al., (2005) found that not only performance but also subjective awareness of the decks' contingencies was comparable between patients with schizophrenia and controls. Similarly, Turnbull et al., (2006) found comparable performance on the IGT between schizophrenic patients, divided by positive and negative symptoms, and control participants. The role of positive and negative symptomatology became relevant during the set-shifting modification introduced after the first 100 trials when the contingencies were progressively altered. It was found that during the set-shifting phase patients with schizophrenia who scored high on measures of negative symptomatology performed worst than those who scored high on measures of positive symptomatology. This finding led the authors to consider that some specific sub-set of symptoms might influence emotion-based learning ability. The flexible emotion-based learning paradigm, despite the promising results, has been used only in one clinical study (i.e., Turnbull et al., 2006). Apart from symtomatological characterization, other aspects have been hypothesized to have an influence on IGT performance. Rodrigiuez-Sanchez et al., (2005) investigated the role of illness duration and drug treatment on emotion-based learning in a group of first episode schizophrenia. A comparison with the control participants' performance found first episode schizophrenics perform equally well. The authors conclude that the

extent of the illness duration and prolonged exposure to antipsychotic medication might produce a negative effect on emotion-based learning.

The extent of the inconclusive findings regarding the investigations conducted on schizophrenia using the IGT were reviewed by Sevy et al. (2007). The authors noted that IGT performance in schizophrenia may be related to other OFC deficits typically observed in schizophrenia such as working and declarative memory, attention and executive function. The authors also proposed that deficits in IGT performance could be due to the co-occurrence of substance abuse disorders (Sevy et al., 2007). Empirical data presented in the same review showed no difference in performance between patients with schizophrenia with and without concurrent cannabis use disorder; a significant difference in IGT performance was, on the contrary, present between the two clinical groups and a control group.

More recently, two studies attempted to correlate IGT performance of schizophrenic patients with structural abnormalities in the frontal lobes (Premkumar, Fannon, Kuipers, Simmons, Frangou, & Kumari, 2008; Nakamura, Nestor, Levitt, Cohen, Kawashima, Shenton & McCarley, 2008). Premkumar et al. (2008) compared OFC gray matter volume to IGT performance in patients with schizophrenia and healthy controls. Results showed patients with schizophrenia performed significantly poor on the IGT, with a general positive correlation between OFC gray matter volume and IGT performance. Similarly, Nakamura et al. (2008) examined IGT performance in a sample of schizophrenics and matched control participants both of whom received MRI scanning for OFC gray matter volume. In this case, the authors found a similar disadvantageous

performance on the IGT of the schizophrenic group but no association with OFC gray matter volume.

The effect of medication and substance intake represent an important variable to factor in any explanatory model of decision-making. Schizophrenics are heavily medicated for long periods of time and this long exposure to neuro-chemicals could have a strong effect per se on behaviour, brain functionality and morphology. By showing no impairment in IGT in first episode psychotic patients the study of Rodrigiez-Sanchez et al., (2005) seems to point in the direction of a contribution of drugs in influencing performance of schizophrenic patients. On the other hand, Kester et al., (2006) found adolescents with early onset of schizophrenia, as well as first episode patients little or no medicated, performed worst than healthy controls. Although the deficit of early onset schizophrenia could be explained by psychotic symptoms, the incidence of impulsivity, which is higher in young adults, could be claimed as a critical difference between the two studies (Glickson et al., 2006).

In the large majority of the studies reviewed, schizophrenia has been clustered as a discrete clinical entity. This conceptualization of the disorder has been largely questioned lately and alternative accounts of its phenotype have been proposed (Johns & van Os, 2001; Peralta, de Leon & Cuesta, 1992). The fact that psychotic features seem to distribute along a continuum in the normal population is not a novel idea (Claridge, 1997). A large body of epidemiological studies has shown how features such as delusion and hallucination occur in seemingly healthy individuals and not only in full blown schizophrenia (Peters, Joseph & Garety, 2004; Tien, 1991). The dimensionality of symptoms and the realization that current diagnostic labels might not be accurate enough

to characterize homogeneously a cluster is an element worth considering in emotion-based learning research in schizophrenia.

In summary, the findings of IGT performance in schizophrenia have been mixed and largely inconclusive. Various studies in this area have tried to control for potentially confounding factors such as medication, co-morbid diagnosis, clinical presentation and heterogeneous group formation but the extent and the possible causes of the emotion-based learning deficit in schizophrenia are still unclear.

Depression. Depression refers to a wide range of mental health problems characterized by the absence of positive affect (loss of interest and enjoyment in ordinary things and experiences), low mood and a range of associate emotional, cognitive, physical and behavioural symptoms (National Institute for Clinical Excellence, 2004, p.13). The lifetime estimated prevalence of depression in the UK ranges between 21 to 98 individuals in every thousand (Meltzer, Gill, Petticrew & Hinds, 1995).

Depressive symptoms have been associated with a variety of cortical and sub-cortical structures such as the amygdala, the ventral anterior cingulated cortex, the orbital, ventro, ventrolateral and dorsomedial portions of the prefrontal cortex (Drevets, 2000). Humans with orbital cortex lesions perseverate in behaviours that are unreinforced and exhibit difficulty in shifting cognitive strategies in response to changing task demands (Rolls, 1995; Bechara et al., 1998). The wide emotional and behavioural disturbance and the proposed cortical areas implicated in depressive symptoms suggested that emotion-based learning aspects could be implicated in the depressive symptomatology.

The first IGT application to mood disorders was by Clark et al., (2001) aiming to investigate decision-making process and the associated ventromedial prefrontal cortex functionality in acutely maniac inpatients. The hypothesis to be tested in this study was the relation between elevated mood and IGT performance. The study showed that maniac patients did chose significantly more from the disadvantageous decks demonstrating a performance similarity with VMPFC patients.

On the other end of the spectrum Dalgleish, Yiend, Bramham, et al. (2004) explored IGT performance in neurosurgery patients receiving stereotactic subcaudate tractotomy as a treatment for depression. Stereotactic subcaudate tractotomy is a surgical procedure performed for the alleviation of intractable affective disorders. It involves the destruction of bifrontal pathways located beneath and in front of the head of the caudate nucleus (Kartsounis, Poynton, Bridges & Bartlett, 1991). The hypothesis behind their investigation was that the neurosurgery would lead to depression recovery by reducing sensitivity to negative information. Four small groups of patients were recruited: a psychosurgery group no longer depressed, a psychosurgery group still depressed, a group of recovered depressed patients treated with neuroleptic and a group of healthy subjects. Results showed that the group of patient recovered from depression after psychosurgery exhibit the worse performance compared to the other three groups. The findings suggest the relevance of prefrontal areas in characterizing sensitivity to negative feedback and underline the centrality of prefrontal cortex to assist emotion-based decision-making. The authors also argue that the sensitivity to negative feedback, notoriously amplified in depression, is the key ability in order to perform advantageously on the IGT. In support of this claim there is a substantially similar performance of control participants,

depressed patients recovered with medication and depressed patients with unsuccessful stereotactic subcaudate tractotomy.

In two recent studies, Must et al. (2006, 2007) investigated IGT performance in patients with major depressive disorder (MDD). In the first study 30 MDD patients were tested with the standard (ABCD) and the reversed (EFGH) version of IGT (Must et al., 2006). The layout of the EFGH task is similar to the ABCD but inverts wins and losses. Every card selection at the EFGH version results in a money loss (either $50 or $100) and sometime a combination of punishment and reward is delivered. Magnitude and schedule of cards is the same as in the ABCD version (Bechara et al., 2000a). MDD patients, compared to controls, showed an impaired performance in the ABCD task but not in the EFGH task suggesting increased sensitivity to reward leading to disadvantageous choices. The results were highly unexpected in light of the idea that depressive symptoms are related to over-sensitivity to punishment and low sensitivity to reward (Dalgleish et al., 2004). The authors hypothesize that the increased sensitivity to positive reward could bias the perception of the high but infrequent punishment in the ABCD version of the task.

A second study conducted by Must et al. (2007) investigated genetic contributions to sub-optimal decision-making in depression with the same two versions of the IGT (i.e., ABCD and EFGH). One hundred and twenty four (124) MDD patients were genotyped for the 5-HTTLPR polymorphism and grouped according to three specific gene variations (allele) namely ss, ls and ll. The polymorphism was chosen for its relation with depression and anxiety as a possible regulator of serotonin transponder deficit implicated in MDD (Gonda, Juhasz, Laszik, Rihmer & Bagdy, 2005). Result showed that patients

with variant ll achieved higher level of performance in the ABCD task compared with patients with genotype ss. This suggests that the ll variant might be related to a better sensitivity to punishment. No association was found instead between the genotype chosen and the EFGH task. As for the study conducted by Dalgleish et al. (2004), Must et al's (2006) findings seems to suggest that impaired performance on the IGT might be due to specific subset of features within the diagnosis of depression.

Recently, a study by Smoski et al. (2008) investigated emotion-based learning with the IGT in a group of depressed patients. Smoski et al. (2008) found that depressed patients performed at comparable levels to healthy participants on the IGT, providing an account of sensitivity to negative feedback in depression. The authors also noted that both good and bad decks deliver losses during the IGT; if depressed patients have an advantageous performance on the task this implies that depressed patients can discriminate effectively between punishments of different entities and prefer the less punishing options. This could be slightly controversial if contextualized in the frame of depression that notoriously shows difficulties in evaluating the magnitude of punishment (Henriques, Glowacki & Davidson, 1994).

The limited number of studies suggests a link between the ineffective decision-making strategy, altered sensitivity to negative consequences and a possible VMPFC functional abnormality in depression. The evidence, however, does not seem to converge fully. The reviewed findings are far from conclusive, in light of the different research questions explored, the partially unaccounted role of medication history and type, and the different patient groups used. It is remarkable that despite the great emotional disturbance experienced and the executive functions deficit shown in the literature, some depressed

patients seem to show normal performance on a challenging task such as the IGT (Rogers et al., 2004). In this respect, investigation of components of the task more related to executive functions, such as flexibility, would characterise more accurately the extent to which depression and its features can influence IGT performance.

The role of subjective experience would also be an important addition to emotion-based learning research in depression; degree of awareness and personal perception of the task it is likely to be different in depressed patients compared to controls due to the illness specific cognitive distortions (Beck, Rush, Shaw & Emery, 1979). This would characterise if the bias in depressed people towards rewards and punishment is implicit or explicit and how this potential bias might fit into emotion-based learning paradigm.

Summary

This review has summarized the relevant aspects of emotion-based learning and contextualized the concept in the frame of neuroscience, experimental psychology and psychopathology. The interest in emotional influence over cognitive process started more than a century ago when the first accounts of patients with prefrontal lobe damage were recorded. Those patients presented a challenging and peculiar profile of intact intellect but a marked deficit to interact effectively with the social environment. Damasio and colleagues, in order to explain this deficit conducted a series of investigation aimed to characterize the influence of specific brain lesions on decision-making. As a mean of assessing decision-making the IGT was first introduced by Bechara et al. (1994) and since used to assess emotion-based decision-making ability. A large number of studies featuring the IGT have been published in the last 20 years investigating emotion-based learning in various subject populations spanning from patients with schizophrenia (Sevy et al., 2007) to Israeli traffic offenders (Lev, Hershkovitz, & Yechiam, 2008).

The role of somatic markers is largely debated and several arguments have been brought forward since its original formulation providing at odds evidence. Factors implicated in IGT successful performance are still largely unclear due to the high proportion of healthy participants failing to reach advantageous learning profile. Moreover, this review has touched upon experimental manipulation of the IGT (e.g., instructions, time constraints) that are able to disrupt normal participants' performance and suggests that emotion-based learning needs certain preconditions in order to operate correctly. Lastly, the role of emotion-based learning in schizophrenia and depression has been reviewed. In schizophrenia, the paradigm has been extensively studied and yielded inconsistent results, while the investigation of emotion-based learning in depression is still in its early days.

The Current Thesis

The present research aims to investigate some issues in relation to emotion-based learning throughout a series of experiments addressing research questions spanning from experimental to clinical psychology. Experiment 1 will explore the role of decision-phase time constraints on emotion-based learning and the bearing of environmental constraint on IGT performance. Chapter 3 will introduce a set-shifting modification of the IGT and characterise the relation between standard emotion-based learning paradigm and flexibility of emotion-based learning. Chapter 4 will examine the autonomic correlates of the set-shifting modification of the IGT. Chapter 5 will then move gradually to the investigation of emotion-based learning in depression and schizophrenia presenting

results from two studies conducted on sub-clinical populations presenting schizotypal and depressive features. The final two empirical chapters will investigate flexibility of emotion-based learning in two clinical samples of depressed and schizophrenic patients.

Chapter 2

Decision-phase time constraints and emotion based learning

A significant number of investigations have reliably shown that learning on the IGT is impaired in people with specific brain lesions and with certain psychiatric disorders (e.g., Bechara et al., 1994; Ritter et al., 2004; Sevy et al., 2007). Although findings with clinical populations seem to depict a clear picture, exactly what constitutes ''unimpaired'' learning remains to be determined (Dunn et al., 2006, p. 251). For instance, variability in IGT performance has been observed with some subgroups of healthy control populations failing to show preference for the advantageous decks at the end of the task (e.g., Caroselli, Hiscock, Scheibel, & Ingram, 2006; Glicksohn et al., 2007; Lehto & Elorinne, 2003). Bechara et al. (2001, 2002) used a mean net score cut-off of 10 to differentiate learners from non-learners, based on normal distribution plots of normal controls and VM lesioned patients. Crone et al. (2004a) distinguished control participants by three levels of performance: bad, moderate and good. This subdivision was achieved by dividing the distribution of total mean net scores into three numerically similar subgroups. The mean number of advantageous selections was 35 for the bad, 48 for the moderate and 58 for good group, respectively. These and other findings showing variability in control group performance on the IGT make interpretation of IGT data difficult because a normative or baseline control group profile is necessary in order to evaluate the performance of experimental (i.e., patient) groups (Dunn et al., 2006, pp. 251–252). Therefore, it is important that further research be conducted into the factors that might influence advantageous performance in IGT control groups.

One possible way of examining variability in IGT performance would be to manipulate methodological features of the task in order to selectively *disrupt* advantageous choice making. According to this logic, if the manipulation successfully disrupts learning, as evidenced by a diminished preference for the advantageous decks, then a profile of unimpaired learning should be observed when the manipulations are absent or removed. This may then permit an analysis of the conditions needed to establish unimpaired learning in control groups, and help make the interpretation of data from IGT studies with clinical populations more reliable (Dunn et al., 2006).

An important consideration when comparing learning profiles across different studies is the differing ways in which the IGT has been administered. Across the years, different versions of the task have been developed. A major improvement with respect to the original table-top procedure has been the computerized version. The manual versus the computerized version of the IGT, in some respects, represents quite a different design. One of the main different aspects is that the time available during the choice phase in the two versions is considerably different; in the manual version, the choice has to be made by pointing to or picking cards from the decks, while in the computerized version only a mouse click is required. Response time, therefore, is on a different scale if left unlimited for the two tasks and is more difficult to implement, track and subject to bias when a non-automated format is used. In addition, facsimile money was used in the manual version of the IGT and participants were allowed more time to make selections (Bowman, Evans & Turnbull, 2005). When Bechara and colleagues moved to a computerized administration of the task (Bechara et al., 1999) they chose to enforce a 6 s time delay between card

selections (i.e., inter trial interval) in order to resemble the choice time in the original manual version of the procedure.

In a recent paper, Bowman, Evans and Turnbull (2005) investigated the role of decision time delays in the manual and the computerised version of the IGT. They adopted a time-constraint of 6 s, which was based on the average inter-trial interval (ITI) developed by Bechara et al. (1999) to record skin conductance responses during the automated IGT. The study design consisted of three experimental conditions: a time-unlimited manual procedure, a time-unlimited computerized procedure and a time-limited computerized procedure with enforced delay. In the *time unlimited manual condition* participants were allowed to select cards freely throughout the duration of the 100 card selections. In the *time unlimited computerised condition* participants were allowed to select cards freely by clicking on the image of one of the four decks displayed on a computer monitor. The *time limited computerised* procedure was equal to the time-unlimited computerised condition apart from the fact that participants were forced to wait 6 seconds between card selections. In this respect the enforced time constraint was not implemented in the critical choice phase, but during the ITI. Once the ITI had elapsed, no time constraint was present during the critical decision making period. It is perhaps unsurprising then that learning rates did not differ significantly either between IGT administration formats or when a 6-s ITI was used (i.e., during the automated task).

Bowman et al. (2005) speculated that an enforced delay of 6 s might evoke feelings of frustration, with participants eager to make their card choices as quickly as possible in order to access the outcomes of their choices. Such unintended frustration might impact upon the IGT because it purportedly recruits emotion-based resources

(Damasio, 1996; Dunn et al., 2006; Turnbull, Evans, Bunce, Carzolio, & O'Connor, 2005). As a result, the possible disruptive effects of time-constraints may be inferred from the subjective experience ratings the participants gave of the relative ''goodness'' and ''badness'' of the decks. However, Bowman et al. (2005) found no significant differences in the subjective ratings of each group suggesting that the 6-s ITI did not evoke feelings of frustration.

It is important that, if the cognitive components of the task are of interest, to examine the potentially disruptive effects of shorter time constraints during the crucial decision-making phase on IGT performance. A number of real-world situations have vital time constraints associated with them, most notably in the interpersonal world, when one often has only a few seconds to judge whether to make a joke, express sympathy at a loss, or respond to an aggressive challenge. In sum, there is much merit in considering the role of time-limitations on the IGT in shorter time durations, and focusing on such time restrictions primarily at the crucial decision-making phase of the task.

The present study, sought to systematically investigate the effect of different time constraints implemented during the decision-making period using an automated IGT format. Two-s and 4-s decision-phase time constraints were selected and learning rates compared with those of control group participants not exposed to any time-constraint. In addition to measuring behavioural performance, subjective experience was also recorded (e.g., Bowman et al., 2005; Evans et al., 2005) in order to examine the effects of time constraints on awareness during the IGT. It is predicted that that the two time constraints groups would show impaired learning in the IGT, relative to the control group, and that

participants' subjective awareness of the ''good'' and ''bad'' decks would be unimpaired.

Experiment 1

Method

Participants

Seventy five participants, 23 male and 52 female, were recruited from the subject pool of the Department of Psychology at Swansea University. Following completion of the study, participants were compensated with £5. Each participant was randomly allocated into one of three groups: 2-s time constraint (n=25), 4-s time constraint (n=25) and a control group with no time constraint (n=25).

Materials and procedure

Upon arrival at the laboratory participants were provided with the information sheet and asked to read it. Participants were, subsequently, given the opportunity to question the experimenter about any aspect of the experiment and finally asked to read and signed the consent form. Once the signed consent form was obtained participants were asked to sit in front of the laboratory computer. The laboratory computer was a Pentium 4 desktop PC loaded with Windows XP, which was arranged on a desk with a chair placed in front of a 17" LCD colour monitor.

One of the three experimental conditions (*no time constraint, 2 seconds time constraint* and *4 seconds time constraint*) was loaded on the machine and participants were asked to read the instructions. All three groups received general instruction about

the task based on Bechara et al. (2000b). Instruction provided to the control no time constraint group were as follow:

In a moment, the computer will present four decks of cards labelled A, B, C, and D. Your task is to select one card at a time, by clicking on the card with the computer mouse, from any deck you choose.

Each time you select a card, the computer will tell you that you have won some money. The amount of money won will be immediately added to the total, which will be displayed in the bottom right-hand side of the screen.

Occasionally, however, when you select a card, the computer will tell you that you have won some money but that you have also lost some money. The amount of money lost will be immediately deducted from your total.

Your task is to try and earn as much money as possible, and if you can't win, to avoid losing as much money as possible.

You will be given a loan of £1000 credit to begin the task. It is important that you try and behave as if this were a real card game and try to win as much money as possible (and lose as little as possible). Treat the £1000 credit of play money, and all money won/lost during the task, as if it were your own real money.

No matter how much you find yourself losing, you can still win. Pay attention to the wins/losses.

Every so often, the computer will ask you to give each deck of cards a score, based on how good or bad you feel they are. Please use the slider scale to rate each of the decks. The computer will show you how to do this.

The computer will not tell you when the task will end, so please keep playing until the tasks ends.

If you have any questions, please read through the instructions again to see if they answer your questions. If they do not, then ask the experimenter to explain.

Remember, your task is to try and earn as much money as possible, and if you can't win, to avoid losing as much money as possible, and be sure to give each deck of cards a score based on how good or bad you feel they are.

Good luck!

The instruction given to 2-s and 4-s time constraint groups differed from those of the control group in that the speed of responding was emphasised (i.e. "your task is to select one card at time *as fast as you can*..."). Clarification about the task was provided by the experimenter if requested by a participant.

A computerized standard version of the IGT was employed for the no time constraint condition as described from Bechara, Damasio and Damasio (2000a). Four decks of cards of the same physical appearance and colour (see Figure 4) were concurrently presented on the screen. Participants were asked to keep playing until the message "please report to the experimenter" was displayed on the screen. Participants were randomly allocated to one of the experimental conditions.

No time constraint

In the no time constraint condition participants where simply asked to choose cards in order to maximize their winnings. No mention was made of any time constraint. Participants could take as long or as short as they liked to make selections.

Two seconds time constraint condition

In the 2 seconds time constraint condition participants where instructed as in the no time constraint condition but forced to choose a card within two seconds.

Four seconds time constraint condition

In the 4 seconds time constraint condition participants where instructed as in the no time constraint condition but forced to choose a card within four seconds.

In both time constraint conditions, if a choice was not made in the time available, a message, "*time out, please be faster*" appeared on the screen for 5 seconds. The number of trials with a time out was recorded but not counted as part of the total number of trials of the IGT. For each condition, the task finished after 100 choice-trials had occurred.

Figure 4: Screen shot of the Iowa Gambling Task computerized version developed at Swansea University.

Apart for the time constraints described above, the task employed standard IGT features (e.g., Bechara et al., 2000a). Participants were asked to select cards form four

concurrently available decks (labelled A, B, C and D). At the beginning, a loan of £1000 of virtual money was given and displayed at the bottom right of the screen. Every win or loss was summed to or subtracted by the total amount of the loan always present on the screen. As in the original version of the IGT (Bechara et al., 1994) deck A and deck B were disadvantageous while deck C and D were advantageous. The computer programme randomly determined which two of the decks were to be the advantageous and disadvantageous, respectively for each participant. That is, unlike previous studies (e.g., Bechara et al., 1994; Bowman et al., 2005; Suzuki et al., 2003), the spatial location of the advantageous and disadvantageous was not restricted to the left (e.g., A & B) or right (e.g., C & D) of the screen. Randomly determining advantageous and disadvantageous decks at the outset of the task for every participant rules out location preference as a potential factor governing performance.

Frequency of reward and punishment differed for each deck. Participants always won £100 if they selected a card from deck A or B and always won £50 if they select a card from deck C or D. The amount of losses was comprised between £150 and £350 for deck A; £1250 for deck B; between £25 and £75 for deck C; and £250 for deck D (see Figure 5). In case of gain, a sentence stating "You won X" appeared on the computer screen and the amount of money won was added to the total. In case of win and loss, the message presented was "You won X but you lost Y". Overall high immediate reward decks (A and B) resulted in a higher magnitude of punishment leading to a net loss of £250 every ten trials, whereas the low immediate reward decks (C and D) resulted in a lower magnitude of punishment leading to a net gain of £250 every ten trials.

Subjective experience ratings: An additional feature to investigate subjective experience was embedded in the task (Bowman et al., 2005). Every twenty selections the game was interrupted and participants were asked to provide subjective experience of "goodness" and "badness" of each deck (A, B, C, D). Ratings were made using a slider-scale from 0 to 10 (where 0 = *very bad* and 10 = *very good*).

Decision time: Decision time was also recorded for every trial during the entire task. Decision time was defined as the time (measured in seconds) elapsing from the onset of the cards until a choice was made.

Figure 5: Schedule of wins (on the card value) and losses (in the circle) occurring every 10 cards in the four decks for all the conditions.

Results

Participants' mean age was 21.66 (SD=3) and mean number of years spent in education was 15.72 (SD=2.17). No significant difference was found between the three groups for the above-mentioned characteristics (all $p > .05$).

IGT Mean Net Score

As in Bechara et al. (1994), the hundred IGT selections were sub-divided into five blocks of 20 trials. The mean net score was calculated for each block by subtracting disadvantageous selections from advantageous selections [(C+D)-(A-B)]. A net score above zero is indicative of advantageous selections, while a net score below zero implies disadvantageous selections. Figure 6 shows the IGT mean net scores for the control, 2-second and 4-second groups. A mixed factor 3 (group) x 5 (block) ANOVA showed a main effect for block, $F(4, 288) = 27.03, p < .001$. All three groups showed a general increase in advantageous selections across trial blocks. There was also a significant main effect for group, $F(2, 72) = 3.83, p < .05$. Tukey HSD post-hoc tests revealed that the control group made significantly more advantageous selections than the 2-second group ($p < .05$), but that the control did not differ significantly from the 4-second group and that the 4-second group did not differ significantly from the 2-second group. The trial block by group interaction was not significant, $F(8, 288) = 1.18, p > .05$.

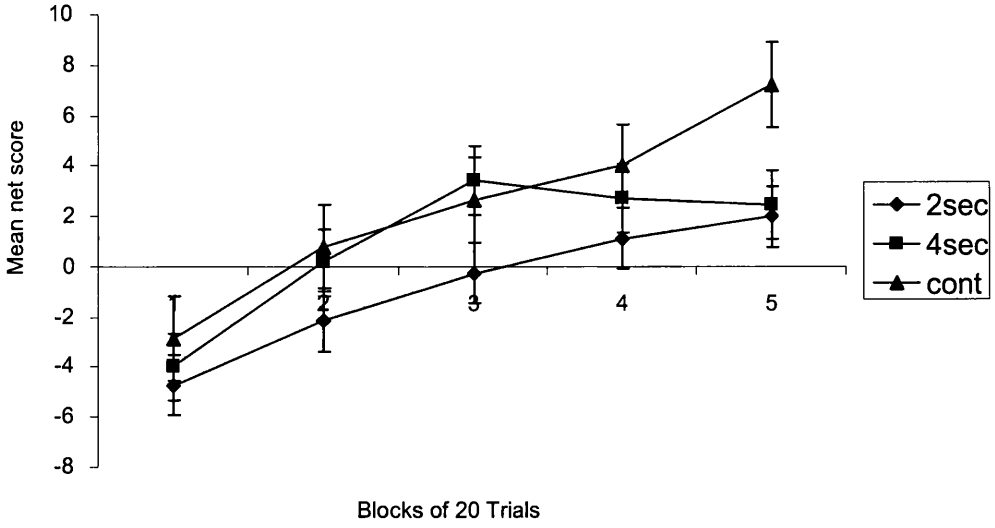

Figure 6: Mean net score for each of the three groups across the five blocks of 20 trials. 2sec: two second time constraint; 4sec: four second time constraint; cont: no time constraint.

IGT and Subjective Ratings

In this case a mean net subjective rating was calculated by subtracting the ratings of the disadvantageous decks (A and B) from the ratings of advantageous decks (C and D). The mean subjective ratings for each group across blocks are shown in Figure 7. A mixed factor 3 (group) x 5 (block) ANOVA showed a main effect for trial block, $F(4, 288) = 8.01, p < .001$. For the three groups, subjective ratings showed a substantial increase from the first to the second blocks of trials. The main effect for group and the group by trial block interaction were not significant, however.

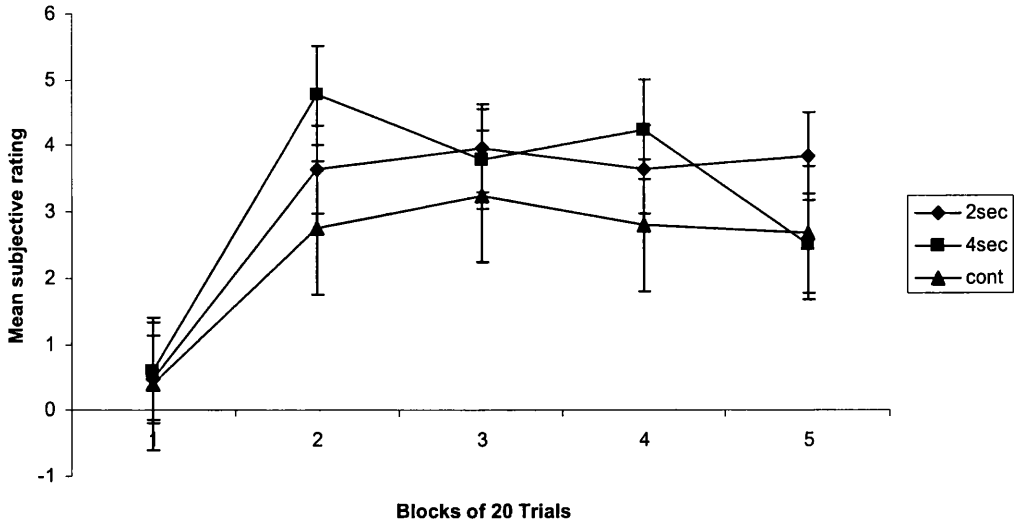

Figure 7: Mean subjective experience ratings for each of the three groups across the five blocks of 20 trials. 2sec: two second time constraint; 4sec: four second time constraint; cont: no time constraint.

IGT and decision Time

Figure 8 shows the mean reaction time for each experimental group across the five trial blocks. A mixed factor 3 (group) x 5 (block) ANOVA found a significant main effect for trial block, $F(4, 288) = 5.62, p < .001$, a significant main effect for group, $F(2, 72) = 12.60, p < .001$ and a significant trial block by group interaction, $F(4, 288) = 3.22$, $p < .01$. Bonferroni-adjusted post hoc tests found that the control group had significantly longer reaction times when compared to the 2-second group across the first three trial

blocks ($p < .01$), and the 4-second group across the first two trial blocks ($p < .01$).

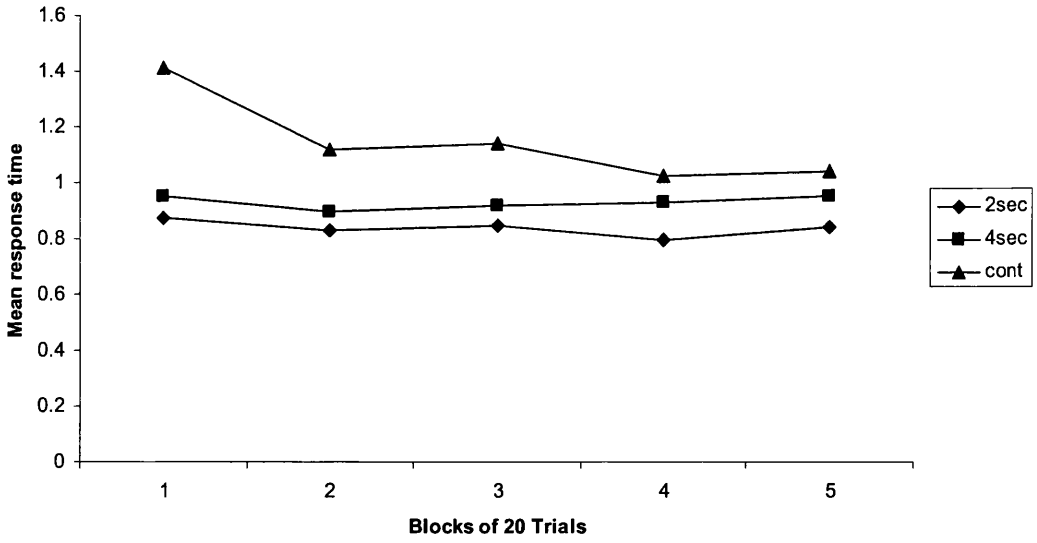

Figure 8: Mean decision-time in seconds for each of the three groups across the five blocks of 20 trials. 2sec: two second time constraint; 4sec: four second time constraint; cont: no time constraint.

Figure 9 shows the total number of 'timeouts' for all participants in the 2-second and 4-second groups. A 2 (group) x 5 (block) ANOVA showed a main effect for group, $F(1, 48) = 17.42, p < .001$, while the main effect for block and the block by group interaction were not significant. Contrast analysis found that the 2-second group had significantly more timeouts than the 4-second group in blocks 1, 2 and 4 ($p < .01$).

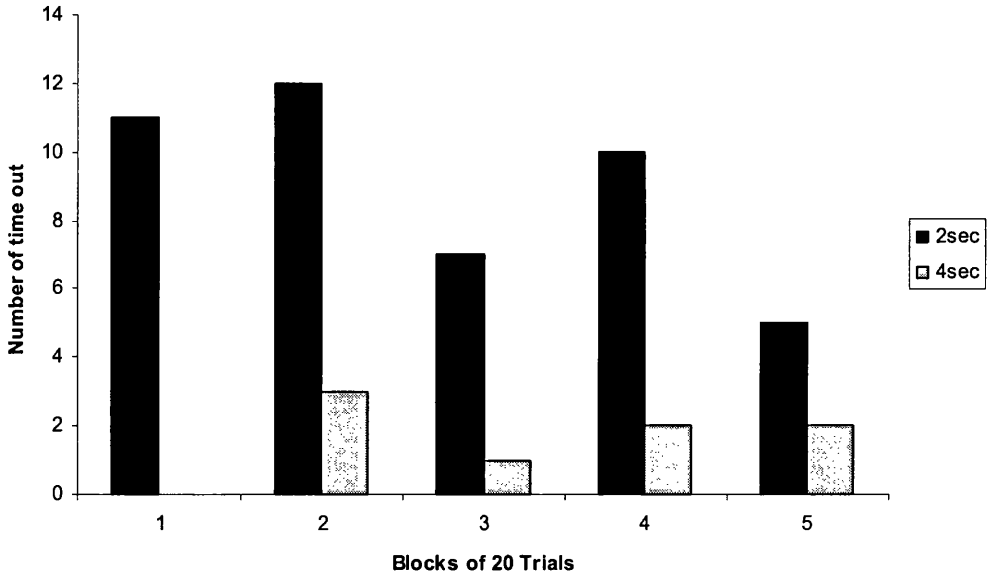

Figure 9: The number of trial time-outs for the 2-second and 4-second groups across the five blocks of 20 trials.

Discussion

The aim of the present study was to investigate the effect of 2 and 4 s time constraints on emotion-based learning during the critical decision-making period in the IGT. Results showed that learning was significantly disrupted in the time constraints conditions if compared with a control group given no time-constraints. All groups initially showed the typical pattern of decision-making below chance but gradually shifted to advantageous above chance levels as the task progressed. This is consistent with previous research conducted with normal populations (i.e., university students; Balodis, MacDonald & Olmstead, 2006; Bowman & Turnbull, 2003; Fernie & Tunney, 2005; Glicksohn et al., 2007). The performance of the three groups showed an increase in the number of advantageous selections across trials and although a common pattern of

learning was displayed by all participants, control group did perform significantly better than the 2-s time constraint group. The present findings are the first to show a significant disruptive effect of decision-phase time constraints on learning during the IGT, with less advantageous choices being made while performing the task under the 2-s time constraints suggesting time as a critical factor impacting on emotion based learning.

Subjective experience ratings also showed a significant increase across blocks, for all groups. However, participants' ratings of which decks were ''good'' or ''bad'' did not appear to be disrupted by the implementation of time-constraints during the critical decision making period. That is, participants from all three groups showed comparable recruitment of emotion-based resources in discriminating the advantageous decks at above chance levels from the first block of trials onwards. This suggests that participants had better awareness of the affective status (or emotion-biasing signals), of the reward and punishment schedule contained within the IGT than may previously have been thought (cf., Bechara et al., 1997, 2000a; see Bowman et al., 2005; Evans et al., 2005; Maia & McClelland, 2004).

The present findings appear also to be relevant to the issue of the ''cognitive impenetrability'' (Dunn et al., 2006, pp. 245– 249) of the IGT schedules claimed by Bechara and co-workers. The creators of the task claimed that advantageous performance on the IGT is entirely dependent on the guidance of emotional signal rather than a rational decision-making process based on the calculation of the schedule of rewards and punishments (Damasio, Adolphs & Damasio, 2003). Subjective experience results from this experiment show that participants can access emotion-based knowledge of the ''goodness'' and ''badness'' of the decks at a surprisingly early stage in the task,

provided that participants are required merely to interrogate their feelings about an object (deck) rather than provide a fully-fledged descriptive account of the basis of the task (Evans et al., 2005; Maia & McClelland, 2004; Turnbull, Berry, & Bowman, 2003). Whether or not the subjective experience ratings measured in the present study can be said to accurately reflect the penetrability of the IGT reward and punishment schedules is, of course, a contested issue that must await the outcome of further research, as well as a greater conceptual clarity about the nature of conscious awareness.

The present findings also include the first reported analyses of reaction time data during IGT performance, and show both significant main effects and interactions of trial block and participant group. As one might expect, the control group took significantly longer to make choices compared to the two time constraint groups, but it is remarkable to notice that the reaction times of all three groups remained below 2-s across all blocks of trials. Also, perhaps unsurprisingly, there were a significantly greater number of ''time outs'' in the 2-s time constraint group compared with the 4-s group, notably in the first and second blocks of trials.

Taken together, decision phase reaction time and time-out data indicate that time constraints initially disrupt advantageous performance, but such constraints are not disruptive when imposed between decision-making phases (Bowman et al., 2005). Nevertheless, while decision-phase time constraints do produce a decrement in both speed and ''accuracy'', participants still showed some adaptability to the reward/punishment schedules.

Overall, the findings demonstrate important effects of time constraints on emotion-based learning in the IGT when these constraints are targeted at the crucial

decision-making phase, and also suggest that the reward/punishment schedules of the IGT are to some extent cognitively penetrable. The methodological features of the present study, such as the randomised positions of the good and bad decks and the use of subjective experience ratings and reaction time data, may be important considerations for future research in helping to identify the necessary and sufficient conditions for ''unimpaired'' IGT control group performance. This is clearly a central issue when investigating a construct such as emotion-based learning that shows substantial variability across the population, and is increasingly understood to be important for the way in which humans make complex decisions in uncertain circumstance.

Chapter 3

The contingency shifting variant IGT: Flexibility and emotion-based learning

The findings of Chapter 2 clearly illustrate that the performance of healthy control participants on the IGT may be systematically disrupted by placing time constraints on the critical decision-making period. Performance was seen to vary as a function of the duration of time constraint that groups of participants were exposed to. It was argued that this systematic *disruption* of learning may provide a novel means of studying the factors responsible for variability in control group performance.

It maybe argued, however, that an exhaustive analysis of variability in IGT performance is both difficult and unnecessary. The myriad of influences exerted over human performance in experimental settings is both widely accepted and extensively studied (McGuigan, 1993), and an investigation with the IGT certainly has considerable merit. At this stage in the research, however, an alternative approach was adopted that involved developing a novel variant IGT as a means of further illustrating the range of factors that may be responsible for variability. In so doing, an empirical analysis of performance on a novel IGT was deemed appropriate. The remaining empirical chapter sought to undertake this investigation.

The original version of the IGT, as used in Chapter 2, typically consists of 100 card selections conventionally divided into five blocks of 20 trials, and involves participants making choices from four concurrently available decks of cards for monetary gain/loss. Two of the decks (labelled A & B) result in immediate high gain per choice (e.g., £100), but produce regular losses, leading to a cumulative long-term loss (i.e., termed "the disadvantageous choice"). The remaining two decks (labelled C & D)

typically result in lower immediate rewards, (e.g., £50), but also generate fewer losses, resulting in a cumulative long-term gain (i.e., termed "the advantageous choice"). A defining feature of IGT performance is the gradual adjustment to the affective consequences of reward and punishment. Participants initially tend to prefer cards from the disadvantageous decks and, around halfway through the task, a shift in the selection strategy is usually observed in favour of the advantageous decks (see Dunn et al., 2006).

In the original IGT, fixed or variable rewards are presented on every trial and fixed or variable punishments are presented intermittently. Advantageous decision-making, then, involves foregoing immediate gains associated with higher long-term losses for lower immediate gains and lower long-term losses. The role of reward and punishment in the IGT has been studied since the original introduction of the task with schedule and magnitude modification of the original procedure. In a variant of the original task, called the EFGH version, Bechara et al. (2000a) arranged the schedules such that the advantageous decks presented high immediate punishment but overall higher rewards, while the disadvantageous decks presented low immediate punishment but overall lower rewards. In this variant task advantageous decks (i.e. E and F) deliver high immediate money loss (i.e. $-100) but overall higher winnings. Conversely, the disadvantageous decks delivered immediate low money loss (i.e. $-50) but lower magnitude winnings. In this respect, sampling cards from decks E and F would lead to a mean net gain of $250 over 10 trials while ten selections from decks G and H would result in a net loss of $250. Patients with VMPFC damage showed preference for the disadvantageous decks on both the standard and variant IGT (Bechara et al., 2000a). However, patients with major depressive disorder show impaired learning on the original,

but not the variant IGT (Must et al., 2006), while typically-developing children and healthy adults show a clear developmental trend towards preferring the advantageous decks on both versions of the task (e.g., Crone & Van der Molen, 2004; Crone, Bunge, Latenstein, & Van der Molen, 2005; Davis et al., 2007).

In recent years there has been interest in the extent to which performance on the standard IGT might rely on reversal learning ability. This argument is based on the claim that for some decks, such as deck B that presents one high magnitude punishment every 10 trials, initial selections result in high temporary rewards, followed by punishment after several selections (See figure 5 chapter 2 for schedule of the task). Therefore initial selections from deck B can be appraised, in the early stages of the task, as advantageous but would need to be reassessed once the low frequency high money losses will occur. In light of this reassessment of preference along the task several authors have suggested that performance on the IGT may rest on reversal learning abilities (e.g. Fellows & Farah, 2003; Hornak et al., 2004; Maia & McClelland, 2004; Rolls, 2000).

Several studies have investigated the issue of reversal learning performance and its influence on decision-making, particularly in individual with brain injury but findings have often been inconclusive. Fellows and Farah (2003) showed that VMPFC damage, but not dorsolateral prefrontal cortex damage, results in impaired reversal learning ability. This claim rest on the finding of an investigation conducted with standard reversal learning task (Fellows & Farah, 2003). During this task, participants were dealt two cards at a time from two different coloured decks. One deck always delivered rewarding cards while the other delivered equal magnitude losing cards (i.e., win $50, lose $50). After 8 consecutive winning selections, contingencies were switched so that the

previously good deck delivered losses and the previously bad deck delivered wins. Participants' performance was rated for number of errors and for the number of trials necessary to complete the task. The task ended after the successful completion of five contingency switches. Fellows and Farah's (2003) results showed that patients with VMPFC damage, but not dorsolateral prefrontal cortex damage or controls, were impaired in this task, providing further support to the crucial role of VMPFC to accomplish reversal learning tasks.

Following the study employing the standard reversal learning task (Fellows & Farah 2003) Fellows and Farah (2005) developed a "shuffled" variant IGT to explore the issue of reversal learning in relation to the IGT. The shuffled variant IGT task used the same 4 decks layout but the card order was changed so that the losses associated with the disadvantageous decks were experienced on the first few trials (i.e., 1-10). The early occurrence of money losses would, in the author's view, eliminate the need for reversal learning as disadvantageous decks would be perceived as such from an early stage of the task and therefore the "advantageousness" of the decks would not need to be reassessed (Fellows & Farah, 2005). Results showed that the learning profile of VMPFC patients was indistinguishable from that of controls. In explaining these atypical findings, Fellows and Farah (2005) suggested that a deficit in reversal learning ability may be involved in IGT performance because "cards are presented in a fixed order that induces an initial preference for the ultimately riskier decks that must then be overcome as losses begin to accrue" (Fellows & Farah, 2005, p. 58). When the card order was changed, as during the shuffled variant, and the need for reversal learning was hence removed or at the very least minimised, the performance of VMPFC patients approximated control levels.

Recently, Brand et al., (2007) found that performance on specific executive function measures, such as the Wisconsin Card Sorting Task (WCST), which involves reversal learning, was correlated with performance on the last blocks of IGT trials only (see also Lehto & Elorinne, 2003; Mitchell, Colledge, Leonard, & Blair, 2002). Performance on the first block of the IGT trials did not correlate with either the WCST measure or other IGT blocks. Brand et al. (2007) suggested that two potentially separable mechanisms, decision-making under ambiguity and decision-making under risk, operate during the first and latter blocks of the IGT trials, respectively. Correlations with the WCST were only found in the later IGT trial blocks (when decisions are made under risk) because reversal learning, which is indexed by the WCST, was not implicated until later in the task after punishment has been experienced.

In the context of these complex, and at times ambiguous findings, there are several limitations in investigating reversal learning with the traditional IGT. Firstly, deck selection is not controlled by the investigator, so that it might take a few trials, or very many trials, before a participant encounters punishment on a particular deck. Secondly, as Fellows and Farah (2003) noted reversal learning claimed in the standard IGT is based on the effects of a *single* negative experience on a deck, rather than the cumulative effects of sustained selection. For deck B, for instance, the schedule allowed nine rewarding experiences followed by one punishment; a money loss, even if of high magnitude, can arguably be claimed to constitute reversal learning after nine wins. It is possible that the IGT performance is at least partially due to 'aggregate learning' over many trials, as evidenced by apparently normal performance with patients with both substantial working memory impairments (Bechara et al., 1998), and profound episodic

memory impairment (Turnbull & Evans, 2006). Finally, the role of reversal learning in IGT performance has been investigated through *correlations* between the original IGT and either different tasks (e.g., reversal learning tasks; Fellows & Farah, 2003) or executive function tests (e.g., WCST; Brand et el., 2007) rather than tasks specifically designed to assess aggregate learning reversal.

Recently, Turnbull, Evans, Kemish, Park, and Bowman, (2006) employed a unique contingency-shifting modification of the IGT. During the contingency-shifting variant IGT, the reward and punishment contingencies were systematically altered following initial exposure to the standard 100 trials. In a non-automated study conducted with people with schizophrenia and healthy controls, Turnbull et al. introduced three successive, signaled "shift-periods" with modified contingencies such that the decks that were previously advantageous became disadvantageous, and vice versa. The contingency shift modification consisted of 120 trials to be completed after the standard 100 IGT trials. During the shift-phase the schedule of advantageous and disadvantageous cards were systematically changed so that decks with positive payout shifted to negative and vice versa. Results showed that healthy participants, after an initial disruption of learning levels, adapt to the changing environment. This typically was show by an improvement during the later trials of each shift-period. The learning profile of controls was comparable to those people with schizophrenia who scored high in positive symptoms, but not from those who scored high in negative symptoms.

These findings highlight potential difficulties in flexible emotion-based learning in schizophrenia, in particular in tasks that involves shifting or reversal learning (e.g., Pantelis, Barber, Barnes, Nelson, Owen, & Robbins, 1999). The contingency-shifting

variant IGT, devised by Turnbull et al. (2006), offers considerable promise as a means of investigating the *flexible* use of emotion-based learning and further elucidating the role played by reversal learning in IGT performance. It is important to note that the use of the term 'contingency-shifting' refers to a progressive modification of the reward and punishment contingencies, and not to abilities described by similar, related terms such as 'set-shifting' (e.g., Dias, Robbins, & Roberts, 1996; Konishi, Nakajima, Uchida, Kameyama, Nakahara, Sekihara et al., 1998).

The present chapter sought to extend the findings of Turnbull et al. (2006) and to explore the potential of the contingency-shifting variant IGT as a putative measure of reversal learning ability. To do so, the procedure used by Turnbull et al. was adapted in the following ways. First, Turnbull et al. used a non-automated version of the task and real-money rewards throughout. Although no significant differences have been observed between automated and non-automated formats (Bowman et al., 2005) or when real and hypothetical rewards have been used (Bowman & Turnbull, 2003), the variability of control group IGT performance (e.g., Dunn et al., 2006, pp. 251-252; Glicksohn et al., 2007) across studies employing identical tasks suggests that a replication and extension of Turnbull et al.'s findings would be useful. Second, Turnbull et al. did not measure participants' subjective experience ratings of the relative "goodness" and "badness" of the decks (Bowman et al., 2005). Recording subjective ratings allows for an examination of the effects of the shift-periods on emotion-based learning, and may permit an identification of when during the task the rules governing choices become explicit (Brand et al., 2006, 2007; Maia & McClelland, 2005). Finally, Turnbull et al. signalled each of the three shift-periods to participants, which may have influenced subsequent choices.

Experiment 2 was undertaken to address these issues and to provide a detailed analysis of set-shifting IGT performance with a large cohort of participants.

Experiment 2

Method

Participants

Two hundred and eight undergraduates (95 male, 113 female) from Swansea University participated in return for course credit. Ages ranged between 18 and 38 (M = 21.38, SD = 4.11). An independent samples t-test revealed no significant difference in age between males and females, $t(206) = -.518$, $p = 0.605$. Participants had a mean of 14.94 (SD = 2.67) years of education.

Materials and Procedure

An automated version of the IGT, programmed in Visual Basic® 6.0, was employed. Participants received general instructions about the task that were based on Bechara et al. (2000a; see Appendix 1) and completed a total of 220 trials of the IGT in two phases: 100 trials of the original version of the task (Phase 1) followed by 120 trials of a contingency-shifting variant IGT involving three successive shifts of reward and punishment (Phase 2).

Phase 1: *Original IGT.* Participants were instructed to select cards from four concurrently available blue-coloured decks (labelled sequentially A, B, C and D). The computer programme randomly determined which two of the decks were to be 'advantageous' and 'disadvantageous', respectively, for each participant (Fernie & Tunney, 2006; Lin, Chiu, Lee, & Hsieh, 2007; Pecchinenda, Dretsch, & Chapman, 2006).

That is, the spatial location of the advantageous and disadvantageous decks was not restricted to the left (i.e., A & B) or right (i.e., C & D) of the computer screen. Randomly determining advantageous and disadvantageous decks at the outset of the task for every participant excludes location preference as a potential factor governing performance. Once determined, the positions of the decks remained unchanged until the end of the task.

A loan of £1000 of virtual money was displayed at the bottom right of the screen and was updated immediately following choices with gains and/or losses. Participants always won £100 if they selected a card from the 'disadvantageous' decks and always won £50 if they selected a card from the 'advantageous' decks. The amount of losses varied between £150 and £350 for deck A; £1250 for deck B; between £25 and £75 for deck C; and £250 for deck D. In the case of gains, a sentence stating, "You won X! X added to your total" appeared on the screen and the amount of money won was added to the total. In the case of gains and loss, the message presented was "You lose £1250! £1250 has been deducted from your total". This onscreen feedback was displayed for 5-s, before a 2-s ITI. Phase 1 ended after 100 trials.

Phase 2: *Contingency-shifting IGT.* Immediately after Phase 1 (i.e., without interruption and/or signaling), three contingency-shift phases, each consisting of two blocks of 20 trials, were introduced (Turnbull et al., 2006). The onset of each unsignalled shift phase involved a systematic modification of the reward and punishment contingencies of Phase 1 (participants' positions within the decks continued into Phase 2). During the three, 40-trial contingency-shift phases, the advantageous decks (C and D) were successively replaced by decks A and D (shift period 1), A and B (shift period 2), and B and C (shift period 3). Each contingency-shift period began immediately following

the 100th (shift period 1), 140th (shift period 2) and 180th trial (shift period 3), respectively. Table 2 shows the net win/loss for each deck in each shift period. Phase 2 consisted of a total of 120 trials.

	A Win/Loss	B Win/Loss	C Win/Loss	D Win/Loss	Good decks	Bad decks
Phase 1	£2000/£2500	£2000/£2500	£1000/£500	£1000/£500	C & D	A & B
Phase 2						
Shift 1	£1000/£500	£2000/£2500	£2000/£2500	£1000/£500	A & D	B & C
Shift 2	£1000/£500	£1000/£500	£2000/£2500	£2000/£2500	A & B	C &D
Shift 3	£2000/£2500	£1000/£500	£1000/£500	£2000/£2500	B & C	A & D

Table 2: Net win/loss per 20 trials for each of the decks during Phase 1 and each of the three shift periods of Phase 2. The two advantageous ('good') and disadvantageous ('bad') decks in each phase/period are also shown.

Subjective experience ratings: After every 20 trials in both phases, participants were asked to provide subjective experience ratings in terms of how "good" or "bad" they felt each deck to be (Evans, Bowman & Turnbull, 2005). Ratings were made using a computer presented slider-scale from 0 to 10 (where 0 = *very bad* and 10 = *very good*).

Results

Mean Net Score and Subjective Ratings

The mean net score was calculated by subtracting disadvantageous selections from advantageous selections [(C+D)-(A+B)]. A net score above zero is indicative of advantageous selections, while a net score below zero implies disadvantageous selections. Figure 10 shows that there was a steady increase in learning for all participants over the five blocks of Phase 1. A repeated measures ANOVA showed that participants significantly improved across the five trial blocks, $F(4, 828) = 44.38, p < .0001$. Contrast analyses showed there were significant increases in learning from block 1 to 2, $F(1, 207) = 28.05, p < .0001$, from block 2 to 3, $F(1, 207) = 10.98, p = .001$, from block 3 to 4, $F(1, 207) = 7.25, p = .008$, but not from block 4 to 5, $F(1, 207) = 2.62, p = .11$. In the first contingency-shift period, Figure 10 shows that there was a substantial impairment in choice of advantageous decks; mean net score for the whole sample returned to slightly below chance levels compared to the final block of Phase 1. This would suggest the initial contingency shift was successful in disrupting the established contingency learning. In terms of performance within each discrete shift period, repeated measures t-tests showed that there was significant change in mean net score within the first, $t(207) = -2.74, p = .007$, and the third, $t(207) = -2.81.58, p = .005$, contingency-shift periods but only a approaching significance trend for the second, $t(207) = -1.88, p = .061$.

A mean net subjective rating was calculated by subtracting the ratings of the disadvantageous decks from the subjective ratings of the advantageous decks. Figure 10 shows that there was a large increase in subjective ratings after the first block in Phase 1. A repeated measures ANOVA showed that subjective ratings differed significantly across

the five trial blocks, $F(4, 828) = 25.17, p < .0001$. Contrast analyses showed there was a significant increase in subjective ratings from block 1 to 2, $F(1, 207) = 60.50, p < .0001$, no significant change from block 2 to 3, $F(1, 207) = 0.198, p = .66$, a significant decrease in subjective rating from block 3 to 4, $F(1, 207) = 8.77, p = .003$, and a significant increase in subjective rating from block 4 to 5, $F(1, 207) = 4.50, p = .035$. Figure 10 further shows a trend of increasing subjective ratings between the first and the second block of each of the contingency-shift periods in Phase 2. Repeated measures t-tests did indeed show that there were significant increases in mean net subjective ratings within the first, $t(207) = -5.32, p < .0001$, second, $t(207) = -4.65, p < .0001$, and third, $t(207) = -3.81, p < .0001$, contingency-shift periods. A Pearson product-moment correlation between the IGT mean net score and subjective experience ratings revealed a positive correlation in Phase 1 ($r = .22, p < .0001$) and Phase 2 ($r = .19, p < .0001$).

Stepwise multiple regression was conducted to investigate factors predicting Phase 2 performance. The dependent variable of the regression model was the total mean-net score of the contingency-shift phase. Predictors entered were: Phase 1 block 1, 2, 3, 4 and 5 mean net score, block 1, 2, 3, 4 and 5 mean net subjective rating, age, years of education and gender. Variables were included and excluded from the final model on the basis of significant values of partial correlation (p in .05 and p out .10, respectively). Only three predictors entered the model accounting for almost 28% of the shift performance ($R^2 = .277, F(3, 207) = 26.11, p < .0001$). The strongest predictor was block 3 mean net score (standardised $b = .39, p < .0001$), followed by block 4 mean net score (standardised $b = -.2, p = .007$) and block 1 mean net score (standardised $b = -.15, p = .013$). Although largely accounted for by block 3 and 4 mean net score, the regression

findings showed that poor performance in block 1 predicts good performance during Phase 2. No other variables were found to significantly predict performance in Phase 2.

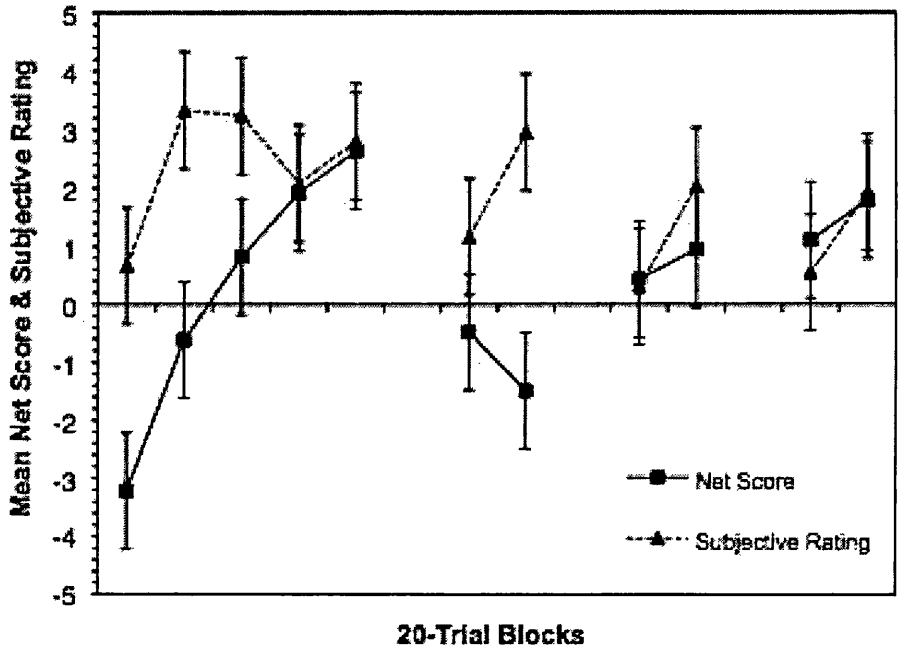

Figure 10: Mean net score and subjective ratings for all participants for the five 20-trial blocks in Phase 1 and the six 20-trial blocks in Phase 2. Error bars represent two standard errors.

Contingency-Shift Learning

The analyses presented above show clear evidence of improvements in learning across the original version of the task (Phase 1) and impairments in learning with the contingency shifts (Phase 2), most notably in the first contingency-shift period. Analyses with the whole sample, however, tend to mask substantial individual differences in learning performance across both the normal and shift phases. As the focus in the current study is the contingency-shift version of the IGT in normal participants, learning levels on each of the contingency-shift were further analyzed.

On the basis that Bechara and Damasio (2002) had previously suggested that a score of 10 or greater on the standard phase of the task characterised advantageous performance, therefore only those individuals who had achieved a mean net score equal to or greater than 10 in the normal IGT phase (N = 69) were included in subsequent analysis. In other words, the focus is on those participants who had shown some success in learning the original reinforcement contingencies. An inspection of contingency-shift performance for this sub-sample revealed substantial differences in performance. Thirty-nine of the participants had a total mean net score above 10 for the contingency-shift phase (M = 35.05, SD = 21.66: *High Performers*), while 26 participants had mean net scores below 0 for the contingency-shift phase (M = -13.04, SD = 13.85: *Low Performers).* Four participants who scored 0 or just above chance on the contingency-shift phase were not considered in subsequent analyses. An independent samples t-test revealed a highly significant difference in mean net score between these two groups, $t(63) = 10.02$, $p < .0001$. Independent t-tests performed on High and Low Performers for age and education did not reveal any significant differences between the groups ($p > .05$);

similarly a chi square test did not reveal a gender difference between the groups, $\chi^2(2) = 0.11, p > .05$. Likewise, a repeated measures t-test did not reveal significant differences in subjective ratings between the High and Low Performer groups in any block of either Phase 1 or 2 (all $p > .05$). Based on the clear differences in contingency-shift performance for the High Performers and Low Performers, these two groups were used in subsequent analyses of contingency-shift performance.

To further explore differences in deck selections between the two groups over the three shift periods, a mixed factor 3 (shift period) x 4 (deck) x 2 (group) analysis was conducted. Of most interest was a significant three-way interaction between group, shift period and deck, $F(6, 378) = 12.63, p < .0001$. Figure 11 shows the pattern of deck selection for the two groups in each shift period. The two groups appear to display more differentiated selection of decks in shift periods 2 and 3, relative to shift period 1. Simple interactions indicated that there was no significant deck by group interaction in shift period 1, $F(3, 189) = 2.13, p = .098$, however there were significant deck by group interactions for shift period 2, $F(3, 189) = 17.98, p < .0001$, and shift period 3, $F(3, 189) = 17.21, p < .0001$.

To further explore deck selection differences within each shift period, Bonferroni-adjusted pairwise comparisons (using a threshold p value of .004) were made across the two groups for each individual deck across each shift period. These showed that there were no significant differences between the groups in all deck selections in the first shift period (all $p > .05$) or in deck C in shift period 3 ($p = .041$), while there were significant differences across all other deck selections in shift periods 2 and 3 (all $p < .001$). Despite the lack of difference in deck selection in shift period 1, Figure 11 indicates that good

performers tend to pick more from the deck that has remained 'good' from the normal phase of the task in the first shift period (Deck D), whereas there were clearly no differences between the groups for the deck that shifted from 'bad' to 'good' (Deck A). These findings also highlight that individual differences in shift ability are more apparent after the first shift period, and further show that differences in performance are relatively stable after the first shift period. The significant deck by group interactions in shift periods 2 and 3 shown in Figure 11 clearly highlight the differential response patterns across the groups that lead to good and poor contingency-shift performance. The poor performers in shift period 2 are characterised by increased responding to the deck that has changed from 'good' to 'bad' for that shift period (Deck D) relative to the deck that has stayed bad from shift period 1 (Deck C). This implies that poor performance is characterised by poor shift ability and/or a combination of response perseveration based on lack of sensitivity to negative feedback. This distinction across 'bad' decks disappears for the poor performers in shift period 3, however, as there are no significant differences in their selections from both 'bad' decks in this shift period ($p > .05$).

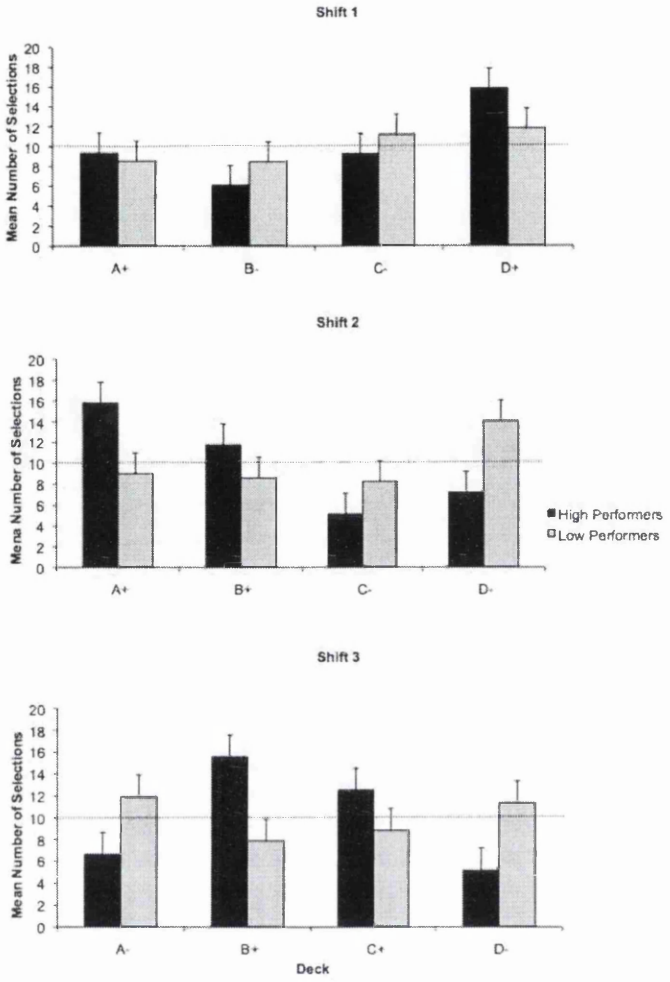

Figure 11: Mean number of deck selections for the High and Low Performers across each of the three contingency-shift periods in Phase 2.

Index of Flexible Learning

As shown in Table 2, each contingency-shift period comprised two decks changing contingencies (from 'bad' to 'good', and vice versa) and two of the decks having the same contingency as the previous shift period. In order to examine differences

in performance as a function of absolute and progressive contingency-shifts an index of flexible contingency-shift learning for each deck was calculated. This *index of flexible learning* was calculated by dividing the cumulative number of selections of each deck by the total number of trials that the deck had a particular contingency immediately after a contingency shift. For example, in the first block of 20 trials in shift period 1, the number of selections of Deck A would be divided by 20 as this is the cumulative number of trials that this deck has been 'good' (i.e., it has changed from being 'bad' in the original phase of the IGT, to 'good' in the first shift block). In the same block of trials, the cumulative selections of Deck B would be divided by 120, as the contingency of this deck has not changed from the original phase of the IGT. The index of flexible learning thus provides a measure of deck selection weighted by the number of trials that a deck has had 'good' or 'bad' contingencies in effect. The weighted scores can range from 0 (no selection in any trials from that particular block) to 1 (deck selected on all trials with the same contingency).

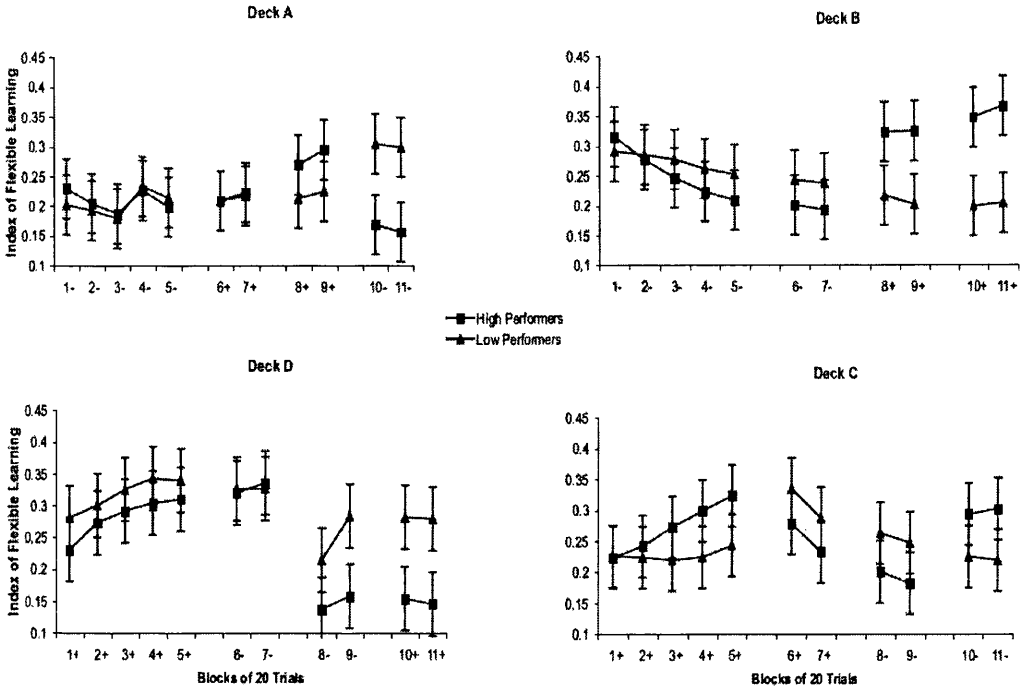

Figure 12: Weighted proportion (index of flexible learning) of deck selections for the high and low performing groups across each of the decks during Phase 1 and Phase 2.

Figure 12 shows the index of flexible learning for the high and low performing groups. A mixed factor 6 (block) x 4 (deck) x 2 (group) analysis showed a significant three way interaction, $F(15, 1410) = 21.33$, $p < .0001$. Figure 12 shows distinct patterns of weighted deck selections for each of the groups across the six blocks of trials. It is noticeable that differences in deck selections across the two groups are more substantial in the latter four blocks of trials, as noted earlier. Focusing on the Low Performers group, there is a differentiation across decks in terms of their disadvantageous selections. With Deck A, this group selected this deck relatively infrequently when the deck was 'good' in the first four blocks of trials, yet responded significantly more frequently when the deck

shifted to 'bad' in the final two blocks, $F(1, 44) = 12.87, p = .001$. With Deck B, there was a relatively undifferentiated pattern of responding across all blocks, with no significant differences in weighted deck selection across all blocks. With Deck C, there was a steadily declining rate of weighted deck selection across the six blocks. There was no significant increase or decrease in selection when this deck shifted to good in the final two blocks of the task. Finally, with Deck D, the Low Performers group had a similar pattern of weighted deck selection to the group that performed well in the first two blocks of trials. However, while they decreased their selections significantly from block 2 to block 3, $F(1, 44) = 25.22, p < .0001$, when this deck turned 'bad', they subsequently increased selections from this deck from block 3 to 4, $F(1, 44) = 22.83, p < .0001$, and maintained a relatively high rate of disadvantageous selections for the remaining blocks.

Discussion

The present findings offer novel insights into the question of flexible emotion-based learning on the contingency-shifting variant IGT, carried out with a sufficiently large sample size so that a range of possible relationships between important variables could be investigated. Participants showed comparable levels of learning to previous studies during Phase 1 (e.g., Bowman & Turnbull, 2004; Turnbull et al., 2006). Similarly, as in the previous study, the onset of the first contingency modification in Phase 2 initially disrupted learning but soon recovered to earlier levels. The two subsequent shift periods resulted in similar decrements in learning. Overall, these findings replicate and extend those of Turnbull et al. (2006), but with a larger cohort of healthy participants, using an automated procedure in which the shift periods were unsignalled.

This is the first time that a study has had sufficient sample size to investigate the key issue of variability in IGT performance with healthy participants, a concern that has been raised previously in relation to this literature (Dunn et al., 2006, pp. 251-252; Glicksohn et al., 2007). In this study, a number of analyses were performed to better understand the ways in which important themes co-vary, and influence flexible decision-making. It is noticeable that there were substantial individual differences in performance on the contingency-shift phase, even with non-clinical participants. A relatively large number of participants who had clearly learned the reinforcement contingencies in the first IGT phase performed poorly in the contingency-shift phase of the task. This suggests that the task is robust to individual differences in performance, and thus may be useful in a range of clinical and non-clinical settings.

Focusing only on participants who had a mean net score equal to or greater than 10 in the original IGT phase, participants were further divided into groups of High and Low Performers, based on their performance during the contingency-shifting phase. Analysis of the contingency-shift phase with these two groups of participants highlighted distinct patterns of deck selection across the contingency-shift periods. The results indicated that responses were more differentiated in the latter periods of the contingency-shift phase, relative to the first shift period. In addition, low performers tended to incorrectly choose decks that had shifted in reinforcement contingency, rather than simply choose decks that were 'bad' in the standard phase. This would suggest the task is sufficiently sensitive to measure reversal learning processes through an inability to shift reinforcement contingency as indicated by the patterns of response perseveration shown by Low Performers (Fellows & Farah, 2005).

Given that the contingency-shifting variant IGT meets the necessary requirements for classification as a measure of reversal learning (i.e., systematic and repeated reversal of reinforcement contingencies), the finding of Experiment 2 do not appear to support the claim of Fellows and Farah (2003, 2005) that reversal-learning ability is implicated primarily during the *initial* IGT trial blocks. The regression model showed that performance during the third block of twenty-trials (i.e., more than halfway through the task) in Phase 1 only partially accounted for shift performance in Phase 2. This notwithstanding, it is perhaps difficult to directly compare across studies because Fellows and Farah's claim rests on findings obtained with the shuffled variant IGT, in which the losses associated with each deck were moved to earlier in the first block of trials, and improvements in performance were measured by comparison with performance on the standard IGT and a separate reversal-learning task. Also, it is noteworthy that in the Fellows and Farah (2003) study, carry-over effects cannot be ruled out as tasks were administered in a fixed order and correlations were not conducted between overall, aggregate performance on the reversal learning task and the two versions of the IGT. Indeed, only "degree of improvement" (Fellows & Farah, 2005, p. 61) was estimated based on performance in the second IGT task (the shuffled variant IGT). Nevertheless, while further research is needed to determine the precise role, if any, played by reversal learning in the original IGT, the present findings suggest that the contingency-shifting variant IGT holds considerable promise as a means of investigating reversal learning.

The present study extended the analysis of subjective experience to the contingency-shifting variant IGT, and reveals greater roles for subjective awareness than might previously have been anticipated (Bechara et al., 1997, 2000a). The subjective

experience ratings of the relative 'goodness' and 'badness' of the decks were initially quite low (although still above-chance) during Phase 1, but by the second block of trials had increased and remained relatively stable. Consistent with previous findings, ratings remained higher than IGT performance across all blocks (Bowman et al., 2005; Evans et al., 2005), suggesting that all participants, both High Performers and Low Performers, had greater awareness of the reward/punishment schedules of the different decks than their behavioral performance implied (cf. Bechara et al., 2000a; but see Evans et al., 2005; Maia and McClelland, 2005). This finding was replicated in Phase 2, with ratings progressively falling during the first block of each shift period, and then increasing by the second block, although the level at which ratings increased gradually declined during each shift period. This suggests that participants may come to rely less and less on intuitive/subjective sources of knowledge as they become more familiar with the parameters of the task. Indeed, it is likely that explicit cognitive strategies play a role in guiding card selections later in the task. Regardless of the precise nature of the relationship between cognitive or emotion-based strategies in IGT performance, the current findings clearly showed that behavioral IGT performance and subjective experience ratings were positively correlated in both phases for all participants (see Evans et al., 2005).

The result of Experiment 2 showed a high level of between-subject variability in participants' performance. As outlined in the introductory section, this is not uncommon to observe (e.g., Caroselli, Hiscock, Scheibel & Ingram, 2006) and there are several factors have been advanced in order to account for this phenomena. The first factor concerns the task instructions used. Previous research with the original IGT has shown

that the type of instructions used can have a systematic effect on learning (e.g., Balodis, MacDonald, & Olmstead, 2006; Fernie & Tunney, 2005). The abbreviated instructions used, which were adapted from Bechara et al. (2000a; see the Appendix 1), may help to explain the finding that the mean net scores in Phase 1 were lower than those typically reported for previous studies presumably employing full task instructions (e.g., Bowman et al., 2005; Fernie & Tunney, 2005). Also, the instruction used in Experiment 2 did not include mention of the contingency-shifting phases, which may explain the lower learning level of the present study compared with that of Turnbull et al. (2006) who explicitly instructed their participants about the upcoming shifts. It is important to note, however, that a limited number of studies provide copy of the actual instructions given prior to the onset of the IGT making comparisons with the present findings somehow difficult. An investigation of the effects of task instructions on contingency-shifting IGT performance is therefore warranted to test the hypothesis that the "variability in control group performance" (Dunn et al., 2006, pp. 251-252) may in fact be a function of instructional control.

The second factor concerns the age of the participants, which is known to influence IGT performance (e.g., Denburg, Tranel, & Bechara, 2005). The mean age of participants in the present study (21.3 years) is almost identical to that of Caroselli et al. (2006) (21.7 years) who also used a relatively large sample of university students (n =141) and noted an overall preference for the disadvantageous decks on the original IGT. While some studies with older samples have also noted poor performance in some of the participants (e.g., Bechara et al., 2001), an important issue for future research is to

determine to what extent the present findings were due to the relatively young age of the sample by extending the contingency-shifting IGT to an older sample.

The final factor to be considered in understanding the control group variability is the potential role of sex differences. More than half (54%) of the current sample were females, and males tend to outperform females on the original IGT (e.g., Overman, 2004; Reavis & Overman, 2001). Thus, it is possible, although unlikely, that the poor performance observed in the present study may have been influenced by the already-identified gender differences on the IGT since the results of the regression analysis failed to find an effect for gender.

Notwithstanding the above-mentioned factors, a possible limitation of Experiment 2 was the absence of specific measures of executive functions, as well as basic reversal learning ability and intelligence. Previous research has shown that IGT performance is correlated with intelligence scores (Olson, Hooper, Collins, & Luciana, 2007), but the relationship with executive function measures, such as the WCST and the Brixton Test (Burgess & Shallice, 1997), remains inconclusive (Brand et al., 2007; Lawrence, Wooderson, Mataix-Cols, David, Speckens & Phillips, 2006; Lehto & Elorinne, 2003; Turnbull et al., 2006). There are several ways in which these findings map onto issues of relevance for experimental and clinical neuropsychology, especially because the contingency-shifting variant IGT focuses on the flexibility of emotion-based learning. The central issue is that tasks which focus on such flexibility are likely to better capture the complex and fluctuating nature of real-world experience, and therefore meet the external validity claims originally suggested in relation to the original IGT (Bechara et

al., 1994). As such, the contingency-shift version of the IGT offers potential for both experimental and clinical research settings.

Experiment 3

Experiment 2 introduced a contingency shifting variant modification to the standard Bechara et al., (1994) IGT. The changing of deck contingencies allowed to test a new form of learning reliant on fast adaptation and ability to relate to previous reward and punishment schedules.

The IGT has been conceptualized as a learning task in which participants progressively modify their behaviour in accordance to the exposure to reward and punishment resulting from card selections (Bechara et al., 2000a; Brand et al. 2006). As for other learning tasks, the plotting of card selections on the IGT generally produces a learning profile showing improvement of performance across the course of the task (Dunn et al., 2006). A rising learning pattern is noticeable for the majority of healthy participants; dissimilarly VM patients have been showing learning profiles displaying little or no improvement across the 100 IGT trials (Bechara et al., 2000b). Bechara et al., (1994) reported that the VM patient's learning impairment is stable over time. Subsequent re-test with the IGT on VM patients produced similarly "flat" learning profiles showing no evidence that any information has been retained form previous exposure to the task. It is also appreciable, from the data presented by Bechara et al (1994; 2000b), that time elapsed between the first and successive exposures has no bearing on the VM patients' performance. Performance after one month, 24 hours and six

months from the initial testing equally resulted in a below chance number of advantageous deck selections. In other words, the VM patients failed to show a significant improvement as a function of repeated testing (Bechara et al., 2000b, p. 299). On the contrary, performance of control participants was reported to improve over time, although data on the number of advantageous selections were never reported. The use of the term "improvement", as in Bechara et al., (1994, p. 13), would suggest that control participants would progress in their learning during subsequent exposure to the task.

The retention of emotion-learnt information in control participants was firstly investigated indirectly by Fernie & Tunney (2005) in a study aimed at clarifying the influence of instruction quality on IGT performance. In this study participants were presented twice with the same IGT version after a 48-hours interval. Participants were randomly allocated to 4 experimental groups: instructions with hint and facsimile money, instructions without hint and facsimile money, instructions with hint and real money, instructions without hint and real money. Although every experimental group improved during the second exposure, level of improvement were different; the groups receiving the instruction hint were generally better than the groups that did not receive it. Apart from showing the influence of instruction quality on IGT, the study had the merit to provide the first learning profiles of controls participants after a second exposure to the task. These showed how learning during the second occasion started from a positive mean net score and that by the end of the task participants almost reached a ceiling effect (i.e., selecting only advantageous decks).

Bechara et al. (1994) firstly described how healthy controls without prior knowledge of the schedule of reward and punishment would initially sample

predominantly from high immediate reward decks and progressively shift their preference towards the so called advantageous decks (i.e., low immediate reward but low punishment resulting in a net money gain). During the course of the game, control participants would gradually modify their selections and eventually gain some level of awareness of the nature of the decks (Bechara et al., 1997, 2000a; Damasio, 1994). Bechara et al. (2000a) have advanced that full awareness of the nature of the decks (i.e., the conceptual phase) is only reached in the last block of the task. Independent investigations have challenged this claim to the point that subjective awareness has been suggested to control, to a large extent, task performance from earlier stages (Bowman et al., 2005; Maia & McClelland, 2004). Notably the description of the "conceptual" phase as proposed by Bechara et al. (2000a) entails participants to acquire full knowledge of the task contingencies. If that would be the case for normal participants, what would be expected from the second exposure to the task would be a ceiling effect of performance where little or no learning occurs. Interestingly, this is not the case for the second exposure as showed by Fernie and Tunney (2005) where substantial learning still occurs. The fact that more learning occurs during the second IGT exposure is indeed interesting and might have different explanations. One aspect recreating the need of learning could be the time elapsed between the first and the second exposure and the consequent loss of knowledge relative to the deck contingencies. A second explanation can be hypothesized in the unreached conceptual phase by some participants so that during the second exposure more learning can still occur. A third explanation can be advanced in support to the role of somatic markers; that is, if unconscious somatic markers guide to a large extent participants' performance, overt knowledge and memories from the previous

participation will produce a benefit only at the beginning of the second exposure. Although somatic marker stored in the VMPFC can be reactivated quickly via the "as if body loop" some degree of interaction with the environment would still be necessary in order to elicit some emotional response (Damasio, 1994; Tranel et al., 1999).

It therefore appears important to consider more carefully the role of emotion-based learning information retention and how specific component such as subjective awareness and implicit emotional biases contribute to the performance. The paradigm of successive exposure to the same task as used by Fernie and Tunney (2005) could provide useful in this respect. In addition to the measure of subjective awareness the following investigation wants to explore participants' ability to retain shifting components as assessed by the contingency shifting modification version of the task used in Experiment 2.

Method

Participants

Twenty students (8 male, 12 female) from Swansea University participated in return for course credits. Their ages ranged between 20 and 26 (mean: 22.6; SD=1.56). An independent t-test revealed no significant difference in age between males and females; $t(18)=.227$, $p=.823$). Mean number of years spent in education was 15.11 (SD=1.89).

Materials and Procedure

An automated version of the IGT, programmed in Visual Basic® 6.0, was employed for this experiment as in Experiment 2. Participants received general instructions about the task that were based on Experiment 2 and completed 2

experimental sessions for a total of 440 IGT trials. Participants were asked to participate in an experiment divided into two sessions. During the first session, each participant was introduced to the nature of the experiment, played the IGT for the first time and booked for a second experimental session. The second experimental session was scheduled between a minimum of 48 and a maximum of 60 hours from the previous session (mean interval in hours was 52.6; SD=4.8). The purpose of the second experimental session was not disclosed and participants were not asked to memorise or pay particular attention to any specific information during the first session. Upon arrival at the lab for the second experimental session, participants were asked, similarly to the first session, to play a computer task. In both sessions the same instructions were presented on the computer screen and option for further clarification given.

As for Experiment 2, the IGT version used in Experiment 3 was divided in two phases: 100 trials of the standard version of the task (Phase 1) followed by 120 trials of a set-shifting variant IGT involving three successive shifts of the reinforcement contingencies (Phase 2). Details of Phase 1, Phase 2 and subjective experience ratings are described in the Method section of Experiment 2.

Results

Mean net score

Mean net score was calculated for the behavioural IGT performance measure by subtracting disadvantageous selections from advantageous selections [(C+D)-(A+B)]. A net score above zero is indicative of advantageous selections, while a net score below zero implies disadvantageous selections. Figure 13 shows that there was a steady increase

in learning for all participants over the five blocks of Phase 1 and 2 for the first and the second exposure.

Phase 1

A 5 (block) x 2 (time) repeated measure ANOVA conducted on Phase 1 mean net score revealed a significant main effect of block $F(4,76)=18.04$, $p=.0001$, a significant effect of time $F(1, 19)=26.38$, $p<.0001$, but no interaction $F(4,76)=18.04$, $p<.0001$ (Fig. 13). Contrast analysis showed significant difference between the scores in block 1 and 2 and between 4 and 5 for first exposure and between block 1 and 2, 2 and 3 and 4 and 5 for the second exposure (Table 3).

Phase 2

A 6 (block) x 2 (time) repeated measure ANOVAs conducted on Phase 2 mean net scores revealed a significant main effect of block $F(5, 95)= 11.19$, $p<.0001$, a significant effect of time $F(1, 19)=64.58$, $p<.0001$, but no significant interaction $F(5, 95)=.26$, $p=.88$ (Fig.13). Contrast analysis showed significant difference between the first contingency shift of the first exposure and in all the contingency shifts of the second exposure (Tab. 3).

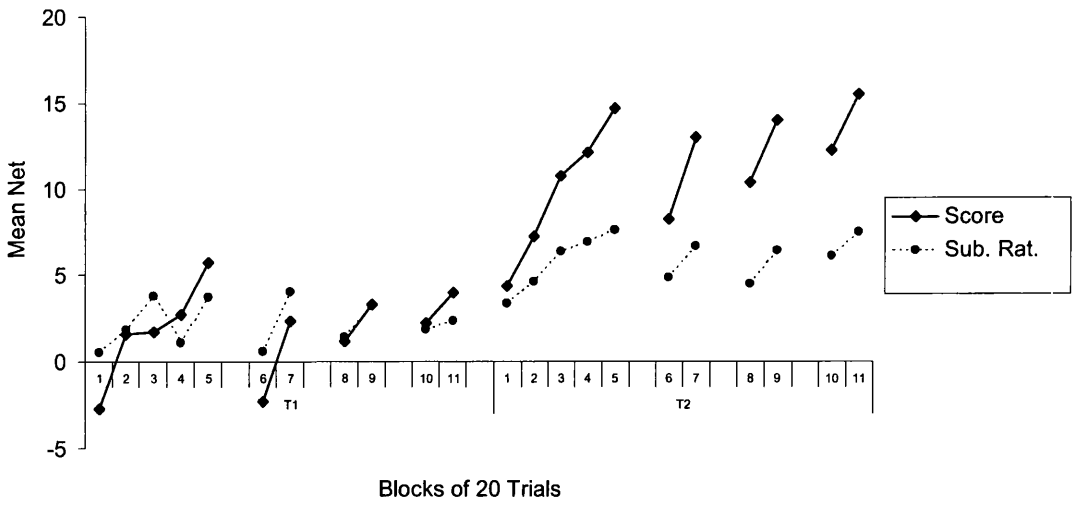

Figure 13: Phase 1 and 2 mean net score and subjective rating for first (T1) and second exposure (T2).

Block	First exposure net score contrast df (1,19)	Second exposure net score contrast df (1,19)
1vs2	F= 4.77 (p=.042)	F=7.31 (p=.014)
2vs3	N/S	F= 16.69 p<.0001
3vs4	N/S	N/S
4vs5	F= 4.22 (p=.05)	F= 5.34 (p=.032)
6vs7	F= 6.01(p=.024)	F= 11.78 (p=.003)
8vs9	N/S	F= 11.76 (p=.003)
10vs11	N/S	F= 8.69(p=.008)

Table 3: Contrast analysis for mean net scores in consecutive blocks of phase 1 and 2.

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Subjective rating

Similar to the mean net score, a mean net subjective rating was calculated by subtracting disadvantageous from advantageous ratings [(C+D)-(A+B)]. A net score above zero is indicative of awareness regarding good and bad deck, while a net score below zero implies poor awareness about the nature of the decks. Figure 13 shows that there was a steady increase in awareness throughout the first and the second exposure for phase 1 while an improved trend within each shift can be seen in both phase 2.

Phase 1

A 5 (block) x 2 (time) repeated measure ANOVAs conducted on Phase 1 mean net subjective rating scores revealed a significant main effect of block, $F(4,76)= 87.27$ $p<.0001$, a significant effect of time, $F(1, 19)=14.03$, $p=.0001$, but no significant interaction, $F(4, 76)=18.03$, $p=.301$ (Fig.13). Contrast analysis showed significant difference between block 2 and 3, 3 and 4 and 4 and 5 for the first exposure and between block 2 and 3 for the second exposure (Tab. 4).

Phase 2

A 6 (block) x 2 (time) repeated measure ANOVAs conducted on Phase 2 mean net subjective rating scores revealed a significant main effect of block, $F(5, 95)= 4.16$, $p<.0001$, a significant effect of time, $F(1, 19)=25.8$, $p<.0001$, but no significant interaction, $F(5, 95)=.99$, $p=.43$ (Fig.13). Contrast analysis showed significant difference in the first shift of the first exposure and in the first and in the second shift of the second exposure (Table 4).

Block	First exposure subjective rating contrast df (1,19)	Second exposure subjective rating contrast df (1,19)
1vs2	N/S	N/S
2vs3	F= 4.61 (p=.045)	F= 5.34(p=.032)
3vs4	F= 4.69(p=.043)	N/S
4vs5	F= 4.78 (p=.041)	N/S
6vs7	F= 12.26 (p=.002)	F= 4.26 (p=.051)
8vs9	N/S	F= 4.34(p=.05)
10vs11	N/S	N/S

Table 4: Contrast analysis of mean net subjective rating scores in consecutive blocks of phase 1 and 2.

Improvement in shifting ability

In order to analyse readiness to shift and its relative improvement between the first and the second exposure, previously-good-now-bad selections were considered. Figure 14 shows the relative improvement in shift ability from the first to the second exposure to the task. Repeated measure t-tests revealed significant differences in the number of previously-good-now-bad selections between the first and second exposure in the first, $t(19)=6.34$, $p<.0001$, second, $t(19)=4.23$, $p<.0001$, and third, $t(19)=8.05$, $p<.0001$, shift.

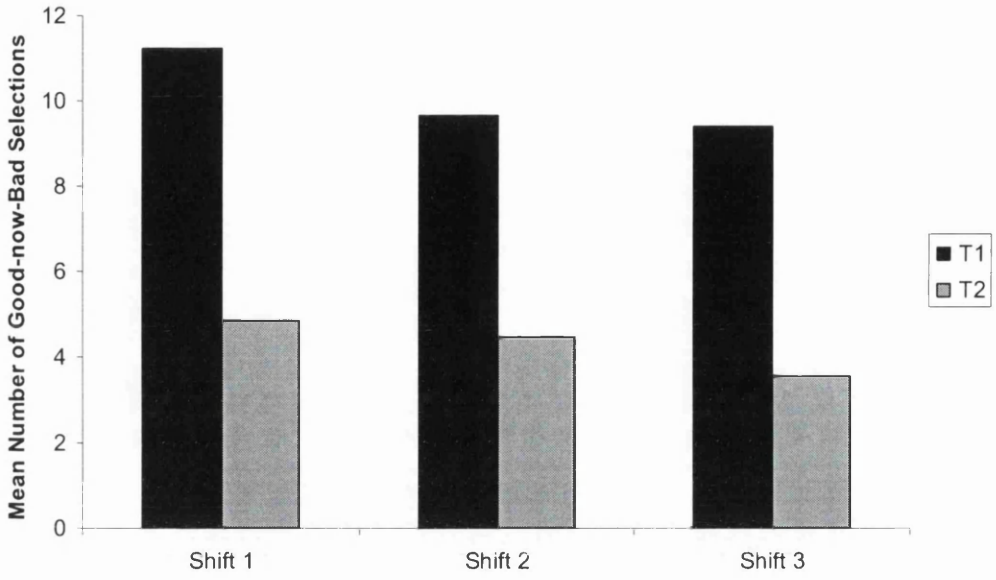

Figure 14: Mean number of selection from the previously-good-now-bad decks in the three contingency shifts during the first (T1) and the second (T2) exposure.

Discussion

The aim of Experiment 3 was to test retention of learning rates between subsequent exposures to the IGT. Participants showed significant improvement in advantageous card selections across the initial exposure to the task. Subsequent exposure, after a time interval, showed a degree of learning retention from the initial testing and a continuation of the learning trend. That is the number of advantageous cards per block continues to improve, even if starting form a positive mean net score. In both sessions, the onset of the contingency shifting modification initially disrupted learning rates that gradually recover during the course of Phase 2. Analysis conducted on the contingency shifting modification showed that during the second exposure participants selected

significantly less from decks that were previously good now bad displaying an enhanced shifting ability improved by practice.

The issue of practice in neuropsychological testing has for long been discussed as an aspect that can account for improvement in performance across subsequent exposures (McCaffrey, Ortega & Haase, 1993). The practice effect (i.e. improvement in performance due subsequent exposure to the same task) is particularly important to account for measures that need to be taken at different point in time to assess the effectiveness of interventions (Beglinger et al., 2005) or the long term impact of training (McCaffrey, Ortega, Orsillo, Nelles & Haase, 1992). The ability to make decision, as measured by the IGT, has traditionally been measured as a present/absent function (e.g. impaired/unimpaired) (Bechara et al., 1999). The limited number of studies conducted on subsequent exposure suggests that VM patients present a stable deficit in IGT performance regardless of the number of exposures whether putatively healthy participants present a degree of improvement between the first and the second performance (Bechara et al., 1994). Where the complete absence of learning from previous experience in VM patients suggests that there is no effect of practice, the result of Experiment 3 suggests that this is not the case for control participants. The high initial mean net score displayed in Experiment 3 showed a noticeable level of procedural retention whereby no re-acclimatisation to the task is needed and participants start the second IGT testing from the learning level achieved at the end of the first session.

The high level of performance seen in the fist block of the second exposure may provide partial support to Bechara et al.'s (2000a, 2000b) claim that by the end of the standard IGT participants have reached some awareness of the task contingencies. This is

consistent, for the first exposure, with the observed levels of subjective awareness that present a similar pattern to the mean net score. Dissimilarly during the second exposure pattern of subjective ratings and mean net score start to diverge, with the mean net scores showing much higher values and steeper learning across blocks. This difference may suggest that even if the good and bad decks are mostly rated according to their actual reward and punishing schedule there is still some degree of ambiguity about the real valence of the decks. This is particularly interesting in light of the behavioural performance that shows a clear pattern of selection for the advantageous decks. Speculatively and according to Damasio (1994), it can be argued that if the behavioural selections have higher mean net score than the subjective rating, participants may still benefit from the emotional signal to achieve a higher level of performance. Another possible explanation to the lower level of subjective experience in the second presentation is the type of instructions given in the current experiment that did not contain the hint sentence, as identified by Fernie and Tunney (2005). Less detailed instructions might not provide enough explicit knowledge so that improvement in the level of awareness is more difficult even after subsequent exposure. Participants also did not know if the task presented was the equal to the one they were presented in the first session. A final possible explanation for the lower levels of subjective awareness showed during the second exposure is the fact that the current experimental procedure used randomised allocation for decks. Therefore in the second testing occasion decks of cards may have had a different label and positioning on the screen with a potentially confusing effect on subjective rating.

Experiment 3 constitutes the first attempt to study the role of past experience in flexible emotion-based learning. Throughout two exposures to the contingency shift variant IGT the current experiment demonstrate that emotion-based learning components can be improved. Participants that have played the IGT once demonstrate, during the second exposure to the task, much higher behavioural and subjective awareness scores. The improved levels of performance seen across subsequent exposures suggest that the IGT performance is affected by practice effect. As a consequence, a possible generalisation of these findings is that subsequent exposure to situation requiring EBL maximise the occurrence of adaptive behaviour. Bechara et al. (2000a) has shown that this improvement is not observed in people with VM damage, demonstrating that some cortical areas are responsible for EBL. It remains unclear whether the initial disadvantageous performance, as seen for some of the healthy participants in Experiment 2, can improve after successive exposure to the task and how this improvement would relate to the neuroanatomical substrates.

Chapter 4

Psychophysiological correlates of flexible emotion-based learning

In Chapter 3, a novel contingency shifting variant IGT, originally developed by Turnbull et al (2006), was adapted for an automated formant and extensively validated with a large sample of healthy controls. The findings make a novel contribution to the research literature and offer further insights into the nature of control group variability. Within the literature, one of the leading theoretical accounts, the SMH, postulates a key role for autonomic signals or markers in governing emotional decision-making (Bechara, 2004). While there are several demonstrations of the autonomic correlates of the original IGT performance there are, as yet, no published studies conducted with the contingency shifting variant IGT. The objective, therefore, of Chapter 4 was to undertake the first investigation of the autonomic correlates of performance on the contingency shifting IGT.

Emotions can be considered as a collection of responses including subjective experience, behavioural expression and physiological activation (Hot, Saito, Mandai, Kobayashi & Sequeira, 2006). Theories aimed at predicting emotional influence on behaviour should therefore employ an array of measures in order to capture the complexity of the phenomena. Physiological correlates, and in particular the skin conductance response (SCR), have long been used as physiological markers of emotional activation (Bradley & Lang, 2002).

Skin conductance responses (SCRs), also known as galvanic skin responses, can be defined as transient modification of homeostatic levels of the skin's sweat gland activity (Bouscein, 1992; Critchley, 2002; Dawson, Schell & Filion, 2000; Venables &

Christie, 1980). Conceptually, variations in sweat production are linked to the activity of the parasympathetic nervous system. The sympathetic and parasympathetic nervous systems regulate peripheral or bodily reactions to the organism stimulation (Damasio, 1999). The sympathetic system primarily facilitates motor action as a consequence of stimulation; for instance, the fight reaction in a threatening situation. The parasympathetic system regulates more "vegetative" functions. Arousal in these two systems is generally referred with the term of autonomic arousal and describes modification in hart rate, body temperature, blood pressure, gut motility and skin sweat (Critchley, 2002). Increased activity of vegetative functions is commonly referred to as autonomic arousal and such arousal is particularly characteristic of specific stereotyped behavioural repertoires (e.g., fight and flight responses; Critchley, 2002). Beside thermoregulation, smell and mechanical friction, sweat gland activity, alongside other autonomic reactions (i.e., piloerection, increased hart rate), serve as a sign of emotional expression (Darwin, 1998). In humans, the interplay between subjective and autonomic bodily feeling has long been thought to influence the individual experience of emotion (Damasio, 1994, 1999; James, 1894)

Although evidence for emotional activation is often recorded via bodily arousal, the trigger to the measured somatic state is mediated via the brain (Critchley, 2005; Phan, Wager, Taylor & Liberzon, 2004; Price, 1999). The exact nature of the specific contributions of cortical and sub-cortical structures in mediating various somatic states is, however, still largely unclear (Anders, Lotze, Erb, Grodd & Birbaumer, 2004; Critchley, 2002; Critchley, Elliott, Mathias & Dolan, 2000). One of the first studies that investigated the neural contribution to somatic states was conducted by Tranel and Damasio (1994). In

this study, the SCRs of 36 patients with well-characterized lesions in various regions of the cerebral hemispheres were recorded while they viewed emotional materials (e.g., pictures of nudes and mutilated bodies). Result showed that several lesion loci were associated with defective electrodermal responding: the ventromedial frontal region, the right inferior parietal region and the anterior cingulate gyrus. Tranel and Damasio found a crucial role of the amygdala in mediating the development of SCRs, further confirming outcomes from fear conditioning studies in lesioned monkeys (Aggleton, 1992; Zola-Morgan, Squire, Alvarez-Royo & Clower, 1991) and aversive Pavlovian conditioning studies (Bechara, Tranel, Damasio, Adolphs, Rockland & Damasio, 1995; LaBar, LeDoux, Spencer & Phelps, 1995; LaBar, Gatenby, Gore, LeDoux, & Phelps, 1998).

Following Tranel and Damasio's (1994) observation of emotional deficits in VM patients, Bechara et al. (1994) conducted the first study using the IGT and measuring SCRs. In this study, SCRs were recorded prior (i.e., anticipatory) and after (i.e., appraisal) every card selection in a group of healthy controls and in VM patients. Results showed how VM patients, compared to healthy controls, failed to develop anticipatory SCRs prior to risky selections (i.e., those involving punishment).

In a further study, Bechara et al. (1999) measured SCRs associated with the IGT performance in a group of patients with amygdala lesions, a group presenting VMPFC lesions and in healthy control participants. Findings pointed at the importance of the amygdala as the eliciting structure for SCRs; amygdala damaged patients were unable, in fact, to produce any SCRs once exposed to the task. On the contrary, VMPFC patients did produce appraisal SCRs but failed to develop anticipatory responses to disadvantageous selections compared to controls. Taken together, the results of these

studies advance the role of the amygdala as a structure responsible for producing the somatic activation (i.e., the feeling of emotion) but suggest the VMPFC as the delegate structure to process this signal effectively in order to reach an advantageous decision-making strategy. Further studies measuring SCRs were undertaken to substantiate the role of the amygdala, as the eliciting structure, and VMPFC, as the processing structure for the somatic marker signals (Bechara & Damasio, 2002; Campbell, Stout, & Finn 2004; Fishbein, Eldreth, Hyde, Matochik, London, Contoreggi, et al., 2005; Kleeberg, Bruggimann, Annoni, van Melle, Bogousslavsky & Schluep, 2004). These SCR studies increasingly support the role of somatic signals in predicting advantageous performance in the IGT. In particular, the increase in anticipatory SCRs displayed by healthy participants in the first part of the IGT prior to disadvantageous selections is considered to be the crucial biasing signal to decision-making (Bechara et al., 2002).

The formulation of the SMH stimulated a number of studies largely employing similar paradigms (Bechara et al., 1996; Bechara & Damasio, 2002). Interestingly, empirical data produced in support of the SMH were mainly gathered using behavioural paradigms, such as the IGT (Dunn et al., 2006). The proponents of the SMH claim that the IGT can be reliably used in the assessment of emotion-based learning because a number of studies have consistently demonstrated a relationship between impaired performance on the task and lack of anticipatory SCRs in people with VMPFC brain damage (Bechara et al., 1996; 2000a; Bechara & Damasio, 2002; Tranel et al., 1999). While the study of VMPFC patients' autonomic activity was the primary focus in the initial years after the formulation of the SMH, recently a number of studies have investigated the SCR correlates of IGT performance with healthy participants (e.g., Crone

et al., 2004a; Suzuki et al., 2003). The value of studying IGT physiological activation in control participants rests on the variability often noted in performance and on the fact that reliable normative data of either behavioural or autonomic performance are missing (Dunn et al., 2006). In fact, as noted by Bechara et al. (2002), not all the control participants learn to select from the advantageous decks over time. It was found that as many as the 20% of control participants showed a behavioural performance similar to the VMPFC patients. Underperforming controls showed great variability and unclear evidence of anticipatory SCR arousal before selecting the disadvantageous decks. In explaining these findings, Bechara et al. (2002) speculatively concluded that those who underperform on the IGT override the emotional signals evoked during the task with conscious, effortful processing.

In recent years, increasing research attention has been paid to determining the autonomic correlates of control group performance on the IGT. Tomb and co-authors (2002) were the first to conduct a study solely with healthy participants. In this study, two groups of participants took part in two experimental conditions. The first experimental condition recorded SCRs during the Bechara et al., (1998) version of the IGT, while the second experimental condition recorded SCRs during an altered schedule version of the IGT. In the altered IGT version, the card outcomes were changed so that good decks were associated with a higher overall magnitude of punishment and reward than bad decks. This change was made in order to clarify the effect of magnitude of reward and punishment (i.e., money at stake for each card choice) on autonomic activation. In particular the authors wanted to test the hypothesis that the amount of money involved in the selection would affect SCRs levels more that the value of the decks. Results indicated

that autonomic activation prior to each card selection was driven by the magnitude of the immediate anticipated reward and not by the long-term consequences, as stated by the SMH. In other words, according to Tomb et al. (2002), SCR correlates of IGT performance are dependent on the relative expected magnitude of reward and punishment. Damasio, Bechara and Damasio (2002) suggested that the modification of the task made by Tomb et al., (2002) might have inverted the somatic marker signal. According to the SMH, in fact, autonomic arousal precedes both decisions with a prospective positive or negative outcome; under conditions of conflict and uncertainty somatic markers help reject or endorse an option or action (Damasio et al., 2002).

Another recent study by Suzuki et al., (2003) recorded SCRs prior to (i.e., anticipatory) and after (i.e., appraisal) each selection, analyzed trials with and without punishment and considered the effect of selection in early and late stages of the task. The procedure used for this study closely resembles the computerized task used by Bechara et al., (1999) although some modifications were adopted. The most substantial modifications were the shortening of the task to 80 trials (this was justified by the fact that, generally, control participants achieve a stable performance by the 80^{th} trial) and a verbal response instead of a key press. Findings showed larger magnitude appraisal SCRs following disadvantageous selections from both advantageous and disadvantageous decks followed by punishment. This latter finding confirms that the SCR emotional response is sensitive to negative values (Fowles, 1980). Furthermore, Suzuki et al. (2003) found an inverse correlation between appraisal SCRs in early trials and disadvantageous selections in late trials, suggesting the importance of appraisal activity in advantageous performance. Findings were less clear for anticipatory responses. The authors found, in

line with Bechara et al., (1999; 1996), higher anticipatory SCR values for disadvantageous selections but failed to find evidence for the temporal pattern described by the SMH; where anticipatory SCRs for disadvantageous decks gradually develops after the first few trials with punishment. The lack of clear findings in relation to anticipatory responses extends to the fact that no relationship was found between anticipatory activation prior to selections from the disadvantageous decks and IGT performance, suggesting relative independence between the two aspects.

Finally, a study by Crone et al. (2004a) investigated SCR and heart rate correlates of controls participants' performance on another modified version of the IGT. The task was originally modified to conduct research with children (Crone et al., 2005). Modifications involved changes to the visual presentation (i.e., help a hungry donkey to collect apples) and to the reward type (i.e., food for the donkey). For the analysis, participants were divided according to their behavioural performance into three groups: poor, moderate and good performers. The mean numbers of advantageous selections per groups were 35 for the poor group, 48 for the moderate group and 58 for the good group. Results showed a slowing of the anticipatory heart rate measure and greater anticipatory SCRs before disadvantageous relative to advantageous choices, but only for good performers. In contrast, all of the groups equally showed decreased heart rate and increased levels of SCRs following loss relative to reward outcomes. The authors interpreted the findings suggesting that decision-making impairment is dependent upon a weak anticipatory activation to risky stimuli rather than an appraisal response to reward and punishment.

These reviewed studies conducted with control participants have shown that anticipatory activation prior to disadvantageous deck selections correlates with an overall good decision-making strategy. Although this appears to be a common finding, the question of variability in control participants' performance seems to have unclear and unexplained physiological correlates (Crone at al., 2004a). The temporal pattern of SCR development is poorly described (Suzuki et al., 2003) and it is not clear whether the magnitude of reward and punishment equally affects the somatic markers (Tomb et al., 2002).

The issue of subjective awareness also appears relevant to investigation of SCR correlates of IGT performance, particularly as the SMH places great emphasis on the suggested preconscious nature of the somatic biasing signal. Not surprisingly, the creators of the task remark that the IGT schedule is opaque to probabilistic reasoning and that participants' performance is largely dependent on emotional bias (Damasio et al., 2003). As outlined in Chapter 1, this claim has been challenged by several authors suggesting that participants are more aware of the nature of the cards schedule than suggested by the Damasio and co-workers (Bowman et al., 2005; Maia & McClelland, 2004; 2005; Turnbull et al., 2003). Until now, only one study has investigated participants' awareness of the task contingencies in conjunction with autonomic correlates of the IGT (Bechara et al., 1997). In this study, participant's awareness of the contingencies of the decks employed in the task was assessed through a verbal question (i.e., "Tell me all you know about what is going on in this game") asked every 20 selections. On the basis of the responses given to the question, the authors concluded that advantageous performance was driven by anticipatory activation prior to bad deck

selections in a phase where participants were not aware of the nature of the decks. This led Bechara and co-workers (1997) to hypothesise that somatic markers help decision-making before individuals become aware of the contingencies.

Taken together, the studies reviewed point to the relevance of emotional activation, as measured by SCRs, in guiding IGT performance. Issues such as the variability in participants' autonomic performance, the role of appraisal SCRs, the relation between autonomic activity and awareness of task contingencies, and the time-course development of SCRs on trials with and without punishment are therefore essential to a further understanding of the factors that influence advantageous decision-making. In addition, identifying the autonomic correlates of performance on the contingency shifting modified IGT can initiate debate on the role of somatic markers in a flexible environment. No prior research to date has explored the role of autonomic activation and its relevance to decision-making performance in a modifying environment. According to the predictions of the SMH, adaptation to fast changing contingencies would require a quick modification of the autonomic arousal, especially the appraisal arousal, in order to successfully guide behaviour. Alternatively, it is possible that other behaviour during the contingency shifting phase may be guided by other autonomic responses dependent on outcomes (i.e., appraisal response).

Experiment 4, therefore, sought to investigate the autonomic correlates of healthy participant's performance on the contingency-shift variant IGT.

Chapter 4

Experiment 4

Method

Participants

Twenty-five participants were recruited from Swansea University's student population. Participants were reimbursed for their time with £10 at the end of the experiment. Fifteen females and 10 males took part in this experiment; average age was 22.04 (SD=3.142) and mean number of years spent in education was 15.64 (SD=1.57). Independent t-tests did not reveal any significant differences between genders for age and education. Participants were self-assessed for traumatic brain injury history, mental health issue and drug abuse problems. One participant failed to produce psychological data due to a technical problem with the power supply; only behavioural data were acquired and used for the analysis.

Procedure

Upon arrival in the laboratory, participants were invited to read and sign the consent form. Once consent was obtained, participants were asked to sit in front of a computer screen and adjust the chair to a comfortable position. The computer mouse was placed on the side of the dominant hand (e.g., on the left side for left-handed) and two fingers of the non-dominant hand were used to record physiological activity. The non-dominant hand rested on a pillow to maximise comfort and minimise movement during the experiment. Two electrodes were attached to the volar surface of the distal phalanges of the index and the middle finger. Participants' electrodermal activity was then monitored for five minutes in order to establish the level of baseline conductivity.

Participants were than left in the laboratory to complete the task and were watched by the experimenter via CCTV. Instructions, as presented on the computer screen, are presented in Appendix 1. At the end of the experiment participants were debriefed and paid.

Apparatus

The IGT contingency shift version used for this investigation was adapted from the procedure used in Experiment 2; details of the adaptations are reported below. Electrodermal activity was acquired via an ADI Instruments ML116 GSR Amp® interfaced with a 2/25 PowerLab® unit. SCR was recorder through the use of two dry, bright plated bipolar electrodes with velcro straps. Electrical conductance values, the measure of how easy electricity flows along a certain path, were displayed in Microsiemens (μS). Chart® software was used to visualize and extract the data.

Electrodermal activity recording

Following a 5-minute baseline SCR assessment phase, SCRs were measured throughout the task without interruption. Two breaks, one after 80 and the other after 160 trials, were scheduled. A Visual Basic® interface provided markers for anticipatory and appraisal SCRs on a parallel channel to the SCR responses so that trial by trial physiological responses could be matched.

In order to record SCRs, the contingency shift IGT as used in Experiment 2 was modified to enforce delay periods between trials. Similar to the procedure employed by Suzuki et al. (2003), each card choice was preceded by a 10-s time period in order to record anticipatory responses. During the anticipatory onset time period, participants were presented with the four decks of card and the message "please consider your choice". The current money earned balance was also presented at the bottom right of the

screen. After the enforced 10-s anticipatory interval had elapsed the mouse pointer appeared on the screen together with the message "please make your choice". During the selection period, participants were not under any time constraint and left free to make their choice. As soon as each choice was made the outcome message (e.g., you won £100) appeared on the screen for 10 s. Display of this outcome message re-presented the appraisal interval. Next, a 6-s inter-trial interval was presented and, following that, the next trial began (see Figure 15).

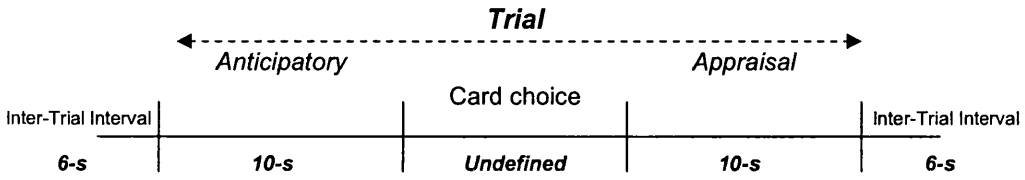

Figure 15: Shows the time course of the phases within each trial and their length, during Experiment 4.

SCR analysis

Data collected were extracted with Chart® for windows version 5.0 (ADI instruments). Individual data were log transformed before analysis. Logarithmic transformation was used to stabilise the variance of the sample (Blad, 2000). As in Suzuki et al., (2003), anticipatory SCRs were defined as the amplitude of the largest SCRs in μS having onset during the 10-s anticipatory interval. Similarly, appraisal SCRs were defined as the amplitude of the largest SCRs in μS having onset during the 10-s interval following the card choice.

The method of data extraction employed here is slightly different for the one used by Bechara et al (1999; 2002). They, in fact, considered the anticipatory response as the area under the curve in a variable interval and divide it by the interval length, in seconds, to obtain the mean SCR magnitude. The methodology used by Suzuki and colleagues (2003) and in this experiment allows for identification of a given oscillation in a standard recording interval, rather than an activation occurring in variable time frame to be divided by time. By using the maximum amplitude, intended as the maximum value within the interval, the experimental design and data extraction process can follow a fixed rule that is not dependent on the quality of each response. This standard process can be therefore automated and easily replicated.

Results

Mean net score

The mean net score for each block was calculated by subtracting disadvantageous selections from advantageous selections [(C+D)-(A-B)]. As for previous experiments reported in this thesis, a net score above zero indicates advantageous selections, while a net score below zero entails disadvantageous performance.

Figure 16 shows the mean net score for Phase 1 and Phase 2. A repeated measures ANOVA performed on the 5 blocks on the net score values showed a significant learning pattern across block, $F(1,96)=20.683$, $p<.001$. Contrast analysis showed a significant improvement in performance between blocks 1 and 2, $F(1,24)=14.31$, $p<.0001$. A repeated measures t-test performed on the three shifts did not show any significant learning pattern within each shift. By considering performance across all of Phase 2, a

repeated measure ANOVA showed improvement across shifts with values approaching significance level, $F(5,120)=3.83$, $p=.061$.

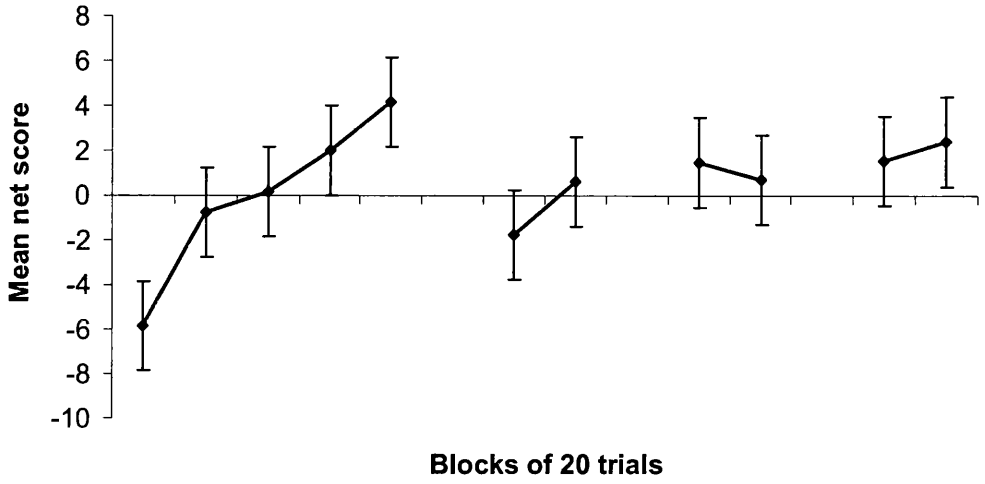

Figure 16: Mean net score for Phase 1 and 2.

IGT and Subjective Ratings

A mean net subjective rating was calculated by subtracting the ratings of the disadvantageous decks from the subjective ratings of the advantageous decks. Figure 17 shows that there was a large increase in subjective ratings after the first block in Phase 1 while awareness decreased in the three shifts of Phase 2. A repeated measures ANOVA showed that subjective ratings improved across the five trial blocks of Phase 1, $F(1, 96) =8.98$, $p < .0001$. Contrast analysis revealed a significant improved performance block 1 and 2, $F(1,24)=17.37$, $p<.0001$. A repeated measures ANOVA performed on Phase 2 did not reach statistical significance, $F(5,120)=2.89$, $p=.10$, although contrast analysis

showed a significant drop in the subjective rating scores between the second and the third shift, F (1,24)=11.59, p=.002.

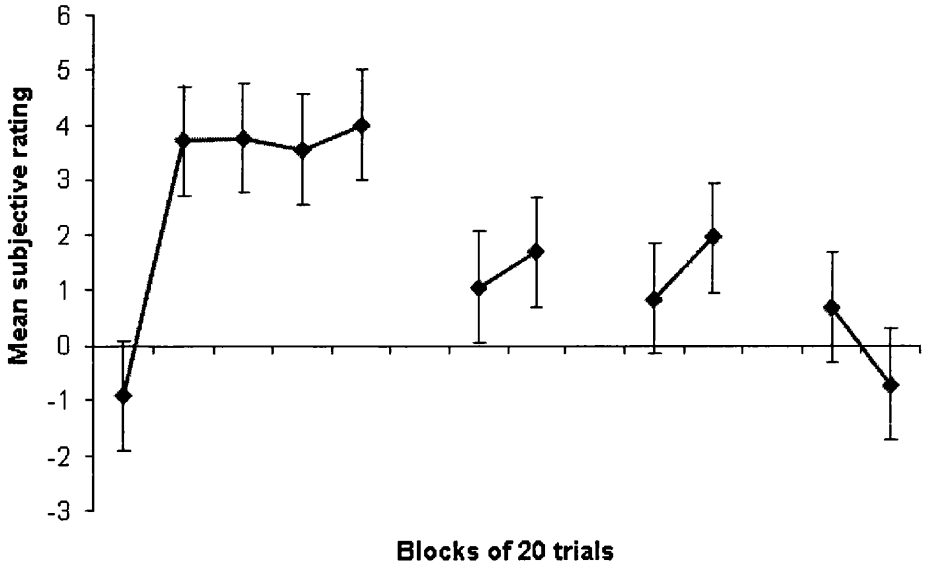

Figure 17: Mean net subjective rating for Phase 1 and 2.

SCR analysis - Deck type

To investigate anticipatory and appraisal SCRs for advantageous and disadvantageous decks, A and B selections and C and D selections were grouped for every block of 20 selections.

Anticipatory: Phase 1

A within-subjects repeated measures ANOVA conducted on the first phase of the IGT found no main effect of block, F(1.96, 45.07)=1.61, p=.212, no significant effect of deck type, F(1,23)= .17, p=.68, and no interaction, F(1.96, 45.07)=.048, p=.995 (see figure 18).

Phase 2

A within-subjects repeated measures ANOVA conducted on the second phase of the IGT found no main effect of block, F(2.97, 68.33)=2.57, p=.062, no effect of deck type, F(1,23)=.26, p.19, and no interaction, F(2.82, 64.88)=.188, p=.89 (see figure 18).

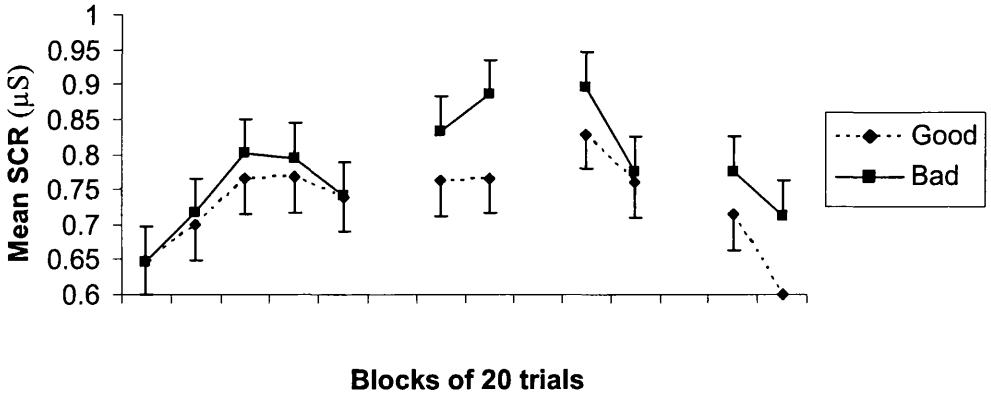

Figure 18: Anticipatory SCRs magnitude by blocks (in Phase 1 and 2) grouped by deck type (Good and Bad).

Appraisal: Phase 1

A within-subjects repeated measures ANOVA conducted on Phase 1 of the IGT found main effect of block, F(1.24, 9.95)=3.24, p=.024, no significant effect of deck type, F(1,8)= .023, p=.88, and no interaction, F(1.25, 10.04)=.244, p=.91. Contrast analysis found significant differences between block 1 and 2, F(1,23)=-2.45, p=.027, and block 2 and 3, F(1,23)=-2.08, p=.50, of the good decks and between block 1 and 2, F(1,23)=-2.07, p=.014, and between block 2 and 3, F(1,23)=-2.15, p=.044, of the bad decks (see figure 19).

Phase 2

A within-subjects repeated measures ANOVA conducted on the second phase of the IGT found no main effect of block, $F(3.47, 79.88)=.56$, $p=.56$, no significant effect of deck type, $F(1,23)= 3.71$, $p=.083$, and no interaction, $F(2.6, 59.8)=.774$, $p=.44$ (see figure 19).

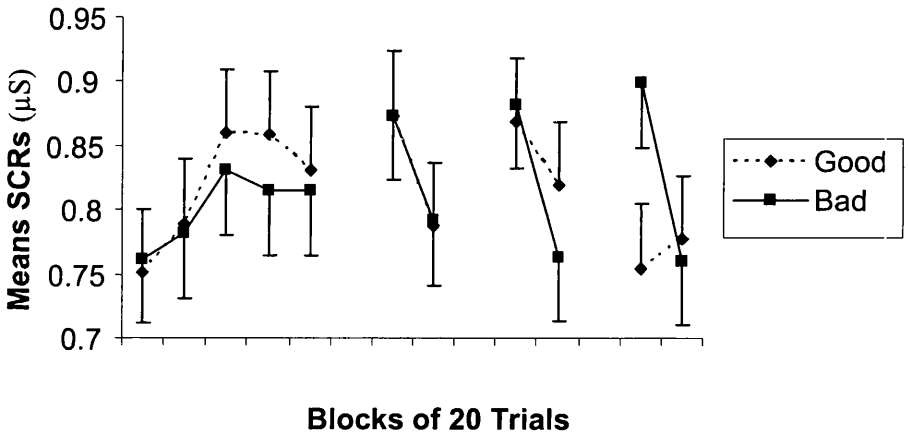

Figure 19: Mean appraisal SCRs for good and bad decks in phase 1 and 2.

Punishment and reward analysis

Anticipatory and appraisal arousal SCRs were investigated for trials with and without money loss. Punishment trials were defined as those trials where a monetary loss occurred, whereas reward trials were defined as those trials where no monetary loss occurs. As can be expected from the IGT schedule used in the current experiments, trials with punishments are less numerous than the trials without punishment. As participants played a fixed schedule and the frequency of trials with punishment is equal in both good and bad decks, a ratio between trials with and without punishment can be calculated. The

ratio between trial with and without punishment in Experiment 4 is 2.33, which means that, on average, a trial with punishment would occur every 2.33 selection of cards without punishment. This ratio also indicates that trials without punishment were more than two times the trials with punishment.

Anticipatory: Phase 1

A within-subjects repeated measures ANOVA conducted on the first phase of the IGT found main effect of block, $F(1.57, 36.2)=4.09$, $p=.033$, no significant effect of punishment, $F(1,23)= .278$, $p=.6$, and no interaction, $F(2.59, 92)=.273$, $p=.81$ (see figure 20).

Phase 2

A within-subjects repeated measures ANOVA conducted on the second phase of the IGT found no main effect of block, $F (1.36, 28.53)=1.03$, $p=.35$, no significant effect of punishment $F(1,21)= .077$, $p=.74$, and no interaction, $F(3.64; 76.54)=1.12$, $p=.35$ (see figure 20).

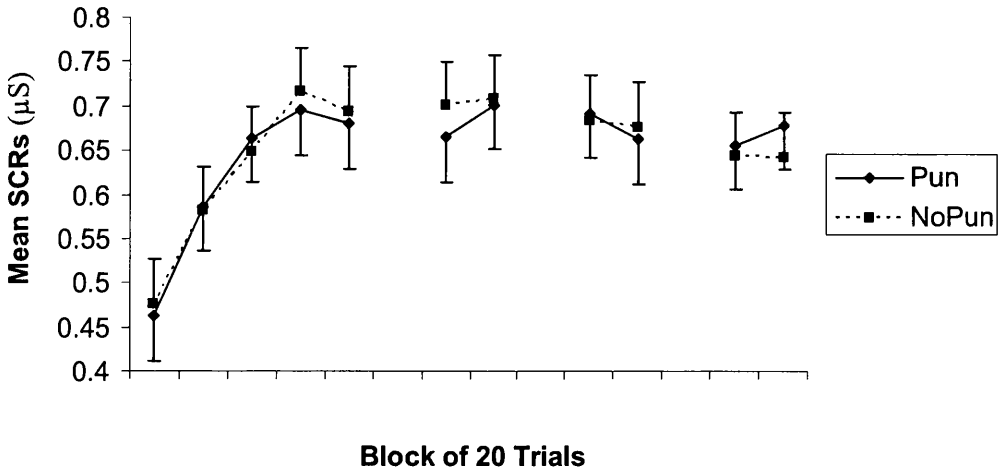

Figure 20: Anticipatory SCRs for decks with and without punishment in phase 1 and 2.

Appraisal: Phase 1

A within-subjects repeated measures ANOVA conducted on the first phase of the IGT found no main effect of block, F (1.58,34.92)=3.19, p=.062, significant effect of punishment, F(1,22)= 9.02, p=.007, but no interaction, F(2.31, 50.98)=.717, p=.51.

Follow-up paired t-test analysis found significant differences in block 2 between Punishment and Non-punishment, t(23)=3.04, p=.006 (see figure 21).

Phase 2

A within-subjects repeated measures ANOVA conducted on the second phase of the IGT found no main effect of block, F(1.51, 34.6)=.388, p=.861, no significant effect of punishment, F(1,23)= 3.816, p=.063, and no interaction, F(5; 115)=1.63, p=.157 (see figure 21).

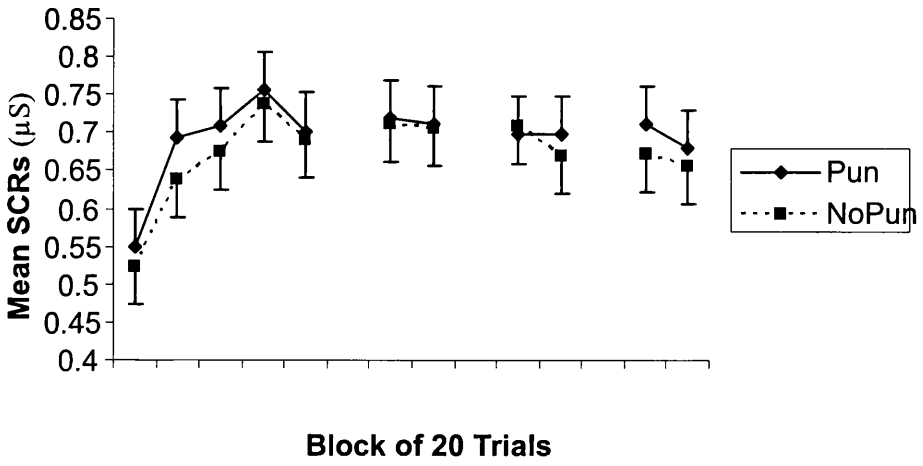

Figure 21: Mean appraisal SCRs for decks with and without punishment in Phase 1 and 2.

Learners and non-learners analysis

In order to perform this analysis the original sample was divided into Learners and Non-learners. Due to the relatively low performance of the overall group, the criteria used in Experiment 2 to define High and Low performers (i.e., High-performers as those with a Phase 1 performance equal or above 10) would have compromised the possibility to carry out statistical analysis. Therefore, a less stringent classification of Learners and Non-learners was adopted for the sample division. Learners were defined as those individuals with an IGT mean net score performance above one, while Non-learners were defined as those participants with a meant net score below -1. Participants with mean net score comprised between -1 and 1 were not included in the analysis. It is important to note that since Bechara and Damasio's (2002) original distinction between advantageous and disadvantageous performance in control participants, different definitions of what is

considered advantageous and disadvantageous have been adopted (e.g., Crone et al., 2004; Davies et al 2007; Glickson et al., 2007) and no one method is preferred over another.

Eleven learners and 10 non learners were identified. Three participants had a score comprised between -1 and 1 and were excluded from this analysis. As previously, behavioural performance and subjective rating were plotted in blocks of 20 trials and divided in Phase 1 (5 blocks) and 2 (6 blocks) (see Figure 22).

Behavioural performance

A 5 (block) x 2 (group) mixed factor ANOVA conducted on Phase 1 IGT revealed a main effect of groups, $F(1,19)=.003$, $p<.0001$, main effect of blocks, $F(4,76)=13.21$, $p<.001$, and significant interaction, $F(4,76)=5.29$, $p=.001$.

A 6 (block) x 2 (group) mixed factor ANOVA conducted on the shift phase of the IGT revealed a main effect of groups, $F(1,19)=32.19$, $p<.0001$, no main effect of blocks, $F(5,95)=1.52$, $p=.191$, and significant interaction, $F(5,95)=3.61$, $p=.005$.

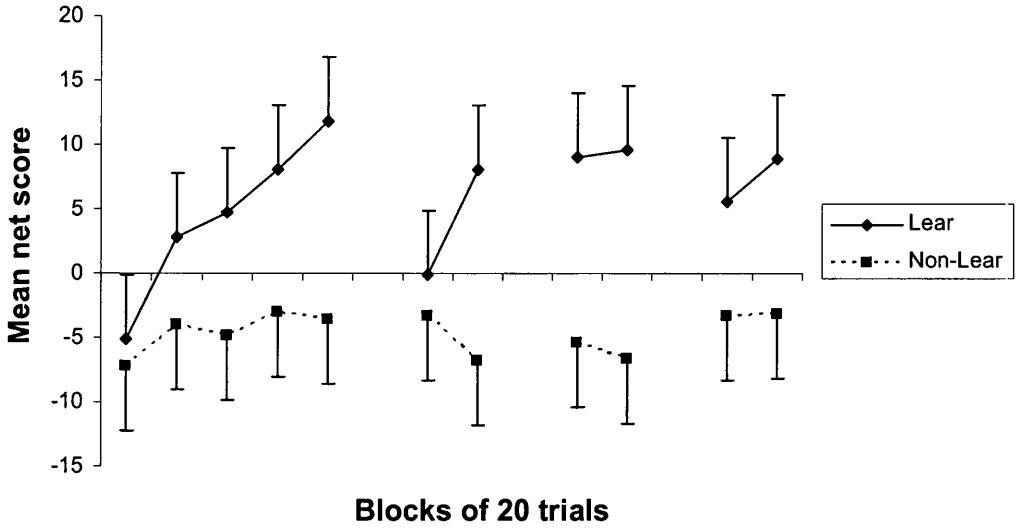

Figure 22: Mean net score for Learners and Non-learners during Phase 1 and 2

Subjective rating analysis

A 5 (block) x 2 (group) mixed factor ANOVA conducted on the standard IGT revealed a main effect of groups, $F(1,19)=9.96$, $p=.005$, main effect of blocks, ($F(4,76)=7.69$, $p<.001$, but no significant interaction, $F(4,76)=1.68$, $p=.163$.

A 6 (block) x 2 (group) mixed factor ANOVA conducted on the shift phase of the IGT revealed no main effect of groups, $F(1,19)=1.23$, $p=.28$, main effect of blocks, $F(2.79,53.06)=4.33$, $p=.01$, and significant interaction, $F(2.79,53.06)=4.36$, $p=.009$.

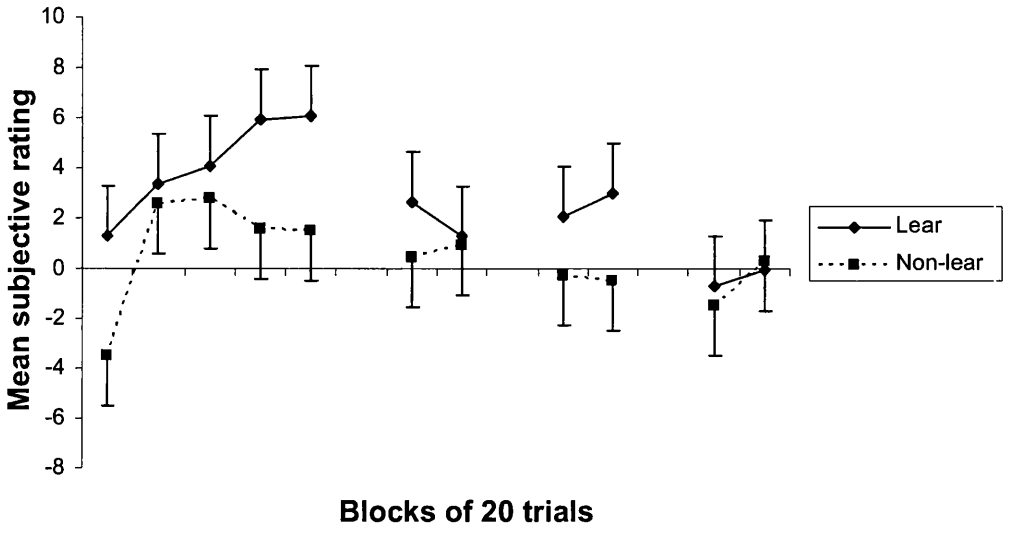

Figure 23: Mean net Subjective Rating for Learners and Non-learners during Phase 1 and 2

Anticipatory bad decks : Phase 1

A 5 (block) x 2 (group) mixed factor ANOVA conducted on the first phase of IGT found main effect of block, F (2.89, 55.4)=2.85, p=.047, no significant effect of group type, F(1,19)= 1.79, p=.122, and no interaction, F(2.89, 55.4)=.85, p=.49. Follow-up independent t-test analysis found significant differences between learners and non-learners for block 2, t(19)=2.46, p=.02, and block 3, t(19)=2.70, p=.017.

Phase 2

A 6 (block) x 2 (group) mixed factor ANOVA conducted on the second phase of IGT found no main effect of block, F(3.8, 72.24)=.412, p=.79, no significant effect of group type, F(1;19)= .142, p=.711, and no interaction, F(3.8, 72.24)=.109, p=.74.

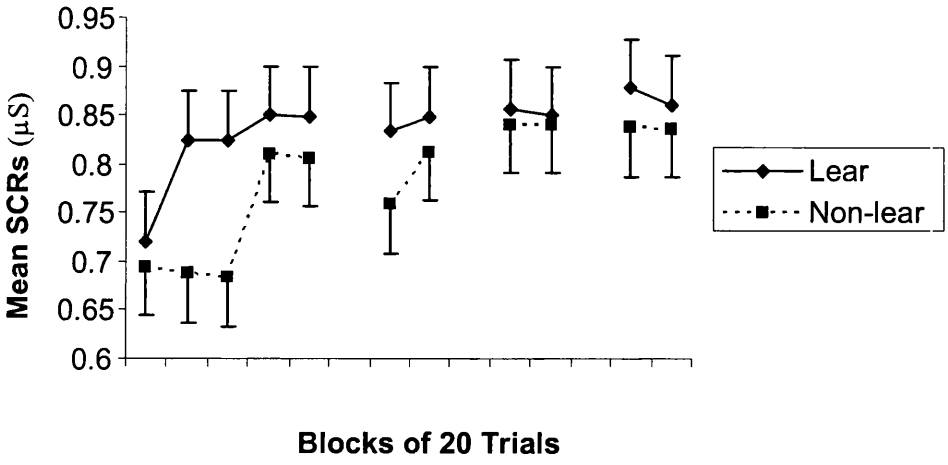

Figure 24: Anticipatory SCR for bad decks in Learners and Non learners for Phase 1 and 2.

Selections with punishment: Appraisal SCRs (Phase 1)

A 5 (block) x 2 (group) mixed factor ANOVA conducted on the first phase of the IGT found main effect of block, $F(4,76)=2.74$, $p=.034$, no interaction, $F(4,76)= .103$, $p=.98$, and no significant effect of group type, $F(1;19)=.004$, $p=.94$.

Phase 2

A 6 (block) x 2 (group) mixed factor ANOVA conducted on the first phase of the IGT found no main effect of block, $F(5,95)=.057$, $p=.98$, no interaction, $F(5,95)= .134$, $p=.964$, and no significant effect of group type, $F(1,19)=3.47$, $p=.076$. Follow-up independent t-test analysis found no approaching to statistical significant values (p comprised between .09 and .06) for clock 6, 7, 8, 9 10 and 11.

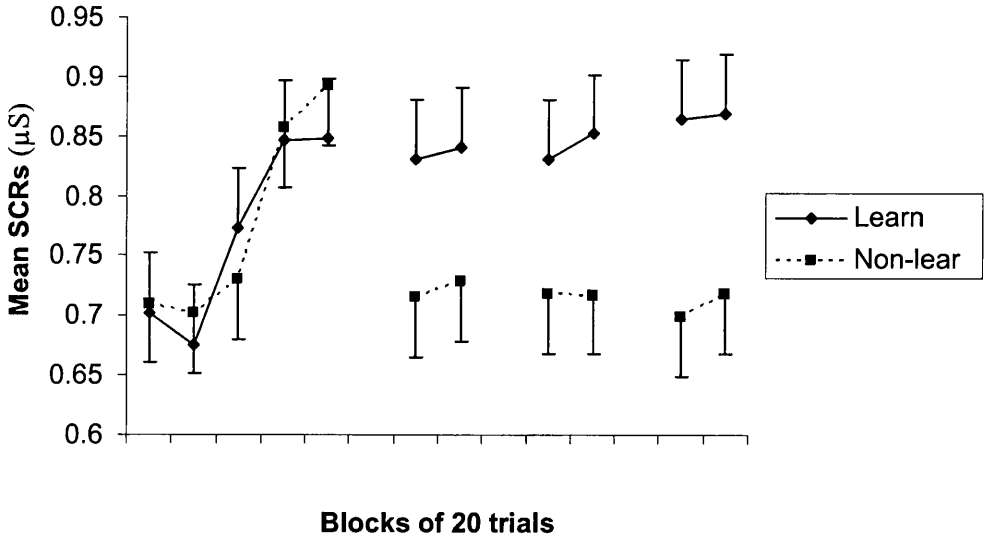

Figure 25: Appraisal SCRs for selection with money loss for Learners and Non-learners.

Discussion

Experiment 4 investigated SCR correlates of the contingency shifting variant IGT. Unlike previous studies, the current experiment did not find different levels of anticipatory SCR prior to card selections from the good and bad decks during Phase 1 (cf. Bechara et al., 1996; 1999; Crone et al. 2004; Suzuki et al., 2003). During the first five blocks, there was no difference in anticipatory SCR levels for good and bad cards and for selections with and without punishment. Similarly appraisal SCRs for Phase 1 did not differ between good and bad decks and punishment and non-punishment. These findings might appear controversial in consideration of the significant learning evidenced from the behavioural performance, although it should be noted that the mean score achieved by the group at the end of Phase 1 was rather low (i.e., 4). In previous work, Bechara and

Damasio (2002) only classified participants with a final mean net score of 10 or above as advantageous performers. Therefore, it can be hypothesized that the similar autonomic arousal between bad and good decks may be due to the relatively poor learning performance of the group.

As in Phase 1, Phase 2 levels of behavioural performance were quite low if compared to Experiment 2 and previously published data (Turnbull et al., 2006). Differences in levels of anticipatory and appraisal SCRs for bad and good decks and for trials with and without punishment were not found for Phase 2, thus replicating the findings of Phase 1. The considerably similar SCR values seen during the 3 contingency shift phases may have been influenced by the lengthy duration of the experiment and/or the high variability of individual behavioural performance. Indeed, a high degree of variance was observed during the analysis (e.g., the homogeneity of variance assumption was often not respected and appropriate sphericity correction applied). Steps taken to sub-divide the group into Learners and Non-learners were aimed at reducing this variance.

As expected, the behavioural performance of Learners and Non-learners was significantly different during Phase 1 and 2. The subjective ratings of the two groups were also significantly different, further confirming the influential role of awareness on performance (Bowman et al., 2005; Maia & McClelland, 2004). In both groups, anticipatory SCRs for bad decks increased across the blocks of Phase 1 providing support for the hypothesis of gradual sensitization at first and habituation later to risky selections. Although there was a general trend for improvement in anticipatory physiological activity for both Learners and Non-learners, it is important to note how the two patterns differed.

The difference between Learners and Non-learners was particularly evident in the second and the third blocks of Phase 1 suggesting that high anticipatory SCRs to bad decks are helpful only in the early stages of the task. Learners, in fact, appeared to develop anticipatory activity more rapidly that Non-learners. It also needs to be noted that the rise in anticipatory levels in Non-learners during the fourth and fifth blocks did not correspond to an improvement in performance. It has previously been argued that the IGT might evaluate two distinct types of decision-making processes, namely decision under ambiguity and decision under risk (Brand et al., 2007). The findings of Experiment 4 seem to suggest that anticipatory markers to risky selections are particularly helpful in the decision under ambiguity stage rather than in the decision under risk stage. In addition, the results seem to suggest that a particular feature of Non-learners' performance is the later development of anticipatory activation. Previous work has found undifferentiated anticipatory activation for good and bad decks in underperforming healthy controls (Bechara & Damasio, 2002). The results of Experiment 4 point at the possibility that low performance on the IGT might be related to the late development of somatic markers and their relative ineffectiveness in influencing the IGT performance. One possible explanation to the late inefficacy of anticipatory responses may be found in the reliance that participants seem to have on different resources across the task (Brand et al., 2007). It is possible that in later stages, when exposure to the contingencies has been maximal, participants' decisions are based on less intuitive processes and draw more resources from executive functions (Brand et al. 2006; 2007).

Anticipatory differences during Phase 2 were attenuated and the two groups appeared to have a similar level of performance. Anticipatory responses for the two

groups remained high and showed little sign of change both across the three shifts and between groups. Again, this may signify that Phase 2 relies less on intuitive mechanisms and more on reward sensitivity. To test this hypothesis, appraisal SCR levels for decks with punishment were investigated. It was found that Learner and Non-learners had comparable performance during Phase 1 but showed a trend approaching significance in favour of Learners during Phase 2. However, the framing of findings from Phase 2 is slightly more complicated due to the novelty of the contingency shift modification and the insufficient number of publications to compare with the present results. The appraisal results for trials with punishment seem to suggest that Learners present a higher sensitivity to negative outcomes compared to Non-learners. This finding might also suggest, although this is speculative, that performance on Phase 2 correlates with the ability to elicit appropriate SCRs following punishment and therefore sensitivity to punishment. Previous studies indicate that reward and punishment sensitivity mediate the psychophysiological response to wins and losses (Goudriaan et al., 2005; Knyazeva, Slobodskayaa & Wilson, 2002; Kilzieh & Cloninger, 1993; Suzuki et al., 2003). Also, it has been argued that decision-making and set-shifting ability is dependent on reward sensitivity (Blair, Peters & Granger, 2004; Franken, & Muris, 2005; Shur & Tsanadis, 2007). SCR correlates with appraisal in trials with punishment implies a relative higher sensitivity to punishment in Learners compared to Non-learners and, therefore, might suggest sensitivity to punishment as an important factor influencing Phase 2 performance. The findings of the Learners group support the SMH, but this is tempered somewhat by the fact that roughly half of the sample failed to perform above chance on the IGT. In other words, if the anticipatory somatic marker signal occurring early in Phase 1 can be

claimed as responsible for the Learners good performance, the issue of what impairs the Non-learners somatic markers remains unknown.

Two are the major achievements of Experiment 4. First, the findings confirm that Learners and Non-learners have different psychophysiological correlates of decision-making. In addition to Crone et al. (2004a), Experiment 4 showed that Non-learners fail to develop adequate anticipatory responses to bad decks in the early stages of the task. The study of different psychophysiological levels prior to and following decisions might help to understand the reasons behind the variability seen in controls participants' performance during the IGT and cast further light on factors influencing decision-making. The second major contribution of this study is the exploration of the SCRs correlates of the contingency shift phases and the characterization of the punishment sensitive nature of advantageous performance.

Nevertheless a number of limitations needs to be considered. First, the length of the study was approximately 90 minutes, which may have influenced participants' level of attention and motivation. Second, the limited number of participants might have curtailed the strength of some trends that approached significance. Finally, the variability in participants' performance coupled with the high variance normally seen in SCRs data is unhelpful for statistical analysis, especially parametric statistical methods. In line with previous research measuring SCRs activation during the IGT the choice of parametric testing was preferred to non-parametric (Bechara et al. 1994). Due to the sometime non-normal distribution of the scores significance values were appropriately corrected (i.e. Greenhouse-Geisser correction). It is debatable whether the use of non-parametric statistic would have proven beneficial for the analysis. As a matter of fact, parametric

statistic provide a more powerful approach to data analysis but more conservative (Field, 2000), therefore the approaching significance levels observed in the results presented could have been significant with a different analysis strategy. The analysis choice made for Experiment 4 was based on previous similar reports with comparable number of participants and variance in the attempt to help the comparability of the findings.

Chapter 5

Flexible emotion-based learning and psychopathological traits

Chapters 3 and 4 have evidenced a degree of variability in IGT participants' performance across different experiments. Those participants with low levels of performance present a learning profile that has been described as similar to those of VM patients (Bechara et al., 2002). Deficits in emotion-based learning are also implicated in several psychiatric disorders and appear related to a wide range of symptoms (Pinkham, Penn, Perkins, & Lieberman, 2003). Extending the use of the contingency shifting IGT to the domain of psychopathology may shed further light on the nature of performance impairment in various clinical groups. However, before so doing it may be salutary to first investigate performance as a function of sub-clinical characteristics. In Chapter 5 the dimensionality of psychopathology approach (Claridge, 1997), as it relates to schizotypal and depressive features, was applied to contingency shifting IGT performance.

The findings of clinical research have shown impaired emotional decision-making in individuals with several psychiatric disorders, such as obsessive-compulsive disorder (Lawrence et al., 2006), substance addiction (Verdejo-García & Bechara, 2009), depression (Must et al., 2006) and schizophrenia (Martino et al., 2007). Dysfunction in structures such as the VMPFC and orbitofrontal cortex (OFC) is evident in schizophrenia (e.g., Pantelis et al., 2003; Quintana et al., 2003) and, accordingly, patients with schizophrenia have been shown to perform more poorly than healthy volunteers on OFC-sensitive decision-making tasks (e.g., Hutton, Murphy, Joyce, Rogers, Cuthbert, Barnes et al., 2002). The evidence from studies employing the IGT is, however, largely inconclusive (Sevy et al., 2007). Some studies (Evans et al., 2005; Ritter et al., 2004)

have shown that patients with schizophrenia perform at levels comparable to healthy participants. Other studies (Lee et al., 2007; Martino et al., 2007; Shurman et al., 2005) have shown that patients with schizophrenia engage in disadvantageous decision-making compared to healthy controls, which suggests a pronounced impairment in emotion-based learning. The interpretation of these inconclusive findings needs to acknowledge the contribution of factors such as the relatively small sample sizes, the influence of medication, comorbid diagnoses, and the heterogeneity of symptoms within the diagnosis of schizophrenia itself (Dunn et al., 2006; Sevy et al., 2007).

Turnbull et al. (2006) suggested that people with schizophrenia might not show consistent deficits on the IGT because the original task does not adequately tap flexibility in emotion-based learning. Flexible adjustment to the affective consequences of reward and punishment is a defining feature of advantageous performance on the IGT as participants initially choose cards from all of the decks before showing, around halfway through the task, a choice preference for the advantageous decks (Dunn et al., 2006). The inconclusive findings from research with people with schizophrenia suggests that measures of emotion-based learning such as the IGT may not be sufficiently sensitive to assess the ability of such individuals to modify or regulate these emotion-based processes.

The investigation of flexible emotion based components in decision-making has relied on the interpretation of set-shifting and reversal learning tasks. A number of studies have shown that people with schizophrenia perform relatively poorly on such tasks (Pantelis et al., 1999; Waltz & Gold, 2007). These deficits may be the outcome of dysfunction in various prefrontal cortex sub-regions including the VMPFC and OFC.

Recently, Rodriguez-Sanchez et al. (2005) reported that first episode schizophrenia patients have unimpaired IGT performance, yet have impaired performance on one of the most widely used measures of executive functioning and set shifting ability: the Wisconsin Card Sorting Test (WCST; see also Prentice, Gold & Buchanan, 2008). These authors also found that performance on the IGT was not correlated with WCST performance. In another recent study with people with schizophrenia, Lee et al. (2007) reported impaired IGT performance, and, similar to Rodriguez-Sanchez et al. (2005), an absence of correlations between WCST ability and IGT performance. Lee et al. (2007) also found that performance on the Simple Reversal Learning Task (SRLT; Fellows & Farah, 2003) was impaired in people with schizophrenia, relative to healthy controls, but was not associated with performance on the IGT in either of the groups. Both the Rodriguez-Sanchez et al. (2005) and Lee et al. (2007) studies failed to find correlations between set-shifting ability, as measured by the WCST, and reversal learning ability, as measured with the SRLT, and IGT performance. This suggests that the standard version of the IGT employed in these and other studies may not be sufficiently sensitive to assess the flexible recruitment of emotion-based resources.

To overcome the lack of tasks assessing flexibility in emotion based learning, Turnbull et al. (2006) developed a contingency shifting variant IGT. This task has been previously described in the present thesis and research conducted with it in several contexts so far. However, it is important to emphasise that Turnbull et al. (2006) first applied the contingency shifting IGT to study individuals with schizophrenia in order to clarify whether or not this group would display a specific impairment in the part of the task that required more flexibility in the adaptation to advantageous contingencies. The

modified version of the task used by Turnbull et al. (2006) was similar to the task used in Experiment 2, 3 and 4 of this thesis. In other words, the reinforcement contingencies of the card decks were shifted following initial exposure to the standard IGT trials. Over three successive contingency shift periods, card decks that had previously been advantageous became disadvantageous, and vice versa. Thus, the contingency-shifting variant IGT was designed to tests the ability of participants to flexibly deal with changing reinforcement contingencies across a more extended period of time than that allowed by the original IGT. As a point of departure from the task used in Turnbull et al. (2006), the contingency shifting IGT used in the Experiments 2, 3 and 4 did not signal the onset of the shifting phase. In their analyses, Turnbull et al. (2006) compared the performance of a group of patients with schizophrenia who were classified as either high or low in positive and negative symptomatology with that of a healthy control group. Results showed that patients high in positive and negative symptoms initially learned at levels comparable to the healthy controls during the standard version of the IGT, supporting some previous studies (e.g., Rodriguez-Sanchez et al., 2005; Ritter et al., 2004). During the contingency shift phase of the task, however, those patients with schizophrenia high in negative symptoms exhibited markedly poorer performance in adjusting to the changing contingencies relative to both healthy controls and those patients high in positive symptoms. The findings of Turnbull et al. (2006) suggest that deficits associated with schizophrenia are specific to the shift phase of the contingency-shifting variant IGT. As previously noted, this is consistent with research showing deficits in set-shifting ability in schizophrenia (Pantelis et al., 1999; Waltz & Gold, 2007).

Emotion-based learning deficits may reflect core pathological processes in schizophrenia and appears important to further clarify the impact of symptomatology on the reported behavioural deficits in order to shade light on the cognitive determinants of psychopathology. An intriguing means of addressing this question is to examine flexible emotion-based learning with the contingency-shifting variant IGT in non-clinical samples that have elevated psychosis proneness or high schizotypal features (Johns & van Os, 2001; Verdoux & van Os, 2002). Hallucination- and delusion-proneness are two of the most prominent features of psychosis-proneness that appear to be dimensionally distributed across the general population (Johns & van Os, 2001; Verdoux, Maurice-Tison, Gay, van Os, Salamon, et al., 1998). The concept of the dimesionality of psychotic features has proven to be a useful research concept to investigate psychosis as well as a valuable clinical notion to inform prevention strategy (Claridge, 1997). People with high psychotic proneness scores are in fact at much higher risk to develop psychosis than the general population; recent research has estimated that this risk can be up to 60 folds higher (Hanssen, Bak, Bijl, Vollebergh & van Os, 2005).

Previous studies have investigated how psychometric measures of psychosis-proneness and schizotypy relate to putative measures of set-shifting, such as the WCST. In clinical samples, poor WCST performance has been more often associated with negative symptoms of schizophrenia (Nieuwenstein, Aleman & de Haan, 2001). In non-clinical samples, findings have been mixed with deficits in WCST performance being related to negative symptoms (e.g., Suhr & Spitznagel, 2001), positive symptoms (e.g., Suhr, 1997) or both (e.g., Gooding, Kwapil, & Tallent, 1999). It should be noted that performance on the set-shifting IGT and WCST is likely to be reliant on a number of

relatively diverse cognitive processes, such as working memory, attention and response inhibition. Some caution is therefore necessary when assuming that previous findings with the WCST will be relevant to the contingency-shifting IGT. Indeed, Turnbull et al. (2006) found low correlations between performance on the contingency-shifting IGT and other set-shifting measures, including the WCST (cf. Lee et al., 2007). Nonetheless, based on previous research, it seems plausible to suggest impairment in IGT contingency-shifting performance in individuals high on schizotypal traits, such as hallucination and delusion proneness.

The aim of Experiment 5, therefore, is to extend the findings of Turnbull et al. (2006) with the contingency-shifting variant IGT by examining the performance of non-clinical groups high on hallucination and delusion proneness scores.

Experiment 5

Method

Participants

There were two stages to participant recruitment for Experiment 5. First, a large cohort of students was screened in order to comprise the participant groups. Second, those participants invited for further study were tested in a laboratory and were compensated with £5.00. This study was reviewed and approved by the Department of Psychology, Swansea University Ethics Committee. Written informed consent was obtained from all participants before their entry in the study.

Two hundred and fifty-three Swansea University students were administered the *Launay-Slade Hallucination Scale* (LSHS; Launay & Slade, 1981; Larøi, Marczewski &

van der Linden, 2004) and *Peters Delusions Inventory* (PDI; Peters, Joseph & Garety, 1999; Peters, Joseph, Day & Garety, 2004). One hundred and seventy seven of these participants were female and 73 were male (3 participants did not record their gender). The mean age of this sample was 20.13 years (SD = 3.27). Scores on the LSHS and PDI served as the basis for inclusion in the study. Participants in the top and bottom 15% of the total score distribution for the PDI and LSHS were placed in to high and low groups for these scales, respectively. These individuals were then invited to participate in a further experimental session comprising administration of the contingency-shifting variant IGT. Seventy-four of the 92 invited participants agreed to complete the second session, yielding a final sample of 28 high- and 27 low-LSHS participants and 27 high- and 26 low-PDI participants. None of the participants involved in the second session reported substance abuse problem, brain injury or mental health condition. The mean total scale scores for each group were as follows: High-LSHS (M = 34.07, SD = 6.29), Low-LSHS (M = 4.52, SD = 2.38), High-PDI (M = 102.81, SD = 33.54) and Low-PDI (M = 9.23, SD = 5.39). There were 10 males and 18 females in the High-LSHS group, 12 males and 15 females in the low-LSHS group, 7 males and 20 females in the High-PDI group and 11 males and 15 females in the Low-PDI group.

Psychosis-proneness Measures

Launay-Slade Hallucination Scale (LSHS; Launay & Slade, 1981; Larøi et al., 2004): Hallucination proneness was assessed using a modified version of the LSHS (Larøi et al., 2004). The scale is composed of 16 items, scored on a 5-point Likert scale, where 0 = "certainly does not apply to me", 1 = "possibly does not apply to me", 2 = "unsure", 3 = "possibly applies to me", 4 = "certainly applies to me". Participants are

asked explicitly not to report any experiences that occurred under the influence of drugs, alcohol or any psychotropic substance. Total LSHS score is the sum of all the item scores and can range form 0 to 54. This scale has been widely used with non-clinical populations (Cronbach's $\alpha = 0.78$; Larøi et al., 2004).

Peters et al. Delusions Inventory (PDI; Peters et al., 1999): Delusion proneness was assessed with the revised 21-item PDI (Peters et al., 2004). The 21-item scale explores life-time prevalence of delusional ideation, using the introductory expression, "Do you ever feel as if [*some people are not what they seem to be*]?" Questions are answered on a yes-or-no basis. When a "Yes" is checked, three additional 5-point rating scales measure distress, preoccupation and conviction associated with the experience. Each "Yes" checked assigns 1 point contributing to a frequency score of reported unusual experiences (range: 0-21). All of the items checked "Yes" also contribute to distress, preoccupation and conviction scores. The final score is the sum of the selection endorsed in the rating subscales. Each subscale can range from 0 to 105. Every "No" answer on the PDI leads automatically to a 0 score for each subscale. Finally, a total PDI score is obtained by adding the frequency of "yes" checked to all the subscales total scores. The 21-item scale has been used reliably in a large body of research and has high internal validity (Cronbach's $\alpha = 0.82$) and test-retest reliability (Spearman's $r = 0.78$; Peters et al., 1999).

Measure of Emotion-Based Learning

Flexible emotion based learning was measure with the *Contingency-Shifting Variant IGT* as employed in Chapter 3, Experiment 2. The same task and instructions were administered to all participants.

Results

Table 5 displays the mean PDI and LSHS scores for the initial large sample, as well as for the high and low PDI and LSHS sub-groups. Reliability scores as established by Cronbach's alphas were .88 for the LSHS, .94 for PDI total, .84 for PDI distress, .84 for PDI preoccupation and .79 for PDI conviction. In the total sample, the PDI and LSHS total scores were positively and significantly correlated ($r = 0.53$, $p < .001$). As expected, a t-test performed on the PDI and LSHS total scores between high and low groups revealed significant differences (both $p < .01$).

	Group	Male/Female	Age (SD)	Mean PDITot	Mean PDIdis	Mean PDIPre	Mean PDICon	Mean LSHS
PDI	All	73/177	20.13	45.95	12.8	12.55	15.4	16.92
	(*n*=253)		(3.27)	(30.42)	(9.27)	(9.14)	(10.16)	(10.54)
	High	7/20	20.04	102.81	30.33	28.52	33.59	27.52
	(*n*=27)		(2.05)	(33.54)	(10.59)	(11.77)	(10.15)	(11.32)
	Low	11/15	21.73	9.23	2.46	2.54	3.12	9.08
	(*n*=26)		(4)	(5.39)	(1.55)	(2.1)	(1.86)	(7.31)
LSHS	All	73/177	20.13	45.95	12.8	12.55	15.4	16.92
	(*n*=253)		(3.27)	(30.42)	(9.27)	(9.14)	(10.16)	(10.54)
	High	10/18	19.68	79.32	23.14	22.29	26.11	34.07
	(*n*=28)		(1.33)	(44.52)	(13.93)	(14.19)	(14.03)	(6.29)
	Low	12/15	21.96	24.33	6.70	6.56	8.31	4.52
	(*n*=27)		(4.01)	(28.69)	(8.06)	(7.98)	(9.03)	(2.38)

Table 5: Gender ratio, mean age and mean values for LSHS and PDI subscales for high and low groups. Note: PDITot = total PDI score, PDIdis = PDI distress subscale score, PDIPre = PDI preoccupation subscale score, PDICon = PDI conviction subscale score, and LSHS = total LSHS score.

Figures 26 and 27 show Phase 1 and 2 mean net score performance for the high and low PDI and LSHS groups, respectively. In Phase 1 of the IGT, both high and low PDI groups showed a positive learning pattern, but there were no significant between-group differences on performance. A 2 (group) x 5 (block) mixed factor ANOVA revealed a main effect of block, $F(4, 204) = 11.70$, $p < .001$. However, there was no significant group main effect, $F(1, 51) = 1.98$, $p=0.17$ or block by group interaction, $F(4, 204) = 1.73$, $p=0.15$. A similar pattern of results was shown for the high and low LSHS groups. In Phase 1 of the IGT, both groups showed a general increase in performance across blocks, but there were no significant group differences. A 2 (group) x 5 (block) mixed factor ANOVA revealed a main effect of block, $F(3.2, 173.32) = 6.25$, $p < .001$. Again, there was no significant group main effect, $F(1,53) = 0.01$, $p=0.92$, or block by group interaction, $F(3.2, 173.32) = 0.82$, $p=0.49$.

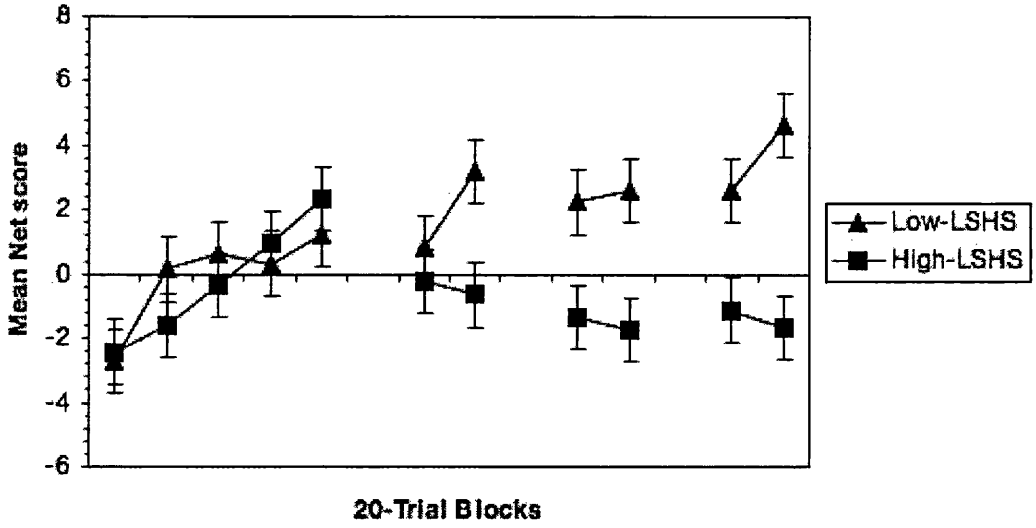

Figure 26: The mean net score performance for the high- and low-LSHS groups for the five 20-trial blocks in Phase 1 and the six 20-trial blocks in Phase 2.

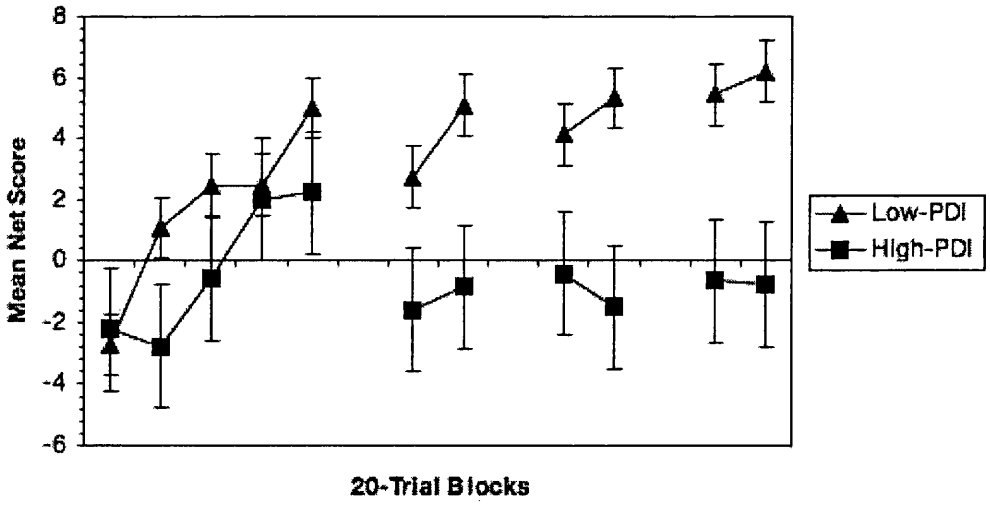

Figure 27: The mean net score performance for the high- and low-PDI groups for the five 20-trial blocks in Phase 1 and the six 20-trial blocks in Phase 2.

Figures 26 and 27 show that across Phase 2, performance between the low and high groups on the PDI and LSHS began to diverge. A 2 (group) x 6 (block) mixed factor ANOVA performed on the shift phase for high and low PDI groups showed a significant main effect for group, $F(1, 49) = 15.24, p < .001$, but no significant main effect for block, $F(3.7, 181.32) = 1.193$ $p=0.2$ nor a significant interaction $F(3.7, 181.32) = .759$, $p=0.58$. Post hoc t-tests showed that the high and low PDI groups significantly differed in mean net score across each of the six blocks (all $p < .05$). A similar set of analyses conducted for the LSHS high and low groups revealed a main effect for group, $F(1,52) = 7.7, p = 0.008$, but no significant main effect for block, $F(4.1, 213.43) = .49$, $p=0.75$, nor significant interaction, $F(4.1, 213.43) = 1.73$, $p=0.14$. Post hoc t-tests showed that the high and low LSHS groups significantly differed in mean net score across blocks 2, 3, 4, and 6 ($p < .05$).

Investigating response perseveration during contingency-shift phases

Performance in Phase 2 was further investigated by examining the selection of decks that from advantageous became disadvantageous from phase 1 to phase 2 and during the contingency shifts of Phase 2 in both LSHS and PDI sub-groups (see Figures 28 & 29). A mixed factor 2 (group) x 3 (shift) ANOVA conducted on the LSHS sample showed a main effect of group, $F(1, 53) = 7.212, p = .005$, but no significant effect of shift period $F(2, 106)=0.96$, $p=0.39$,nor interaction $F(2, 106)=0.24$, $p=0.79$. Post-hoc tests showed that high-LSHS participants made significantly more good-now-bad selections in

the second, t(53)=−2.35, p=0.02, and in the third shift periods, t(53)=−2.01, p=0.05, but not in the first shift period, t(53)=−1.61, p=0.11.

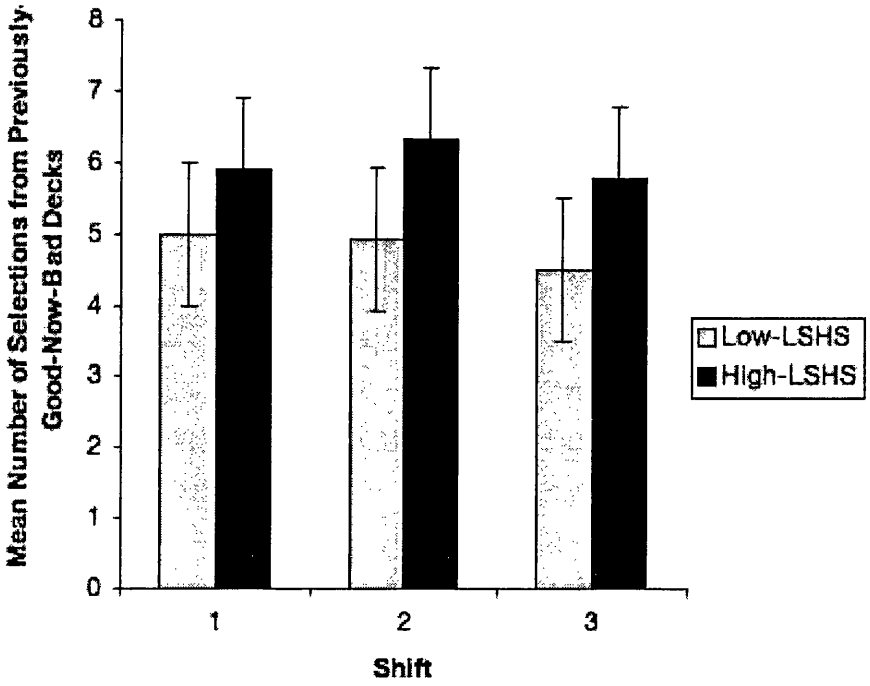

Figure 28: The mean number of previously-good-now-bad selections by the high- and low-LSHS groups during each of the three shift periods of Phase 2. Error bars represent two standard errors.

A mixed factor 2 (group)×3 (shift) ANOVA conducted on the PDI sample showed a main effect of group, F(1, 51)=6.41, p<0.0001, but no significant effect of shift period, F(2, 102)=1.10, p=0.34, nor interaction, F(2, 102)=0.02, p=0.98. Post-hoc tests showed that high-PDI participants made significantly more good-now-bad selections in the third shift period, t(51)=−1.99, p=0.05, with trends towards significantly more good-now-bad selections in the first, t(51)=−1.92, p=0.06, and second, t(51)=−1.87, p=0.07, shift periods.

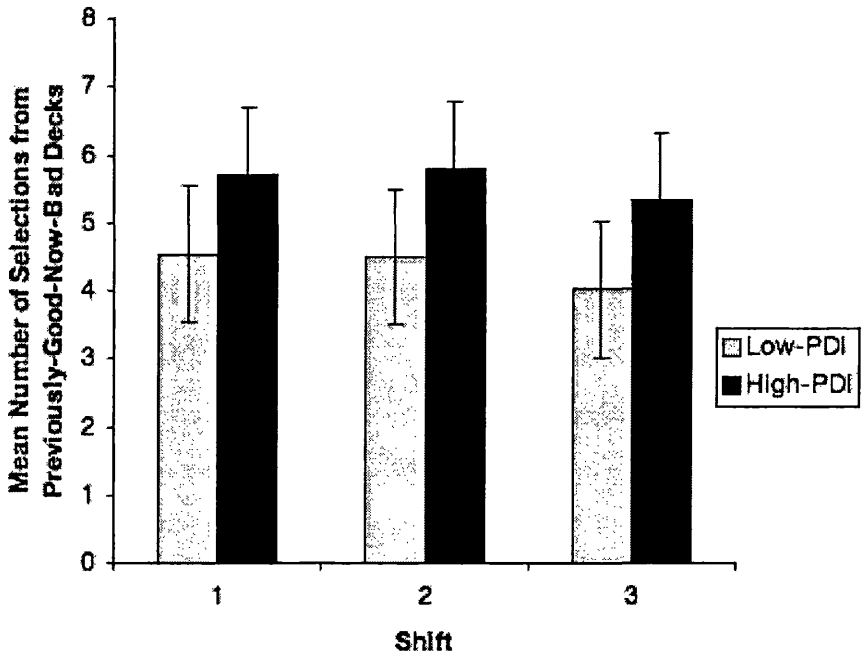

Figure 29: The mean number of previously-good-now-bad selections by the high- and low-PDI groups during each of the three shift periods of Phase 2. Error bars represent two standard errors.

Chapter 5

Discussion

The findings of Experiment 5 revealed no significant differences between the performance of individuals classified as high and low in delusion- and hallucination-proneness during the standard IGT phase (i.e., Phase 1). Differences in performance only emerged between the groups following the onset of the contingency shift phases (i.e., Phase 2): individuals high in delusion- and hallucination-proneness had impaired emotion-based learning performance, as measured by mean net score, during all three contingency shift sub-phases, compared with low delusion- and hallucination-prone individuals. Indeed, during the shift phases, high delusion- and hallucination-prone individuals showed a general impairment in their IGT performance as evidenced by consistent disadvantageous decision strategy (i.e., mean net score below zero).

It is remarkable, in the context of previous experiments showing variability in participants (e.g. Experiment 2), that high- and low-psychosis proneness individuals display a within group homogeneous performance both in Phase 1 and 2. This may suggest that variability in controls participants could be dependent from a predisposition to certain traits and psychosis proneness could be a relevant aspect to control for in future studies. It is possible that a variety of traits may affect IGT performance and create the variability in performance. Clearly, more research is needed to investigate the relevance of personality and psychopathological traits in decision-making performance.

The IGT contingency shift impairment observed in high delusion- and hallucination-prone individuals may be compared with the results obtained from previous studies that investigated emotion-based learning in schizophrenia patients classified on the basis of negative (i.e., symptoms relating to the absence of normal functioning) or

positive symptoms (i.e., symptoms relating to the presence of abnormal experiences). Ritter et al. (2004) found impaired performance during standard IGT trials in patients with schizophrenia compared to a group of healthy controls, and observed that WCST performance was impaired in both groups. This study also failed to find any correlations between IGT scores and measures of negative symptom whereas measures of positive symptoms were not reported. In the other previous study that examined the relationship between positive and negative symptomatology and IGT performance, Turnbull et al. (2006) employed the set-shifting variant IGT and found that patients with high scores on measures of positive symptoms showed Phase 1 and Phase 2 learning at levels comparable to that of controls. Differently patients with high scores on measures of negative symptoms performed well during Phase 1 but showed below-chance level performance in the contingency-shifting Phase 2. Thus, it would appear that the findings of Experiment 5 are at odds with those of Turnbull et al. for patients high in positive symptoms as participants with high hallucination- and delusion proneness showed unimpaired performance in Phase 1 and below-chance performance in Phase 2. On a more general level, however, the findings demonstrate that impairments associated with hallucination and delusion proneness are specific to the shift phase of the contingency shifting variant IGT, which supports Turnbull et al.'s findings with patients with schizophrenia.

Similar to a number of previous studies conducted with patients with schizophrenia, the results suggest that features of psychosis might not alter performance on the standard version of the IGT during Phase 1 (Evans et al., 2005; Rodriguez-Sanchez et al., 2005). An alternative explanation for the similar performance during the

standard IGT trials might be the fact that psychosis proneness, as measured by the instruments employed, is an indicator of psychopathological propensity, rather than actual psychopathological symptomatology. It follows that the intensity of the traits expressed by the participants in this study can be considered of lower intensity than those of patients with schizophrenia. Therefore, symptom severity and symptomatological composition should be taken into consideration by future studies investigating emotional decision-making in psychosis.

The effect of confounding factors such as medication, institutionalization, substance abuse, and illness length cannot be ruled out in explaining the results of the studies showing schizophrenic deficits on the standard IGT (Sevy et al., 2007). Such potential confounds make comparisons between the present findings and those from research conducted with patients with schizophrenia difficult. For instance, of the twenty participants in Ritter et al's (2004) study, 3 participants were prescribed typical anti-psychotic medication, while the majority (n = 17) were prescribed atypical medication, and the average illness duration was 25.8 years. It has been suggested that patients on typical anti-psychotics are more impaired on the IGT than on the WCST compared with patients on atypical anti-psychotics (Beninger et al., 2003; but see Martino et al., 2007). Clearly, medication-type or duration of illness, or both, may have contributed to the results obtained in previous studies. The current study can rule out the effect of medication and clinical history and provides some insight into their importance in affecting IGT performance. Nevertheless, further research is indeed necessary to disentangle the effects of different medication-types and illness duration on emotion-based learning abilities in schizophrenia.

A number of studies have advanced the importance of different prodromal factors in the development of psychosis (e.g., Cella, Cooper, Dymond & Reed, 2008; Dean, Bramon, & Murray, 2003; Seeber, & Cadenhead, 2005). The present findings suggest that that emotion-based learning impairments generally, and the contingency-shift variant IGT specifically, may have potential implications as experimental indicators of psychosis risk. In particular, the extended version comprising the contingency-shift phase seems to be particularly sensitive to features of schizophrenia-proneness (Fusar-Poli, Perez, Broome, Borgwardt, Placentino, Caverzasi, et al., 2007). Advantages of using an emotion-based learning paradigm in sub-clinical and clinical research are: the neuropsychological background upon which the task was developed (Bechara 2004), the finding that impaired performance in tasks such as the IGT has been shown to be related to PFC and VMPFC damage (Bechara et al., 1994; 2005), that research has identified brain abnormalities in the PFC in people at risk of psychosis (Fusar-Poli et al., 2007), and that poor performance on the task has been shown to correlate highly with social and functional impairment in people with PFC damage (Shamay-Tsoory, Aharon-Peretz, & Levkovitz, 2007).

The result of Experiment 5 may have relevance to the literature on response perseveration in schizophrenia (Brazo, Delamillieure, Morello, Halbecq, Marié & Dollfus, 2005). Findings showed that during the contingency-shift phases, hallucination- and delusion-prone participants were more likely to continue to select the previously-good-now-bad decks, indicating a persistence of previously learned reinforcement contingencies and an impaired ability to adapt to the changing outcomes (i.e., perseverative errors). Response perseveration of this kind has typically been observed

with tasks requiring repeated reversals of reinforcement contingencies, such as the WCST (Haut et al., 1996). Compared to the WCST, the contingency-shift variant IGT allows for a more extended analysis of the effects of progressive modifications to the underlying reward/punishment contingencies on choices from each of the four decks. In this way, the contingency-shift variant IGT may offer promise as an alternative means of investigating response perseveration with an ecologically-valid emotional decision-making task.

In conclusion, this study examined the effect of hallucination and delusion proneness on the contingency shifting modification of the IGT. The results showed there were no significant differences between those classified as high and low on hallucination and delusion proneness on the standard phase of the IGT while difference in performance emerged during the contingency shifting modification. Several limitations should, however, be noted when considering the data. Firstly, no other behavioural measures of contingency-shifting, reversal learning or executive functions were administered, making it difficult to generalise the findings to previous studies that have used such measures (e.g., Lee et al., 2007; Turnbull et al., 2006). Secondly, only university students were included in the sample, which may not be representative of the general population and due to their young age are at higher risk of developing psychosis (Häfner, & an der Heiden, 1997). This was however consistent with the recruitment of previous experiment in this thesis and helpful in order to compare the results across experiments. Finally, hallucination and delusion proneness, although highly prodromic, only represent two particular facets of psychosis proneness. This limits the potential applicability of these findings to research using clinical schizophrenic groups. Despite these limitations, this study has extended previous research by demonstrating that the impairment in flexible

emotion-based learning in patients with schizophrenia is also observed in sub-clinical groups with elevated scores on measures of hallucination and delusion proneness.

Experiment 6

The syndrome of depression is characterised by cognitive impairment including problem solving, attentional set-shifting, planning and inhibition process (Elliott, Sahakian, McKay, Herrod, Robbins & Paykel, 1996; Harvey, Le Bastard, Pochon, Levy, Allilaire, Dubois et al., 2004). Evidence from neurofunctional and neurostructural studies on depression disorders suggests that several areas are implicated with particular reference to the prefrontal cortex (Drevets, 2000a,b; 2003; Kanner, 2004). The PFC has been acknowledged as the anatomical structure largely responsible for executive functions and complex behaviours such as decision-making (Krawczyk, 2002). Decision-making and emotional difficulties are often seen at clinical level in patients with depression and represents landmark symptoms of the disorder (Mansell, Colom, & Scott, 2005; Shenal, Harrison & Demaree, 2003). Research evidence suggests that depression's decision-making ability could be biased by altered sensitivity to reward and punishment (Elliott et al., 1996; Henriques et al., 1994).

Must et al. (2006) investigated the issue of reward sensitivity and emotion based learning in depression using the IGT. By assessing patients with the ABCD and the EFGH version of the IGT (Bechara et al., 2000a, see also Chapter 1 and 3) the authors found altered sensitivity to reward and punishment in depressed patients compared to controls. Major Depressive Disorder (MDD) patients showed high sensitivity to

immediate large reward leading to long-term losses and relative low sensitivity to low frequency high punishment. This pattern of selection lead MDD patients to a sub-optimal performance compared to controls further supporting the findings that depressive features might alter decision-making. Nevertheless the results of Must et al. (2006) are difficult to compare to similar studies investigating reward sensitivity in depression with the IGT.

Dalgleish et al. (2004) explored the effect of a specific psychosurgery procedure for depression (Stereotactic Subcaudate Tractotomy) to reward sensitivity. In this study the IGT performance was tested in 4 groups: patients recovered from depression after psychosurgery, patients not recovered from depression after psychosurgery, patients recovered from depression after drug treatment and healthy controls. Results showed that only patients recovered from depression after psychosurgery presented impaired performance. The psychosurgery group pattern of selection across blocks also suggested altered sensitivity to negative feedback compared to the other three groups. Interestingly the IGT performance of depressed patients did not differ from those of controls, unlike in Must et al. (2006), where depressive features per se do not alter IGT performance. Sensitivity to reward and punishment in depression, as measured by the IGT, has been further investigated in a recent study by Smoski et al. (2008). The authors found a rather paradoxical effect in depressed patients who displayed a better performance at the IGT compared to controls. In attempting to explain the unusual findings the authors advance the hypothesis that depressed participants were less likely to choose from risky decks due to a more effective risk aversive strategy rather than being better learners. Such an interpretation of the finding stresses the possibility that the IGT performance could be affected by factors others than the one outlined by the SMH (Naqvi et al., 2006).

Although the issue of reward and punishment sensitivity in relation to the IGT schedules have been studied in previous research (e.g., Bechara et al.2000a; Tomb et al., 2002) it is not clear how a possible altered sensitivity to reward and punishment, such the one advanced for depression, would interact with the task. A possible way of analysing the issue of depression reward and punishment sensitivity in the context of decision-making is to systematically modify contingencies and investigate how patients and matched controls adjust. Set shifting ability as measured by the WCST has produced inconclusive finding with some studies suggesting impairment related with MDD and bipolar symptoms (Elliott et al., 1996; Martin et al., 1991; Rogers et al., 2004) and other showing no bearing of depressive symptoms (Must et al., 2006). The contingency shift variant IGT used in Experiment 2 could prove useful to investigate both reward and punishment sensitivity issue and assess decision-making ability. Results from Experiment 2 showed how shifting components can further discriminate between controls participants ability to perform the standard IGT proving that performance on phase 2 tap on relatively different resources. The results of Experiment 4 further suggest that the autonomic activations profiles during the contingency shifting phase were different from the standard IGT; with anticipatory activation guiding performance on the standard IGT and appraisal correlating with good performance during the shift.

Borkowska and Rybakowski (2001) suggested that WCST performance of people affected by mood disorders can be influenced by symptom severity. Symptom severity and heterogeneity of presentation within the same diagnostic label could greatly affect the results of specific clinical groups and the comparability across similar studies (Chen, Eaton, Gallo & Nestadt, 2000). Similarly, the use of different medications and comorbid

diagnosis are often under-considered aspects that could influence the results. An interesting way to control for symptom severity and account for medication history would be to investigate reward sensitivity and decision-making ability in the depressive features of the general population. Mood, unlike psychotic experiences has for long been thought of as a dimensional and fluctuating aspect present in the general population (Lucht, Schaub, Meyer, Hapke, Rumpf, Bartels, et al., 2003; Karasz, 2008). Rating instruments, such as the Beck Depression Inventory, have been used to screen for depressive features and to assess intervention improvement (Beck et al., 1996). It is, therefore, possible to distinguish high and low level depression at the non-clinical level and compare the extreme of non-clinical distributions. Similarly to Experiment 5 this was the approach used in Experiment 6. Depression features were screened in a population of healthy students and the extremes of the distribution obtained were invited to take part in an experimental session evaluating decision-making through the use of the contingency shift variant IGT.

Method

Participants

There were two stages of participants' recruitment for Experiment 6. First, a large cohort of students was screened in order to comprise the participant groups. Second, those participants invited for further study were tested in a laboratory and were compensated with £5.00. This study was reviewed and approved by the Department of

Psychology, Swansea University Ethics Committee. Written informed consent was obtained from all participants before their entry in the study.

Two hundred and twenty seven Swansea University students were administered the Beck Depression Inventory (BDI, Beck et al., 1996), Launay-Slade Hallucination Scale (LSHS; Launay & Slade, 1981; Larøi et al., 2004) and Peters Delusions Inventory (PDI; Peters et al., 1999, 2004). Psychosis proneness measures were administered due to the effect shown on the contingency-shift phase in experiment 5. One hundred and fifty three of these participants were female and 74 were male. The mean age of this sample was years 21.11 (SD = 4.75). Scores on the BDI served as the basis for inclusion in the study. Participants in the top and bottom 15% of the total score distribution BDI were placed in to high and low groups for these scales, respectively. These individuals were then invited to participate in a further experimental session comprising administration of the contingency-shifting variant IGT. Fifty of the 64 invited participants agreed to complete the second session, yielding a final sample of 25 High- and 25 Low-BDI. None of the participants involved in the second session reported substance abuse problem, brain injury or mental health condition.

Measures: Depression

Beck Depression Inventory (BDI; Beck et al., 1996) is a self-report measure for depression widely used in clinical and research settings. The BDI is a 21-item questionnaire asking about feelings over the past week. The score is a simple sum of the positive answers; each items' score can range form 0 to 3. Total BDI score can range between 0 and 63. Scores are generally interpreted according to four indicative ranges: 0–9 non-depressed, 10–15 not likely to meet diagnostic criteria (dysphoric), 16–23 likely to

meet diagnostic criteria (mild, moderate depression), 24 or above very likely to meet diagnostic criteria (severe depression, MDD) (Kendall & Flannery-Schroeder, 1995). For non clinical young adult population BDI internal consistency scores range form 0.80 to 0.90 with a mean α=0.86 (Canals, Bladé, Carbajo & Domènech-Llabería, 2001; Dozois, Dobson & Ahnberg, 1998) and has a test re-test reliability coefficient of 0.67 reported at 1 month interval (Roberts, Lewinsohn & Seeley, 1991).

Measures: Psychosis proneness

Launay-Slade Hallucination Scale (LSHS; Launay & Slade, 1981; Larøi et al., 2004): Hallucination proneness was assessed using a modified version of the LSHS (Larøi et al., 2004). The scale is composed of 16 items, scored on a 5-point Likert scale, where 0 = "certainly does not apply to me", 1 = "possibly does not apply to me", 2 = "unsure", 3 = "possibly applies to me", 4 = "certainly applies to me". Participants' total LSHS score is the sum of all the item scores and ranges from 0 to 54.

Peters et al. Delusions Inventory (PDI; Peters et al., 1999): Delusion proneness was assessed with the revised 21-item PDI (Peters et al., 2004). The 21-item scale explores life-time prevalence of delusional ideation, using the introductory expression, "Do you ever feel as if [*some people are not what they seem to be*]?" Questions are answered on a yes-or-no basis. When a "Yes" is checked, three additional 5-point rating scales measure distress, preoccupation and conviction associated with the experience. Each "Yes" checked assigns 1 point contributing to a frequency score of reported unusual experiences (range: 0-21). All of the items checked "Yes" also contribute to distress, preoccupation and conviction scores. The final score is the sum of the selection endorsed in the rating subscales. Each subscale can range from 0 to 105. Every "No" answer on the

PDI leads automatically to a 0 score for each subscale. Finally, a total PDI score is obtained by adding the frequency of "yes" checked to all the subscales total scores. The 21-item scale has been used reliably in a large body of research and has high internal validity (Cronbach's $\alpha = 0.82$) and test-retest reliability (Spearman's $r = 0.78$; Peters et al., 1999).

Emotion Based learning measure

Flexible emotion based learning was measure with the *Contingency-Shifting Variant IGT* as employed in Experiment 2. The same task and instructions was administered to all participants.

Results

Table 6 presents mean BDI, LSHS and PDI values for the large sample and the high and low groups. There were 10 females and 15 males in the High BDI group and 10 females and 15 males in the Low BDI group. Reliability scores as assessed by Cronbach's alpha were .84 for the LSHS, .92 for the PDItot, .89 for PDIdis, .85 for the PDIpre, .82 for the PDIcon and .89 for the BDI. Positive correlations were observed between the BDI and LSHS (r=.32, p=0.02) and PDIdis (r=.31, p=0.03).

The High and the Low BDI group were not different in term of age, $t(48)$=-.194, p=.847. T-tests conducted between High and Low BDI group revealed no significant difference in all the PDI scales (all p> .05) and in LSHS score, $t(48)$=-1.69, p=.097. As expected the high and low BDI group were significantly different on BDI scores, $t(48)$=-20.48, p<.0001.

	Group	M/F Ratio	Age (SD)	Mean BDI	Mean PDI Tot	Mean PDI Dis	Mean PDI Pre	Mean PDI Con	Mean LSHS
BDI	All (*n*=227)	74/153	21.11 (4.75)	9.22 (4.67)	43.16 (29.51)	11.95 (8.88)	11.73 (8.96)	14.72 (10.32)	16.34 (10.2)
	High (*n*=25)	10/15	20.48 (2.01)	17.9 (2.99)	62.2 (31.88)	18.16 (10.32)	17.52 (9.44)	21.56 (12.29)	17.9 (2.99)
	Low (*n*=25)	10/15	20.36 (2.18)	1.18 (.99)	43.76 (38.87)	12.4 (12.51)	11.68 (13.21)	14.52 (13.67)	14.18 (10.67)

Table 6: Shows genders ratio, mean age, and mean score (standard deviation) for BDI, PDI total, PDI distress, PDI preoccupation, PDI convinction and LSHS in all participants and in the subsequent High and Low BDI grouping.

Mean net score

Figure 30 shows Phase 1 and 2 mean net score performance for the High and Low BDI groups. In Phase 1 of the IGT, both High and Low BDI groups showed a positive learning pattern, but there were no significant between-group differences on performance. A 2 (group) x 5 (block) mixed factor ANOVA revealed a main effect of block, $F(4, 192) = 6.01$, $p < .0001$. However, there was no significant main effect of group, $F(4, 192) = 1.16$, $p=.33$, or block by group interaction, $F(1, 48) = .96$, $p=.75$.

Figures 30 shows that across Phase 2, performance between the Low and High groups on the BDI began to diverge. A 2 (group) x 6 (block) mixed factor ANOVA performed on the shift phase for High and Low BDI groups showed a significant main effect for group, $F(1, 48) = 5.27, p = .026$, but no significant main effect for block, $F(3.87, 185.6) = 1.49, p = .21$ nor a significant interaction, $F(3.87, 185.6) = .829, p = .53$. Post hoc t-tests showed that the High and Low BDI groups significantly differed in mean net score in blocks 9, 10 and 11 (all $p < .05$).

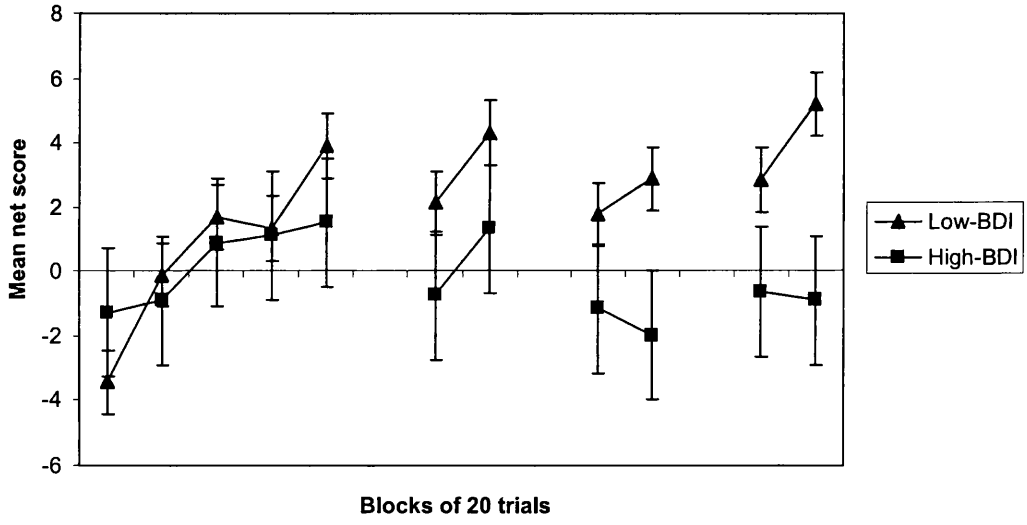

Figure 30: Mean net score performance for the High- and Low-BDI groups for the five 20-trial blocks in Phase 1 and the six 20-trial blocks in Phase 2.

Mean subjective rating

Figure 31 shows Phase 1 and 2 mean subjective rating scores for High and Low BDI groups. In Phase 1 both groups show a similar pattern of awareness increasing substantially from the first to the second block but Low BDI participants display consistently higher scores. A 2 (group) x 5 (block) mixed factor ANOVA revealed a main effect of block, $F(3.2, 153.98) = 3.86$, $p = .005$ and group, $F(1,48)=10.93$, $p=.002$, however, there was no significant block by group interaction ($p > .05$).

During Phase 2 subjective ratings were somehow similar for the two groups. Repeater measure ANOVA showed no effect of block, group or interaction (all $p > .05$).

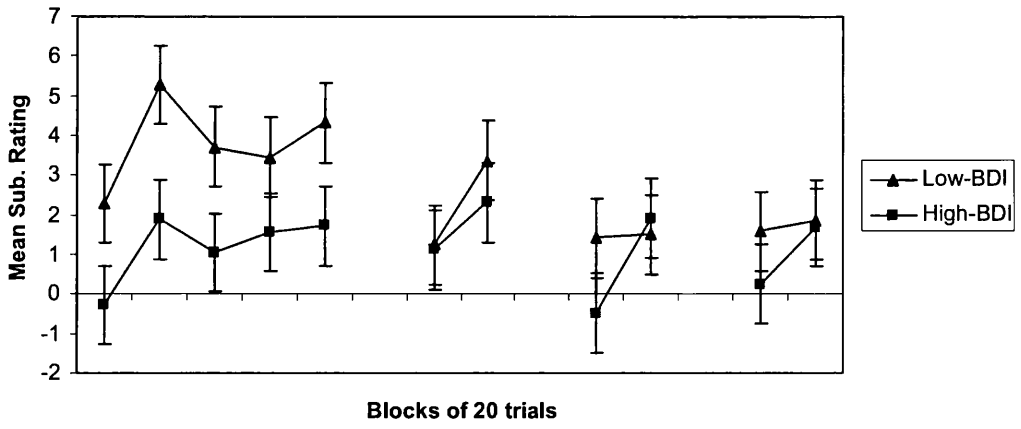

Figure 31: Mean net subjective rating performance for the High- and Low-BDI groups for the five 20-trial blocks in Phase 1 and the six 20-trial blocks in Phase 2.

Investigating sensitivity to reward and punishment in Phase 2

A set of analysis was conducted in order to investigate adaptation to reward and punishment changing scheduled in High and Low BDI scores' group. In particular the current analysis wants to explore how previous contingency history can influence future selections. In order to perform this analysis, levels of Previously Good-Now-Bad selections (PGNB) and Previously Bad-Now-Good (PBNG) were calculated. PGNB selections were those from decks of card that were advantageous in the previous shift or phase and become disadvantageous (i.e. deck C for shift 1, deck D for shift 2 and deck A for shift 3). Reversely PBNG selections were those from decks of card that were disadvantageous in the previous shift or phase and become advantageous (i.e. deck A for shift 1, deck B for shift 2 and deck C for shift 3).

A 2 (group) x 3 (shift) mixed factor ANOVA conducted on levels of PGNB revealed a main effect of shift, $F(2,96)=5.29$, $p=.007$, and group, $F(1,48)=6.79$, $p=.013$ but no interaction, $F(2,96)=.34$, $p=.71$. Follow-up t-test conducted on PGNB selections across the three shifts revealed that the Low BDI score group sampled more from PGNB in shift 1, $t(48)=-1.988$, $p=.05$, and shift 2, $t(48)=-2.23$, $p=.023$.

The same analysis conducted on levels of PBNG did not reveal a main effect of shift, group or an interaction but independent t-test showed a significant difference, $t(48)=2.26$, $p=.028$, between High and Low BDI group in the third shift.

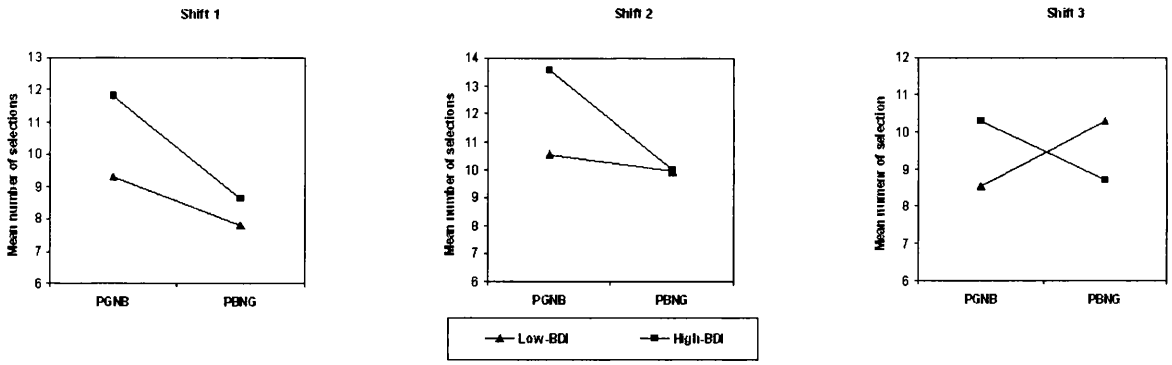

Figure *32:* Mean number of Previously Good-Now-Bad selections (PGNB) and Previously Bad-Now-Good (PBNG) in the Low and the High BDI groups across the three shifts.

Discussion

Experiment 6 investigated the influence of depressive features on flexible emotion-based learning in a general population of young adult non-clinical sample. Participants, grouped according to High and Low BDI scores, showed similar performance during Phase 1 of the IGT. Differently during the contingency shifting phase, the performance of the two groups progressively diverged with the Low BDI group exhibiting a progressive learning pattern and the High BDI group showing performance worsening across the three shifts. Further analysis conducted to investigate difference in performance during Phase 2 showed different PGNB selections across the three shifts for the two groups. In particular High BDI participants selected more from the PGNB decks, compared to the Low BDI participants, in the first and in the second shift. This difference in PGNB selection could be interpreted as a lack of flexibility

displayed by participants with high depressive features. Similarly to the finding gathered with WCST, the ability to adjust to IGT changing contingency might be altered in depression (Martin et al., 1991; Rogers et al. 2004). It is interesting to note the relative stability of levels of PGNB selections in the High BDI group across the three shifts. This might suggest that shifting ability from rewarding to punishing contingencies might be a factor implicated in depression. The temporal trend of PGNB selections is also pointing at the lack of adaptation displayed by High BDI participants. Inflexibility has for long been proposed as an important feature in depressive disorders (Channon, 1996). The results of the current experiment suggest that the altered sensitivity to reward and punishment seen in people with high depressive features may relay on altered emotional based learning process.

The findings of the PBNG are also proving to be interesting. While the PGNB performance seems to be little adjusted across the three shifts for both groups, the PBNG performance is relatively stable for the High BDI group but changes substantially in the Low BDI group. Participants with Low BDI score show, by the third shift, a significantly higher number of selections from the PBNG decks compared to the High BDI group. This might be interpreted as a finer sensitivity to rewarding choices and the ability to apply less stable negative values to shifting contingencies. The difficulty in detaching from previous learnt negative consequences might be also inferred by the progressive worsening seen in the High BDI group during Phase 2. The findings confirm that depressive features are more sensitive to good-bad shifting rather than bad-good and further advance the role of relative higher sensitivity to negative punishment in depression and/or diminish responsiveness to reward (Dalgleish et al., 2004; Henriques et

al., 1994; Shankman, Klein, Tenke & Bruder, 2007). What it is new to this investigation is the notion that depressive features may compromise the ability to perceive unrewarding contingencies becoming rewarding in a changing environment.

Together with the results of Experiment 2 and 5, the results of Experiment 6 show that dissociation is possible between Phase 1 and 2 of the new contingency modified IGT. Participants can perform well during the standard 100 trials of the task and then be affected by the sudden shifting of contingencies during Phase 2. This further suggests that the two phases of the newly modified task may preferentially tap into dissimilar functions and be differentially affected by psychopathological traits.

Subjective rating findings showed the High BDI group display higher levels during Phase 1 compared to the Low BDI group. This finding could be potentially challenging to explain given that previous experiments in this thesis found positive correlations between IGT subjective ratings and performance (e.g., Experiments 2 and 3). Where the relative difference in subjective rating between the two experimental groups might be dependent on depressive features it remains difficult to explain the lack of influence on IGT behavioural performance. One possibility is that the subjective rating of the Low BDI is sufficient to aid the behavioural choice. It is in fact noticeable that the mean subjective rating levels of the Low BDI group across Phase 1 is largely positive and with a similar trend to the High BDI group. It is plausible that subjective awareness would require a minimum level in order to assist behavioural performance or that above a certain level there is no perceived benefit. Alternatively it can be hypothesised that depressive features have little reliance on overt subjective judgment. Subjective awareness levels during Phase 2 proved to be undifferentiated and perhaps lead support

to the hypothesis that subjective ratings might not be an important biasing aspect in individuals with depressive features. Depressed and prone to depression individuals are known, in fact, to be incline to discount their opinion as little accurate or not worth of consideration (Clark, 2001).

The use of non-clinical population, although permit to infer some important process that may relate to depression, does not allow to translate the finding to clinical depression. The finding of the current study might serve as a useful platform for future examination on clinical population. The current results can inform subsequent research on clinical depression regarding the role of medication and long-term clinical history of depression. It is also possible, given the self-assessed nature of the depression screening that some of the participants in the High BDI group were undiagnosed cases of depression. The average BDI value for the High BDI group fell into the moderate depression range therefore it is plausible that some of the High BDI participants could be on the pathway to depression. In this respect the result could contribute to the understanding the role of potential prodromal features related to the development of clinical depression.

Taken together the findings confirm the role of high sensitivity of depression to punishment and support the notion that people with depression have difficulties in adapting to a changing environment (Channon, 1996; Rogers et al., 2004). Previous work conducted on emotion-based learning and depression showed that depressed patients could not perform as well as controls on the IGT (Must et al., 2006). The current findings partially disconfirm this claim showing that depressive features in non-clinical population do not affect IGT performance. It is therefore possible that only exacerbation of symptom

is responsible for the impaired performance observed by Must et al. (2006) or that other factor specific to the their sample composition might have produced the effect. In line with Somski et al. (2008) and Dalgleish et al. (2004) in this study it was found that depressive features do not impair the IGT performance. Further, this study analyse the role of depressive features during the contingency shift variant IGT finding participants with High BDI scores showing altered sensitivity and difficulties to adapt to reward and punishment contingency changes.

Chapter 6

Flexible emotion-based learning in schizophrenia

Chapter 5 investigated the influence of dimensional features of psychopathology using the contingency-shifting modification IGT. The results showed individuals with higher psychopathological features performing sub-optimally during the shifting phase. Individuals with high delusion- and hallucination-proneness, in Experiment 5, showed dissociation during their performance on the Phase 1 and 2 suggesting that proneness to positive symptoms of psychosis negatively influence decision-making in a changing environment. The current Chapter 6 sought to extend the sub-clinical findings to the clinical research domain by recruiting patients diagnosed with schizophrenia and administering the contingency shifting IGT. This design also allows for a timely replication of Turnbull et al's (2006) study with patients with schizophrenia using a fully automated task.

Patients with schizophrenia have been shown to perform badly on the rule-shifting task such as the one indexed by the WCST (Prentice et al., 2008; Stratta et al., 2004). At the cortical level performance on rule shifting task has been associated with the PFC and in particular the dorsolateral portions of the PFC (Miller, 2000). Several studies have employed the WCST together with the IGT in the assessment of PFC functions in people with schizophrenia. The large majority of the studies found that schizophrenic patients would complete fewer categories and made more preseverative errors on the WCST irrespectively of the IGT performance (e.g., Lee et al. 2007; Martino et al., 2007). In other words where the notion of impaired WCST in schizophrenia appears to gather consensus across investigations the IGT findings remain unclear. No study to date has

showed a positive correlation between impaired performance on the WCST and the IGT in schizophrenia, although Brand et al. (2007) found a positive correlation between the last trials of the IGT and the WCST score in a sample of healthy university students.

Areas associated with rule shifting and decision-making have for long been implicated in etiopathological models of schizophrenia (Frith & Dolan, 1996; Nakamura et al., 2008). Cognitive functions anatomically related to the PFC such as working memory, executive functions and social cognition have reliably shown to be impaired in schizophrenia (Bowie & Harvey, 2005; Chan, Chen, Cheung & Cheung, 2004; Lee & Park 2005). Notwithstanding, the prefrontal cortex encompasses numerous sub-regions and larger number of cognitive functions has been hypothesised to have a strong reliance on these regions. In recent years much interest has been gathered by schizophrenia abnormalities in the OFC and VMPFC with a number of studies showing structural and functional abnormalities and neurophatological evidence of impairment (Antonova et al., 2004; Crespo-Facorro, et al., 2000; Pantelis et al., 2003).

The OFC and VMPFC have been indicated to play a critical role in complex decision-making (Krawczyk, 2002). Evidence from this claim comes from a series of studies conducted on patients with acquired VM brain injury exhibiting distinct deficits in real life decision-making especially in situation where social and emotional aspects form integral part of the decision-making process (Bechara, 2004). These studies, as it has been seen in the introduction, were conducted with the IGT. This is why the IGT took a prominent role in the study of decision-making in schizophrenia (see Sevy et al., 2007 for a review).

Although a considerable number of studies have used the same experimental paradigm results are far from consistent. Of the studies that have investigated decision-making performance with the IGT some showed schizophrenic patients underperforming on the task (e.g., Ritter et al., 2004) and some others found schizophrenic patients showing a comparable performance to healthy controls (e.g. Wilder et al., 1998). In the attempt to disentangle possible aspects responsible for the low mean net scores observed in patients with schizophrenia subsequent studies have focussed on various aspects such as different medications (Beninger et al., 2003), co-occurring substance abuse (Sevy et al., 2007), symptoms severity (Rodriguez-Sanchez et al., 2005) and specific symptoms such as catatonia (Bark et al., 2005). Although investigations have spanned a broad range, results do not have a common frame of interpretation and are largely inconclusive (Sevy et al., 2007).

It is remarkable that despite being both PFC related tasks, the IGT and the WCST have showed somehow dissociation in findings. Unlike the WCST, in fact, the IGT has not been found consistently impaired in schizophrenia, hinting at the fact that different process or clinical presentation may influence selectively performance on the IGT. Where both tasks are likely to use a basic number of cognitive resources such as attention, working memory and information processing, the IGT, according to its original formulation it is claimed to require the assistance of an emotional biasing signal (Naqvi et al., 2006). On the other hand the WCST does not account for the biasing influence of emotion and presents frequent variations in the reward schedule across trials. The systematic modification of the contingencies has proven to be highly ecologically valid and problematic in individuals with schizophrenia. Turnbull et al. (2006) suggested that

the variability observed in people with schizophrenia might be dependent on the relative low degree of flexibility implicated in the IGT. Gradual, flexible adjustment to the affective consequences of reward and punishment is a defining feature of performance on the IGT as participants initially choose cards from all of the decks before showing, around halfway through the task, a choice preference for the advantageous decks (Dunn et al., 2006).

In order to test flexibility in the frame of the IGT this thesis has developed, based on Turnbull et al. (2006), a contingency shifting version of the IGT. As described in Experiment 2 the contingency shifting IGT progressively alter the reinforcement contingencies of the card decks following initial exposure to the standard IGT. Over three successive contingency shift periods, card decks that had previously been advantageous became disadvantageous, and vice versa. Thus, the contingency-shifting variant IGT tests the ability of participants to flexibly deal with changing reinforcement contingencies learnt via EBL. Turnbull et al. (2006) compared the performance of a group of patients with schizophrenia classified according to their symptoms (high or low in positive and negative symptomatology) with that of a healthy control group. Results showed comparable learning levels in patients with high positive and negative symptoms and healthy controls during the standard version of the IGT, supporting some previous studies (e.g., Rodriguez-Sanchez et al., 2005; Ritter et al., 2004). During the contingency shift phase of the task, however, patients with schizophrenia high in negative symptoms exhibited markedly poorer performance in adjusting to the changing contingencies relative to both healthy controls and patients high in positive symptoms. The findings of Turnbull et al. (2006) suggest that deficits associated with schizophrenia are specific to

the contingency-shifting phase of the IGT. In addition the results of Experiment 5 seem to support this claim suggesting that high schizoptypal features may impair flexible emotion based learning. In particular positive rather than negative features, in non-clinical populations, account for disadvantageous performance during Phase 2.

In the attempt to consolidate and further expand the findings of Experiment 5, Experiment 7 was conducted to investigate the performance of an outpatient schizophrenic group on the contingency shifting variant IGT. Patients were assessed for positive and negative symptoms, medication, clinical history and demographic information and variables. It is expected that the schizophrenia groups will be outperformed during the contingency shifting phase by the controls but it is difficult to advance any predictions in term of positive or negative symptoms. The study also recorded subjective ratings and explored its potential relevance in interpreting the results.

Experiment 7

Method

Participants

Twenty-five outpatients with schizophrenia and 24 healthy controls were recruited for this experiment. Patients were recruited in the Swansea NHS trust area throughout different Community Mental Health Teams (CMHT) and the local NHS psychiatric hospital. The diagnosis of schizophrenia and schizo-affective disorder was established by the centre psychiatrist on the basis of a structured clinical interview (SCID; First et al., 1996); a comprehensive review of medical records was also

conducted. Patients with a history of neurological disorders or medical conditions known to influence cognition were excluded. Patients with a co-morbid diagnosis of substance abuse were excluded; patients presenting minor addiction issues during the clinical interview were included and addiction type and severity recorded on a scale from 0 to 100. Addiction problem and severity was clarified with the care stuff and clinical notes. All patients were medicated with stable dosage of atypical antipsychotics (risperidone, clozapine, olanzapine or aripiprazole) with no less than a month from the last medication change. All patients recruited stated that medication compliance had been optimal in the two weeks prior to testing. More than half of the patients (n=15) received additional psychotropic medication, most frequently benzodiazepine.

The healthy control group was selected in the local community based on age, gender and education. All normal controls were psychotropic medication free and did not have any history mental illness as assessed by a brief interview. Similar to the patient group, controls did not have history of neurological or medical condition known to affect cognition.

After receiving a detailed description of the research protocol both patients and control participants provided written consent. Swansea NHS trust ethic committee approved this study (REC number: 07/WMW02/31).

Procedure

All the participants with schizophrenia underwent clinical interview aiming to confirm and clarify unclear aspects of the case as appraised from consultation with the care stuff and personal record search. Symptom assessment was undertaken using the

PSYRAT and SANS. The contingency shift modified version of the IGT, as used in Experiment 2 was employed to assess emotion based learning.

Materials

Psychotic Symptom Rating Scale (Haddock et al.,1999): The *Psychotic Symptom Rating Scale* (PSYRATS) is a 17-item scale assessing the multidimensional features of delusions and auditory hallucination in schizophrenic patients (Haddock, McCarron, Tarrier & Faragher, 1999). The scale is administered via an interview; the rater's task is to select the option that best described patient's account. Every item was on a 5 point likert scale (0-4) and provided rating options with increasing severity (e.g. 0= voice not present and 4=voices occur continuously). The scale is designed to rate the multidimensionality of symptoms' severity over the course of the last week providing an accurate account of recent positive symptomatology. The PSYRATS provides two scores: Auditory Hallucinations (11 items) and Delusion Scale (6 items), in addition to this score patients are asked about the presence of other forms of hallucinations. Each of the two scales provides a separate set of multidimensional attributes. The dimensions of the Auditory Hallucination scale are: frequency, duration, location, loudness, beliefs about the origin, negative content, intensity of negative content, amount of distress, intensity of distress, disruption of life and control. The dimensions of the Delusion scale are: amount of preoccupation, duration of preoccupation, conviction, amount of distress, intensity of distress and disruption of life. Total score for Auditory Hallucination scale can range from 0 to 44 whilst total score for the delusion scale can range from 0 to 24.

Scale for the Assessment of Negative Symptom (Andreasen, 1982, 1983): The *Scale for the Assessment of Negative Symptom* (SANS) is a 20-item scale assessing

negative symptoms associate with schizophrenia. The items of the scale are grouped in 5 complexes: affective flattering (7 items), alogia (4 items), avolition-apathy (3 items), anehdonia-asociality (4items) and attentional impairment (2 items). Each item is rated on a 6 point scale ranging from 0 (absence of the feature) to 5 (severe presence). A global rating score item and a subjective rating score item (both ranging from 0 to 5) are included in each complex and accounted in the total score. Total score can range from 0 to 150. The scale is administered via an interview but also draws on subjective observation from care staff and family members.

Contingency Shifting Variant IGT

Phase 1 & Phase 2: The *Contingency-Shifting Variant IGT* as employed in Experiment 2, with the same decks contingencies and instructions, was administered to all participants. In addition to the version used in previous experiments the version employed in this study played tones after each card selection. Two types of tones were included in this task, one following trials with positive outcome (i.e. no money loss) and another following trials with punishment. This additional feature was according to the Bechara et al. (1999) IGT computer version. Patients were given few mock trials in order to provide familiarization with the computer and the requirements of the task.

Results

Sociodemographic and clinical characteristics

Sociodemographic and clinical characteristics of the schizophrenia and the control group are presented in table 7. There were no differences between the groups for age, $t(47)=1.41$, $p.=166$, gender distributions, $\chi^2(1)=.214$, $p=.77$, ethnicity $\chi^2(1)=1.06$, $p=.47$ and marital status $\chi^2(1)=4.19$, $p=.12$ (Yates' corrected), but a significant difference was detected for years of education, $t(47)=-3.53$, $p=.002$ and employment status $\chi^2(1)=45.99$, $p<.0001$(Yates' corrected).

Table 8 shows PSYRATS and SANS mean (standard deviation) scores for the clinical group. As suggested by Steel, Garety, Freeman et al. (2007) PSYRATS items are presented separately. Values of the SANS and PSYRATS are comparable to previous investigation (Drake et al., 2007; Klimidis, Stuart, Minas, Copolov & Singh, 1993).

	Schizophrenia (N=25)	Controls (N=24	t or χ^2
Age	39.24 (10.54)	35 (10.51)	$t(47)=1.41$ p=.166
Gender (M/F)	15/9	11/14	$\chi^2(1)=.214$ p=.432
Education (yrs)	13.4 (2.12)	15.38 (1.76)	$t(47)=-3.53$ p=.001
Ethnicity			
White	25	23	$\chi^2(1)=1.06$ p=.47
Black	0	1	
Employment			
Unemployed	23	0	$\chi^2(1)=45.99$ p<.0001
Working	0	20	
Student	2	3	
Retired	0	1	
Cigarette per day	13.01 (2.59)	4.84 (.99)	$t(47)=5.42$ p<.0001
Substance abuse problem (number)	13	0	
Substance abuse severity (from 0 to 100)	14.2 (21.6)		
Last hospitalization (weeks)	75.36 (75.38)		
Age of onset	23.04 (6.33)		
Illness duration (yrs)	16.44 (8.96)		
Psychiatric hospitalization	5.12 (4.88)		
CBT for psychosis	16/25		

Table 7: Demographic and clinical information for the schizophrenia and the control groups. Difference was tested with t-test or chi square test as appropriate, p values are reported.

		Mean (SD)
PSYRATS Hallucination	Frequency	1.12 (1.2)
	Duration	1.36 (1.44)
	Location	1.64 (1.7)
	Loudness	2.12 (1.01)
	Beliefs about origin	2.04 (1.09)
	Amount of negative content	1.44 (1.66)
	Intensity negative content	1.28 (1.51)
	Amount of distress	1.52 (1.66)
	Intensity of distress	1.32 (1.41)
	Life disruption	1.16 (1.28)
	Control	1.32 (1.55)
	Total Auditory Hallucination	16.16 (13.4)
PSYRATS Delusion	Amount of preoccupation	1.08 (.95)
	Duration of preoccupation	1.2 (1.04)
	Conviction	1.52 (1.04)
	Amount of distress	1.56 (1.32)
	Intensity of distress	1.24 (1.2)
	Life disruption	1.32 (1.14)
	Total delusion	7.52 (6.31)
SANS	Affective flattering	9.08 (9.05)
	Alogia	3.44 (5.12)
	Avolition-apathy	2.84 (3.43)
	Anehdonia-asociality	6.7 (4.88)
	Attentional impairment	4.32 (3.55)
	Global rating	4.16 (4.17)
	Total SANS	30.52 (25.99)

Table 8: PSYRATS and SANS mean (standard deviation) scores for the clinical group.

Table 9 shows the correlations between positive and negative symptoms dimensions and history of mental illness variables. In this case both positive and negative symptoms correlate negatively with the length of time elapsed (in weeks) since the last psychiatric hospitalization.

	PSYRATS Hallucination	PSYRATS Delusion	PANS
Last Hospitalization	-.27*	-.526**	-477*
Illness Duration	-.04	.15	.224
Number of Hospitalization	.34	.27	.35

*p<0.01 **p<.001

Table 9: Correlations between PSYRATS delusion, PSYRATS hallucination and SANS with history of mental illness variables.

IGT Performance

Figure 33 shows mean net score performance of the schizophrenia and the control group during Phase 1 and Phase 2. A quite distinct pattern of learning can be observed, with the controls displaying improvement across the first 5 blocks whilst the schizophrenia group displays a constantly below chance pattern. A 2 (group) x 5 (block) mixed factor ANOVA conducted on phase 1 revealed a main effect of block $F(2.9, 138.39)=8.87$, $p<.0001$, group $F(1, 47)=18.84$, $p<.0001$ and interaction F(2.9,

138.39)=9.41, $p<.0001$. Within group contrast analysis showed a significant decrease between block 2 and 3 in the schizophrenia group, F(1,24)=4.41, $p=.046$, and a significant increase in the control group between block 1 and 2, F(1,23)=24.9, $p<.0001$. Follow-up between group ANOVA showed a significant higher performance of the control group for block 3, 4 and 5 (all $p<.05$).

A similar analysis was conducted for phase two. A 2 (group) x 6 (block) mixed factor ANOVA revealed a significant main effect of group, F(1,47)=25.82, $p<.0001$, but no significant main interaction, F(3.47, 163,09)=.249, $p=.88$, or block, F(3.47, 163,09)=.1.84, $p=.13$. Post-hoc independent t-test conducted on each block of the phase two revealed a significant difference in all the comparisons ranging from $p<.0001$ of block 9 and 10 to $p=.006$ of block 7. Repeated measure t-test conducted within the schizophrenia groups did not show any significant performance improvement in any of the three contingency shifts. Similarly for the control participants a significant improvement between the first and the second block of each shift was not observed.

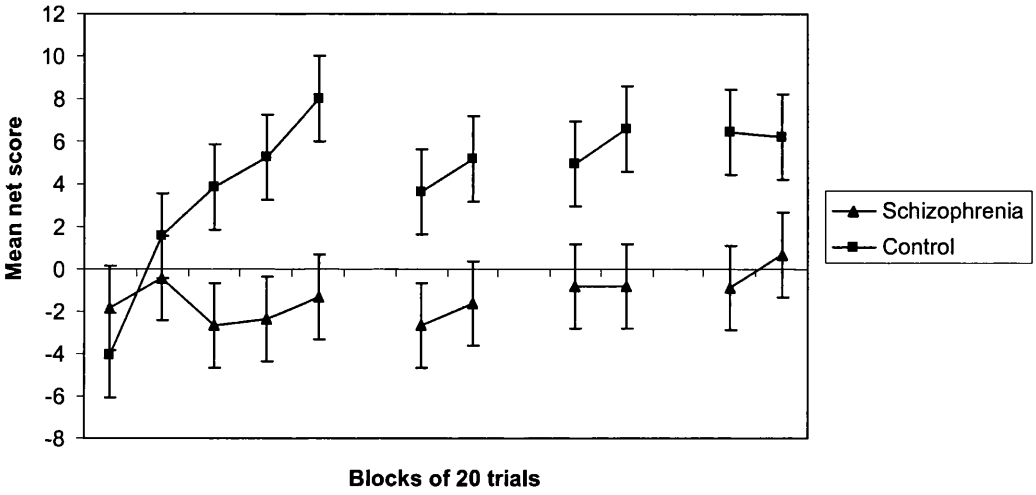

Figure 33: Mean net score performance for schizophrenic patients and control group during the five 20-trial blocks of Phase 1 and the six 20-trial blocks of Phase 2.

IGT Subjective Rating

Figure 34 shows mean net subjective rating for the two groups during Phase 1 and 2. A 2 (group) x 5 (block) mixed factor ANOVA conducted on Phase 1 revealed a main effect of block, $F(3.37, 158.6)=10.05$, $p<.0001$, group, $F(1, 47)=13.34$, $p=.001$, and interaction, $F(3.37, 158.6)=13.04$, $p=.009$. Within group contrast analysis showed a significant improvement in subjective rating between block 1 and 2, $F(1,23)=4.33$, $p=.049$, and block 2 and 3, $F(1,23)= 11.78$, $p=.002$, for the control participants and between block 1 and 2 for the schizophrenia group, $F(1,24)= 7.01$, $p=.014$. Follow-up between group ANOVA showed significantly higher performance of the control group for block 3, 4 and 5 (p values between .04 and <.0001).

A 2 (group) x 6 (block) mixed factor ANOVA was conducted to investigate groups subjective rating on Phase 2 revealing a significant main effect of block, F(3.76,

176.62)= 4.83, p<.001, but failing to show any significant main effect for group, F(1,47)= 3.67, p =.061, or any interaction, F(3.76, 176.62)= 1.36, p=. 241. Post-hoc independent t-test conducted on each block of Phase 2 revealed a significant difference in block 6, t(47)=-3.19, p=.003, but failed to show any significant difference in the remaining blocks. Repeated measure t-test conducted on the schizophrenia groups showed significant subjective rating improvement during the first contingency shift, t(24)= -3.41, p=.002. Differently significant improvement in subjective rating during Phase 2 was noted for the control group in the second shift, t(23)= -2.31, p=.03.

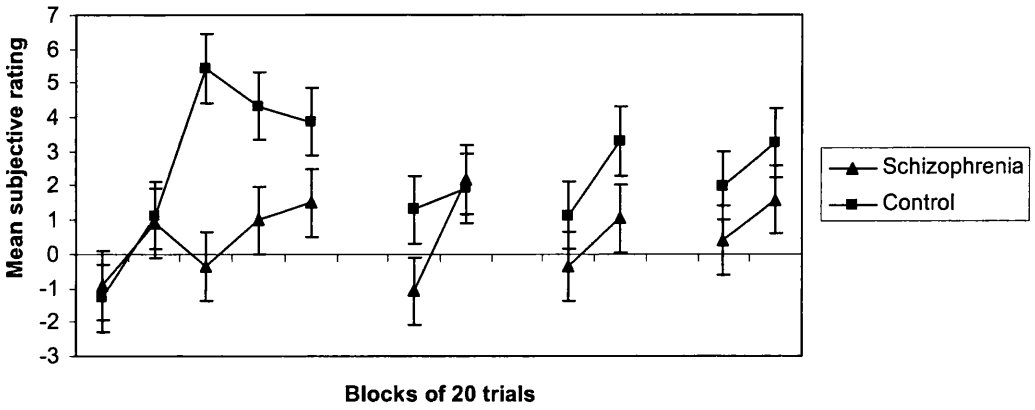

Figure 34: Mean net subjective rating for schizophrenic patients and control group during the five 20-trial blocks of Phase 1 and the six 20-trial blocks of Phase 2.

Investigating schizophrenia failure

The previous analysis showed schizophrenic patients underperforming in both Phase 1 and 2 compared to controls. To clarify the contribution of different symptoms to the task a further set of analysis was conducted. For the purpose of the analysis the schizophrenic groups was subdivided in high (n=11) and low (n=14) delusional ideation

(cut-off score =10), high (n=12) and low (n=13) hallucinations (cut-off score =15) on the basis of the PSYRATS scores and in high (n=13) and low (n=12) negative symptom (cut-off score =20) on the basis of the SANS scores.

A 2 (group) x 5 (block) mixed factor ANOVA conducted on Phase 1 for the high and low delusion groups did not reveal a significant effect of block, F(2.69,62)=1, p=.412, group, F(1,23)=.13, *p*=.719, or interaction, F(2.69,62)=2.19, *p*=.076. A 2 (group) x 5 (block) mixed factor ANOVA conducted on Phase 1 for the high and low hallucination groups did not reveal a significant effect of block, F(2.48, 57.19)=.83, *p*=.464, group, F(1,23)=.3.39, *p*=.08, or interaction, F(2.48,57.19)=3.43, *p*=.76. A 2 (group) x 5 (block) mixed factor ANOVA conducted on Phase 1 for the high and low negative symptoms groups did not reveal a significant effect of block, F(2.51,57.85)=.81, *p*=.47, group, F(1,23)=.72, p=.4, or interaction, F(2.51,57.85)=.23, *p*=.84.

Similar set of analysis was performed on phase two. A 2 (group) x 6 (block) mixed factor ANOVA conducted on Phase 1 for the high and low delusion groups did not reveal a significant effect of block, F(2.8,64.2)=.93, *p*=.46, group, F(1,23)=2.41, p=.134, or interaction, F(2.8,64.2)=.93, *p*=.88. A 2 (group) x 6 (block) mixed factor ANOVA conducted on Phase 1 for the high and low hallucination groups did not reveal a significant effect of block, F(2.89, 66.44)=.93, *p*=.43, group, F(1,23)=.088, *p*=.77, or interaction, F(2.89, 66.44)=1.22, *p*=.30. A 2 (group) x 6 (block) mixed factor ANOVA conducted on Phase 1 for the high and low delusion group did not reveal a significant effect of block, F(2.74, 63.1)=.99, *p*=.423, group, F(1,23)=.038, *p*=.85, or interaction, F(2.74, 63.1)=.69, *p*=.62.

To further explore the contribution of the clinical scales to other variables implicated in schizophrenia poor performance in the both Phase 1 and 2, two stepwise multiple regression models were performed on the clinical group IGT results. Variables were included and excluded from the final model on the basis of significant values of partial correlation (p in .05 and p out .10, respectively). The first model investigated predictors of total Phase 1 IGT mean net scores. Independent variables as entered in the model were: PSYRATS delusion, PSYRATS hallucination, SANS total, years of education, last hospitalization (weeks), number of hospitalization, flattening affect, alogia, avolition, anhedonia, attention and total subjective rating of Phase 1. Result yielded subjective rating as the only significant predictor of Phase 1 performance (Standardized b= .728 p=.015). Similar analysis was conducted for Phase 2 except from the fact that the dependent variable was the total Phase 2 mean net score and Phase 2 total subjective rating was added to the list of independent variables. Regression model showed two variables significantly contributing to explain performance in Phase 2: the subjective rating of phase 1 (standardized b= 1.38 p=.01) and number of hospitalization (standardized b= -.75 p=.034). Correlation analysis confirmed the positive and significant relation between subjective rating and mean net score in both Phase 1 and 2 with values ranging between .407 to .741 (all $p<.05$).

Finding subjective rating of decks' goodness as a reliable predictor of both phases of the task's performance is not surprising, as it has been shown that good awareness of the nature of the task is usually achieved by the last blocks. In the attempt to clarify the contribution of positive and negative symptoms to subjective awareness two stepwise multiple regression models were performed. The first regression model had subjective

rating during Phase 1 IGT as a dependent variable and SANS score, PSYRATS delusion and hallucination score as independent variables. PSYRATS hallucinations scale was found to be the only significant predictor (standardized b= -.592, p=.002). Differently the same set of independent variables used as predictors for Phase 2 did not reveal any significant predictor.

Discussion

Experiment 7 investigated flexible emotion based learning in schizophrenia using the contingency shifting variant IGT. Compared to controls, patients with schizophrenia displayed significantly poorer performance in both Phase 1 and 2. Although the gap in performance persisted until the end of Phase 2, differences in mean net score appear statistically stronger in Phase 1; it is therefore possible that difference in Phase 2 may result as a consequence of the initial poor learning. The onset of the shifts, in fact, produced a marked decrease in the control group while only marginally influence the performance schizophrenia group. This may be due to the fact that initial learning was not achieved by patient with schizophrenia and therefore the onset of the contingency shift had little to disrupt.

Subjective experience ratings during the task were similarly different during Phase 1 but not in Phase 2. Although the role of subjective experience in clinical IGT performance is still controversial (e.g., Evans et al., 2005), the results of this study suggest awareness of the relative "goodness" and "badness" of the decks may be an important contributor to the behavioural performance. The present findings are in contrast with Evans et al. (2005) where both patients with schizophrenia and control participants

showed advantageous performance and comparably high rates of subjective awareness. Evans et al. concluded that subjective awareness is of substantial assistance to the IGT performance but that it is not impaired in patients with schizophrenia. The result of Experiment 6 supports the claims of the positive correlation between subjective awareness and IGT performance but showed that people with schizophrenia have difficulties both in selecting and identifying advantageous decks. This finding is also supported by previous research that has suggested that awareness of the nature of emotional experience and decision-making ability is impaired in schizophrenia (Bar-on et al., 2003; Koren, Seidman, Poyurovsky, Goldsmith, Viksman, Zichel et al., 2004; Lane & Schwartz, 1987).

Regression results in the schizophrenia group further strength the influence of subjective experience on performance even over symptom severity. The findings suggest the possible role of subjective awareness as a moderator between positive symptoms and IGT performance. For both phases subjective rating resulted as the most reliable predictor of IGT performance and its levels were affected by symptoms severity (i.e. hallucinations).

Symptom severity is known to be one of the factors with the greatest influence on IGT performance (Martino et al., 2007; Rodríguez-Sánchez et al., 2005; Turnbull et al., 2006). Yet, the current study did not find an effect of symptomatology or symptom severity on IGT selections per se. Both the regression analysis and the between group comparisons showed no direct but mediated influence through subjective experience. Notwithstanding the role of subjective experience there are several possible factors that may have contributed to the lack of a direct influence between symptom severity and

decision-making performance. First, the small number of participants employed. All the studies employing the IGT in the context of schizophrenia typically recruited 20 to 30 individuals. This number would allow a straightforward comparison between controls and patients but would fall short of statistical power if further subdivided by symptom typologies or severity. As in this thesis, many investigations have advanced claims on the bases of small between group comparison that would benefit from replication in larger samples. Second, the large standard deviation observed in the PSYRATS and SANS instruments might have affected the results. Future research should aim to characterize emotion based learning in more homogeneous groups of patients presenting similar severity and symptoms by, for instance, selecting individuals with similar sympotmatological profile (e.g., auditory hallucination with paranoid theme). Clinical group homogeneity will enhance the accuracy of the analysis and will provide more clear indication to which aspect impairs decision- making ability within the schizophrenia spectrum. It is also possible that the disadvantageous performance seen in the clinical group was not dependent on one factor (e.g., positive, negative, disorganized) but could result from the interaction between different factors. In larger samples this can be investigated by comparing the characteristics of those failing at the task with those having a less disadvantageous performance or an advantageous performance. Alternatively regression model could be applied to relatively large samples of patients.

Interestingly, and despite the limitation in the sample composition noted above, a negative association was found between subjective awareness and hallucinations. This novel finding shows how hallucination severity may play a directly negative influence on awareness of the deck contingencies. Perhaps one possible explanation to the largely

inconclusive findings seen in IGT research with people with schizophrenia could be that symptomatology has a direct influence on mediating factors, such as subjective awareness, in the decision-making process. Emotion-based learning has often been described as a process sourcing different cognitive ability to be deployed effectively and dependent on various neuroanatomical structures (LeDoux, 1996; Turnbull et al., 2003). Positive and negative symptoms therefore might influence only a subset of the resources mediating the deployment of EBL. The results of Experiment 5 showed proneness to delusion and hallucination producing a negative effect on performance in Phase 2. In the present experiment, patients with schizophrenia underperformed, compared to healthy controls, from Phase 1. The severity of symptoms, again, may influence performance at various levels with clinical chronic features presenting a bearing on performance form the outset. It also needs to be noticed that disadvantageous performance on Phase 1 is unlikely to result in an advantageous performance on Phase 2 as the contingency shift phase adds further complexity to an already poorly understood task. This was indeed the case for the IGT performance but not, largely, for the subjective rating given by the clinical group. Patient with schizophrenia showed a level of improvement in their subjective ratings during Phase 2. This finding result somehow difficult to explain but could reflect the first step into the understanding of the contingency changing schedules. Speculatively it can be argued that the low performance and subjective rating in the first part of the task suggest that schizophrenic patient do not benefit form emotional biasing signal in order to adjust their behaviour but would need conscious knowledge in order to master a changing environment. It is ascertained by both previous research and the findings of Experiment 5 that positive symptoms affect the experience of reality in

schizophrenia (Sass & Parnas, 2003). The rise in subjective ratings during later stages of Phase 2 could reflect a slow rise in awareness due to habituation to the task.

Although the methodology employed was similar, the findings of Experiment 7 appear in contrast with those of Turnbull et al. (2006). Firstly, in this investigation people with schizophrenia were found to perform significantly worst than control groups in both Phase 1 and 2 of the IGT. On the contrary, Turnbull et al. (2006) found that only a particular sub-group of patients with high negative symptoms underperformed during the contingency shift phase. In contrast with Experiment 6, the between group comparisons performed by Turnbull et al. (2006) included the control group (i.e. control group, high negative symptoms group and low negative symptom group). The analysis presented showed a main effect of group, but in the absence of a post-hoc test the claim that negative symptoms affect contingency-shifting can not be accurately supported. At first sight, the groups reported in the current Chapter could have been used in a similar fashion although a more conservative statistical analysis (i.e., compare high and low symptoms in clinical population sub-groups) discounted a direct bearing of symptoms on performance. In Experiment 7, direct comparisons between high and low symptom sub-groups did not reveal any difference in performance. Turnbull et al. (2006) claimed that negative symptoms are implicated in flexible emotion based learning ability rest only on a approaching significance value ($p=.077$) of a regression model having IGT Phase 2 as a dependent variable and negative symptoms as independent variable. The results of Turnbull et al, (2006) do not provide strong evidence in support of detrimental influence of negative symptoms on Phase 2 within the schizophrenia group. Similarly, the findings

of Experiment 7 do not provide support to a direct implication of symptom severity, as measured by PSYRATS and SANS, on IGT performance in schizophrenia.

A number of limitations need to be noted in the interpretation of the current findings. First, the average number of years of education was significantly different between the clinical and control group. Although having more years of education is regarded to have a positive effect on neuropsychological tests this has been showed to have a negative correlation with the IGT performance (Evans et al., 2004). Second, as suggested by Sevy et al. (2007), the large variance in clinical and control groups performance coupled with a relative low number of subjects in each group could affect results. Third, more than half of the clinical sample received adjuvant psychotropic medication. The effect of this add on medication was difficult to control in the analysis given that patients were prescribed with different medications and dosage. Future studies should devote effort to control for clinical heterogeneity and attempt to clarify emotion-based learning performance in well-defined clinical groups.

In conclusion, Experiment 7 found that patients with schizophrenia showed impaired performance during the contingency shifting variant IGT and showed no adjustment during the shift phases. Subjective experience in the group with schizophrenia was lower than controls and had a significant bearing on performance. The hallucination subscale of the PSYRATS was the only symptom dimension that predicted subjective awareness.

Chapter 7

Flexible emotion-based learning in depression

Chapter 6 showed that clinically relevant psychopathological features can substantially impair the decision-making performance on the contingency shifting IGT. The results of Experiment 6 suggested the relevance of depressive features to emotion-based learning in the general population. In particular, Experiment 6 showed that people with high depressive features failed in performing advantageously during the course of Phase 2 of the contingency shifting IGT, demonstrating that depressive features can compromise shifting ability. Findings gathered with non-clinical populations, as in Experiment 5 and 6, may help to inform subsequent studies conducted on clinical populations and clarify the effect of symptom severity and medication on decision-making performance in depression. The current Chapter 7 sought to extend the sub-clinical findings on depressive features to patients diagnosed with clinical depression.

A large number of cognitive impairments are characteristic of clinical depression including set-shifting and decision-making ability (Elliott, et al., 1996; Harvey et al., 2004). At the cortical level, the contribution of the prefrontal cortex has often been claimed to be crucial from the ethiopathogenesis of depressive traits and especially for executive functions impairment (Drevets, 2000a,b; 2003; Kanner, 2004). The wide emotional disturbance seen in depressive patients in conjunction with cognitive and neurofunctional deficits leads to the hypothesis that the decision-making impairment seen in depressive patients could be due to a deficit in the emotion-based learning system (Must et al., 2006). In particular, the abnormalities observed in emotional arousal following reward and punishment have been proposed as the main dysfunctional

mechanism accounting for the poor decision-making observed in people with mental illness (Dunn et al., 2006). The results of Experiment 6 showed that during Phase 1 of the IGT individuals with high depressive features did not differ in their decision-making performance compared to participants with low depressive features. However, during Phase 2 high depressive features compromised flexible emotion based learning and the ability to adapt to changing contingencies. According to this result it is possible to expect that those diagnosed with clinical depression will display similar impairment during Phase 2. Unlike Phase 2, it is difficult to predict the performance of depressive patients on Phase 1. Previous investigations have showed mixed performance of depressed patients on the standard IGT, with one study showing impairment of clinically depressed patients (Must et al., 2006), another study showing similar performance between depressed and control participants (Dalgleish et al., 2004) and a more recent study showing depressive patients outperforming control participants (Smoski et al., 2008). Although these studies had similar research questions, they present several potentially critical differences that might have affected the results. Firstly, in the study by Smoski et al., (2008), depressed patients were identified only on the basis of Hamilton depression scale (HAM-D, Miller, Bishop, Norman & Maddever, 1985) scores of 13 or higher. Even if highly prodromic, high scores on this scale does not represent a sole criterion for clinical diagnosis for depression. Further, in the same study, participants were not recruited through clinical settings but recruited from the normal population through a newspaper advertisement. The lack of help seeking behaviour and the missing information about co-morbid diagnosis might make Smoski et al.'s depressed sample different from the participants recruited in the other two studies conducted by Must et al.

(2006) and Dalgleish et al. (2004). Secondly, medication was sparsely accounted throughout the three studies; Smoski et al. (2008) did not record medication history, Must et al. (2006) detailed various different medications taken by the depressed patients, while Dalgleish et al. (2004) only recorded that one of the clinical groups tested took antidepressant medication and recovered. Thirdly, Dalgleish et al., (2004) compared four small groups of patients (i.e., ten or less) and some patients in these groups had a diagnosis of bipolar disorder. Clark et al. (2001) have shown that manic features have a particular effect on IGT performance. Manic patients tend, in fact, to select more often from disadvantageous decks than controls but overall they select more cards from the advantageous decks. The presence of bipolar patients in the depressed group, therefore may have influenced the findings of Dalgleish et al.

Experiment 8 sought to investigate the performance of depressed patients on the contingency shifting IGT. The potential advantage of this study would be to contrast the findings with the results of Experiment 6 and clarify whether symptom severity affects the performance on the IGT and if depressed patients would show a comparable performance to healthy controls during Phase 1.

Experiment 8

Method

Participants

Nineteen outpatients with major depressive disorder (MDD) and 20 healthy controls were recruited for this experiment. Patients were recruited from the Swansea NHS trust area via several Community Mental Health Teams. Demographic characteristic

of the participants are summarised in Table 9. The diagnosis of depression was established by a trained member of the mental health team (e.g., psychiatrist, psychologist, mental health nurse) with structured clinical interview (SCID; First et al., 1996). A comprehensive review of medical records was also conducted. Patients with a history of neurological disorders or medical conditions known to influence cognition were excluded as well as patients with a history or presence of substance abuse. Presence of psychotic and maniac features was considered an exclusion criterion.

All patients were taking stable dosage of antidepressant medications (i.e.,venlafaxine, fluoxetine, zoloft, imipramine, duloxetine) with no less than a month form the last prescription change. All patients recruited stated that medication compliance had been optimal in the two weeks prior testing. Only two patients received adjuvant psychotropic medication (in both cases mood stabiliser: lithium carbonate).

The healthy control group was selected in the local community based on age, gender and education. All normal controls were psychotropic medication free and did not have any history of mental illness as assessed by a brief psychiatric interview. Similar to the patient group, controls did not have history of neurological or medical condition known to affect cognition.

After receiving a detailed description of the research protocol both patients and control participants provided written consent. Swansea NHS trust ethic committee approved this study (REC number: 07/WMW02/31).

Materials: Beck Depression Inventory, BDI-II (Beck, Steer and G.K. Brown, 1996).

The Beck Depression Inventory-II (BDI-II) is a self-report questionnaire assessing depression over the past fortnight. The scale consists of 21 items assessing

symptoms relating to physical concerns, such as sleep disturbance and loss of weight, emotional state, hopelessness, sorrow, motivation, willingness to work, and cognitive aspects, such as concentration and self-evaluation. Each item presents 4 sentences ranging from neutral (0) to a maximum level of severity (3), and the subject chooses one according to his/her experience during the previous fortnight. The BDI total score is the sum of the points across the items. Indicative cutoffs scores for depression severity are suggested: 0–13: minimal depression; 14–19: mild depression; 20–28: moderate depression; and 29–63: severe depression (Richter, Werner, Heerlein et al. 1998). Higher total scores indicate severe depressive symptoms

Measure of Emotion-Based Learning

Flexible emotion based learning was measured with the *Contingency-Shifting Variant IGT* as employed in Experiments 7. The same task and instructions were administered to all participants. Patients were given few mock trials in order to provide familiarization with the computer and the requirements of the task.

Results

Sociodemographic and clinical characteristics

Sociodemographic and clinical characteristics of the depression and the control groups are presented in Table 10. There were no differences between the groups for age $t(37)=-.19$, $p=.84$, years of education, $t(37)=-.57$, $p=.57$, gender distributions, $\chi^2=.24$ $p=.75$, ethnicity and employment status $\chi^2=6.31$, $p=.17$(Yates' corrected). Not surprisingly the two groups present a highly significant difference in BDI scores $t(37)=17.96$, $p<.0001$.

	Depression (N=19)	Controls (N=20)	t or X^2
Age	35.79 (10.65)	35.15 (9.38)	$t(37)$=-.19 p=.84
Gender (M/F)	11/8	10/10	X^2=.24 p=.75
Education (yrs)	14.47 (2.5)	14.9 (2.2)	$t(37)$=-.57 p=.57
Ethnicity			
White	19	20	
Other	0	0	
Employment			
Unemployed	4	0	
Working	9	15	X^2=6.31 p=.17*
Student	1	3	
Retired	5	2	
BDI	30.11 (7.2)	0.85 (1.08)	$t(37)$=17.96 p<.0001
Age of onset	25.58 (6.44)		
Illness duration (years)	10.21 (6.17)		
Last hospitalization (weeks)	41.63 (37.17)		
Number of Hospitalization	0.68 (1.06)		

Table 10: Demographic and clinical information for the depression and the control groups. Difference was tested with t-test or chi square test as appropriate, p values are reported. *Yates corrected

IGT Performance

Figure 35 shows mean net score performance of the depression and the control groups during Phase 1 and Phase 2. Pattern of learning during Phase 1 is similar for both groups, although controls seem to learn at a faster pace. The mean net score of the depression group did not approach advantageous levels (i.e., above 0) until after the final block of trials in Phase 1. The onset of the shifts in Phase 2 clearly differentiates between the two groups. A 2 (group) x 5 (block) mixed factor ANOVA conducted on Phase 1 revealed a main effect of block, $F(4,148)=10.01$, $p<.0001$, group, $F(1, 37)=12.48$, $p=.001$, but no significant interaction, $F(1. 148)= 1.48$, $p=.21$. Contrast analysis revealed a significant performance improvement for depressed patients and control participants between the first and the second block, $F(1,37)=20.09$, $p<.0001$. A follow-up between groups ANOVA showed a significant higher performance for the control group for block 2, 3, 4 and 5 (all $p<.05$).

A similar analysis was conducted for Phase 2. A 2 (group) x 6 (block) mixed factor ANOVA revealed a significant main effect of group, $F(1,37)=11.37$, $p=.002$, but no significant main effect for interaction, $F(5, 185)=2.11$, $p=.066$, or block, $F(1, 185)= 0.154$, $p=.98$. Follow-up, between groups, ANOVA conducted to investigate difference in levels of performance during Phase 2 revealed significant difference for blocks 7, 9, 10 and 11 (all $p<.05$).

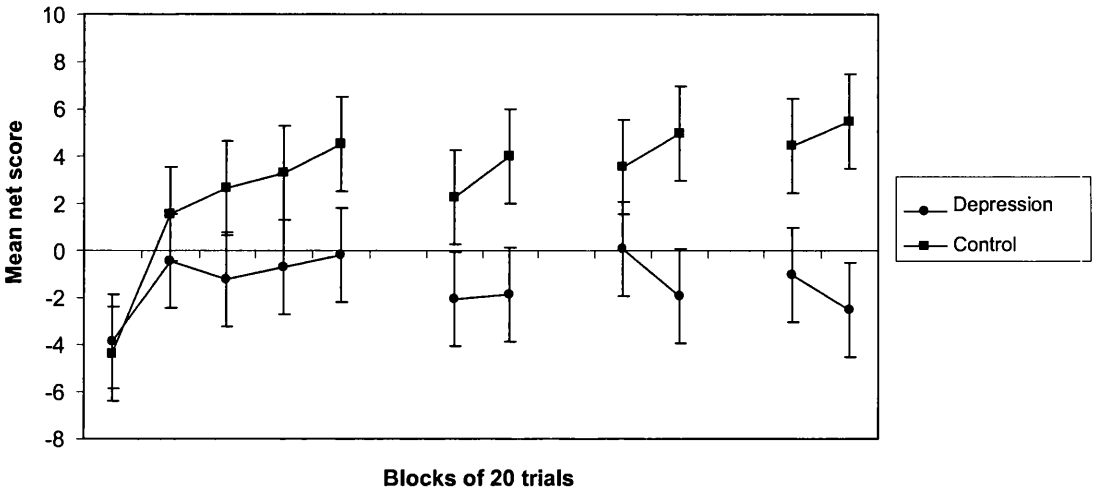

Figure 35: The mean net score performance for depressed patients and control group during the five 20-trial blocks of Phase 1 and the six 20-trial blocks of Phase 2.

IGT Subjective Rating

Figure 36 shows mean net subjective rating for the two groups during Phase 1 and 2. A 2 (group) x 5 (block) mixed factor ANOVA conducted on Phase 1 revealed a main effect of block, $F(3.22, 119.32)=13.83$, $p<.0001$, but no group, $F(1, 37)=1.28$, $p=.28$, or interaction, $F(3.22, 119.32)=0.59$, $p=.6$, effect. Contrast analysis showed a significant improvement in subjective rating between block 1 and 2, $F(1,37)=12.43$, $p=.001$, and block 2 and 3, $F(1,37)= 11.19$, $p=.002$.

A 2 (group) x 6 (block) mixed factor ANOVA was conducted to investigate groups subjective rating on Phase 2 revealing a significant main effect of block, $F(3.39, 125.46)= 5.03$, $p=.002$, but failing to show any significant main effect for group, $F(1,37)= 17.5$, $p=.57$, or any interaction, $F(3.39, 125.46)= 2.47$, $p=. 058$. Post-hoc independent t-

test conducted on the each block of the phase two did not reveal any significant difference between the two groups.

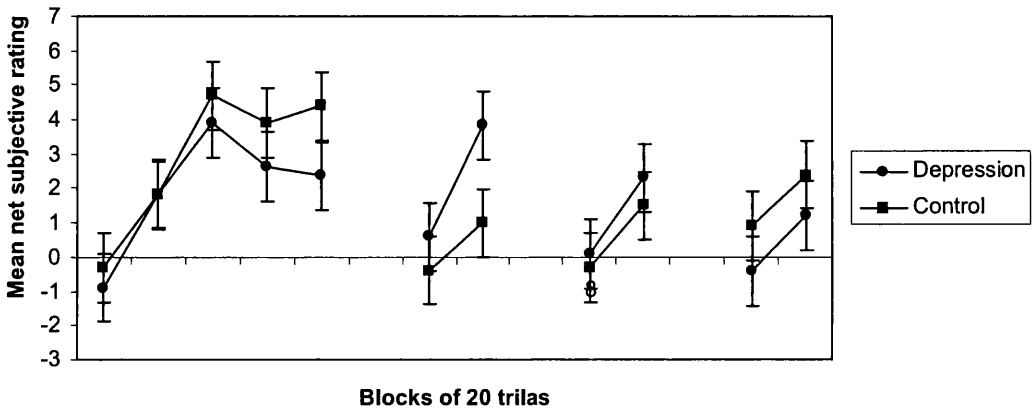

Figure 36: The mean net subjective rating for depressed patients and control group during the five 20-trial blocks of Phase 1 and the six 20-trial blocks of Phase 2.

Deck Preferences

To investigate cause of depression lack of advantageous selections during Phase 1, a 5 (blocks) x 2 (group) ANOVA was performed for each of the four IGT decks. Results revealed depressed patients showing preference for deck A over controls, $F(1,37)=3.74$, $p=.041$, and control participants showing preference for deck D over depressed, $F(1,37)=5.24$, $p=.028$. Levels of Previously Good-Now-Bad selections (PGNB) and Previously Bad-Now-Good (PBNG) were calculated to further explore the cause of the depressed patients' failure during Phase 2. PGNB selections were those from decks of card that were advantageous in the previous shift or phase and become disadvantageous (i.e. deck C for shift 1, deck D for shift 2 and deck A for shift 3).

Reversely PBNG selections were those from decks of card that were disadvantageous in the previous shift or phase and become advantageous (i.e. deck A for shift 1, deck B for shift 2 and deck C for shift 3).

Independent t-test revealed significant difference in the mean selections of PGNB decks in shift 1, $t(37)=2.86$, $p=.007$, and 3, $t(37)=2.93$, $p=.006$, and in PBNG selections in shift 3, $t(37)= -2.04$, $p=.04$, (figure *37*).

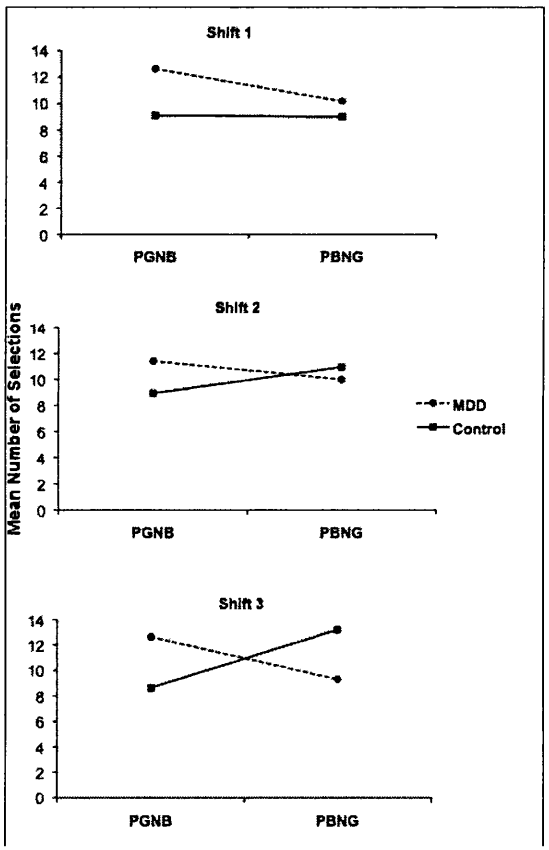

Figure 37: Mean previously good now bad (PGNB) and previously bad now good (PBNG) selection for depression and control group during the three shifts of Phase 2.

Discussion

The results of Experiment 8 showed that depressed patients displayed lower mean net scores compared to healthy controls throughout Phase 1 and 2 of the contingency shifting IGT. Levels of subjective ratings were slightly different for both groups and almost never significant. The findings of Phase 1 provide support for Must et al.'s, (2006) investigation where depressed patients performed worse than controls. The findings of Experiment 8 and those of Must et al. (2006) look remarkably similar, as in both investigations significant differences between the two groups become evident in the third, fourth and fifth block of Phase 1. A main difference between the depressed patients performance in the two studies is the trend. In Experiment 8, depressed patients failed to show improvements in learning after chance level was reached, whereas in Must et al. (2006) depressed patients seem to have a performance involution during the last blocks of the IGT whereby after having reached positive levels of mean net score by the fourth block depressed patients performance returns under chance in the fifth block. In the context of the current work, the performance showed by depressed patients during the contingency shift variant phase resembles the pattern observed for schizophrenic patients seen in Experiment 7. Even if both clinical populations failed to perform advantageously during Phase 1 and 2, the subjective rating of the two clinical groups showed some differences. Experiment 7 has shown that in schizophrenia patients a low level of subjective awareness may be partially responsible for the low performance in the IGT. This cannot be said for depressed patients, as comparable levels of subjective awareness were displayed by the depressed and control groups but in the absence of advantageous

performance. Consistent with Experiment 6, this study found depressed patients showing little or no sensitivity to decks that were disadvantageous and became advantageous.

Although some level of similarity can be found with one of the few studies conducted on depressed people's decision-making ability's (Must et al., 2006), the results of the current experiment appear controversial in respect to other investigations. Dalgleish et al. (2004) and Smoski et al. (2008), for example, presented results showing depressed patients performed at the same or better levels than controls, respectively, on the IGT. As mentioned in the introduction, there are several possible relevant differences between these studies that might have contributed to the heterogeneous findings.

The argument of altered sensitivity to reward and punishment in depression has been used both ways to explain advantageous and disadvantageous performance in depressed patients compared to controls. The results of the current investigation seem to support the view that altered sensitivity could be responsible for the low performance of patients and propose a somehow different picture from Dalgleish et al. (2004) hypothesis that learning on the task could be achieved only by paying attention to the punishing components. The current study found depressed patients selected more from disadvantageous decks with higher frequency punishment of relative lower magnitude than controls (i.e., deck A). This pattern of preference lends partial support to Dalgleish et al.'s hypothesis that only high magnitude punishments are avoided by depressed patients whereas lower magnitude punishments are not perceived as disadvantageous. On the contrary, control participants tended to prefer advantageous decks with low frequency but relatively high magnitude punishment (i.e., deck D). This finding does not support the high magnitude punishment avoidance in depression and suggest how focussing only on

certain aspects of the task (e.g., avoid large punishments) may not be sufficient to achieve advantageous performance. Avoiding large punishments without paying attention to rewards is most likely the strategy that depressed people used during Phase 1. The nature of the IGT implicates that participants have to attend to all the components of their selections and it can be advanced that failing to produce substantive emotional biasing signals for rewards can alter the background of punishment perception.

Must et al. (2006) found that depressed patients with lower HAM-D (i.e. Hamilton depression scale) score more frequently neglected high punishment than did depressed patients with higher HAM-D score. In addition, the results of Experiment 6 provide a further account of the severity of depressive features on decision-making performance in Phase 1. This effect can be related to a selective influence of medication on reward and punishment sensitivity. As advanced by Dalgleish et al. (2004) antidepressants may enhance sensitivity to negative outcomes in order that they can be perceived and avoided. While enhanced sensitivity to reward and punishment is a crucial target of antidepressant medications, the results presented in this experiment suggest that in real life environments a sufficient integration between the sensitivity to positive and negative outcomes is necessary to achieve advantageous decision-making. This is perhaps why Experiment 6 showed a difference between high and low BDI scores only in more challenging environments such as the one that occurred in Phase 2.

During Phase 2, depressed patients showed a lack of ability to adjust to the changing shifting contingences. Interestingly, and similarly to the results of Experiment 6, there was a worsening trend within each shift. The depressed group in this respect present a performance that tend to worsen in the second block of each shift in opposition

to the improvement seen in the same block for the control group. If improvement in the second block can, for the controls, be interpreted as an insight or a correct behavioural adjustment to the changed contingencies; the decline in performance seen in depression can perhaps be interpreted as not only a lack of adjustment but as the pursuit of an ineffective strategy.

PGNB selections showed the depressed group being more attached to the affective consequences of previous positive contingencies and displaying less flexible behaviour to adapt to changing positive pattern. For both controls and depressed participants, there seem to be little adjustment in PGNB throughout the three contingency shifts. Controls showed a better ability to detach themselves from previous good contingency when they become bad. On the contrary the ability to shift from bad to good contingences appears to improve quite substantially in control participants but does not change in depression. In that respect controls and depressed patients create by the third shift a clear example of a double dissociation where controls shows low PGNB and high PBNG levels of selections and depressed patient shows high PGNB and low PBNG levels.

Chapter 8

General Discussion

The work contained in this thesis has explored the concept of emotion-based learning in experimental and clinical settings. Across each of the 8 experiments, the current thesis investigated a range of issues with relevance for understanding the affective components of the decision-making process using the original and contingency shifting variant IGT. This final chapter will attempt to summarise and discuss the main themes that have arisen. The first part of this chapter will summarise and review the findings from each of the experiments presented, while the second part will discuss the overarching topics that have emerged from the empirical studies and the contributions made by the thesis to the broader research literature.

Chapter 1: Emotion based learning overview and critical issues

Chapter 1 presented an overview of the research conducted in the area of emotion-based learning from experimental, clinical and neuroscience perspectives. The term "emotion-based learning" was used to refer to a specific class of learning that occurs in uncertain situations and that is achieved via a substantial contribution of the emotion system (Turnbull et al., 2005). This process aids uncertain decisions by activating previously learnt emotional reactions attached to the outcomes of a similar scenario such as when individuals are required to make rapid decisions in the absence of a clear understanding, or when advantageous outcomes of a decision do not result in an immediate gain (Damasio, 1996; LeDoux, 1996).

The VMPFC was described as the key brain region involved in emotion based learning and the processing of emotional situations in social contexts (Bechara et al., 1999). Further support for the role played by the VMPFC and in general the role of the OFC in emotion-based decision-making comes from clinical studies with brain injured patients. These findings contributed to Damasio's formulation of the Somatic Marker Hypothesis (SMH; Damasio, 1994). The SMH postulates that visceral responses to events in the environment are used to "mark" (positively or negatively) the consequence of actions. In this framework, the VMPFC plays a key role as the structure capable of eliciting visceral responses that reflect the anticipated value of choices (Naqui et al., 2006).

The IGT was developed as an experimental paradigm to test the SMH (Dunn et al., 2006) by measuring decision-making in a way that simulates real world complexity. Initially used to investigate decision-making deficits in people with acquired brain injury,the IGT has more recently become an accepted means of measuring complex decision-making performance in a wide range of participant groups. Chapter 1 described the IGT as requiring participants to select 100 cards (although some studies have employed fewer trials: e.g., Suzuki et al., 2003), one at time, from up to four concurrently available decks of identical physical appearance. Every card selection results in a variable monetary reward or a combination of reward and loss. Over the course of the 100 card choices, neurologically normal participants tend to learn that in order to win money, decks with immediate lower reward but overall positive balance have to be preferred to higher immediate reward decks with overall negative balance. This pattern of selection adjustment is not observed in VM patients (Bechara et al., 1994). Performance on the

IGT is generally defined by an aggregate score of positive minus negative selections called the mean net score. A positive mean net score is indicative of advantageous performance while a negative mean net score corresponds to disadvantageous performance. A number of studies showed an association between VM patients overall negative mean net score on the IGT and lack of anticipatory autonomic activation for negative decks (e.g., Bechara et al., 1994)

In Chapter 1, several issues were advanced as relevant to the interpretation of the burgeoning IGT research findings. First, variability in control participants' performance has been observed in several studies, raising the question of what factors might influence IGT performance in the healthy population. This issue is particularly pertinent given the important comparison role played by healthy control groups in interpreting performance deficits in clinical groups. Second, the cognitive penetrability of the task, a term used to describe the intelligibility of the schedule of wins and losses, has been advanced as a potential problem for the SMH. The creators' claim that the underling reward and punishment schedule of the IGT is impenetrable via conscious cognitive awareness and rests upon the assumption that performance is instead guided by the influence of somatic markers. In this way the cognitive penetrability of the task it is not necessary for learning to occur (Bechara et al., 2005.). A penetrable schedule, measured via concurrent awareness rating or post experimental questioning, would rule out the unconscious influence of emotional activation or at least represent a significant challenge to the theoretical status of the SMH (Dunn et al., 2006; Maia & McClelland, 2004). Finally, the role of reversal learning, the ability to reverse a learned contingency, has also been claimed to have a bearing on decision-making performance as measured by the IGT

(Fellows & Farah, 2005). This argument has been stressed to the point that the VMPFC deficits observed on the IGT have been hypothesised to be entirely dependent on a lack of prior reversal learning ability (Rolls, 2005). The relationship between the IGT and reversal learning ability was highlighted as an empirical testable hypothesis that may further illustrate the interaction between emotional and cognitive factors in determining IGT performance.

Despite these and other potential confounding issues related to the task, the IGT has been extensively used to explore a variety of research questions in many different populations. Chapter 1 described prominent examples of the applications of the IGT in psychopathology (Dunn et al., 2006). Perhaps unsurprisingly, a conspicuous number of studies found that patients with a range of psychopathological disorders display sub-optimal learning profiles on the IGT. Patients with schizophrenia, depression, substance misuse, anorexia and OCD, for instance, displayed, if not consistently, a similar degree of impairment on the IGT compared to the unimpaired learning of control participants (e.g. Cavedini et al., 2002a; 2004a; Dalgleish et al., 2004; Sevy et al., 2007; Verdejo-García & Bechara, 2009). In this way, the variability observed within some clinical groups resembles that seen in some healthy control groups studied using the same task.

Of the clinical disorders mentioned above, research on schizophrenia has gathered perhaps the most inconclusive findings, with a proportion of the studies showing that patients are impaired at the IGT compared to controls and other studies showing identical performance between controls and patients. These inconsistent findings have sparked the hypothesis that particular features (e.g., symptomatology, medication or illness length, concomitant substance abuse) may moderate the decision-making performance within

schizophrenia. In a similar fashion, although with fewer published studies, the research picture on depression looks as inconclusive as the one on schizophrenia, with one study showing patients with depression underperform on the IGT compared to controls (Must et al. 2006), another study showing similar performance (Dalgleish et al., 2004) and a third report showing depressed patients exhibiting superior performance (Smoski et al., 2008).

From the topics reviewed in the first Chapter 1, a number of worthwhile research questions were identified and subsequently investigated in the experimental chapters. Two broad areas of investigation formed the empirical focus of the subsequent chapters: experimental psychology and experimental psychopathology. In particular, the role of variability in control group IGT performance was systematically studied, and findings lead to the development of a novel variant IGT that was deployed with several healthy, sub-clinical and clinical groups.

Chapter 2: The role of time constraints on decision-making

Chapter 2 explored the role of decision-making time constraints on IGT performance (Cella, Dymond, Cooper & Turnbull, 2007). In Experiment 1 the critical decision-making interval was experimentally manipulated in order to study one of the potential factors that may disrupt learning. The research hypothesis was that a shorter available time to make a decision would negatively impact on decision-making performance as measured by the IGT (Bowman et al, 2005). In Experiment 1, the influence of time constraints on decision-making was explored by comparing the performance of health volunteers playing two modified version of the IGT with time constraints (2 s and 4 s, respectively) with a control group playing the original, no time

constraint 100-trial version of the IGT. In addition to selections, the automated procedure systematically measured participants' subjective experience of the decks. Every twenty trials, subjective ratings of the relative "goodness" and "badness" of each of the decks were provided. This measure was introduced to clarify the contribution of overt knowledge on performance and how this may mediate the more intuitive components claimed to shape the decision-making strategy (Turnbull et al., 2005).

Findings showed that reducing the time available during the critical decision-making phase can significantly decrease the number of advantageous selections. Learning profiles were shown to decrease linearly as a function of the time constraint imposed. Therefore, being subjected to time constraints negatively affects decision-making performance. Experiment 1 also showed that participants in each of the experimental conditions had a higher level of subjective awareness ratings than that suggested by previous research (Bechara et al., 1997), hinting at the possibility that covert knowledge of the task contingencies could be an important and under-considered factor in explaining overt IGT performance.

Chapter 3: *Flexible emotion based learning*

Chapter 3 introduced the contingency shifting modified version of the IGT. The experiments reported in this chapter explored the effect of contingency changes on decision-making performance and how quickly normal participants can adapt to sudden modification of a learned pattern of reward and punishment.

In recent years, the role of reversal learning has increasingly been considered essential to perform well on the IGT (Fellows, 2007). This argument is based on the

claim that for some decks, such as deck B that presents one high magnitude punishment every 10 trials, initial selections result in high temporary rewards, followed by punishment after several selections. The paradigm tested in Chapter 3 introduced a contingency shift phase to the standard 100 trial IGT in which the wins and losses of decks are progressively shifted. Immediately after Phase 1, three contingency-shift phases, each consisting of two blocks of 20 trials, were introduced. The onset of each shift phase involved a systematic modification of the reward and punishment contingencies. In order to perform advantageously, participants need to progressively adapt their behaviour to the changing environment.

In the two experiments described in Chapter 3 (Experiment 2 and 3), the potential usefulness of the contingency shifting IGT in assessing emotion based learning profiles of healthy control participants was investigated. Experiment 2 trialled the modified task on a large sample (n= 208) of university students (Dymond, Cella, Cooper & Turnbull, 2009). Learning profiles showed that the onset of each contingency shift produced a disruption in learning rates and that participants progressively adapted to the shifting environment by taking less time to recognise and select advantageous decks. Experiment 2 also supported the findings of Experiment 1 on subjective awareness by showing that early levels of awareness can support or complement performance. Unlike Experiment 1, Experiment 2 showed considerable variability in control participants' performance. It was surprising to find that roughly only one third of the participants reached the advantageous mean net score of plus 10, previously used by Bechara et al. (2002), to classify advantageous performance. The variability in participants' performance observed prompted the distinction between two sub-groups of healthy controls; Learners and Non-

Learners. This classification helped describing two typologies of control participants by exploring their choice selection profiles, subjective ratings and flexible emotion-based learning performance.

In order to determine whether the variability in control participants performance observed in Experiment 2 could be overcome by providing additional learning experience, Experiment 3 exposed another group of participants to the contingency shifting IGT in a second learning session. The findings of the contrast analysis revealed that, in the first block of the second exposure, participants showed immediate positive mean net scores demonstrating that learning was retained from the first exposure. Retention of emotionally learned information has been advanced by the SMH but rarely tested (Bechara et al., 1994; Fernie & Tunney, 2005). The results of Experiment 3 suggested that decision-making performance on the contingency shifting IGT benefits from good level of retention and would need minimal reappraisal.

Chapter 4: Psychophysiological correlates of flexible emotion based learning

Chapter 4 explored, for the first time, the psychophysiological correlates of the contingency shifting IGT. This chapter sought to confirm the role of anticipatory responses in the original 100-trial IGT and clarify the contribution of psychophysiological arousal to learning during the contingency shifting phases.

As in Bechara's studies (1994), the psychophysiological correlates of IGT performance were measured via SCRs. Experiment 4 used a fully automated procedure to record anticipatory and appraisal SCRs responses in a group of healthy individuals. Similar to Experiment 2, the findings of Experiment 4 revealed a large degree of

variability in control participants' behavioural performance. Because of this variability, the psychophysiological data were analysed by contrasting two sub-groups of participants defined by their performance: Learners and Non-learners. This between-group analysis proved useful and showed higher anticipatory SCRs for disadvantageous selections in Learners compared to Non-learners during the standard IGT phases (i.e. Phase 1). Later in the task, during the contingency shift phases, Learners showed higher levels of appraisal SCRs for selections with punishment. The findings suggest that different emotional processes may influence IGT performance in Phase 1 and 2, at least in groups defined on the basis of their behavioural performance. It was argued that anticipatory SCRs may help decision-making in uncertain scenarios while appraisal SCRs sustain decision-making in a changing environment by pairing outcome values with psychophysiological modification.

Chapter 5: Flexible emotion based learning and the dimensionality of psychopathology

In Chapter 5, the relevance of clinical features to flexible emotion based learning was investigated. This chapter explored the usefulness of dimensional features of psychopathology to study decision-making in people with depression and schizophrenia. The conceptual background to the studies contained in Chapter 5 was that milder and non-pathological expression of psychopathological traits as postulated by the dimensional view of psychopathology may influence complex decision-making (Helzer, Kraemer, Krueger, 2006; Linney, Peters & Ayton, 1998).

In Chapter 5, the concept of dimensionality was used to study decision-making processes in the schizophrenia and depression continuum (Johns & van Os, 2001). Two

large samples of young adults were screened for depression, hallucination- and delusion-proneness. The extremes of the distribution obtained were than tested with the contingency-shift variant IGT and their performance compared.

Experiment 5 showed the influence of schizotypal features on the contingency shifting learning profiles. Participant with high delusion and hallucination prone scores (as measured by the PDI-21 and the LSHS) displayed lower levels of advantageous selections during Phase 2 compared to participants with lower scores on the same scales.

Experiment 6 showed that Phase 2 performance was significantly different between putatively healthy participants with high and low depressive features (as measured by the BDI). Participants with high BDI scores found it difficult to learn and adapt to the shifting contingencies of Phase 2.

Taken together, the findings suggest that depression and schizotypal features affect decision-making only when the contingencies start to shift and in general when an increased level of difficulty is added to the environment. People prone to depression and schizotypal individuals do not, per se, have difficulties in dealing with uncertain scenarios but shifted contingencies may alter their ability to deploy emotional signals in order to assist learning.

Chapter 6: Flexible emotion based learning in schizophrenia

Chapter 6 progressed the investigation of how psychotic features may influence decision-making performance. In this chapter, the contingency shifting performance of a group of clinical individuals affected with schizophrenia was examined. Previous research has shown inconsistent findings in relation to schizophrenic performance on the

original and variant IGT with a number of studies showing schizophrenic with impaired learning profile while other showing patient having similar learning profiles to controls (e.g., Beninger et al., 2003; Martino et al., 2007).

In Experiment 7, a sample of outpatients with a diagnosis of schizophrenia and sample of healthy controls were recruited and tested with the contingency shifting IGT. Patients were screened for positive and negative symptoms with the PSYRATS and the SANS (Andreasen, 1983; Haddock et al., 1999). Patients with schizophrenia showed a marked preference for disadvantageous decks throughout Phase 1 and 2, compared to healthy controls. Findings suggest that symptom-severity may impair not only the more complex shifting part of the task but also the initial learning process. When analysed within the patient group, none of the symptom dimensions measured (i.e., positive and negative) were found to have a direct bearing on IGT performance, but it was found that hallucination severity significantly influenced the patients' subjective experience (as measured via subjective ratings). As for most of the previous experiments, subjective experience was found to be a significant predictor of IGT performance. It was postulated that high positive symptom-severity may have negatively influenced IGT performance indirectly by compromising subjective experience.

The results of Experiment 7 support some of the research conducted with the IGT in the context of psychosis and suggest that patients with schizophrenia have impaired emotion-based learning abilities and display difficulties in flexible environments (Martino et al., 2007; Turnbull et al., 2006). It was concluded that inconsistent findings in this area may be due to the unaccounted role of a number of important factors such as medication, diagnostic heterogeneity and co-morbid diagnosis (Sevy et al., 2007).

Chapter 7: *Flexible emotion based learning in depression*

Chapter 7 investigated flexible emotion based learning in depression. The topic of decision-making ability in depression has been largely debated around the theme of altered sensitivity to reward and punishment (Dalgleish et al., 2004). Experiment 8 recruited patients referred for depression to an outpatient mental health clinic and were administered the contingency shifting variant IGT. Results from the depressed outpatients showed a below-chance learning profile during both Phase 1 and 2, compared to healthy controls. Similar to those participants in Chapter 6 (Experiment 6) who were prone to depression, the depressed participants' low level of performance during Phase 2 was associated with decreased sensitivity to select from decks shifting form disadvantageous to advantageous.

Key Findings

The following sections of this final chapter will attempt to discuss the findings of the thesis grouped by topic. Reference to the experimental chapters will be made across the themes extracted in the following sections as different experiments in the course of this thesis have provided evidence for a particular topic.

The use of the IGT as a research tool

This thesis employed the IGT in various settings (i.e., laboratory and applied) and in modified formats (i.e., time constrained original and contingency shifting variant). The findings support the view that the IGT is a complex and multifaceted task capable of providing insight into many aspects related to decision-making such as variability in performance, sensibility to environmental constraint and emotional influence. The task proved to be reliable for both clinical and experimental applications and sensitive to a range of individual differences. Studies with large samples, such as Experiment 2, often showed a considerable degree of variability. In the course of the thesis, participants' variability in performance was investigated through potential contributions made by individual differences (Experiments 6 and 7) and by experimental manipulation of the task related parameters (Experiment 1).

The large pool of variables affecting IGT performance gives credit to the creators' of the task claim that the IGT mimics real life decision-making scenarios (Bechara et al., 1994; 1996; Damasio, 1994). In the real world, it is difficult to predict human decision-making due to the large number of variables present in the environment. In this respect, the IGT may function as a task capable of summing the environmental complexity and contrast effectively the performance of individuals showing less proficiency in social contexts, such as people with psychopathology, compared to healthy individuals.

Although the sensitivity of the IGT to a wide range of factors constitutes a measure of its ecological validity, it renders comparison between studies difficult due to the lack of normative data. A large proportion of the published studies have compared IGT performance with a between-groups experimental design, defining impaired

performance in relative terms (e.g., clinical vs control group). Unlike other neuropsychological tests (e.g., WAIS, BADS), the IGT does not have normative scores that define normal or advantageous performance (Dunn et al., 2006). This thesis has used the IGT both in between-group comparisons (e.g., Experiments 1 & 7) and in a large single group study (Experiment 2). Although the between-group design has shown, in the experiments presented in this thesis and previous published material, several noteworthy findings, clinical applications of the task to individual participants can only be achieved with validated instruments with clear normative scores. In this respect, the present thesis includes one of the first large sample studies to be conducted with the IGT on putatively healthy individuals (Experiment 2). As such, the data contained within the present thesis may help to provide a profile of normative performance that may help clarify the nature of the impairment often seen in clinical groups.

Subjective awareness

All the experiments described in this thesis employed a measure of subjective awareness Based upon Bowman et al. (2005), the method of assessing awareness used in this thesis required participants to provide a quantitative rating of goodness or badness for each deck of cards, every block of 20 trials. The automated, Likert-style ratings allowed in depth evaluation of the levels of awareness across the course of the task and removed the social constraint of providing a verbal a post-experimental self-report to an experimenter (Bechara et al., 1997; 2000a). The systematic and standardised recording of subjective experience allowed the current thesis to accumulate a large body of data

around the topic of awareness, its importance in decision-making and what factors might influence it.

Across all of the experiments, it was reliably found that healthy participants consistently rated advantageous decks better than disadvantageous from a very early stage in the task. In contrast with Bechara et al.'s (2000a) claim that awareness of the task contingencies is reached after two thirds of the game (i.e., by block 60), this work showed that participants' awareness significantly improves after the second block to stabilise around the third block until the end of the task. The subjective experience data suggest that participants are more aware of the task contingencies than previously thought (Bowman et al., 2005; Maia & McClelland, 2004; Turnbull et al., 2005). Such findings ought to prompt a re-thinking of the potential role played by subjective awareness during the IGT and, in general, in decision-making.

However, the role of subjective awareness remains controversial especially in its relation to performance; this can be exemplified using the findings of Experiment 2 and Experiment 7. Experiment 2 showed no difference in subjective awareness between Learners and Non-learners suggesting that high degree of awareness might not be necessarily related to good performance. The performance of schizophrenic patients, in Experiment 7, revealed a different picture where learning rates, as well as levels of subjective awareness, were substantially compromised in the clinical group compared to controls. In summary, subjective awareness, in the course of this thesis, has been found to contribute to, and dissociate from, IGT performance. It is possible that for IGT performance, a number of factors can moderate or mediate subjective awareness (such as hallucination severity in schizophrenia). Based on the data presented in this thesis, it is

plausible to advance that subjective awareness may be an important aspect that contributes to IGT performance, although it may not be necessary. This notwithstanding, the early awareness showed by participants across the experiments suggests that emotion-based learning interacts with conscious processing from an early stage of the task (Bowman et al. 2005; Evans et al., 2005; Maia & McClelland, 2004).

Variability in control performance

In the last fifteen years, a number of research papers have raised the issue of variability in control participants' performance during the course of the IGT (e.g., Bechara et al., 2002; Dunn et al., 2006; Glicksohn et al., 2007). That is, a significant number of IGT participants present a learning profile similar to those obtained with the orginial VMPFC patient groups (Bechara et al., 1994). The term "variability" is used here to refer to the relatively high variance observed in control participants' performance. This is defined by a large standard deviation and a consequent high variance in the control's group total mean net score obtained at the end of Phase 1.

In the experiments presented in this thesis variability was often observed, particularly in Experiment 2. Accounting for a substantial proportion of control participants that fail to perform advantageously on the task is not easy, particularly as few studies have tried to study the phenomenon directly (cf. Caroselli et al., 2006; Crone et al., 2004; Dunn et al., 2006; Glickson et al 2007). Nevertheless, the empirical data presented throughout the thesis showed that variability is indeed often present.

The direct study of behavioural variability (Sidman, 1961) was not in the remit of this thesis and therefore limited material can be used in order to clarify this issue. The

distinction between Learners and Non-learners, adopted in Experiment 2 and 3, proved to characterise well the two sub-groups of healthy participants. The proportion of Non-learners varied between experiments and showed slightly lower levels of subjective awareness. It is also worth noting that the clinical control groups recruited for Experiment 7 and 8 did not include individuals with impaired learning profiles. The university student samples that showed higher levels of variability were generally younger and more educated than the matched controls groups used in the clinical studies. Previous research has shown that both of these factors, young age (Caroselli et al., 2006; Glicksohn et al., 2007) and years spent in higher education (Evans, Kemish, & Turnbull, 2004) are associated with lower learning levels on the IGT. It is possible, therefore, that either of these factors individually, or in combination, may have influenced control groups performance in the present thesis. This area is clearly understudied and warrants further attention by researchers interested in the determinants of behavioural variability.

Clearly, complex decision-making, as indexed by the IGT, it is likely to rest on a multitude of influences. While the SMH seeks to account for a broad and overarching process capable of explaining decision-making, other factors might have a bearing on sub-components of decision-making. For instance, attention to the task contingencies could be affected by high trait anxiety, and have a bearing on learning potentials of the individual (Coles & Heimberg, 2002). Similarly, heavy loading of cognitive functions, such as working memory, could have a detrimental effect on the IGT performance suggesting that emotion-based learning is unlikely to be a "stand-alone" process (Hinson et al., 2002; 2003; Pecchinenda et al., 2006; Turnbull et al., 2005). Nevertheless, a finer

grade understanding of what influences decision-making, such as personality, aging, cognitive impairment, and psychopathology is needed.

The contingency shifting variant IGT

As Bechara et al. (1994; 1997; 2000a) pointed out, the main feature of the IGT is the ability to detect real life decision-making problems in neurological patients with seemingly intact neuropsychological profile but profound decision-making impairment. Although the IGT represented a considerably novel form of neuropsychological testing, and one that has been enormously successful, it did not capture a considerable characteristic of a dynamic environment: variability. Real life situations, in fact, also require attention to change and consequent behavioural adjustment (Goldfried, & Davison, 1994).

In the first attempt to encompass this feature, this thesis adapted the contingency shifting modification of the IGT proposed by Turnbull et al. (2006). The contingency shifting modification of the IGT involved three subsequent modifications of the deck contingencies following the original 100-trial IGT. The relevance of this modification, both to the understanding of possible reversal learning components associated with performance on the original IGT and in exploring flexible behaviour, has been a central theme of the current thesis. Experiment 2 introduced the contingency shifting IGT and explored its usage with a large sample of young adults. Performance on the shift phases was partially dissociable from the performance in the standard/original IGT; this was shown by the fact that some participants with advantageous performance showed a poor performance profile during the contingency shifting phase. The partial dissociation

observed in healthy participant groups hints very strongly that performance during Phase 2 is influenced by several different aspects and that various resources might come into play in governing performance. As a confirmation of the fact that different components might influence performance on Phase 2, Experiment 5 and 6 showed how sub-clinical characteristics of depression and schizophrenia can disrupt learning during Phase 2 but not during Phase 1. This is a finding of particular interest as it shows dissociation in performance between Phase 1 and 2 and suggests how the contingency shifting modification may tap on partially different functions compared to the standard IGT.

The findings of the current thesis illustrate that it has proven very challenging for some groups of patients, as well as for some control participants, to perform advantageously on the contingency shifting phase, showing how complex deciding advantageously and adjusting to new, changing contingencies can be. There is no doubt that the difficulty of the task coupled with the relatively short time available to learn, required a higher order cognitive functions to achieve advantageous performance. Future investigation of flexibility in the emotion based learning environment should focus on factors like sensitivity to reward and punishment (e.g., Must et al., 2006), ability to detach from previously learnt contingencies (e.g., Turnbull et al., 2007) and how history of past emotions modify emotion-based learning (e.g., Turnbull et al., 2007).

Physiological correlates of emotion-based learning

In Chapter 4, if considered as a single homogeneous sample, anticipatory SCR arousal during the standard IGT phase did not follow the predictions advanced by the SMH (Naqvi et al., 2006). Interestingly, an analysis of Learners and Non-learners

demonstrated that higher anticipatory SCR responses for bad decks developed only for Learners. Using a similar between group analysis in Experiment 4 further, confirmed that similar demographic samples holds considerable variability and that low performance on the task corresponded to diminished anticipatory activation during the early trials of the standard IGT. Advantageous performers showed higher SCR activations prior to the selection of bad decks but, at the same time, a substantial proportion of healthy participants fail to perform advantageously in the task and did not produce anticipatory SCRs before disadvantageous selections.

The findings of Experiment 4 neither disconfirm nor provide support for the SMH. The primary contribution of the data presented is in pointing to the limitations of the SMH framework and advocates more research in order to better describe the influence of emotion to human decision-making behaviour. Whether or not the SCR results of Phase 1 can be reconciled with the majority of the previous published literature, the findings concerning Phase 2 autonomic arousal are the first of their kind. The results of Experiment 4 showed that unlike Phase 1, Phase 2 seems to be relying more extensively on the appraisal responses. Learners tended to have higher appraisal SCRs prior to selections with punishment suggesting that emotional reaction to feedback governs subsequent performance rather than the initial, autonomic intuition.

It is difficult to say if the behavioural adjustment leading to advantageous performance in the shifting phase is only dependent on the autonomic response to punishment, as learners in Phase 2 are also those with an advantageous performance profiles in Phase 1. As shown in several experiments presented in this thesis, it is extremely unlikely that disadvantageous performance in Phase 1 results in an

advantageous performance in Phase 2. Therefore, it is possible to advance that sensitivity to punishment, which showed a strong influence on Phase 2 performance, is related to the initial development of anticipatory SCR activation prior to disadvantageous selections (Suzuki et al., 2003).

Participants initially face a novel environment with little certainty about the reward and punishment contingencies embedded within it. As awareness increases and participants extend their experience with the task, anticipatory arousal might become less important in influencing decision-making. At this stage, when the experience with the task is high participants might prefer to base their decisions on the emotional consequences of their behaviour rather on a more intuitive feeling. The adaptation to shifting contingencies necessary to perform advantageously on Phase 2 needs to be seen in the context of past experience on Phase 1. In other words, the appraisal response, that has been showed to be related to advantageous performance in Phase 2, may be related to the anticipatory arousal displayed during Phase 1. The value of anticipatory responses to appraisal is claimed, as part of the SMH, to be a mechanism that serves to consolidate learning into conscious information (Damasio, 1994). The physiological data gathered in this thesis support and extend this claim suggesting that anticipatory responses can influence appraisals even if the learning environment changes.

The dimensionality of psychopathology and its usefulness in understanding clinical phenomena

Experiments 5 and 6 approached the study of IGT performance in schizophrenia and depression using a dimensional approach. Both studies used non-clinical participants

screened for depression, delusional and hallucination proneness and compared high with low ends of the distributions. The dimensionality of psychopathology approach (i.e., considering clinical features as dimensions rather that dichotomous entities; Claridge, 1997) has been increasingly used to study clinically relevant issues. This approach has the advantage of accessing largerer samples, allow higher level of control on confounding variables (e.g., medication influence) and minimal adaptation required of existing experimental task (e.g., Linney et al., 1998; Henry, Bailey & Rendell, 2008). In terms of how this approach may benefit clinical research, both Experiment 5 and 6 provided examples of similar and different effects between clinical and non-clinical populations with high proneness to certain psychopathological features. In Experiment 6, for example, participants with high BDI scores showed, similar to clinically depressed patients (Must et al., 2006), poor performance in Phase 2 evidencing the same lack of adjustment for previous-bad-now-good decks. Findings from Phase 1 showed that the learning profile of the High BDI group is different from the profile of the clinically depressed group.

In general, applying the dimensional approach to psychopathology permits researchers to study relevant features without being constrained by traditional challenges inherit when conducting research in clinical settings and may also allow for identification of potential prodromic signs towards developing clinical disorders (Claridge & Davis, 2003). Recent research has shown that people with high levels of cognitive and emotional disturbances are at greater risk of developing mental illness (Hanssen et al., 2005; Krabbendam, Myin-Germeys, DeGraf, Vollebergh, Nolen, Iedema et al., 2004; Morrison, French, Lewis, Roberts, Raja, Neil et al., 2006). The notion of the dimensionality of

psychopathology, as used in this thesis, can clarify the pre-morbid decision-making performance, provide useful insights with regards to what differentiates clinical and non-clinical population and inform on what may be prodromic the exacerbation of symptoms and their transition to clinical relevance.

Emotion-based learning and schizophrenia

Experiments 5 and 7 explored the theme of emotion-based learning in psychosis. As seen in the first chapter and in the introduction to the specific experimental chapters, this area of research has gathered inconclusive findings with respect to whether or not schizophrenia patients present impairment in emotion-based learning tasks. Some of the studies conducted in this area showed no difference between patients with schizophrenia and control participant (e.g., Cavallaro et al., 2003; Wilder et al., 1998) while other investigations have suggested that patients with schizophrenia present a deficit in emotion based learning (Lee et al., 2007; Martino et al., 2007; Shurman et al., 2005).

The findings gathered in this thesis suggest that emotion-based learning deficits in psychosis follow a gradient of symptom-severity and perhaps interact with medication (Beninger et al., 2003; Rodríguez-Sánchez, et al., 2005). Experiment 5 showed that high-delusion and–hallucination-prone participants presented marked decrements in decision-making performance during the shifting phase, suggesting that shifting and reversal learning deficits can be seen in individuals presenting non-clinical features of schizophrenia (Laurent, Duly, Murry, Foussard, Boccara, Mingat, et al., 2001). Further, in relation to the performance of schizophrenic patients during the standard IGT phase, Experiment 7 showed impaired performance of patients compared to controls.

Unsurprisingly, schizophrenic patients show impaired performance during the shifting phase.

The inconclusive findings of previous research gathered using the standard IGT may suggest that the impaired performance in emotion-based learning tasks in schizophrenic patients could be dependent on different factors such as concomitant substance misuse (Sevy et al., 2007), medication (Beninger et al., 2003) and symptom classification (Bark et al., 2005). The research conducted in this thesis used dimensional measures of symptom assessment, the PSYRATS. The PSYRATS gives a multi-dimensional value of delusion and hallucination severity in the two weeks prior to investigation (Haddock et al., 1999). The patients recruited for Experiment 7 were mainly actively psychotic individuals (e.g., having trouble with voices and presenting some level of delusional ideation) although well enough to be outpatients. The active nature of the symptoms is the most likely the cause of the low performance of the clinical group compared to controls on the IGT.

The results of Experiment 7 do not provide support to the only previous study that investigated flexible emotion-based learning in schizophrenia (Turnbull et al., 2007). This could be due to the different composition of the clinical groups, a problem that reflects the general concern of the heterogeneity of the schizophrenia diagnosis. The results of the study conducted in this thesis suggests that there is no distinction between the IGT performance of patients with high and low positive and negative symptoms; positive symptom ratings were, instead, found to be predictive of awareness. Taken together, the result of Experiments 5 and 7 suggested that there is a gradient in the effect

of psychotic symptoms on the IGT and advance the role of awareness as an important factor in predicting performance.

Emotion-based learning and depression

Previous research on IGT performance in clinical depression has also been largely inconsistent, with some studies showing depressed patients have worst performance than controls on the IGT (Must et al., 2006) while other studies showing depressed patients have better performance on the IGT compared to controls (Smoski et al., 2008). Similar to the experimental work conducted with the schizophrenia spectrum, a dimensional approach was used in Experiment 6 to investigate contingency shifting IGT performance in putatively healthy participants with high and low BDI scores. Experiment 8 replicated Experiment 6 but contrasted clinically depressed outpatients with healthy controls.

The results of both experiments showed that depression and depressive features can substantially influence IGT performance. Experiment 6 showed that putatively healthy young adults with high scores on the BDI underperformed during the shifting phase showing little ability to adjust to shifting contingencies. In-depth analyses of participants' selection patterns revealed that individuals with high BDI scores showed little adjustment to contingencies shifting from bad to good. Interestingly, this finding was replicated in Experiment 8, although, in this case clinical depressed patients underperformed from the start of the task.

Building upon the predictions made by SMH, the insensitivity to reward observed in depression could be explained as a lack of emotional activation in consequence to rewarding outcomes (Dalgleish et al., 2004). Although the creators of the task claim that

attending only to punishing outcomes is not sufficient to perform advantageously on the IGT, the SMH does not address the importance of somatic arousal in relation to positive outcomes (Damasio, 1994). While depressed patients have repeatedly shown to be sensitive, or even oversensitive, to the outcomes of losses (Dalgleish et al., 2004), little research has examined sensitivity to positive outcomes. The findings presented support the idea of altered sensitivity to reward in depression and suggest the role of balance between positive and negative affect could be crucial in influencing decision-making performance. In other words, the biasing signal claimed to influence decision-making may result from a history of positive and negative emotional arousals. In the case of depression, an altered sensitivity to positive outcomes (i.e., very low) may create a sufficient unbalance to the system and compromise emotion-based learning.

By using a dimensional approach to the study of depression this thesis has been able to clarify the contribution of symptoms severity to decision-making in an uncertain and flexible environment. Clinically depressed patients showed impaired performance, compared to controls, in both the standard and the contingency shifting phase of the task. This more impaired learning profile it is likely to be related to more severe symptoms, history of mental illness and medication. Certain symptoms, in fact, may make decision strategies increasingly ineffective (Bark et al., 2005). For example, avoiding social activity for a long time may make social decision-making particularly hard because of a lack of practice and altered emotional activation. A long history of depression can also create regularities in biased decision-making strategy that can be more difficult to reverse or overcome. Finally, the influence of medication is worth taking into account as it is

possible that various substances may act differently on each patient symptom profile and therefore diversely affect the decision-making process.

In a different manner to the learning plots displayed by the schizophrenic patients, depressed patients demonstrated more awareness for the good and bad decks. This trait may connote a slightly different process behind depressed patients' low performance. The depressed group, by showing comparable level of awareness with respect to controls, further characterizes their difficulty in using emotional signals to mark behavioural consequences. Thus, depressed patients did not show a substantial problem in identifying the good and bad decks but failed to elicit appropriate levels of emotional arousal in response to those accurately identified contingencies.

Potential limitations of the present research

A number of general limitations can be pointed out for the experiments conducted in this thesis. First, a complete neuropsychological screening for control participants was not conducted. Although previous studies have already confirmed the relative independence between emotion-based learning, as measured by the IGT, and other neuropsychological functions, a complete neuropsychological assessment may have detected a correlation between Phase 2 performance and specific cognitive functions (Naqvi et al., 2006). A neuropsychological assessment would have also provided a useful index of concurrent validity especially with tasks such as the WCST that has been often used in combination with the IGT but never with the contingency shifting variant modification.

A second limitation can be acknowledged in the use of a student population for the basic experimental studies. Students indeed constitute a limited proportion of the general population proving to be a difficult sample when attempting to generalise the findings. Yet, a substantial amount of experimental research, as a matter of convenience, uses university student samples. This has eventually created a common ground for comparison of studies. The use of college students was, however, integral to one of the main themes of the thesis: the role of variability in control group IGT performance.

A third limitation is the lack of an accurate screening instrument for mental health symptoms and diagnoses in the control participants. The small and preferential nature of the control participants selected to match the clinical groups was used as a first line of screening for mental health problem. In addition, control participants were asked about their mental health history and psychoactive medications. Although the brief interview held for eligibility to the study was structured, it was not validated and therefore it is impossible to exclude the possibility that all the controls participants did not experience a mental health problem during their life course. Future studies may benefit from adopting validated clinical assessments such as the SCID (First et al., 1996; 1997) or the CIS-R (Brugha, Bebbington, Jenkins, Meltzer, Taub, & Janaset, 1999).

A fourth aspect worth mentioning relates to the possible ecological validity limitations of the IGT. As seen earlier in this chapter, the real-life mimicking component of the task it is often claimed as one of the main advantages. In comparison with other neuropsychological tests, this characteristic can be truly argued to be an advantage of the IGT. Nevertheless, when considered in absolute terms, the ecological validity attribute of the task, presents a few flaws. In the first instance, a card game resembling a gambling

scenario might not be common to many participants. Indeed, the extent to which the task actually mirrors any real world gambling task is itself subject to debate. Card-based gambling tasks that resemble the IGT present more than one deck of cards simultaneously with revealed "outcomes" (e.g., Texas Hold 'Em Poker, Blackjack). Therefore, the real-world validity of the IGT may rest on its counterbalancing of uncertain reward and punishment rather that its formal similarity with gambling games. Secondly, decisions in real life can rely strongly on the social context. Although the influence of other individuals on decision is intuitive, the implementation of the social constraint in decision-making tasks is in its early days (Turnbull, Worsey & Bowman, 2007). A further point with regards to the task limitation is the assumed initial emotional neutrality. That is none of the decks has emotional value prior to the commencement of the card selection due to their similar physical appearance. However, in real life situation people often judge on the basis of preconception and pre-existing attitudes (e.g., on the basis of clothes people might infer wealth).

Future research

The results of the studies presented in this thesis can suggest future interesting avenues of research. Several patients with schizophrenia expressed, at the end of the task, the impression that the subjective rating was capable of controlling the reward schedule embedded in the decks. Although it is reasonable to think that delusion and in particular idea of reference could have influenced patients perception of the task the possibility of altering the schedule according to the rating seems an excellent idea. People tend to adjust their behaviour not just according to the outcomes but also according to the

cognition associated with it (Plassmann, O'Doherty, Shiv & Rangel, 2008). In this respect, it would be interesting to investigate how a schedule of rewards that changes in accordance or not with the subjecting rating, will impact on performance. This line of investigation would be particularly interesting in the context of delusional disorders and may help to clarify the extent to which delusional thinking can influence the decision-making behaviour of individuals.

A second interesting development of the work conducted in this thesis would be to change the affective value of the stimulus presented as reward and punishment. This line of investigation could be exploited in several different ways and provide an insightful view into the affective components of decision-making. One possible way to characterize the extent of the emotional signal would be to try to disrupt it in the same fashion as Experiment 1. By presenting emotionally salient pictures in-between trials participants should be able to elicit emotion possibly functioning as confounders to the somatic marker signal. A recent theory has advanced the possibility that decisions can be pursued by two separate and competitive systems: the "hot" decision-making system, that deals with emotionally salient material, and the "cold" decision-making system, that deals with more neutral material and can optimize the use of cognitive resource (Weber, Shafir & Blais, 2004). Fidgner et al. (2009) found adolescents engaged in higher risky behaviours when playing a "hot" version of the Columbia Card (CCT) decision-making task (i.e., the CCT) compared to when they played a "cold" version of the same task. This suggests that emotions can generally alter the decision-making process not necessarily for the good.

Another possible way of disrupting the emotional signal could be to replace the monetary reward and punishment with emotionally salient stimuli either visual or auditory. For instance, an emotionally salient modified version of the task could replace the monetary losses with different volumes (to resemble the different magnitude) loud aversive tones. Likewise, it is possible to present affectively consistent or inconsistent information prior to card selections by, for example, positioning affectively pleasant or unpleasant images from the International Affective Picture System (IAPS) on the card decks.

A further interesting development of the work conducted in this thesis would be the study of IGT performance with joint functional imaging and psychophysiology methods (i.e., SCRs). Functional imaging studies of the IGT are currently underway and they will most likely clarify the cortical involvement during specific part of the task (Lawrence, Jollant, O'Daly, Zelaya, & Phillips, 2009; Lin, Chiu, Cheng & Hsieh, in press). Future investigations should consider linking functional MRI with SCR measures of emotional arousal. The link between information processing, emotional activation and neural functioning it is still largely unclear (Critchley, 2005). Decision-making, given its aggregate process nature resulting from a number of more basic functions, will prove to be difficult to investigate. Nevertheless its importance for the human behaviour will contribute to cast some light on more complex cognition and eventually understand the psychophysiological and affective underpinnings of executive functions.

Two of the ideas proposed above, the emotional manipulation and the customized manipulation of the schedule of reward and punishment, could be used to investigate clinical phenomena and findings could inform therapies approaches. For example, by

interspersing the schedule of the IGT decks with emotionally negative stimuli (one before and one after the choice) might help people with depression recognise a rewarding outcome due to the higher relative difference between the emotional values of successive events.

References

Ackerly, S.S., & Benton, A.L., (1948). Report of a case of bilateral frontal lobe defect. *Res Publ Assoc Res Nerv Ment Dis (Baltimore).* 27: 479-504.

Adolphs, R. (1999). Social cognition and the human brain. *Trends Cogn. Sci., 3*, 469–479.

Adolphs, R., Cahill, L., Schul, R., & Babinsky, R. (1997). Impaired declarative memory for emotional material following bilateral amygdala damage in humans. *Learn. Mem.* 4(3):291-300.

Adolphs, R., Tranel, D., & Damasio, A. R., (1998).The human amygdala in social judgment. *Nature.* 4; 393(6684):470-4.

Aggleton, J.P. (1992). *The amygdala: neurobiological aspects of emotion, memory, and mental dysfunction.* Wiley-Liss, New York.

Aleman, A., David, A.S., & Medford N. (2006). *The Cognitive Neuropsychiatry of Emotion and Emotional Disorders.* Psychology press.

Anders, S., Lotze, M., Erb, M., Grodd, W. & Birbaumer, N. (2004). Brain activity underlying emotional valence and arousal: a response-related fMRI study. *Hum Brain Mapp.* ;23(4):200-9.

Andreasen, N.C. (1982). Negative symptoms in schizophrenia. *Arch Gen Psychiatry.*;39:784-788.

Andreasen, N.C. (1983). *The scale for the assessment of negative symptoms (SANS).* University of Iowa, Iowa city, IA, USA.

Antonova, E., Sharma, T., Morris, R.., & Kumari, V. (2004). The relationship between brain structure and neurocognition in schizophrenia: a selective review. *Schizophr Res*. 2004 Oct 1;70(2-3):117-45.

Balodis, I. M., MacDonald, T. K., & Olmstead, M. C. (2006). Instructional cues modify performance on the Iowa Gambling Task. *Brain Cogn*, 60(2), 109–117.

Bark, R., Dieckmann, S., Bogerts, B., & Northoff, G., (2005). Deficit in decision making in catatonic schizophrenia: an exploratory study. *Psychiatry Res.* 134, 131–141.

Bar-On, R., Tranel, D., Denburg, N.L., & Bechara, A. (2003). Exploring the neurological substrate of emotional and social intelligence. *Brain.* ;126(8):1790-800.

Barrash, J., Tranel, D., & Anderson, S.W. (2000). Acquired personality disturbances associated with bilateral damage to the ventromedial prefrontal region. *Dev Neuropsychol.* 18(3):355-81.

Barratt, E.S., Stanford, M.S., Kent, T.A & Felthous, A. (1997). Neuropsychological and cognitive psychophysiological substrates of impulsive aggression. *Biol. Psychiatry* 41, 1045–1061.

Bechara, A. (2001). Neurobiology of decision-making: risk and reward. *Semin Clin Neuropsychiatry*. 6(3):205-16.

Bechara, A. (2004). The role of emotion in decision-making: evidence from neurological patients with orbitofrontal damage. *Brain Cogn.* 55(1):30-40.

Bechara, A., & Damasio H. (2002). Decision-making and addiction (part I): impaired activation of somatic states in substance dependent individuals when pondering decisions with negative future consequences. *Neuropsychologia*, 40:1675–89.

Bechara, A., Damasio H., & Damasio, A.R., (2003). The role of the amygdala in decision making. In: Shinnick-Gallagher P., Pitkanen H., Shekhar A., Cahill L.,(Eds.), The amygdala in brain functioning: Basic and clinical approaches. *Annual New York Academy of science*, 985:356-369.

Bechara, A., Damasio, A., Damasio, H., & Anderson, S., (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition,* 50, 7-15.

Bechara, A., Damasio, H., & Damasio, A.R. (2000b). Emotion, decision making and the orbitofrontal cortex. *Cereb Cortex.* ;10(3):295-307.

Bechara, A., Damasio, H., Damasio, A. R., & Lee, G. P. (1999). Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making. *J Neurosci. 19*(13), 5473–5481

Bechara, A., Damasio, H., Tranel D., & Damasio A.R. (1997). Deciding advantageously before knowing the advantageous strategy. *Science* 275, 1293-1295.

Bechara, A., Damasio, H., Tranel, D., & Anderson, S.W., (1998). Dissociation of working memory from decision-making within the human prefrontal cortex. *J Neurosci.* 18 (1), 428–437.

Bechara, A., Damasio, H., Tranel, D., & Damasio, A.R. (2005). The Iowa Gambling Task and the somatic marker hypothesis: some questions and answers. *Trends Cogn Sci.* 2005;9(4):159-62.

Bechara, A., Dolan, S., & Hindes, A. (2002). Decision-making and addiction (part II): Myopia for the future or hypersensitivity to reward?. *Neuropsychologia*, 40, 1690–1705.

Bechara, A., Tranel D., Damasio, H., Adolphs, R., Rockland C., & Damasio A.R., (1995). Double dissociation of conditioning and declarative knowledge relative to the amygdala and hippocampus in humans. *Science*. 25; 269(5227):1115-8.

Bechara, A., Tranel, D., & Damasio, H. (2000a). Characterization of the decision-making deficit of patients with ventromedial prefrontal cortex lesions. *Brain*, 123, 2189-2202.

Bechara, A., Tranel, D., Damasio, H., & Damasio, A. R., (1996). Failure to respond autonomically to anticipated future outcomes following damage to prefrontal cortex. *Cereb Cortex* 6(2):215-25.

Beck, A.T., Rush, A.J., Shaw, B.F., & Emery, G., (1979) *Cognitive Therapy of Depression*. The Guilford Press.

Beck, A.T., Steer, R. A., & Brown, G. K. (1996). *BDI-II Manual.* The Psychological Corporation, San Antonio, TX (1996).

Beglinger, L.J., Gaydos, B., Tangphao-Daniels, O., Duff, K., Kareken, D.A., Crawford, J., Fastenau, P.S. & Siemers, E.R. (2005). Practice effects and the use of alternate forms in serial neuropsychological testing. *Arch Clin Neuropsychol.* 20(4):517-29.

Beninger, R.J., Wasserman, J., Zanibbi, K., Charbonneau, D., Mangels, J., & Beninger, B.V., (2003). Typical and atypical antipsychotic medications differentially affect two nondeclarative memory tasks in schizophrenic patients: a double dissociation. *Schizophr Res* 61, 281–292.

Bersani G, Clemente R, Gherardelli S, Pancheri P. (2004). Deficit of executive functions in schizophrenia: relationship to neurological soft signs and psychopathology. *Psychopathology*. 37(3):118-23.

Bertollo, D.N., Cowen, M.A., & Levy, A.V. (1996). Hypometabolism in olfactory cortical projection areas of male patients with schizophrenia: an initial positron emission tomography study. *Psychiatry Res.* 29;60(2-3):113-6.

Bland, M. (2000). *An Introduction to Medical Statistics (3rd edition)*. Oxford Medical Publications.

Borkowska, A. & Rybakowski, J.K. (2001). Neuropsychological frontal lobe tests indicate that bipolar depressed patients are more impaired than unipolar. *Bipolar Disord.* 3(2):88-94.

Botvinick, M., Nystom, L., Fissell, K., Carter, C.S., & Cohen J.D., (1999). Conflict monitoring versus selection for action in anterior cingulated cortex. *Nature*, 402:179-181.

Bouscein, W. (1992). *Electrodermal activity*. New York: Plenum.

Bowie, C.R., & Harvey, P.D. (2005). Cognition in schizophrenia: impairments, determinants, and functional importance. *Psychiatr Clin North Am.*. 28(3):613-33, 626.

Bowman, C.H, & Turnbull, O.H. (2004). Emotion-based learning on a simplified card game: the Iowa and Bangor Gambling Tasks. *Brain Cogn.* 55(2):277-82.

Bowman, C.H., Evans, C.E., & Turnbull, O.H. (2005). Artificial time constraints on the Iowa Gambling Task: the effects on behavioural performance and subjective experience. *Brain Cogn.* ;57(1):21-5.

Bradley, M.M., & Lang, P.J. (2002). Measuring Emotion: Behavior, Feeling, and Physiology. In Lane R.D. & Nadel L. (2002) *Cognitive neuroscience of emotion.* Oxford University press.

References

Brand, M., Fujiwara, E., Borsutzky, S., Kalbe, E., Kessler, J., & Markowitsch, H.J. (2005a). Decision-making deficits of korsakoff patients in a new gambling task with explicit rules: associations with executive functions. *Neuropsychology*. 19(3):267-77.

Brand, M., Kalbe, E., Labudda, K., Fujiwara, E., Kessler, J., & Markowitsch, H.J. (2005b). Decision-making impairments in patients with pathological gambling. *Psychiatry Res.* 30;133(1):91-9.

Brand, M., Labudda, K., & Markowitsch, H.J. (2006). Neuropsychological correlates of decision-making in ambiguous and risky situations. *Neural Netw.* ;19(8):1266-76.

Brand, M., Recknor, E.C., Grabenhorst, F., & Bechara, A. (2007). Decisions under ambiguity and decisions under risk: correlations with executive functions and comparisons of two different gambling tasks with implicit and explicit rules. *J Clin Exp Neuropsychol.*;29(1):86-99.

Brazo, P., Delamillieure, P., Morello, R., Halbecq, I., Marié, R.M. & Dollfus, S., (2005). Impairments of executive/attentional functions in schizophrenia with primary and secondary negative symptoms. *Psychiatry Res* 30, 45-55.

Breiter, H.C., Aharon, I., Kahneman, D., Dale, A., & Shizgal, P., (2001). Functional imaging of neural responses to expectancy and experience of monetary gains and losses. *Neuron*; 30:619-639.

Brugha, T.S., Bebbington, P.E., Jenkins, R., Meltzer, H., Taub, N.A., Janas, M. & Vernon, J. (1999). Cross validation of a general population survey diagnostic interview: a comparison of CIS-R with SCAN ICD-10 diagnostic categories. *Psychol Med.* 29(5):1029-42.

Brunet-Gouet, E., & Decety, J. (2006). Social brain dysfunctions in schizophrenia: a review of neuroimaging studies. *Psychiatry Res*. 1;148(2-3):75-92.

Buehner, M. J., & May, J. (2004). Abolishing the effect of reinforcement delay on human causal learning. *Q J Exp Psychol, 57B*(2), 179–191.

Buelow, M.T. & Suhr, J.A. (2009). Construct validity of the Iowa Gambling Task.. *Neuropsychol Rev.* 19(1):102-14.

Burgess, P.W. & Shallice, T. (1997). *The Hayling and Brixton Tests*. Thames Valley Test Company Bury St. Edmonds, England

Calder, A.J., Lawrence, A.D., & Young A.W. (2001). Neuropsychology of fear and loathing. *Nat Rev Neurosci.* 2(5):352-63.

Campbell, M.C., Stout, J.C. & Finn, P.R.(2004). Reduced autonomic responsiveness to gambling task losses in Huntington's disease. *J Int Neuropsychol Soc.* ;10(2):239-45.

Canals, J., Bladé, J., Carbajo, G. & Domènech-Llabería, E. (2001). The Beck Depression Inventory: Psychometric Characteristics and Usefulness in Nonclinical Adolescents. *Europ J Psych Ass*, 17, 1 :63-68.

Caroselli, J.S., Hiscock, M., Scheibel, R.S., & Ingram, F. (2006). The simulated gambling paradigm applied to young adults: an examination of university students' performance. *Appl Neuropsychol.*;13(4):203-12

Carter C., Braver T.S., Barch D.M., Botvinick M.M., Noll D., & Cohen J.D., (1998). Antrior cingulated cortex, error detection, and the on-line monitoring of performance. *Science*; 280:747-781.

Cavada, C., Company, T., Tejedor, J., Cruz-Rizzolo, R. J., & Reinoso-Suarez, F., (2000). The anatomical connections of the macaque monkey orbitofrontal cortex. A review. *Cereb cortex*, 10:220-242.

Cavallaro, R., Cavedini, P., Mistretta, P., Bassi, T., Angelone, S.M., Ubbiali, A. & Bellodi, L (2003). Basal-corticofrontal circuits in schizophrenia and obsessive-compulsive disorder: a controlled, double dissociation study. *Biol Psychiatry.* 15;54(4):437-43.

Cavedini, P., Bassi, T., Ubbiali, A., Casolari, A., Giordani, S., & Zorzi, C., (2004a). Neuropsychological investigation of decision-making in anorexia nervosa. *Psychiatry Res* 127, 259–266.

Cavedini, P., Bassi, T., Zorzi, C., & Bellodi, L., (2004b). The advantages of choosing antiobsessive therapy according to decision-making functioning. *J Clin Psychopharmacol* 24 (6), 628–631.

Cavedini, P., Riboldi, G., D'Annucci, A., Belotti, P., Cisima, M., & Bellodi, L., (2002a). Decision-making heterogeneity in obsessive compulsive disorder: ventromedial prefrontal cortex function predicts different treatment outcomes. *Neuropsychologia* 40, 205–211.

Cavedini, P., Riboldi, G., Keller, R., D'Annucci, A., & Bellodi, L., (2002b). Frontal lobe dysfunction in pathological gambling patients. *Biol Psychiatry* 51 (4), 334–341.

Cella, M., Cooper, A., Dymond, S.O., & Reed P. (2008). The relationship between dysphoria and proneness to hallucination and delusions among young adults. *Compr Psychiatry*. 49(6):544-50.

Cella, M., Dymond, S., & Cooper, A. (in press). Impairment in flexible emotion-based learning in hallucination- and delusion-prone individuals. P*sychiatry Res.*

Cella, M., Dymond, S., Cooper, A., & Turnbull, O. (2007). Effects of decision-phase time constraints on emotion-based learning in the Iowa Gambling Task. *Brain Cogn.* ;64(2):164-9.

Chan, R.C.K., Chen, E.Y.H., Cheung, E.F.C. & Cheung, H.K. (2004). Executive dysfunctions in schizophrenia: relationships to clinical manifestation. *Eur Arch Psychiatry Clin Neurosci.* 254: 256–262.

Channon, S. (1996). Executive dysfunction in depression: The Wisconsin Card Sorting Test. *J Affect Disord*, 39, 2, 8 :107-114.

Chen, L., Eaton, W.W., Gallo, J.J., & Nestadt, G. (2000). Understanding the heterogeneity of depression through the triad of symptoms, course and risk factors: a longitudinal, population-based study. *J Affect Disord*, 59(1), 1-11.

Chwalisz, K., Diener, E., & Gallagher, D. (1988) Autonomic arousal feedback and emotional experience: evidence from the spinal cord injured. *J Pers Soc Psychol.*;54(5):820-8.

Claridge, G. & Davis, C. (2003). *Personality and psychological disorders.* London, England: Arnold.

Claridge, G. (1997). *Schizotypy: Implications for Illness and Health.* Oxford, UK: Oxford University Press.

Clark, D. (2001). The persistent problem of negative cognition in anxiety and depression: New perspectives and old controversies. *Behav Ther*, 32, 1:3-12.

Clark, L., & Manes, F. (2004). Social and emotional decision-making following frontal lobe injury. *Neurocase*. ;10(5):398-403.

Clark, L., Iversen, S.D., & Goodwin, G.M., (2001). A neuropsychological investigation of prefrontal cortex involvement in acute mania. *Am J Psychiatry* 158 (10), 1605–1611.

Clark, L., Manes, F., Antoun, N., Sahakian, B.J., & Robbins, T.W., (2003). The contributions of lesion laterality and lesion volume to decision-making impairment following frontal lobe damage. *Neuropsychologia* 41 (11), 1474–1483.

Coles, J., & Heimberg, F., (2002). Memory biases in the anxiety disorders: current status. *Clin Psychol Rev*. 22(4):587-627.

Convit, A., Wolf, O.T., de Leon, M.J., Patalinjug, M., Kandil, E., Caraos, C, Scherer, A., Saint Louis, L.A., & Cancro, R. (2001).Volumetric analysis of the pre-frontal regions: findings in aging and schizophrenia. *Psychiatry Res* 25;107(2):61-73.

Crespo-Facorro, B., Kim, J., Andreasen, N.C., O'Leary, D.S., & Magnotta, V. (2000). Regional frontal abnormalities in schizophrenia: a quantitative gray matter volume and cortical surface size study. *Biol Psychiatry*. 15;48(2):110-9.

Critchley, H.D. (2002). Electrodermal responses: what happens in the brain. *Neuroscientist*. 8(2):132-42.

Critchley, H.D. (2005). Neural mechanisms of autonomic, affective, and cognitive integration. *J Comp Neurol*. 5;493(1):154-66.

Critchley, H.D., Elliott, R., Mathias, C.J., & Dolan, R.J. (2000). Neural activity relating to generation and representation of galvanic skin conductance responses: a functional magnetic resonance imaging study. *J Neurosci.* 15;20(8):3033-40.

Critchley, H.D., Mathias, C.J., Dolan, R.J., (2001). Neural activity in the human brain relating to uncertainty and arousal during anticipation. *Neuron*, 29:537-545.

Crone, E.A., & van der Molen, M.W., (2004). Developmental changes in real life decision making: performance on a gambling task previously shown to depend on the ventromedial prefrontal cortex.. *Dev Neuropsychol.*;25(3):251-79.

Crone, E.A., Bunge, S.A., Latenstein, H., & van der Molen, M.W. (2005). Characterization of children's decision making: sensitivity to punishment frequency, not task complexity. *Child Neuropsychol.* ;11(3):245-63.

Crone, E.A., Somsen, R.J., Van Beek, B., & Van Der Molen, M.W. (2004). Heart rate and skin conductance analysis of antecendents and consequences of decision making. *Psychophysiology*. 41(4):531-40.

Cummings, J. (1995). Anatomic and behavioral aspects of frontal–subcortical circuits. *Ann NY Acad Sci* 769 , pp. 1–13.

Dalgleish, T., Yiend, J., Bramham, J., Teasdale, J.D., Ogilvie, A.D., Malhi, G. & Howard, R. (2004). Neuropsychological processing associated with recovery from depression after stereotactic subcaudate tractotomy. *Am J Psychiatry* 161(10):1913-6.

Damasio, A. R., (1999). *The feeling of what happens: body and emotion in the making of consciousness.* Harcourt Brace & Co. New York.

Damasio, A., Adolphs, R. & Damasio, H. (2003). The contribution of lesion method to the functional neuroanatomy of emotion. In: *Handbook of affective sciences*. Eds. Davidson, R.J., Scherer, K.R., Goldsmith, H.H. Oxford University press, US.

Damasio, A.R. (1996). The somatic marker hypothesis and the possible functions of the prefrontal cortex.. *Philos Trans R Soc Lond B Biol Sci.* 1996 29;351(1346):1413-20.

Damasio, A.R., (1994). *The Descartes error: emotion, reason and the human brain.* Avon, New York,.

Damasio, A.R., (2001). Fundamental feelings. *Nature*, 413:781.

Damasio, A.R., (2003). *Looking for Spinoza: joy, sorrow and the feeling brain.* Harcourt Brace & Co. New York.

Damasio, A.R., Damasio, H., Christen, A.R., (1995). *Neurobiology of decision making.* New York: Sprinnger.

Damasio, A.R., Tranel, D., Damasio, H. (1990). Individuals with sociopathic behavior caused by frontal damage fail to respond autonomically to social stimuli. *Behav Brain Res.* 14;41(2):81-94.

Damasio, H. (1995). Human neuroanatomy relevant to decision-making. In: Damasio, A.R., Damasio, H., Christen, A.R., editors. *Neurobiology of decision making.* New York: Sprinnger,1-12.

Damasio, H., Grabowski, T., Frank, R., Galaburda, A.M., Damasio, A.R. (1994). The return of Phineas Gage: clues about the brain from the skull of a famous patient. *Science.* 20;264(5162):1102-5.

Darwin, C. (1998). *The expression of the emotions in man and animals.* 3rd ed, P Ekman, editor. Oxford, UK: Oxford Univ Press.

Davis, C., Patte, K., Tweed, S., & Curtis, C. (2007). Personality traits associated with decision-making deficits. *Pers Individ Dif.* 4(2): 279-290.

Dawson, M.E., Schell, A.M., Filion, D.L. (2000). The electrodermal system. In: Cacioppo, J.T., Tassinary, L.G., Berntson, G.C. editor. *Handbook of psychophysiology*. 2nd ed. Cambridge, MA: Cambridge University Press. p 200–23.

Dean, K., Bramon, E., & Murray, R.M., (2003). The causes of schizophrenia: neurodevelopment and other risk factors. *J. Psychiatr. Pract.* 9, 442-454.

Denburg, N.L., Tranel, D. & Bechara, A. (2005). The ability to decide advantageously declines prematurely in some normal older persons. *Neuropsychologia.* 43(7):1099-106.

Dias, R., Robbins, T. W., & Roberts, A. C. (1996). Dissociation in prefrontal cortex of affective and attentional shifts. *Nature, 380*, 69–72.

Dozois, D.A., Dobson, K. S., & Ahnberg, J.L. (1998). A Psychometric Evaluation of the Beck Depression Inventory–II. *Psychol Ass*, 10, 2:83-89.

Drake, R., Haddock, G., Tarrier, N., Bentall, R., & Lewis, S. (2007). The Psychotic Symptom Rating Scales (PSYRATS): their usefulness and properties in first episode psychosis. *Schizophr Res.* ;89(1-3):119-22.

Drevets, W.C. (2000). Functional anatomical abnormalities in limbic and prefrontal cortical structures in major depression. *Prog Brain Res.*;126:413-31.

Drevets, W.C. (2000). Neuroimaging studies of mood disorders. *Biol Psychiatry* 15;48(8):813-29.

Drevets, W.C. (2003). Neuroimaging abnormalities in the amygdala in mood disorders. *Ann N Y Acad Sci.* 985:420-44.

Drewe, E.A. (1975) Go–no go learning after frontal lobe lesions in humans. *Cortex* 11 (1975), pp. 8–16.

Dunn, B. D., Dalgleish, T., & Lawrence, A. D., (2006). The somatic marker hypothesis: a critical evaluation. *Neurosci Biobehav Rev.* 30(2):239-271.

Dymond. S., Cella, M., Cooper, A., & Turnbull, O.H. (2009).The contingency-shifting variant Iowa Gambling Task: An investigation with young adults. *J Clin Exp Neuropsychol.* 22:1-11.

Elliott, R., Dolan, R., & Frith, C.D., (2000). Dissociable functions in the medial and lateral orbitofrontal cortex. *Cereb cortex*;10:308-317.

Elliott, R., Friston, K., & Dolan, R.,(2000). Dissociable neural responses in human reward system. *J neurosci*;20:6159-6165.

Elliott, R., Sahakian, B.J., McKay, A.P., Herrod, J.J., Robbins, T.W., & Paykel, E.S. (1996). Neuropsychological impairments in unipolar depression: the influence of perceived failure on subsequent performance. *Psychol Med* 26, 975–989.

Eslinger, P., & Damasio A.R.,(1985) Severe disturbance of higher cognition after bilateral frontal lobe ablation :patient EVR. *Neurology* 35:1731-1741.

Evans, C.E., Bowman, C.H., & Turnbull, O.H. (2005). Subjective awareness on the Iowa Gambling Task: the key role of emotional experience in schizophrenia. *J Clin Exp Neuropsychol.* 27(6):656-64.

Evans, C.E., Kemish, K., & Turnbull, O.H. (2004). Paradoxical effects of education on the Iowa Gambling Task.. *Brain Cogn.*;54(3):240-4.

Eysenck, S.B., Pearson, P.R., Easting G., & Allsopp, J.F. (1985). Age norms for impulsiveness, venturesomeness and empathy in adults. *Pers Individ Dif* 6 ,613–619.

Fellows, L.K. (2007). The role of orbitofrontal cortex in decision making: a component process account. *Ann N Y Acad Sci.* ;1121:421-30.

Fellows, L.K., & Farah, M.J. (2005). Dissociable elements of human foresight: a role for the ventromedial frontal lobes in framing the future, but not in discounting future rewards. *Neuropsychologia.* ;43(8):1214-21.

Fellows, L.K., & Farah, M.J., (2003). Ventromedial frontal cortex mediates affective shifting in humans: evidence from a reversal learning paradigm. *Brain* 126 (Pt 8), 1830–1837.

Ferguson, M.L, & Katkin, E.S. (1996). Visceral perception, anhedonia, and emotion. *Biol Psychol.* 5;42(1-2):131-45.

Fernie, G., & Tunney, R., (2005). Some decks are better than others: The effect of rein forcer type and instructions on learning in the Iowa Gambling Task. *Brain Cog.* 60: 94-102.

Field, A. (2000). *Discovering statistics using SPSS.* Sage, London..

Figner, B., Mackinlay, R.J., Wilkening, F., & Weber, E.U. (2009). Affective and deliberative processes in risky choice: age differences in risk taking in the Columbia Card Task.. *J Exp Psychol Learn Mem Cogn.* 35(3):709-30.

First, M.B., Gibbon, M., Spitzer, R.L, Williams, J.B., & Benjamin, L.S. (1997). *Structured Clinical Interview for DSM IV Axis II Personality Disorders (SCID-II).* Washington, DC: American Psychiatric Press.

First, M.B., Spitzer, R.L., Gibbon, M., & Williams, J.B.W. (1996). *Structured clinical interview for Axis I DSM-IV disorders—Patient Edition (with psychotic screening) SCID-I/P (W/ psychotic screen) (version 2)*. New York: Biometrics Research Department, New York State Psychiatric Institute.

Fishbein, D.H., Eldreth, D.L., Hyde, C., Matochik, J.A., London, E.D., Contoreggi, C., Kurian, V., Kimes, A.S., Breeden, A., & Grant, S. (2005). Risky decision making and the anterior cingulate cortex in abstinent drug abusers and nonusers. *Brain Res Cogn Brain Res*. 23(1):119-36.

Fitzgerald, P.B., Oxley, T.J., Laird, A.R., Kulkarni, J., Egan, G.F., & Daskalakis, Z.J. (2006). An analysis of functional neuroimaging studies of dorsolateral prefrontal cortical activity in depression. *Psychiatry Res.* 22;148(1), 33-45.

Fowles, D.C. (1980). The three arousal model: implications of Gray's two-factor learning theory for heart rate, electrodermal activity, and psychopathy. *Psychophysiology* 17, 87–104.

Franken, I.A., & Muris, P. (2005). Individual differences in decision-making. *Personality and Individual Differences*, 39,(5), 991-998.

Frith, C., & Dolan, R. (1996). The role of the prefrontal cortex in higher cognitive functions. *Brain Res Cogn Brain Res.*;5(1-2):175-81.

Frith, C.D. (2004). Schizophrenia and theory of mind. *Psychol Med.* ;34(3):385-9.

Fusar-Poli, P., Perez, J., Broome, M., Borgwardt, S., Placentino, A., Caverzasi, E., Cortesi, M., Veggiotti, P., Politi, P., Barale, F. & McGuire, P. (2007). Neurofunctional correlates of vulnerability to psychosis: a systematic review and meta-analysis. *Neurosci Biobehav Rev.*;31(4):465-84.

Fuster, J. M., (1999). Cognitive functions of the frontal lobes. In Miller, B. L., & Cummings, J. L., (Eds.). *The human frontal lobes: functions and disorders* (pp. 187-195). New York: Guilford.

Fuster, J. M., (2001). The prefrontal cortex-an update: time of the essence. *Neuron*; 30:319-333.

Gladwell, M. (2005). *Blink.* New York: Little, Brown.

Glicksohn, J., Naor-Ziv, R., & Leshem, R. (2007). Impulsive decision making: learning to gamble wisely? *Cognition;* 105(1):195-205.

Goel, V., Grafman, J., Tajik, J., Gana S., & Danto D., (1998). A study of the performance of patients with frontal lobe lesions in a financial planning task. *Brain*; 120:1805-1822.

Goldberg, E. (2001). *The executive brain.* Oxford University Press.

Goldfried, M.R., & Davison, G.C. (1994). *Clinical behavior therapy.* Wiley, New York.

Goldman-Rakic, P.S. (1992). Working memory and the mind. *Scientific Am.* 267:111–117.

Gonda, X., Juhasz, G., Laszik, A., Rihmer, Z., & Bagdy, G. (2005). Subthreshold depression is linked to the functional polymorphism of the 5HT transporter gene. *J Affect Disord.*;87(2-3):291-7.

Gooding, D.C., Kwapil, T.R. & Tallent, K.A. (1999). Wisconsin Card Sorting Test deficits in schizotypic individuals. *Schizophr Res.* 21;40(3):201-9.

Goudriaan, A.E., Oosterlaan, J., de Beurs, E., & van den Brink, W., (2005). Decision making in pathological gambling: a comparison between pathological gamblers, alcohol dependents, persons with Tourette syndrome, and normal controls. *Cog Brain Res* 23, 137–151.

Grant, D.A., & Berg, E.A.(1948). A behavioral analysis of degree of reinforcement and ease of shifting to new responses in a Weigl-type card sorting problem, *J Exp Psych* 38 (1948), pp. 404–411.

Green, M.F., Penn, D.L., Bentall, R., Carpenter, W.T., Gaebel, W., Gur, R.C., Kring, A.M., Park, S., Silverstein, S.M. & Heinssen, R. (2008). Social cognition in schizophrenia: an NIMH workshop on definitions, assessment, and research opportunities. *Schizophr Bull.* 34(6):1211-20.

Haaland, V.Ø., & Landrø, N.I.(2007). Decision making as measured with the Iowa Gambling Task in patients with borderline personality disorder. *J Int Neuropsychol Soc.*, 13(4):699-703.

Haddock, G., McCarron, J., Tarrier, N., & Faragher, E.B. (1999). Scales to measure dimensions of hallucinations and delusions: the psychotic symptom rating scales (PSYRATS). *Psychol Med.* 29(4):879-89.

Häfner, H. & an der Heiden, W. (1997). Epidemiology of schizophrenia. *Can J Psychiatry*. 42(2):139-51.

Hamann, S. B., Ely, T. D., Grafton, S. T., & Kilts C. D., (1999).Amygdala activity related to enhanced memory for pleasant and aversive stimuli. *Natl Neurosci*; 2(3):289-93.

Hanson, K.L., Luciana, M., & Sullwold, K. (2008). Reward-related decision-making deficits and elevated impulsivity among MDMA and other drug users. *Drug Alcohol Depend.* 1;96(1-2):99-110.

Hanssen, M., Bak, M., Bijl, R., Vollebergh, W., & van Os, J. (2005). The incidence and outcome of subclinical psychotic experiences in the general population. *Br J Clin Psychol,* 44, 181-191.

Harvey, P. O., Le Bastard, G., Pochon, J. B., Levy, R., Allilaire, J. F. Dubois, B., & Fossati P. (2004). Executive functions and updating of the contents of working memory in unipolar depression. *J Psychiatr Res*, 38 (6), 567-576.

Haut, M.W., Cahill, J., Cutlip, W.D., Stevenson, J.M., Makela E.H., & Bloomfield S.M., (1996). On the nature of Wisconsin Card Sorting Test performance in schizophrenia. *Psychiatry Res* 65, 15–22.

Heims, H.C., Critchley, H.D., Dolan, R., Mathias, C.J., & Cipolotti L. (2004). Social and motivational functioning is not critically dependent on feedback of autonomic responses: neuropsychological evidence from patients with pure autonomic failure. *Neuropsychologia.* 2004;42(14):1979-88.

Helzer, J.E., Kraemer, H.C., & Krueger, R.F. (2006). *The feasibility and need for dimensional psychiatric diagnoses. Psychol Med.* 36(12):1671-80.

Henriques, J.B., Glowacki, J.M., & Davidson, R.J. (1994). Reward fails to alter response bias in depression. *J Abnorm Psychol.* 103(3):460-6.

Henry, J.D., Bailey, P.E., & Rendell, P.G. (2008). Empathy, social functioning and schizotypy. *Psychiatry Res.* 15;160(1):15-22.

Hinson, J.M., Jameson, T.L., & Whitney, P. (2002). Somatic markers, working memory, and decision making. *Cogn Affect Behav Neurosci.* ;2(4):341-53.

Hinson, J.M., Jameson, T.L., & Whitney, P. (2003). Impulsive decision making and working memory. *J Exp Psychol Learn Mem Cogn.* 29(2):298-306.

Hoffman, J.L. (1949) Clinical observations concerning schizophrenic patients treated by prefrontal leukotomy. *N. Engl. J. Med.* 241:233-246.

Hornak, J., O'Doherty, J., Bramham, J., Rolls, E.T., Morris, R.G., & Bullock, P.R. (2004). Reward related reversal learning after surgical excisions in orbito-frontal or dorsolateral prefrontal cortex in humans. *J Cogn Neurosci* 16 (3), 463–478.

Hot, P., Saito, Y., Mandai, O., Kobayashi, T., & Sequeira, H. (2006). An ERP investigation of emotional processing in European and Japanese individuals. *Brain Res.* 29;1122(1):171-8.

Hutton, S.B., Murphy, F.C., Joyce, E.M., Rogers, R.D., Cuthbert, I., Barnes, T.R., McKenna, P.J., Sahakian, B.J., Robbins, T.W. (2002). Decision making deficits in patients with first-episode and chronic schizophrenia. *Schizophr Res.* 1;55(3):249-57.

Iversen, S.D., & Mishkin, M. (1970). Perseverative interference in monkeys following selective lesions of the inferior prefrontal convexity. *Exp Brain Res.* 11: 376–386.

James, W. (1894). Physical basis of emotion. *Psychol Rev* 1:516–29, reprinted in 1994. Psychol Rev 101:205–10.

James, W., (1884). What is an emotion? *Mind*, 19,188-205.

James, W., (1890). *The principles of psychology*. Holt, New York.

Jameson, T.L., Hinson, J.M., & Whitney, P., (2004). Components of working memory and somatic markers in decision making. *Psycho Bulletin Review.* 11 (3), 515–520.

Johns, L. C., & van Os, J., (2001). The continuity of psychotic experiences in the general population. *Clin. Psychol. Rev.* 21(8) 1125-41.

Kahneman, D., & Tversky, A. (1979). Prospect theory: an analysis of decision under risk. *Economica*, 47(2):263-291.

Kanner, A.M. (2004). Structural MRI changes of the brain in depression. *Clin EEG Neurosci.* 35(1):46-52.

Karasz, A. (2008). The development of valid subtypes for depression in primary care settings: a preliminary study using an explanatory model approach. *J Nerv Ment Dis.* 196(4):289-96.

Kendall, P.C., & Flannery-Schroeder, E.C. (1995). Rigor, but not rigor mortis, in depression research. *J Pers Soc Psychol.* 68(5):892-4.

Kester, H.M., Sevy, S., Yechiam, E., Burdick, K.E., Cervellione, K.L, & Kumra, S. (2006). Decision-making impairments in adolescents with early-onset schizophrenia. *Schizophr Res.* 85(1-3):113-23.

Kilzieh, N., & Cloninger, C. R. (1993). Psychophysiological antecedents of personality. *J. Pers. Disorders* 7, 100–117.

Kleeberg, J., Bruggimann, L., Annoni, J.M., van Melle, G., Bogousslavsky, J., & Schluep, M. (2004). Altered decision-making in multiple sclerosis: a sign of impaired emotional reactivity? *Ann Neurol.* 56(6):787-95.

Klimidis, S., Stuart, G.W., Minas, I.H., Copolov, D.L., & Singh, B.S. (1993). Positive and negative symptoms in the psychoses. Re-analysis of published SAPS and SANS global ratings. *Schizophr Res.* ;9(1):11-8.

Knyazev, G.G., Slobodskaya, H. R., & Wilson, G. D. (2002). Psychophysiological correlates of behavioural inhibition and activation. *Pers. Indiv. Differences* 33, pp. 647–660.

Knyazeva, G.G., Slobodskayaa, H.R. & Wilson, G.D. Psychophysiological correlates of behavioural inhibition and activation. *Pers. Indiv. Differences*. 33(4):647-660.

Konishi, S., Nakajima, K, Uchida, I., Kameyama, M., Nakahara, K., Sekihara, K., & Miyashita, Y., (1998). Transient activation of inferior prefrontal cortex during cognitive set-shifting. *Nat Neurosci, 1*, 80–84.

Koren, D., Seidman, L.J., Poyurovsky, M., Goldsmith, M., Viksman, P., Zichel, S., & Klein, E. (2004). The neuropsychological basis of insight in first-episode schizophrenia: a pilot metacognitive study. *Schizophr Res.* 1;70(2-3):195-202.

Krabbendam, L., Myin-Germeys, I., De Graaf, R., Vollebergh, W., Nolen, W.A., Iedema, J., Van Os, J. (2004). Dimensions of depression, mania and psychosis in the general population. *Psychol Med.* 34(7):1177-86.

Krawczyk, D.C., (2002). Contributions of the prefrontal cortex to the neural basis of human decision making. *Neurosci Biobehav Rev*, 26, 631-664.

Kudadjie-Gyamfi, E., Rachlin, H. (2002). Rule-governed versus contingency-governed behavior in a self-control task: effects of changes in contingencies. *Behav Processes.* 28;57(1):29-35.

LaBar, K.S., Gatenby, J.C., Gore, J.C., LeDoux, J.E., & Phelps, E.A. (1998). Human amygdala activation during conditioned fear acquisition and extinction: a mixed-trial fMRI study. *Neuron.* 20(5):937-45.

LaBar, K.S., LeDoux, J.E., Spencer, D.D., & Phelps, E.A. (1995). Impaired fear conditioning following unilateral temporal lobectomy in humans. *J Neurosci.* 15(10):6846-55.

Lane, R.D., & Schwartz, G.E. (1987). Levels of emotional awareness: a cognitive-developmental theory and its application to psychopathology. A*m J Psychiatry.* ;144(2):133-43.

Lang, P.J. (1994). The varieties of emotional experience: a meditation on James-Lange theory. *Psychol Rev.*, 101(2):211-21.

Larøi, F., Marczewski, P., Van der Linden, M., (2004). Further evidence of the multi-dimensionality of hallucinatory predisposition: factor structure of a modified version of the Launay–Slade Hallucinations Scale in a normal sample. *Eur Psychiatry* 19, 15–20.

Launay, G. & Slade, P. (1981). The measurement of hallucinatory predisposition in male and female prisoners. *Pers Individ Dif* 2, 221–234.

Laurent. A., Duly, D., Murry, P., Foussard, N., Boccara, S., Mingat, F., Dalery, J., & d'Amato, T. (2001). WCST performance and schizotypal features in the first-degree relatives of patients with schizophrenia. *Psychiatry Res.* 1;104(2):133-44.

Lawrence, N.S., Jollant, F., O'Daly, O., Zelaya, F., & Phillips, M.L. (2008). Distinct Roles of Prefrontal Cortical Subregions in the Iowa Gambling Task. *Cereb Cortex.*

Lawrence, N.S., Jollant, F., O'Daly, O., Zelaya, F., & Phillips, M.L. (2009). Distinct Roles of Prefrontal Cortical Subregions in the Iowa Gambling Task.. *Cereb Cortex,.*19(5):1134-43.

Lawrence, N.S., Wooderson, S., Mataix-Cols, D., David, R., Speckens, A. & Phillips, M.L. (2006). Decision making and set shifting impairments are associated with distinct symptom dimensions in obsessive-compulsive disorder. *Neuropsychology.* 20(4):409-19.

LeDoux, J., (1996). *The emotional brain: the mysterious underpinnings of emotional life.* Simon and Schuster, New York.

LeDoux, J.E. (2000). *Emotion circuits in the brain. Annu. Rev. Neurosci.* 23:155-184.

Lee, J., & Park, S. (2005). Working memory impairments in schizophrenia: a meta-analysis. *J Abnorm Psychol* 114, 599–611.

Lee, Y., Kim, Y.T., Seo, E.., Park, O., Jeong, S.H., Kim, S.H., & Lee, S.J. (2007). Dissociation of emotional decision-making from cognitive decision-making in chronic schizophrenia. *Psychiatry Res.* 30;152(2-3):113-20.

Lehto, J. E., & Elorinne, E. (2003). Gambling as an executive function task. *Appl Neuropsychol, 10 (4)*, 234–238.

Lev, D., Hershkovitz, E., & Yechiam E. (2008). Decision making and personality in traffic offenders: a study of Israeli drivers. *Accid Anal Prev.*;40(1):223-30.

Lewinsohn, S., & Mano, H. (1993). Multi-attribute choice and affect: the influence of naturally occurring and manipulated moods on choice processes, *J. Behav. Decis. Mak.* 6 (1) 33– 51.

Liao, P.C., Uher, R., Lawrence, N., Treasure, J., Schmidt, U., Campbell, I.C., Collier, D.A., & Tchanturia, K. (2008) An examination of decision making in bulimia nervosa. *J Clin Exp Neuropsychol.,* 11:1-7.

Lin, C.H., Chiu, Y.C., Cheng, C.M., & Hsieh, J.C. (in press). Brain maps of Iowa gambling task.. *BMC Neurosci.* 26;9:72.

Linney, Y.M., Peters, E.R., & Ayton, P. (1998). Reasoning biases in delusion-prone individuals. *Br J Clin Psychol.* 37 (Pt 3):285-302.

Lovibond, P.F. & Shanks, D.R. (2002). The role of awareness in Pavlovian conditioning: empirical evidence and theoretical implications. *J Exp Psychol Anim Behav Process*. 28(1):3-26.

Lucht, M., Schaub, R.T., Meyer, C., Hapke, U., Rumpf, H.J, Bartels, T., von Houwald, J., Barnow, S., Freyberger, H.J., Dilling, H., & John, U. (2003). Gender differences in unipolar depression: a general population survey of adults between age 18 to 64 of German nationality. *J Affect Disord.* ;77(3):203-11.

Luria, A.R. (1966). *Higher Cortical Functions in Man.* Basic Books, New York.

MacLean, P. D. (1949). Psychosomatic disease and the "visceral brain": Recent developments bearing on the Papez theory of emotion. *Psychosom. Med.* 11:338–353.

Macmillan, M. (1996). Phineas Gage: A case for all reasons. In C. Code, C-W. Wallesch, A-R. Lecours, & Y. Joanette (Eds.), *Classic Cases in Neuropsychology* (pp. 243-262). East Sussex: Erlbaum.

Macmillan, M. (2000). *An Odd Kind of Fame: Stories of Phineas Gage.* Cambridge, MA: MIT Press.

Maia, T. V., & McClelland, J. L., (2004). A reexamination of the evidence for the somatic marker hypothesis: what participants really know in the Iowa gambling task. *Proc Natl Acad Sci U S A* 9;101(45):16075-80.

Maia, T.V., & McClelland J. L. (2005). The somatic marker hypothesis: still many questions but no answers: Response to Bechara et al. *Trends Cogn Sci.* 9 (4), 2005, 162-164.

Mansell, W., Colom, F., & Scott, J. (2005). The nature and treatment of depression in bipolar disorder: a review and implications for future psychological investigation. *Clin Psychol Rev.* ;25(8):1076-100.

Martin, D.J., Oren, Z., & Boone, K. (1991). Major depressives' and dysthmics' performance on the Wisconsin Card Sorting Test. *J Clin Psychol.*;47(5):684-90.

Martino, D.J., Bucay, D., Butman, J.T., & Allegri, R.F. (2007). Neuropsychological frontal impairments and negative symptoms in schizophrenia. *Psychiatry res*, 30;152(2-3):121-8.

McCaffrey, R.J., Ortega A., & Haase, R.F. (1993). Effects of repeated neuropsychological assessments. *Arch Clin Neuropsychol* 8,. 519–524.

McCaffrey, R.J., Ortega, A., Orsillo, S.M., Nelles, W.B., & Haase, R.F., (1992). Practice effects in repeated neuropsychological assessments. *Clin Neuropsychol* 6, 32–42.

McGuigan, F.J. (1993). *Experimental psychology: Methods of research*. Prentice Hall.

Mellers, B., & Biagini, K., (1994). Similarity and choice. *Psychol review*. 101: 505-518.

Meltzer, H., Gill B., Petticrew, M., & Hinds K. (1995). *The prevalence of psychiatric morbidity among adults living in private households (OPCS Surveys of Psychiatric Morbidity in Great Britain, Report 1: Office of National Statistics)*, HMSO, London (1995).

Miller, B.L., & Cummings, J.L.. (2006). *The Human Frontal Lobes: Functions and Disorders*. Guilford Press, New York.

Miller, E. K., & Cohen, J. D., (2001). An integrative theory of prefrontal cortex function. *Annu Rev Neurosci* 24, 167-202.

Miller, E.K. (2000). The prefrontal cortex and cognitive control. *Nat. Rev., Neurosci.* 1,59–65.

Miller, L. (1985). Cognitive risk taking after frontal and temporal lobectomy: the synthesis of fragmented visual information. *Neuropsychologia*, 23:359-369.

Miller, L. (1992). Impulsivity, risk-taking, and the ability to synthesize fragmented information after frontal lobectomy. *Neuropsychologia*, 23:359-369.

Miller, L., & Milner, B. (1985). Cognitive risk taking after frontal and temporal lobectomy: the synthesis of phonemic and semantic information. *Neuropsychologia*, 23:371-379.

Miller, W., Bishop, S., Norman, W.H., & Maddever, H. (1985). The Modified Hamilton Rating Scale for Depression: reliability and validity. *Psychiatry Res* 14:131–142.

Miner, B. (1963). Effects of Different Brain Lesions on Card Sorting. *Arch Neurol.*;9(1):90-100.

Mitchell, D.G., Colledge, E., Leonard, A. & Blair, R.J. (2002). Risky decisions and response reversal: is there evidence of orbitofrontal cortex dysfunction in psychopathic individuals? *Neuropsychologia.*;40(12):2013-22.

Miu, A.C., Heilman, R.M., Houser, D. (2008). Anxiety impairs decision-making: psychophysiological evidence from an Iowa Gambling Task. *Biol Psychol.* 77(3):353-8.

Morris, J. S., Ohman, A., & Dolan, R.J. (1999). A subcortical pathway to the right amygdala mediating "unseen" fear. *Proceedings of the national academia of science USA.* 96(4) :1680-1685.

Morrison, A.P., French, P., Lewis, S.W., Roberts, M., Raja, S., Neil, S.T., Parker, S., Green, J., Kilcommons, A., Walford, L., & Bentall, R.P. (2006). Psychological factors in people at ultra-high risk of psychosis: comparisons with non-patients and associations with symptoms. *Psychol Med.*;36(10):1395-404.

Must, A., Juhász, A., Rimanóczy, A., Szabó, Z., Kéri, S., & Janka, Z. (2007). Major depressive disorder, serotonin transporter, and personality traits: why patients use suboptimal decision-making strategies*? J Affect Disord.* ;103(1-3):273-6.

Must, A., Szabó, Z., Bódi, N., Szász, A., Janka, Z., & Kéri, S. (2006). Sensitivity to reward and punishment and the prefrontal cortex in major depression. *J Affect Disord.* 90(2-3):209-15.

Nakamura, M., Nestor, P.G., Levitt, J.J., Cohen, A.S., Kawashima, T., Shenton, M.E., & McCarley, R.W. (2008). Orbitofrontal volume deficit in schizophrenia and thought disorder. *Brain.* 131(Pt 1):180-95.

Naqvi, N., Tranel, D., & Bechara, A. (2006). Visceral and decision-making functions in the ventromedial prefrontal cortex. In: Zald, D., & Rauch, S. (2006). *The orbitofrontal cortex.* Oxford University Press.

National Institute for Clinical Excellence (2002). *Clinical Guideline 1. Schizophrenia: core interventions in the treatment and management of schizophrenia in primary and secondary care*, NICE, London. http://www.nice.org.uk/nicemedia/pdf/cg001fullguideline.pdf (accessed 1 August 2008)

National Institute for Clinical Excellence (2004). *Depression: management of depression in primary and secondary care.* NICE, London. www.nice.org.uk/pdf/CG023quickrefguide.pdf (accessed 1 August 2008).

Nielen, M.M., Veltman, D.J., de Jong, R., Mulder, G., & den Boer, J.A. (2002). Decision making performance in obsessive compulsive disorder. *J Affect Disord.* 69(1-3):257-60.

Nieuwenstein, M.R., Aleman, A. & de Haan, E.H. (2001). Relationship between symptom dimensions and neurocognitive functioning in schizophrenia: a meta-analysis of WCST and CPT studies. Wisconsin Card Sorting Test. Continuous Performance Test. *J Psychiatr Res.* 35(2):119-25.

North, N.T., & O'Carroll, R.E. (2001). Decision making in patients with spinal cord damage: afferent feedback and the somatic marker hypothesis. *Neuropsychologia.*;39(5):521-4.

O'Doherty, J., Kringelbach, M.L., Rolls, E.T., Hornak, J., & Andrews C. (2001). Abstract reward and punishment representations in the human orbitofrontal cortex. *Nat Neurosci.*4(1):95-102.

Olson, E.A., Hooper, C.J., Collins, P. & Luciana, M. (2007). Adolescents' performance on delay and probability discounting tasks: contributions of age, intelligence, executive functioning, and self-reported externalizing behavior. *Pers Individ Dif.* 43(7):1886-1897.

Öngur, D., & Price, J.L (2000). The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans, *Cereb Cortex* 10, 206–209.

Overall, J., & Gorham, D. (1962) The brief psychiatric rating scale. *Psycholl Rep,* 10, 799-812.

Overman, W.H. (2004). Sex differences in early childhood, adolescence, and adulthood on cognitive tasks that rely on orbital prefrontal cortex. *Brain Cogn.* 55(1):134-47.

Ovsiew, F. (1999). *Neuropsychiatry and Mental Health Services.* American Psychiatric Press, Washington, D.C.

Panksepp, J. (1998). *Affective neuroscience: the foundations of human and animal emotions.* New York: Oxford University Press.

Pantelis, C., Barber, F.Z., Barnes, T.R., Nelson, H.E., Owen, A.M., & Robbins, T.W. (1999). Comparison of set-shifting ability in patients with chronic schizophrenia and frontal lobe damage. *Schizophr Res.* 22;37(3):251-70.

Pantelis, C., Velakoulis, D., McGorry, P.D., Wood, S.J., Suckling, J., Phillips, L.J., Yung, A.R., Bullmore, E.T., Brewer, W., Soulsby, B., Desmond, P., & McGuire, P.K. (2003). Neuroanatomical abnormalities before and after onset of psychosis: a cross-sectional and longitudinal MRI comparison. *Lancet*. 25;361(9354):281-8.

Paulus, M., (2005). Neurobiology of decision-making: quo vadis?. *Cognitive Brain Res* 23; 2-10.

Pecchinenda, A., Dretsch, M., & Chapman P. (2006). Working memory involvement in emotion-based processes underlying choosing advantageously. *Exp Psychol.*;53(3):191-7.

Peralta, V., de Leon, J., & Cuesta, M.J. (1992). Are there more than two syndromes in schizophrenia? A critique of the positive–negative dichotomy. *Br. J. Psychiatry* 161, 335– 343.

Peters, E., Joseph, S., Day, S., & Garety, P. (2004). Measuring delusional ideation: the 21-item Peters et al. Delusions Inventory (PDI). *Schizophr Bull.*30(4):1005-22.

Peters, E.R., Joseph, S., & Garety, P.A., (1999). The assessment of delusions in normal and psychotic populations: Introducing the PDI (Peters et al. Delusions Inventory). *Schizophr Bull* 25, 553-576.

Phan, K.L., Wager, T.D., Taylor, S.F., & Liberzon, I. (2004) Functional neuroimaging studies of human emotions. *CNS Spectr*. 9(4):258-66.

Phelps, E.A., LaBar, K.S., & Spencer, D.D. (1997). Memory for emotional words following unilateral temporal lobectomy. *Brain Cog*. 35(1):85-109.

Pinkham, A.E., Penn, D.L., Perkins, D.O. & Lieberman, J. (2003). Implications for the neural basis of social cognition for the study of schizophrenia. *Am J Psychiatry*. 160(5):815-24.

Plassmann, H, O'Doherty, J., Shiv, B., & Rangel, A. (2008). Marketing actions can modulate neural representations of experienced pleasantness. *Proc Natl Acad Sci U S A*. 22;105(3):1050-4.

Premkumar, P., Fannon, D., Kuipers, E., Simmons, A., Frangou, S., & Kumari, V. (2008). Emotional decision-making and its dissociable components in schizophrenia and schizoaffective disorder: a behavioural and MRI investigation. *Neuropsychologia*.;46(7):2002-12.

Prentice, K.J., Gold, J.M., & Buchanan, R.W. (2008). The Wisconsin Card Sorting impairment in schizophrenia is evident in the first four trials. *Schizophr Res* 106(1):81-7.

Price, J.L. (1999). Prefrontal cortical networks related to visceral function and mood. *Ann N Y Acad Sci*. 29;877:383-96.

Quintana, J., Wong, T., Ortiz-Portillo, E., Kovalik, E., Davidson, T., Marder, S.R. & Mazziotta, J.C. (2003). Prefrontal-posterior parietal networks in schizophrenia: primary dysfunctions and secondary compensations. *Biol Psychiatry*. 1;53(1):12-24.

Rabbitt, P. (1997). *Methodology of Frontal and Executive Function*. Psychology press, London.

Rankin, K.P. (2006). Social cognition in frontal lobes in Miller B.L. & Cummings J.L. (2006). *The Human Frontal Lobes: Functions and Disorders*. Guilford Press, New York.

Reavis, R., & Overman, W. H. (2001). Adult sex differences on a decision-making task previously shown to depend on the orbital prefrontal cortex. *Behav Neurosci, 115*, 196–206.

Rempfer, M., Hamera, E., Brown, C., & Bothwell, R.J. (2006). Learning proficiency on the Wisconsin Card Sorting Test in people with serious mental illness: what are the cognitive characteristics of good learners? *Schizophr Res.* 87(1-3):316-22.

Richter, P., Werner, J., Heerlein, A., Kraus, A., & Sauer, H. (1998). On the validity of the Beck Depression Inventory. A review. *Psychopathology.* ;31(3):160-8.

Ritter, L.M., Meador-Woodruff, J.H., & Dalack, G.W., (2004). Neurocognitive measures of prefrontal cortical dysfunction in schizophrenia. *Schizophr Res* 68, 65–73.

Robbins, T.W. (2007). Shifting and stopping: fronto-striatal substrates, neurochemical modulation and clinical implications. *Philos Trans R Soc Lond B Biol Sci.* 29;362(1481):917-32.

Roberts, R.E., Lewinsohn, P.M., & Seeley, J.R. (1991). Screening for adolescent depression: a comparison of depression scales. *J Am Acad Child Adolesc Psychiatry.* ;30(1):58-66.

Rodríguez-Sánchez, J.M., Crespo-Facorro, B., Perez-Iglesias, R., González-Blanch, C., Alvarez-Jimenez, M., Llorca, J., & Vázquez-Barquero, J.L. (2005). Prefrontal cognitive functions in stabilized first-episode patients with schizophrenia spectrum disorders: a dissociation between dorsolateral and orbitofrontal functioning. *Schizophr Res.* 15;77(2-3):279-88.

Rogers, M.A., Kasai, K., Koji, M., Fukuda, R., Iwanami, A., Nakagome, K., Fukuda, M., & Kato, N. (2004). Executive and prefrontal dysfunction in unipolar depression: a review of neuropsychological and imaging evidence. *Neurosci Res.* ;50(1):1-11.

Rogers, R.., Everitt, B.J., Baldacchino, A., Blackshaw, A.J., Swainson, R., Wynne, K., Baker, N.B., Hunter, J., Carthy, T., Booker, E., London, M., Deakin, J. F. W., Sahakian, B.J., & Robbins, T.W. (1999). Dissociable deficits in the decision making cognition of chronic amphetamine abusers, opiate abusers, patients with focal damage to the prefrontal cortex, and tryptophan depleted normal volunteers: evidence for monoaminergic mechanism. *Neuropsychopharmachology*, 20:322-339.

Rolls, E. T. (1995). A theory of emotion and consciousness, and its application to understanding the neural basis of emotion. In Gazzaniga, M. S. (Ed.) *The cognitive neurosciences* (pp. 1091-1106). Cambridge, MA:MIT Press.

Rolls, E.T. (1999) The functions of the orbitofrontal cortex. *Neurocase 5*: 301-312.

Rolls, E.T. (2000). The orbitofrontal cortex and reward. *Cereb Cortex 10*: 284-294.

Rolls, E.T. (2005) *Emotion explained.* Oxford University Press.

Rolls, E.T., Hornak, J., Wade, D., & McGrath, J., (1994). Emotion-related learning in patients with social and emotional changes associated with frontal lobe damage. *J Neurol Neurosurg Psychiatry.* 57 (12), 1518–1524.

Sabbatini, R.M.E. (1997). The History of Psychosurgery. *"Brain & Mind" Magazine*, June/August.

Sass, L.A, & Parnas J. (2003). Schizophrenia, consciousness, and the self. *Schizophr Bull.*;29(3):427-44.

Saver, J. L., & Damasio, A. R., (1991). Preserved access and processing of social knowledge in a patient with acquired sociopathy due to ventromedial frontal damage. *Neuropsychologia.* 29(12):1241-9.

Schmitt, W.A., Brinkley, C.A., & Newman, J.P. (1999). Testing Damasio's somatic marker hypothesis with psychopathic individuals: Risk takers or risk averse? *J Abnorm Psychol, 108*(3), 538–543.

Schultz, W., Tremblay, L., & Hollerman, J.R., (2000). Reward processing in the primate orbitofrontal cortex and basal ganglia. *Cereb cortex*; 10:272-283.

Seeber, K., & Cadenhead, K.S..(2005). How does studying schizotypal personality disorder inform us about the prodrome of schizophrenia? *Curr Psychiatry Rep.* 7(1):41-50.

Sevy, S., Burdick, K.E., Visweswaraiah, H., Abdelmessih, S., Lukin, M., Yechiam, E., & Bechara, A. (2007). Iowa gambling task in schizophrenia: a review and new data in patients with schizophrenia and co-occurring cannabis use disorders. *Schizophr Res.* 92(1-3):74-84.

Shamay-Tsoory, S.G., Aharon-Peretz, J. & Levkovitz, Y., (2007). The neuroanatomical basis of affective mentalizing in schizophrenia: comparison of patients with schizophrenia and patients with localized prefrontal lesions. *Schizophr Res* 90, 274-283.

Shankman, S.A., Klein, D.N., Tenke, C.E., & Bruder, G.E. (2007). Reward sensitivity in depression: a biobehavioral study. *J Abnorm Psychol.* 116 (1), 95–104.

Shenal, B.V., Harrison, D.W., & Demaree, H.A. (2003). The neuropsychology of depression: a literature review and preliminary model. *Neuropsychol Rev* ;13(1):33-42.

Shurman, B., Horan, W.P., & Nuechterlein, K.H., (2005). Schizophrenia patients demonstrate a distinctive pattern of decision making impairment on the Iowa Gambling Task. *Schizophr Res* 72, 215–224.

Sidman, M., (1961). *Tactics of scientific research.* Authors' Cooperative inc., Boston, MA.

Smith, E. E., & Jonides J. (1999). Storage and executive processes in the frontal lobes. *Science*, 283, 1657-1661.

Smoski, M.J., Lynch, T.R., Rosenthal, M.Z., Cheavens, J.S., Chapman, A.L., & Krishnan, R.R. (2008). Decision-making and risk aversion among depressive adults. *J Behav Ther Exp Psychiatry.* 39:567-576.

Smoski, M.J., Lynch, T.R., Rosenthal, M.Z., Cheavens, J.S., Chapman A.L., & Krishnan, R.R. (2008). Decision-making and risk aversion among depressive adults. *J Behav Ther Exp Psychiatry* (in press).

Steel, C., Garety, P.A., Freeman, D., Craig, E., Kuipers, E., Bebbington, P., Fowler, D., & Dunn, G. (2007). The multidimensional measurement of the positive symptoms of psychosis. *Int J Methods Psychiatr Res.;*16(2):88-96.

Stratta, P., Arduini, L., Daneluzzo, E., Rinaldi, O., di Genova, A., & Rossi A. (2004). Relationship of good and poor Wisconsin Card Sorting Test performance to illness duration in schizophrenia: a cross-sectional analysis. *Psychiatry Res.* 1;121(3):219-27.

Strauss, E., Sherman, E. M. S., & Spreen, O. (2006). *A Compendium of Neuropsychological Tests: Administration, Norms and commentary*. Oxford University Press.

Suhr, J.A. & Spitznagel, M.B. (2001). Factor versus cluster models of schizotypal traits. II: relation to neuropsychological impairment. *Schizophr Res.* 1;52(3):241-50.

Suhr, J.A. (1997). Executive functioning deficits in hypothetically psychosis-prone college students. *Schizophr Res.* 17;27(1):29-35.

Suhr, J.A., & Tsanadis, J. (2007). Affect and personality correlates of the Iowa Gambling Task.. *Persy Individ Diff*, 43, 1, :27-36.

Suzuki, A., Hirota, A., Takasawa, N., & Shigemasu, K. (2003) Application of the somatic marker hypothesis to individual differences in decision making. *Biol Psychol.* ;65(1):81-8.

Tien, A., (1991). Distribution of hallucinations in the population. *Soc. Psychiatry Psychiatr. Epidemiol.* 21, 287-292.

Tierney, A. J. (2000). Egas Moniz and the Origins of Psychosurgery: A Review Commemorating the 50th Anniversary of Moniz's Nobel Prize. *J Hist Neurosci* 9, 22-36.

Tomb, I., Hauser, M., Deldin, P., & Caramazza, A. (2002). Do somatic markers mediate decisions on the gambling task? *Nat Neurosci.* 5(11):1103-4.

Tranel, D., & Damasio, H. (1994). Neuroanatomical correlates of electrodermal skin conductance responses. *Psychophysiology.*;31(5):427-38.

Tranel, D., Bechara, A., & Damasio, A. R., (1999). *Decision making and the somatic marker hypothesis*. In: Gazzaniga, M. S.,(Ed.), The new cognitive neuroscience. MIT press, Cambridge, Massachusetts, pp.1047-1061.

Turnbull, O. H., Worsey, R.B., & Bowman, C. H. (2007). Emotion and intuition: Does schadenfreude make interns poor learners *Philoctetes.* 1, (1) 5-43.

Turnbull, O.H., Berry, H., & Bowman, C.H., (2003). Direct versus indirect emotional consequences on the Iowa Gambling Task. *Brain Cog* 53 (2), 389–392.

Turnbull, O.H., Evans, C.Y., Bunce, A., Carzolio, B., & O'Connor, J., (2005). Emotion based learning and central executive resources: an investigation of intuition and the Iowa Gambling Task. *Brain Cog* 57 (3), 244–247.

Turnbull, O.H., Evans, C.Y., Kemish, K., Park, S., & Bowman, C.H. (2006). A novel 'set-shifting' modification of the Iowa Gambling Task: flexible emotion-based learning in schizophrenia. *Neuropsychology*. 20(3):290-298.

van der Bos, R., Houx, B.B., & Spruijt, B.M., (2005). The effect of reward magnitude differencies on choosing disadvantageous decks in the Iowa Gambling Task. *Biol Psychology*. 71: 155-161.

Venables, P.H., & Christie, M.J. (1980). Electrodermal activity. In: Martin, I., & Venables P.H., editors. *Techniques in psychophysiology*. New York: John Wiley. p 3–67.

Verdejo-García, A., & Bechara, A. (2009). A somatic marker theory of addiction. *Neuropharmacology*, 56(1), 48-62.

Verdoux, H., & van Os, J., (2002). Psychotic symptoms in non-clinical populations and the continuum of psychosis. *Schizophr Res* 54(1-2):59-65.

Verdoux, H., Maurice-Tison, S., Gay, B., van Os, J., Salamon, R., & Bourgeois, M., (1998). A survey of delusional ideation in primary care patients. *Psychol. Med.* 28, 127-134.

Vuilleumier, P., & Schwartz, S., (2001b). Modulation of visual perception by eye gaze direction in patients with spatial neglect and extinction. *Neuroreport.* 20;12(10):2101-4.

Vuilleumier, P., & Schwartz, S.,(2001a). Emotional facial expressions capture attention. *Neurology*. 23; 56(2):153-8.

Waltz, J.A. & Gold, J.M. (2007). Probabilistic reversal learning impairments in schizophrenia: further evidence of orbitofrontal dysfunction. *Schizophr Res.* 93(1-3):296-303.

Waltz, J.A., Knowlton, B.J., Holyoak, K.J., Boone, K.B., Mishkin F.S., de Menezes Santos, M., Thomas, C.R., & Miller B. L., (1999). A system for relational reasoning in human prefrontal cortex. *Psychol Science*; 10: 119-125.

Weber, E.U., Shafir, S., & Blais, A.-R. (2004). Predicting risk sensitivity in humans and lower animals: Risk as variance or coefficient of variation. *Psychol Review*, 111, 430–445.

Weinberger, D. R., & Berman, K. F., (1996). Prefrontal function in schizophrenia: confounds and controversies. *Philos Trans R Soc Lond B Biol Sci* 29;351(1346):1495-503.

Welt, L., (1888). Uber charaktervaranderungen des menschen infoldge von lasionen des stirnhirns. *Detusch arch. Klin. Med.* 42, 339-390.

Wilder, K.E., Weinberger, D.R., & Goldberg, T.E., (1998). Operant conditioning and the orbitofrontal cortex in schizophrenic patients: unexpected evidence for intact functioning. *Schizophr Research* 30, 169–174.

WOS: Web of Science. http://apps.isiknowledge.com/WOS_General search_input.do?highlighted_tab=WOS&product=WOS&last_prod=WOS&SID=N 1OLDoFidl@mHlnM2n2&search_mode=GeneralSearch. Website accessed on 20th of October 2008.

Yudofsky, S.C., & Hales, R.E., (1997). *The American Psychiatry Press Textbook of Neuropsychiatry*. American Psychiatric Press, 3rd ed., Washington, D.C.

Zola-Morgan, S., Squire, L.R., Alvarez-Royo, P., & Clower, R.P. (1991). Independence of memory functions and emotional behavior: separate contributions of the hippocampal formation and the amygdala. *Hippocampus*. 1991 1(2):207-20.

Appendix 1

Bechara et al. 1999 original instruction

1. In front of you on the screen, there are four decks of cards A, B, C, and D.

2. I want you to select one card at a time, by clicking on the card, from any deck you choose.

3. Each time you select a card from a deck, the color of the card turns red or black, and the computer will tell you that you won some money. I won't tell you how much money you will win. You will find out along the way. Every time you win, the green bar gets longer.

4. Every so often, however, when you click on a card, the computer tells you that you won some money, but then it says that you also lost some money. I won't tell you when you will lose or how much you will lose. You will find out along the way. Every time you lose, the green bar gets shorter.

5. You are absolutely free to switch from one deck to another any time you wish.

6. The goal of the game is to win as much money as possible and, if you find yourself unable to win, make sure you avoid losing money as much as possible.

7. I won't tell you for how long the game will continue. You must keep on playing until the computer stops.

8. You will get this $2000 credit (see the green bar) to start the game. At the end, we will see how much you won or lost. The red bar here is a reminder of how much money you borrowed to play the game.

9. It is important to know that the colors of the cards are irrelevant in this game. The computer does not make you lose money at random. However, there is no way for you to figure out when the computer will make you lose. All I can say is that you may find yourself losing money on all of the decks, but some decks will make you lose more than others. You can win if you stay away from the worst decks.

Appendix 2

Contingency shifting variant IGT instructions

In a moment, the computer will present four decks of cards labelled A, B, C, and D. Your task is to select one card at a time, by clicking on the card with the computer mouse, from any deck you choose.

Each time you select a card, the computer will tell you that you have won some money. The amount of money won will be immediately added to the total, which will be displayed in the bottom right-hand side of the screen.

Occasionally, however, when you select a card, the computer will tell you that you have won some money but that you have also lost some money. The amount of money lost will be immediately deducted from your total.

Your task is to try and earn as much money as possible, and if you can't win, to avoid losing as much money as possible.

You will be given a loan of £1000 credit to begin the task. It is important that you try and behave as if this were a real card game and try to win as much money as possible (and lose as little as possible). Treat the £1000 credit of play money, and all money won/lost during the task, as if it were your own real money.

No matter how much you find yourself losing, you can still win. Pay attention to the wins/losses.

Every so often, the computer will ask you to give each deck of cards a score, based on how good or bad you feel they are. Please use the slider scale to rate each of the decks. The computer will show you how to do this.

The computer will not tell you when the task will end, so please keep playing until the tasks ends.

If you have any questions, please read through the instructions again to see if they answer your questions. If they do not, then ask the experimenter to explain.

Remember, your task is to try and earn as much money as possible, and if you can't win, to avoid losing as much money as possible, and be sure to give each deck of cards a score based on how good or bad you feel they are.

Good luck!