Decision Making

The Significance of Cognition, Emotion, and Impulsivity

University of Copenhagen
Department of Psychology

By: Linn Øfsti

Supervisor: Anders Gade

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Abstract

This thesis investigates the cognitive, emotional and neurobiological basis for decision making, and examines how impulsivity may lead to inferior choices. Cognitive theories stress that decision making is based on the thoughtful deliberation of intentions, attitudes and subjective norms. Whereas emotional theories stress that decision making is guided by emotions and gut feelings. The importance of emotion in decision making is especially highlighted in the somatic maker hypothesis and demonstrated in the Iowa gambling task. Although many models posit distinct cognitive and emotional contributions to decision making, they both play an important role in guiding decisions. Cognition and emotion work together to guide decision making, however, they may be engaged to a different degree depending on the situation. Furthermore, may various biases affecting emotion and cognition lead to decision making deficits. Inferior decision making may therefore result from cognitive and emotional biases. However, this thesis also shows that there may also be other reasons for disadvantageous decision making. Individuals with neurological lesions in the ventromedial prefrontal cortex are found to produce severe decision making impairments. Also lesions to other neurological structures such as the amygdala, dorsolateral prefrontal cortex, the anterior cingulate cortex, and the nucleus accumbens may produce decision making deficits. Impaired decision making has also been found in impulsive individuals, showing risk seeking behavior and an inability to delay reward. Disorders believed to be related to impulsivity, such as substance abuse and pathological gambling, are also associated with disadvantageous decision making. One of the underlying reasons for impulsive behaviors are thought to result from abnormalities in the serotonergic and dopaminergic system, where especially low levels of 5- HT have been implicated in poor decision making. In relation to the serotonergic system, this thesis also includes 2 empirical studies which are part of two major research programs: Cimbi and Agenda. The first study, which is part of the Cimbi research program, compares MDMA users and healthy controls to investigate whether serotonergic downregulation due to MDMA abuse may affect decision making. The second study, which is part of the Agenda research program, compares the effect of SSRI treatment on decision making in healthy first degree relatives of patients with depression.

1. Introduction

Imagine a brilliant composer, creating a magnificent musical masterpiece. In the process of creating the masterpiece, the composer has to decide from a limited set of notes which to include. Even though the set of notes is limited, the possibility to create beautiful music is almost endless. In the same way, decisions that we are faced with every day may be equally varied. Some decisions may be small, like deciding to go for a walk, or deciding what to wear, or what to eat for dinner. However there are also bigger decisions which may have a huge impact on our lives, like choices of education, work, whom to marry and whether to buy a house or not. These decisions may have long term consequences, and shape your life. It has been said that "life is the art of living without an eraser" (Rasmanesh, 2006, p.269). Although this may be true in some cases, many of our choices are reversible. However, considering the long term impact many decisions may have on our lives, could make the decision making process rather challenging. Furthermore, the uncertainty of not knowing what the future might bring may put an extra strain on the decision making process. Thus, there is always a certain risk involved in making any decision. When making decisions, we may never know what the outcome would have been had we followed another path. Considering the impact that decision making can have on our lives, it would be interesting to examine more closely factors that influence the decision making process. The notion that people use their gut feeling when deciding is well known, thus many of our decisions are based on emotions. However, at other times, our decision making is more elaborate and involves cognition. The main aim of this thesis is therefore to examine the cognitive, emotional and neurobiological basis for decision making and to explore how impulsivity may lead to inferior choices. The two questions this thesis seeks to answer are:

How does cognition and emotion influence our decisions?
How may impulsivity lead to disadvantageous decision making?

The first part of the thesis will start with a theoretical overview and further consider how cognition and emotion influence decision making. The thesis will next explore the neurobiological basis for decision making, and the somatic marker hypothesis of Damasio (1994). In the subsequent part, the thesis will explore how impulsivity, and various

disorders related to impulsivity, may lead to poor decision making. Finally, the thesis will include two empirical studies examining the effect serotonergic modulation has on decision making.

2. General framework for decision making

*"Life is the sum of all your choices," Albert Camus (*Buchanan & O'Connell, 2006)

Explaining human behavior in all its complexity is a difficult task, and can be approached at many levels (Ajzen, 1991). Decision making behavior can sometimes emerge spontaneously and automatically, with presumably no conscious choice. In other cases, decision making behavior involves conscious thought (Carver & Scheier, p. 476). The core ingredients for any decision making analysis are acts, states and outcomes. The set of acts are the options that the decision maker must choose between; the set of states correspond to external uncertainties. The set of outcomes are the different possible consequences of each act given each possible state (Newell, Lagando, Shanks, 2007 p.103). Even though the decision framework based on acts, states and outcomes is standard in most analyses of decision making, it can be construed in several different ways. First there is a distinction between normative and descriptive models. A normative model of decision making tells us how people should make decisions; a descriptive model tells us how people actually do make decisions. Second, there is the distinction between the "as if" and "process" models that applies to both normative and descriptive models of decision making. Essentially, the 'as if' models predict the output of an agent in terms of the input it receives, but don't specify exactly how this is achieved. Thus, 'as if' models are often referred to as computational or rational models. They seek to establish what an agent is trying to compute, rather than how the agent is actually computing it. In contrast, a process model describes how the agent actually carries out these computations, and strives to describe the actual cognitive mechanisms underpinning decision behavior (Newell et al. 2007, p.106, 107).

3. Theoretical overview

3. 1 Expected Utility theory

Von Neumann and Morgenstern (1947, cited in Newell et al., 2007) are usually accredited for putting forward the first theory of decision making in modern time. In 1947 they proposed the expected utility theory (EU), which came to be one of the most influential normative theories of how people make decisions. EU was developed within the discipline of economics but has nevertheless had a strong and lasting influence on psychological investigations of decision making (Newell et al., 2007, p. 20-22). Rooted in economics and mathematics, EU theory is a normative theory about how people theoretically should make decisions. The basic idea of EU is that the value of each possible outcome should be weighted by the probability of its occurrence when contemplating the various options. The expected utility of each act is computed by the weighted sum of the utilities of all possible outcomes of that act. Once the expected utility of each possible act is computed, the principle of maximizing expected utility advises that the act with the highest value is chosen (Newell et al.,2007 p. 105, 106). Von Neumann and Morgenstern suggested that decision makers are rational, consistent, and act according to a set of assumptions and axioms when making decisions (Buchanan & O'Connell, 2006). If decision makers would violate these axioms, expected utility would not be maximized.

An important aspect in the development of EU was the distinction between money and its utility, and the idea that in general money has diminishing marginal utility. This is illustrated by the fact that the same amount of money has a different value for different people. For instance will $100 be of more value for someone financially disadvantaged than a multimillionaire. The subjective value of money is also illustrated in the concave EU function of money and utility. Hence, people value the move from $100 to $200 more than the move from $1100 to $1200. The idea that people evaluate outcomes in terms of changes of wealth rather than financial status of wealth has strong parallels in psychophysics. The responses to sensory and perceptual stimuli are based on relative changes rather than absolute changes, and exhibit a similar relation of diminishing sensitivity to such changes (Newell et al., 2007, p. 115-116).

After Von Neumann & Morgenstern proposed their theory of expected utility, a number of other theorists developed extensions and variations. Savage (1954, cited in Newell et al., 2007 p. 20) proposed the subjective utility theory based on von Neumann & Morgenstern's work by incorporating the notion of subjectivity into the maximization of expected utility. In the subjective utility theory frame, decision makers select the option that maximizes their subjective expected utilities, and minimize the pain or the negative utility in a decision making process. Savage argued that a person whose choices satisfy all the axioms of the theory, chooses as if he/she were maximizing his/her expected utility, while assigning subjective probabilities to the possible outcomes of a choice (Newell et al., 2007 p.20). The EU function is presented in figure 1.

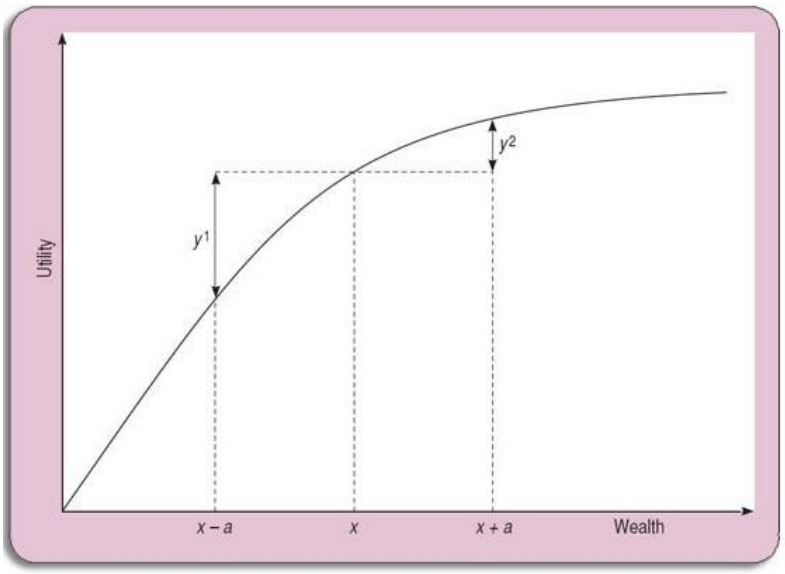

Figure 1: The expected utility function illustrate that at the utility of an increase (+a) in wealth is less than the disutility of a decrease (-a) in wealth. any point x. (Adapted from the Open University, 2009)

Even though the EU theories had a strong normative appeal of how rational actors would behave if certain assumptions were met, it was not useful as a descriptive model of how people actually make decisions (Plous, 1993, p. 95). Observations of human behavior demonstrated that people systematically violated one or more of the axioms of the theory. Objections were therefore raised to the Von Neumann & Morgenstern/Savage version of EU. Together with the increasing amount of evidence showing the insufficiency of EU and the puzzles and paradoxes put forth by Allais in 1953 and Ellsberg in 1961, a renewed

interest was spurred in the judgment and decision making research (Newell et al., 2007, p. 21). One of the main figures in this respect was Simon (1955) who suggested that humans were boundedly rational when making decision. Simon (1955) argued that due to limitations in both cognitive processing and environmental information, it would be inconceivable that a real person would act perfectly rational when making decisions. Instead of being fully rational, Simon (1955) argued that humans should be viewed as being boundedly rational. The idea behind this notion was that even though humans could not make optimal decisions due to limitations in cognitive resources and environmental constraints, they could still make good enough decisions. That is, people could make satisfying decisions if they choose an option that satisfied their minimum requirements, even if that option was not the optimal choice (Sternberg, 2003 p. 407).

3. 2 Prospect theory

The accumulation of evidence showing violations of EU also encouraged other researchers to develop better theories that accounted for decision making in a more descriptive way (Newell et al., 2007, p.22) Perhaps the most influential of these theories was the prospect theory, proposed by Kahneman & Tversky (1979). Prospect theory preserved the idea that people's choices involved maximizing some kind of expectation. However, Kahneman & Tversky (1979) suggested that both utilities and probabilities of outcomes undergo systematic cognitive distortions when they are evaluated. Moreover, prior to this evaluation, the decision maker must construe a mental representation of the choice problem (Newell et al., 2007, p.115). Instead of basing these mental representations on thorough reflection and thought, Tversky and Kahneman (1974) suggested that people are likely to make decisions based on heuristics. Timesaving and easy as heuristics may be, it nevertheless allows a greater chance of error. Hence, heuristics may both limit and sometimes distort the ability to make rational decisions. Identifying factors why humans make errors when making decisions were therefore influential for their proposal of the prospect theory (Sternberg, 2003, p. 409).

The Prospect theory described actual decision making process when decisions were made under uncertainty. In presenting the prospect theory, Kahneman & Tversky (1979) brilliantly demonstrated in an experiment how actual choice deviated from EU theory, and how decisions are affected by the way value and probabilities are framed. In their

experiment, Kahneman & Tversky (1979) constructed a set of choice problems. For example, when offered a choice between $3000 for sure versus a 0.8 probability to win $4000, most subjects preferred the safe option, the $3000. However, when faced with a choice between a sure loss of $3000 versus a 0.8 probability to loose $4000, people often preferred to gamble. This "framing effect" showed that people's choices vary as a function of how a situation is described or framed. Thus, people tend to behave risk-averse in gain situations, but risk seeking in loss situations. Consequently, people do not evaluate outcomes of gambles in terms of the overall state of wealth to which they lead, but evaluate it as gains or losses relative to a neutral reference point (Kahneman & Tversky, 1979). Furthermore, this neutral reference point from which people evaluate a gamble is malleable, and open to manipulation. This means that the same underlying choice problem can be given different reference points, and consequently lead to divergent choices. So people might make very different choices depending on their reference frame (Newell et al., 2007, p.116). Such shifts in risk attitudes are inconsistent with the invariance principle in EU theory which stated that a decision maker should not be affected by the way choices are presented (Newell et al., 2007, p.108). The function of the prospect theory is presented in figure 2.

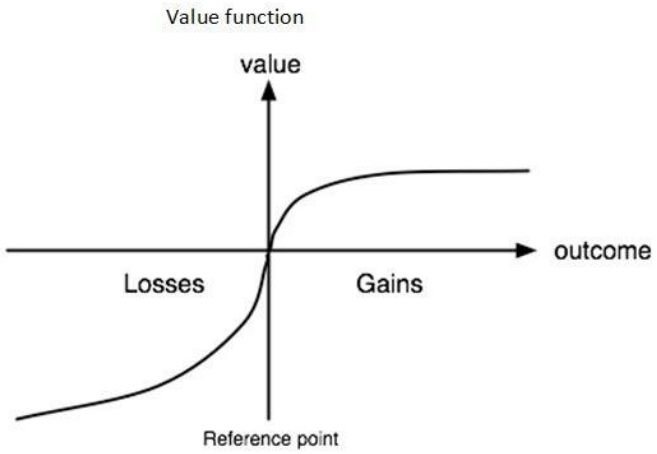

Figure 2: Illustration of the Prospect Theory (Adapted from, Kahneman & Tversky, 1979)

A crucial feature of the prospect theory is that people experience loss much more intensely than corresponding gains. Kahneman and Tversky (1979) called this property loss aversion

and said that "the aggravation that one experiences in losing a sum of money appears to be greater than the pleasure associated with gaining the same amount" (p. 279). The simplest illustration of loss aversion is the fact that people dislike gambles that offer an equal probability of winning or losing the same amount of money. That is, they tend to reject gambles that offer a 50% chance of winning $x and a 50% chance of loosing $x (Newell et al., 2007, p. 118). A demonstration of the loss aversion is the endowment effect (Thaler, 1980) in which a good is perceived as more valuable when in risk of being lost, than when it is viewed as a potential gain (Kahneman, 2003). The endowment effect has been demonstrated in numerous experiments. One of the best known was conducted by Kahneman, Knetsch & Thaler (1990), where university mugs (worth about $5) were randomly given to some of their student's. The student's who had received the mugs, were then asked how much they would be prepared to sell their mugs for, whereas student who had not received mugs, were asked how much they would pay for it. The results showed that the students who received the mug were willing to sell the mug for $7, whereas the student's who were evaluating how much they would pay for the mug, were willing to pay about $3.

The prospect theory does not only account for how people behave in gain and loss situations, it also includes how people view probabilities of outcomes. When people evaluate decision options they often seem to distort the stated or experienced probabilities. Just as the decision makers transform the objective utility of a gain or a loss into a subjective value, they also transform the objective probability of an outcome into a decision weight. Prospect theory postulates that decision weights tend to overweight small probabilities and underweight moderate and high probabilities. These decision weights may help to explain why people engage in risk seeking gambles that offers small probabilities of positive outcomes, like buying lottery tickets. It also accounts for why people act risk aversely to small probabilities of negative outcome, which is the case when people buy insurances (Newell, et al., 2007, p. 120, 121).

3. 2. 1 Criticism of prospect theory

Even though prospect theory has done a very good job in explaining a wide variety of choice behavior, it has a few shortcomings. One criticism concerns that prospect theory does not give a deep psychological explanation for many of the processes it proposes.

There are for example no detailed accounts of how people frame decision problems, select reference points, or edit their options. Neither is there a clear cognitive account of how people integrate decision weights and values to yield a final decision (Newell et al., 2007, p. 125). Another deficiency concerns the fact that there are certain factors that prospect theory does not include, but that seem to have a strong influence on people's decision making. One such prominent factor is the notion of regret in decision making (Loomes & Sudgen). When people make a decision that turns out badly compared to other possible outcomes, they regret the decision. Similarly, if decisions lead to a much better outcome than the other alternatives, people rejoice in their decision. Thus, when making decisions, people usually take these possibilities of regret or rejoicing into account. They anticipate how much they might regret or rejoice in a particular decision by comparing its outcome with other possibilities. However, no theory can account for all aspect of decision making, so the most fruitful direction would be to supplement prospect theory rather than to replace it (Newell, p. 125-126).

3. 3 Theory of reasoned action

Although prospect theory (Kahneman & Tversky, 1979) gives an excellent description of how people actually make decisions, it does not, as noted by Newell et al., (2007, p.125) give a clear cognitive account of how people integrate decision weights and values to yield a final decision. One model that seeks to explain the cognitive mechanisms underpinning decision making is the theory of reasoned action proposed by Ajzen and Fishbein (1975). The *theory of reasoned action* holds that an individual's intention to perform a given behavior is an important factor in explaining behavior. Intentions are assumed to capture the motivational factors that influence a behavior, and manifests itself in how hard people are willing to try, and how much effort they are planning to exert in order to perform the behavior. As a general rule, the stronger the intention to engage in a behavior, the more likely the behavior will be. Furthermore, an individual's behavioral intention depends on the person's attitude about the behavior, which refers to the degree to which a person has a favorable or unfavorable evaluation or appraisal of the behavior in question. The behavioral intention also depends on a person's subjective norms, referring to the perceived social pressure to perform or not to perform the behavior. The attitude and the subjective norm are then weighed together in forming the intention, which subsequently influences the behavior (Ajzen, 1991). The theory of reasoned action has shown to be a

good prediction of choice making. Sheppard, Hartwick & Warshaw (1988) stressed that this model performed extremely well in the prediction of goals and in the prediction of activities involving an explicit choice among alternatives.

In an extension of the theory of reasoned action (Fishbein & Ajzen, 1975), Ajzen (1991) proposed the theory of planned behavior which stressed the importance of perceived behavioral control in predicting behavior. According to this theory, the intentions to perform a behavior can be predicted with high accuracy from the attitudes people hold toward the behavior, their subjective norms, and their perceived behavioral control. Ajzen (1991) view of perceived behavioural control is compatible with Bandura's (1982) concept of perceived self-efficacy, which "is concerned with judgments of how well one can execute courses of action required to deal with prospective situations" (Bandura, 1982, p.122). As a general rule, the more favorable the attitude and subjective norm with respect to a behavior, and the greater the perceived behavioral control, the stronger should an individual's intention to perform the behavior under consideration be. The interaction between attitudes, social norms and perceived control then, seems to be important factors when considering the processes that influence decision making. The relative importance of attitude, subjective norm, and perceived behavioral control in the prediction of intention is expected to vary across behaviors and situations (Ajzen, 1991). Another crucial factor that is influential in this respect is how accurate people's perceptions are. Whether perceived behavioral control reflects actual control depends on the accuracy of the perceptions (Ajzen, 1991). Further, the attitudes and social norms are also dependent upon how a person perceive and interprets various situations. This is why it would be beneficial to take a closer look at how people process information, and to what extent their perceptions reflects reality.

4. The role of information processing and cognition on decision making

All of the stimuli in the environment are interpreted by our perceptual system that organizes and integrates all the inputs into meaningful frameworks. Thus, when people sample these inputs, they construct a personal vision of how reality is organized. So, even

though the objective world around us is the same for everyone, people's experience of the world varies (Carver & Scheier, 2004, p. 415). Cosmides (1989) suggest that humans possess something like a schema acquisition device, which facilitates our ability quickly to glean important information from our experiences and to organize that information into a meaningful structure. According to Cosmide (1989) these schemas are highly flexible, but they are also specialized for selecting and organizing information that will effectively aid people in adapting to various situations. These mental representations then provide the basis for future perceptions, interpretations and actions (Jussim, 1991). Existing schemas does not only influence attention, but also memory. Furthermore, as these schemas are highly subjective and develop over experience, people differ both in how readily they develop schemas, and in the content and complexity of the schemas (Carver & Scheier, 2004, p. 446).

Before making any major decision people often attempt to gather information in the hope that it will lead to a better decision. Often, they will use their schemas as a guideline of 'where to look', but at other times, people still have to work out how much information to look at, and in what order. Acquiring too much information can be extremely costly; acquiring to little can lead to excessive risk of making the wrong decision. Such situations are ubiquitous in day to day life, and involve the trade -off between the costs and benefits of acquiring further information (Newell Lagnado & Shanks, 2008, p .30).

4. 1 Attention

One of the first and essential aspects of decision making is to discover the information we need (Newell et al. 2008, p. 30). Although this may sound relatively easy, people are as previously mentioned, biased by their schemas. All of us experience a richly detailed visual world, where all the visual information is potentially available for attentive processing (Simons & Chabris, 1999). This richness of our visual experience may lead people to believe that their visual representations will include and preserve the same amount of detail (Levin, Momen, Drivdahl & Simons, 2000). However, most of the perceptual processing occurs outside of conscious awareness. Most of the time, our senses are bombarded with a large amount of stimuli which we are unable to fully process. When overloaded with input, the 'bottleneck' in processing allows only a small part to become fully processed. That is why our attention acts as a filter that quickly examines sensory

input and selects a small percentage for full processing and for conscious perception. The unattended information is therefore unnoticed and lost (Atkinson, Atkinson, Smith, Bem & Nolen- Hoeksema, 1996, p.170).

There are several factors that can direct our attention to objects of interest. One crucial factor is people's expectations, which are grounded on previous experiences. Bruner & Postman (1949, p. 222) acknowledged this as they stated that "perceptual organization is powerfully determined by expectations built upon past commerce with the environment". Thus, individuals do not perceive and remember material in isolation. Instead, they may use a top down mechanism or schema to interpret new information in light of past experience and the context in which the material occurs (Plous, 1993, p.38). Hence, when people have enough experience with a particular situation, they often 'see' what they expect to see (Plous,1993 p. 16). Even though expectations can ease the attention process, it may also lead people to miss important cues in the environment. Consequently, failing to notice and attend to information in the environment may narrow down the available decision options.

4. 2 Learning and Memory

Without learning and memory, it would be very difficult to predict the outcome of future events, and consequently decide which actions to take in a given situation. When making a decision, remembering how one solved a decision problem in the past and the outcome that resulted from that choice, may greatly influence the way one solves a new decision problem. Therefore, if a choice produced a good outcome, the tendency to produce the same behavior will be strengthened or reinforced. If an outcome turned out bad on the other hand, the tendency to perform the same behavior in a similar situation will be reduced. Being able to learn from and remember past events are therefore indispensible in decision making (Carver & Scheier, 2004, p. 345).

However, learning from past experiences is not as clear cut as is might seem. Many factors may be influential in this aspect. Not only do people's expectancies concerning events and outcomes influence their response, but people also bring schema-consistent information from memory to fill in potential gaps (Carver & Scheier, 2004, p. 444). Another influential factor is whether people attribute an outcome to their own actions or external events.

Rotter (1966) holds that people who expect their outcomes to be determined by their own actions, learn from reinforcers, but people that expect their outcome to be unrelated to their actions do not learn from reinforcers. Thus, people may therefore differ from each other in the extent to which they see a cause and effect link between their behaviors and situational outcomes (Carver & Scheier, 2004, p. 356).

Even though expectancies and belief in personal responsibility over a situational outcome are influential in decision making, a person's recollection of past situations may be equally important. Remembering how one chose in a specific situation, may serve as a guideline in similar situations. However, people have a tendency to distort their memories. Loftus (2003) argues that memories for specific events are constructed at the time of retrieval, which makes the remembering process prone to errors. One reason for this is the intrusion of associative memory processes (Newell et al., 2008, p. 83). Consequently, we do not always remember events in a way that accurately reflects how they were experienced. A person's recollection may therefore often be distorted, and past events may furthermore be misrecalled in terms of how enjoyable or unpleasant they were (Newell, 2008, p. 135). Distortions in memory often try to rewrite the past in a way that is more consistent with a person's current lay theories, expectations and desires. One's recall of the reasoning behind a decision made in the past may therefore be driven more by current values than by the ones actually held at the time (Newell et al., 2008, p.141).

4. 3 Biases influencing decision making

In addition to biases in attention and memory, there are also several biases that can occur in people's thinking, which subsequently may be influential in decision making. Kahneman & Tversky (1982) identified a number of these biases or heuristic which introduce errors and fallacies into people's thinking.

4. 3.1 Representativeness heuristic

One central heuristic is the representativeness heuristic. This heuristic is defined as a subjective judgment of the extent to which the event in question "is similar in essential properties to its parent population" or "reflects the salient features of the process by which it is generated" (Kahneman & Tversky, 1972, p. 431.) Representativeness heuristics are

something people often rely on because it is easy to use and it often works. For example, if we have not heard the weather report prior to stepping outside, we informally judge the probability that it will rain based on how well the characteristics of this day represent the characteristics of rainy days (Sternberg, 2003, p. 411). Another related representativeness fallacy is the gambler's fallacy, in which the gambler mistakenly believes that the probability of a random event like winning or losing a game of chance is influenced by previous random events. One reason that people misguidedly use the representativeness heuristic is because they fail to understand the concept of base rates, which concerns the prevalence of an event or characteristic within its population of events or characteristics. (Sternberg, 2003, p.411)

4. 3.2 Availability heuristics

Another common heuristic is the availability heuristics (Tversky & Kahneman, 1973) which is a rule of thumb in which decision makers assess the frequency of a class, or the probability of an event by the ease with which instances or occurrences can be brought to mind. Usually this heuristic works well, as common events are easier to remember or imagine than are uncommon events. As with any heuristic, however, there are cases in which the general rule of thumb breaks down and leads to systematic biases (Plous, 1993, p.121). The availability may also be influenced by recency of presentation, unusualness, or distinctive salience of a particular event or event category for the individual (Sternberg, 2003, p. 413). Also the simple act of imagining an event may elicit the availability heuristic.

A common error is *overconfidence*, where an individual over evaluate his/her own skills, knowledge and judgment. This was demonstrated in a study by Fischhoff, Slovic & Lichtenstein (1977) where they gave subjects 200 two alternative statements, such as "Absinth is a) a liqueur, b) a precious stone." The subjects were asked to choose the correct answer and to state the probability that their answer was correct. The results showed that when people were 100 percent confident in their answers, they were right only 80 percent of the time. In general, people tend to overestimate the accuracy of their judgments (Kahneman & Tversky, 1996). Due to overconfidence, people often make poor decisions based on inadequate information and ineffective decision making strategies (Sternberg, 2003, p. 415).

Much of the work on judgment and decision making has focused on the errors we make. However, we do not act irrationally all the time. Cohen (1981) points out a reason for this by claiming that human irrationality is also limited because we do act rationally in many instances. All of us can improve our decision making through practice, particularly if we obtain specific feedback regarding how to improve our decision making strategies. Another key way to improve decision making is to gain accurate information for the calculation of probabilities and to use probabilities appropriately in decision making. Further, it would also be beneficial to avoid overconfidence in our intuitive guesses regarding optimal choices. Yet another way to enhance decision making is to use careful reasoning in drawing inferences about the various options available to us (Sternberg, 2003, p. 416, 417).

4. 3.3 Heuristics as advantageous to decision making

It is however, important to realize that heuristics do not always lead us astray. Sometimes heuristics can be amazingly simple ways of drawing sound conclusions. Gigerenzer & Goldstein (1996) showed that a 'fast-and-frugal' heuristics of "taking the best" option can be remarkably effective in decision making. In their study, Gigerenzer & Goldstein (1996) asked participants to answer questions such as: 'which German city has a larger population. Hamburg or Cologne?' The results showed that subjects relying on the 'fast-and- frugal' heuristics were not only fast but also accurate. The principle behind this heuristic is to only choose the recognized alternative when faced with a decision of many options. If more than one alternative is recognized, people are thought to search the cues in descending order of feature validity until they discover a feature that discriminates one alternative from the other. Once this single discriminating feature has been found, the search is terminated, and the feature is used to make a decision (Goldstein & Gigerenzer, 2002). Thus heuristics can give rise to advantages in terms of simplicity and speed of the decision process without suffering any concurrent loss in the accuracy of judgment and decisions (Newell et al., 2008, p.39).

5. Reasoning and intelligence

5. 1 Reasoning and decision making

When faced with a tough decision, the ability to reflect and reason towards a choice is crucial. Reasoning involves the process of drawing conclusions from principles and from evidence, and moving on from what is already known to infer a new conclusion or to evaluate a proposed conclusion. By using deductive reasoning, individual reasons from one or more general statements regarding what is known to reach a logically certain conclusion. When applying deductive reasoning, people may engage in many heuristic shortcuts to ease the cognitive load, which may lead to inaccurate conclusions. People may also engage in inductive reasoning, which is the process of reasoning from specific facts or observations to reach a likely conclusion that may explain the facts. As a consequence, the inductive reasoner may use a probable conclusion to attempt to predict future specific instances (Sternberg, 2003, p. 417). Using inductive reasoning is intuitive to all of us as it helps to make sense out of the great variability in the environment and predict future events. Inductive reasoning therefore often involves the process of generating and testing hypotheses (Sternberg, 2003, p. 433).

However, there are alternative ways to look at reasoning. Sloman (1996) took a closer look at the empirical data regarding how people reason, and found two complementary systems of reasoning; an associative system and a rule based system. The associative system may lead to speedy responses that are highly sensitive to patterns and to general tendencies. Through this system people detect similarities between observed patterns and patterns stored in memory (Sternberg, 2003, p. 438). The rule based system usually requires more deliberate, sometimes painstaking procedures for reaching conclusions. Through this system, people carefully analyze relevant features of the available data, based on rules stored in memory (Sternberg, 2003, p. 439). According to Sloman (1996) both complementary systems are necessary. It is important to be able to respond quickly and easy to everyday situations, yet it is also crucial to have a means for evaluating responses deliberately (Sternberg, 2003, p. 439).

5. 2 Intelligence and decision making

Closely connected with the ability to reason is intelligence, as people mindfully have to apply their intelligence to their problems and choices (Sternberg, 2003, p.417). So how does cognitive ability affect people's decision making? According to Sternberg (2003, p.417) people may be intelligent in a conventional test based sense, yet show exactly the same biases and faulty reasoning of someone with a lower test score. Thus Sternberg (2003, p.417) argues that people often fail to fully utilize their intellectual competence in their daily life such as in decision making. According to Brand, Heinze, Labudda, & Markowitsch, (2008) on the other hand, advantageous decision making seems to be related to executive functions and calculative strategies rather than intuitive strategies. Brand et al. (2008) demonstrated in a study that participants who applied calculative strategies performed better on the 'Game of Dice Task' than participants who followed intuitive strategies when making decisions under risky conditions. In another study based on the Game of Dice Test, Brand, Laier, Pawlikowski & Markowitsch (2009) examined the effect of intelligence, decision making strategies and the role of feedback in making decisions under risk. The main findings were that participant's with high intellectual abilities, as well as those who used calculative decision strategies, made advantageous decisions in risky situations independent of whether or not they received feedback for their choices. In contrast, individuals with lower intelligence, and those using intuitive decision strategies made more risky and disadvantageous decisions when they did not receive feedback. However, when given feedback they performed significantly better. Brand et al. (2009), interpretation of this was that participants with higher cognitive functioning and logical abilities would recognize the explicit rules and contingencies more easily and could therefore perform well even without feedback. Participants with lower intelligence on the other hand, would benefit more from feedback in order to develop a decision strategy or to learn to avoid risky decisions.

Related to this, Frederick (2005) showed that test scores on cognitive reflections are predictive of the types of choices people make. Frederick (2005) found that individuals who scored high on the cognitive reflection test, were less vulnerable to the various framing biases proposed by the prospect theory. Thus, Frederick (2005) stressed that individuals with high cognitive reflection were less prone to risk taking in gambles framed as "loss". Individuals with a high cognitive reflections score were not only found to be less

affected by the framing effect, they were also less impulsive, and favored larger future rewards to smaller immediate rewards.

Even though there is research showing that cognitive ability has an effect on decision making, the relation between cognitive ability and choice preference does not, by itself, establish that there is one "correct" choice. Two individuals with different cognitive abilities may experience outcomes differently, which may warrant different choices (Fredericks, 2005). Sternberg (2003) stresses that people with high SAT score should not be characterized as those who set the norm for what is true or right. Sternberg (2000, pp. 698) argued: "People with high SAT scores have high levels of certain kinds of cognitive abilities. They have no monopoly on quality of thinking and certainly no monopoly on truth."

6. The effect of emotions in decision making

Decision making is not only dependent upon cognitive reasoning, but also emotions. This link between decision making and emotion was something that Robert Zajonc (1980) acknowledged. Zajonc (1980) stressed that affective reactions to stimuli may precede cognitive reactions and thus require no cognitive appraisal. Zajonc (1980) went on to argue that people sometimes delude themselves into thinking that they make rational decisions by weighing all the pros and cons of various alternatives, when in fact their choices are determined by no more than simple likes and dislikes: "we buy the cars we like, choose the jobs and houses we find attractive and then justify these choices by various reasons (Zajonc, 1980, p. 155). Thus, considering that decision making does not occur in an emotional vacuum, is important to take a closer look at how emotion affect decision making (Newell et al., 2008, p.186).

Traditionally, emotions have been said to interfere with logical reasoning and have therefore been regarded as impedimental to rationality (Mellers, 2000). Folk wisdom suggests that emotions seriously hinder the ability of people to make good decisions.

Baumeister, DeWall., Zhang, in Vogh,Baumeister & Loewenstein (2007, p. 11) stress that people who are emotionally distraught frequently engage in rash, reckless, and destructive behaviors. Furthermore, they say and do things that they regret later, take foolish risks and fail to appreciate the potentially harmful consequences of their choices. On the other hand, emotions may facilitate decision making. Thus, people who disregard the emotional impact of their choices neglect a crucial aspect of the situation. People frequently use their gut feeling when faced with a decision, and people who act against this gut feeling are often sorry later. Moreover, emotions may help people differentiate right from wrong, and help them learn from their mistakes (Baumeister et al., 2007, p. 12). This seemingly paradoxical effect of emotions might be better understood if the effect of emotion is scrutinized even further. One way to get a better understanding of how emotions affect decision making, is to consider how emotion affect information processing and how current and anticipated emotions may affect decision making differently. Simplified one might say that current emotions often distort reasoning capabilities and induce people to make bad decisions, whereas anticipated emotions may be a great resource when contemplating which option to choose.

6. 1 Effect of emotion on information processing

Easterbrook (1959) proposed that emotions can impair information processing. Based on the Yerkes – Dodson law of the relationship between arousal and performance, Easterbrook (1959) argued that increased emotional arousal could narrow down the information processing capacities. According to this perspective, a certain amount of arousal would be beneficial for the performance by aiding people in screening out irrelevant information. Once this irrelevant information has been screened out, however, any additional arousal would cause a person to overlook potentially helpful, task relevant information. This perspective fits with the results of Leith & Baumeister (1996) study that found that high arousal emotions had deleterious effect on decision making as a result of reduced cognitive processing.

It is not only level of arousal that affects information processing strategies, but also positive and negative moods are associated with different information processing strategies. In line with this notion, Schwarz & Clore (1983) proposed the *affect- as-information hypothesis* to account for how contextually elicited affect can serve as a source

of information about a target of judgment. Schwarz & Clore (1983) telephoned individuals and asked them to report their life satisfaction. Participants were either called on a warm and sunny day, or a cold and rainy day. As expected, participants who were contacted on sunny days were in happier moods and reported higher life satisfaction than those called on rainy days. The affect-as-information hypothesis predicts that people monitor how they feel at the present time when evaluating a situation. Subsequently, the current feelings affect people's judgments or choices, and are experienced as reactions to the imminent judgment or decision. Therefore, if current feelings happen to be positive, then the evaluation of a specific decision-making option being contemplated is likely to be positive. If however, the feelings are attributed to a source other than the target of judgment or decisions, their impact is reduced or eliminated (Loewenstein, Weber, Welch, & Hsee, 2001).

6. 2 Current emotions and decision making

Current emotions are real emotions experienced at the time of decision making, and produce consistent alterations in decision making and other behaviors (Baumeister, et al., 2007, p. 22). Current emotional states probably do more harm than good in terms of shaping the decisions that people make. The traditional folk wisdom that emotions produce irrational behavior emphasizes current emotional states. If people make decisions when feeling emotionally distraught, or even possibly euphoric they may do foolish things and make irrational decisions (Baumeister, et al., 2007, p. 16).

Several studies have directly tested whether one's current emotional state has a positive or negative effect on decision making. Leith & Baumeister (1996) manipulated participants' emotions, and then had participants select among different lotteries that varied in the degree of risk and reward. Lottery selections were intentionally arranged so that lotteries with high rewards were statistically less promising in terms of expected gain. Choosing these high reward low gain lotteries could have therefore been considered as irrational, self- defeating and high risk decision making. The results revealed that participants whose mood was experimentally induced to anger or embarrassment were more likely to choose high risk lotteries compared to the other participants. Thus, some emotions, particularly those linked with personal distress, caused people to make unwise decisions. Leith & Baumeister (1996) conducted an additional study to identify the mechanism that could

account for the link between current emotional state and impaired decision making. In this study, participants were exposed to a mood manipulation to elicit either anger or a neutral emotion, and were then asked to choose among a set of lotteries as in the previous studies. Before making their decisions, some participants were instructed to list the cost and benefit of each lottery option before making their decision. The results replicated the shift toward unwise decision making among people who were experiencing anger, and showed that this effect was mediated by reduced cognitive processing. Thus emotional distress impaired the capacity for optimal decision making by reducing cognitive processing (Baumeister, et al., 2007, p. 19).

Additional evidence has shown how current emotional states, particularly negative emotions can lead people to abandon their long term priorities for immediate gratification. In a study by Knapp & Clark (1991) participants were asked to solve a resource-management task in a simulated fishing game. The optimal strategy in the game would be to harvest fish somewhat slowly and on sporadic occasions, which would allow the lake to replenish its fish and sustain over time. An alternative less optimal strategy would be to take out as much profit as possible from the start, which would deplete the lake of its capacity to replenish its fish and would reduce the long term gain. Knapp & Clark (1991) found that participants who were induced to feel sad chose the less optimal, short term benefit strategy more often than participants in neutral moods. Thus, a current emotional state caused people to make shortsighted, irrational decisions.

6. 3 Anticipated emotions

Anticipated emotions play a prominent and beneficial role in the human decision making processes. These emotions do not signify what a person feels right now, but rather what the person anticipates feeling as a result of a particular behavior. Anticipated emotions are therefore closely connected with learning and the recollection from past experiences. Baumeister et al. (2007, p. 27), stresses that conscious emotion, as opposed to automated affect, is instrumental in enabling people to learn. Conscious emotions develop too slowly to guide behavior at the time, but this does not hinder the learning process. In fact, the slowness of conscious emotions can be beneficial in terms of keeping one's attention focused on the recently concluded event, and subsequently prompt rumination about the event. This rumination allows the person to translate the recent events into an appropriate

lesson to be learned from the variety of interpretations that might accompany the situation. One particular relevant example of how emotions facilitate learning is the stimulation of counterfactual thinking (Baumeister et al., 2007, p. 27). Counterfactual thinking frequently arises from a negative emotional experience, which in turn causes a person to reconsider events and how they might have had different outcomes (Roese, 1997). From this perspective, emotions causes people to engage in counterfactual thinking in order to learn from a recent event in terms of how they could have adjusted their behavior so as to bring about a more desirable action (Baumeister et al., 2007, p. 27).

Anticipating whether and to what degree a decision will produce a positive or negative emotional experience, may therefore be a powerful and effective guide to decision making (Baumeister et al., 2007, p. 15). The view that anticipated emotional outcomes play a role in predicting the choices people make comes from the *decision affect theory* proposed by Mellers, Schwartz and Ritlov (1999). The decision affect theory was based on studies where participants were presented with pairs of monetary gambles on a computer screen. The studies found that the emotions that people experienced after a decision depended on a comparison between the actual outcome and the outcome that would have come about if another response option has been chosen (Mellers, Schwartz, Ho, & Ritov, 1997; Mellers, et al., 1999) Mellers et al. (1999) found that emotional reactions to monetary outcomes of gamble varied systematically with the participants subjective probabilities. Each gamble was evaluated by balancing the anticipated pleasure against the anticipated pain. The decision-maker considered the average pleasure of each gamble, and chose the gamble with the greater expected pleasure. The results showed that the participants were disappointed if the option they chose produced a less beneficial outcome than other alternatives, but were pleased if their response led to a superior outcome. Thus the emotions that people experienced after a decision depend on a comparison between the actual outcome and the outcome that would have come about if another response option has been chosen. However, it is interesting to note that the emotions related to the outcome of a choice had asymmetrical effects; the disappointment and regret was greater than the elation and rejoicing for an outcome (Mellers et al., 1999).

The finding that the negative feelings are subjectively greater than the positive feelings for a choice outcome (Mellers et al., 1999) may perhaps play a role in our social interactions with other people. Anticipating negative emotions may inhibit socially sanctioned

behaviors. The anticipation of feeling guilty may prevent people from performing immoral or antisocial acts, and the anticipation of regret might prevent people from doing things that will make them feel sorry in the future. Hence, choices made with the intention of maximizing positive future emotions and minimizing negative future emotions may result in good outcomes (Baumeister et al., 2007, p. 16, 23). Baumeister et al., (2007, p. 16) stresses that people who base their decisions on conscious emotional experiences as well as anticipated future emotional outcomes will frequently arrive at reasonable and wise decisions. However, people do not always make optimal decisions. There may be many reasons for this, but biases of anticipated emotions may be one of them.

6. 3.1 Biases of anticipated emotions

If people make choices by comparing the average anticipated pleasure of options, the accuracy of their predictions becomes a critical concern. Imprecise predictions could easily lead to peculiar choices (Mellers & McGraw, 2001). Even though emotions keep people attuned as to how they might feel about best and worst- case outcomes, the emotion system is inaccurate in finetuning these judgments (Baumeister, et al., 2007, p. 24). Research has shown consistently that people overestimate the duration and intensity of their emotional responses to future events (Baumeister, et al., 2007, p. 25). This will subsequently have an effect on people's behavior, where people who overestimate the pleasure of favorable outcomes, would tend to be overly risk seeking, whereas people who overestimate the displeasure of unfavorable outcomes would tend to be overly risk averse (Mellers & McGraw, 2001). Thus, one of the main errors in affective forecasting is when people focus on whatever is salient in the moment, something Schkade and Kahneman (1998) call the focusing illusion. This illusion was demonstrated in a study by Schkade and Kahneman (1998) where students in the Midwest and California were asked to judge their own happiness and the happiness of the students at the other location. The comparison highlighted the advantages of California, such as better climate, more cultural opportunities, and greater natural beauty. The results showed that both students in the Midwest and those in California predicted that Californians were happier, but in fact, students at the two locations were equally happy.

The focusing illusion can also lead people to base affective predictions on transitions rather than final states (Meller & McGraw, 2001). Gilbert, Pinel, Wilson, Blumberg & Wheatley

(1998) asked untenured college professors to anticipate how they would feel about receiving or not receiving tenure. Not surprisingly, the professors expected to be happy if given tenure and extremely unhappy otherwise. Actually, however, the professors who were denied tenure were not as unhappy as they expected to be. Thus, people often predict a prolonged and intense emotional response to possible future events, but when those events do come to pass, the emotional reactions may be relatively brief and modest. Even though these biases in affective forecasting show that people may overestimate the duration and intensity of their emotional responses to events, they still correctly predict the type of emotion they will feel. Furthermore, the overestimation of emotional responses may also be a beneficial decision making strategy compared with underestimating emotional outcomes. The impact of the anticipated emotional outcome, although it would be likely to be overestimated, is helpful to decision making insofar as it motivates a person to consider carefully the possible consequences of his/her decisions (Baumeister, et al., 2007, p. 24, 25).

6. 4 Regret and decision making

Most people can readily recall or imagine situations in which a poor decision led to painful regret (Connolly & Zeelenberg, 2002). It is therefore no surprise that anticipated regret has been investigated more than the anticipation of any other emotions (Baumeister et al., 2007, p. 24). Loomes and Sugden (1982) and Bell (1982) suggested in their *regret theory* that decision makers anticipate regret if their outcome is worse than that of another choice, and rejoice if their outcome is better. Thus when an individual considers an uncertain prospect, the individual forms some prior expectation about that prospect. If the outcome of the prospect falls short of the prior expectation, then the individual experiences disappointment; whereas if the consequence is better than the prior expectation, the individual feels elation (Loomes & Sudgen, 1986). Decision makers then seem to evaluate their outcome relative to 'what might have been' under another choice (Mellers, 2000). People normally adjust their decisions so as not to experience regret in the future (Baumeister, et al., 2007, p. 24). This was shown in a study by Parker, Stradling, and Manstead (1996) where beliefs and attitudes about unsafe driving dramatically changed after people were reminded about the regret they would feel if their dangerous driving led to accidents involving persons and property.

However, decision makers minimize their chances of experiencing regret in many different ways. Zeelenberg and Beattie (1997) showed how regret avoidance can lead to greater risk seeking or risk aversion, depending on the exact form of outcome feedback. Josephs, Larrick, Steele & Nisbett (1992) demonstrated that regret avoidance varies with the individual's vulnerability to regret, operationalized as self-esteem. They found that decision makers with higher self-esteem were unaffected by outcome feedback, whereas those with lower self-esteem made choices to avoid regret if they expected complete feedback, but not otherwise. Decision makers have also been found to be more likely to feel regret if the negative events that occur are under their control (Markman, Gavanski, Sherman, & McMullen, 1995).

Another feature of regret is whether the negative event is a result of actions or inactions. Kahneman & Tversky, (1982) suggested that decision makers are more likely to feel regret from negative events that are the result of actions, rather than inactions. Contrary, Gilovich and Medvec (1995) showed that even though people felt greater regret about actions than inactions in the short term, they felt greater regret about inactions than actions in the long term. Gilovich and Medvec (1995) argued that when looking back, people experience more regret over paths not taken. Connolly & Zeelenberg (2002) proposed an alternative regret model to accommodate the conflicting results of regret in decision making. Their model, *decision justification theory*, postulates two core components of decision-related regret, one associated with the comparative evaluation of the outcome, the other with the feeling of self-blame for having made a poor choice. Connolly & Zeelenberg (2002) argues that the overall feeling of regret of some decision is a combination of these two components.

6. 5 Emotion and risk-taking behaviors

The powerful effect of current and anticipated emotions both color and shape peoples decisions. However, emotions are particularly important when it comes to people’s perception of risks. Alhakami & Slovic (1994) observed that the relationship between perceived risk and perceived benefit was linked to people’s general affective evaluation of hazards. If an activity was `liked', people tended to judge its risks as low and its benefits as high. If the activity was `disliked', the judgments were perceived as high risk and low benefit. Alhakami & Slovic (1994) suggested therefore that risk and benefit may be inversely related in people's minds.

The feelings that become salient in a judgment or decision making process depend on characteristics of the individual and the task as well as the interaction between them. Individuals differ in the way they react affectively, and in their tendency to rely upon experiential thinking (Slovic, Finucane, Peters & MacGregor, 2002)**.** Nevertheless, representations of objects and events in people's minds are always tagged to varying degrees with affect. Furthermore, Finucane, Alhakami, Slovic & Johnson (2000) suggest that these positive and negative feelings guide decision making. In their proposal of *the affect heuristics,* Finucane et al. (2000) argue that using an overall, readily available affective impression is easier and more efficient than weighing the pros and cons of various reasons or retrieving relevant examples from memory. This is especially true when the required judgment or decision is complex or mental resources are limited. Finucane et al., (2000) found support for the affective heuristic in a study which revealed that the inverse relationship between perceived risks and benefits increased greatly under time pressure, when opportunity for analytic deliberation was reduced. This demonstrates that affect influences judgment directly, and is not simply a response to a prior analytic evaluation. As with other heuristics, the affect heuristic enables us to be rational actors in many important situations. It works brilliantly when our experience enables us to anticipate accurately the consequences of our decisions. However, it nevertheless fails miserably when the consequences turn out to be much different in character than we anticipated (Slovic et al., 2002).

The affect heuristic has much in common with the model of "risk as feelings" proposed by Loewenstein, Weber, Hsee & Welch (2001). Loewenstein et al. (2001) stresses that decision makers emotional states can affect their cognitive evaluations of a risk. These cognitive evaluations, in turn, can affect individuals emotional state. Loewenstein et al. (2001) suggest that people react to the prospect of risk at two levels: they evaluate the risk cognitively, and they react to it emotionally. Thus emotional reactions and cognitive evaluations work ' in concert to guide reasoning and decision making'. Although the two reactions are interrelated, with cognitive appraisals giving rise to emotions and emotions influencing appraisals, the two types of reactions have different determinants. Cognitive evaluations of risk are sensitive to probabilities and outcome valences. In contrast to cognitive evaluations, emotional reactions are sensitive to the vividness of associated imagery, proximity in time, and a variety of other variables that play a minimal role in

cognitive evaluations. Subsequently, emotional reactions to risks can diverge from cognitive evaluations of the same risks (Loewenstein et al., 2001). In these cases, emotions may often lead to behavioral responses that depart from what individuals view as the best course of action. Thus, risk estimates are more often guided by internal feelings than by objective evidence about risks and probabilities. Risky decisions then, are highly connected with emotions which need to be recognized as a great influencing factor.

7. Decision making- influenced by both emotion and cognition

Many models of judgment and decision making posit distinct cognitive and emotional contributions to decision-making, however, they both play an important role in guiding decision making (Quartz, 2009). Lowenstein et al. (2001) stress that emotion and cognition does not operate in isolation but work in concert to guide reasoning and decision making. The way emotional and cognitive system influence decision making was addressed by Epstein (1990) in the cognitive-experiential self theory. This theory assumes that people experience reality by two interactive, parallel processing systems. The analytic system is slow and deliberative, and functions by way of established rules of logic and evidence. The experiential system is intuitive, automatic, nonverbal and encodes reality in images, metaphors, and narratives to which affective feelings have become attached. Epstein believes that both systems are always at work, and that they jointly determine behavior (Epstein, 1990). In the same vein, Metcalfe & Mischel (1999) proposed the Hot/Cool-System of analysis. Metcalfe & Mischel (1999) suggested that there is a hot system that's emotional, impulsive, and reflexive, and a cold system that is cognitive, strategic, flexible, slower and unemotional. The hot system is viewed as the "go" system, whereas the cool system is known as the "know" system and is the seat of self-regulation and self-control. In accordance with the cognitive-experiential self theory, the hot and cool systems are also seen as working in concert.

Even though the cognitive and emotional systems work together, they may be engaged to different degrees depending on the situation. For instance, asking people to give strictly

logical responses to hypothetical events tend to place them in the analytical rational mode. Asking them how they would respond if the events happened to them on the other hand, tends to place them in an experiential mode (Epstein, Lipson, Holstein & Huh, 1992). The more emotionally charged a situation is, the more people's thinking will be dominated by the experiential system. One characteristic of the experiential system is that it encodes information primarily in the form of concrete representations. Thus, absolute numbers, which are more concrete than ratios, are more comprehensible to the experiential system (Denes- Raj & Epstein, 1994). This characteristic of the experiential system was demonstrated in a study by Denes-Raj & Epstein (1994), where participants were offered a chance to win $1.00 by drawing a red jelly bean from an urn. The results showed that the participants often elected to draw from a bowl containing a greater absolute number of beans, but a smaller proportion of red beans, than from a bowl with fewer beans but with a better probability of winning. The participants reported that, although they knew the probabilities were against them, they felt they had a better chance when there were more red beans. This shows that the experiential system can override the rational system, even when people are fully aware that their resultant behavior is irrational.

In light of the cognitive-experiential self theory (Epstein, 1990) decision making is dependent upon both by the experiential and the analytical system, but one or the other system may exert a greater influence on behavior depending on the situation. In some situations, people cognitively and systematically contemplate various options before making a decision, whereas at other times, people follow their gut feeling when deciding. Both strategies may yield equally good results, but then again, both strategies may also lead to less optimal outcomes due to various biases affecting emotion and cognition. Ideally, the experiential and the analytical system should work in collaboration for optimal decision making (Slovic et al., 2002). Subsequently, the effect that cognition and emotion have on decision making should be viewed as complementary.

8. The neuroanatomical basis for decision making

Decision-making is a complex process involving the synthesis of a variety of kinds of information, such as multimodal sensory inputs, autonomic and emotional responses, past experiences, and future goals. These inputs must be integrated with information about uncertainty, timing, cost-benefit, and risk and then be applied to select the appropriate actions. Additionally, decision making also requires some degree of flexibility due to the changing environment (Fellows, 2004). In debilitating a decision, the decision maker often realizes that there usually is more than one correct action. Consequently, it is crucial to assess and attribute value to the available options as well as the consequences associated with the possible outcomes. In addition, the decision maker also has to execute the action. To accomplish this, a range of action related processes is necessary, such as the sequencing of actions, the inhibition of competing actions, and the appropriate timing of the intended actions. Finally, the individual have to evaluate the outcome by linking the action to the outcome. This serves as a key for guiding and adjusting future decision making (Ernst & Paulus, 2005). Considering the many processes involved in decision making, it is not surprising that there are several brain structures involved in making a decision.

8. 1 The ventromedial prefrontal cortices.

In neuropsychological studies, it has been shown that a specific area in the prefrontal cortex, the ventromedial prefrontal cortex (VMPFC) is a chief structure in decision making (Naqvi, Tranel & Bechara, 2006, p. 326). The ventromedial sector includes both the gyrus rectus and mesial half of the orbital gyri, as well as the inferior half of the medial prefrontal surface, from its most caudal aspect to its most rostral in the frontal pole. Areas 11, 12, 13, 25, 32 and 10 of Brodmann are also included in this sector (Bechara, Damasio, & Damasio, 2000). The VMPFC has been found to integrate the input from several neural regions, such as the dorsolateral prefrontal cortex, amygdala, anterior cingulate cortex and nucleus accumbens, to make an evaluation of a choice. By incorporating information about factors such as risk, delay, ambiguity and reward, the VMPFC will evaluate the current value of a choice option. This information will further guide decision making to produce complex goal oriented behaviors (Fellows, 2007). The key role VMPFC plays in decision making

becomes apparent when considering the consequences of VMPFC lesions. Acquired damage to the VMPFC often leads to profound alternations in the ability to make advantageous decisions in the personal, social and financial domain. Previously well-balanced individuals become unable to observe social conventions and unable to decide advantageously on matters pertaining to their own lives. Remarkably, these patient's intellectual abilities are generally well preserved, in the sense that they have normal learning, memory, language and attention capabilities. Although these patients have preserved intellectual abilities, they have abnormal processes of emotion and feeling, which account for their decision making impairments (Bechara, Damasio, & Damasio, 2000).

The first known example of a VMPFC lesioned patient came from the famous case of Phinneas Gage. In 1848, Gage was a successful foreman on the railway with a respectable social life. Following a blasting accident, a tamping iron went through his eye socket and passed out through the top, leading to extensive damaged in the frontal cortex. Remarkably, Gage survived and at first appearance seemed to have no intellectual impairment. Even though his intellect seemed intact, his personality changed radically and people noted that Gage was no longer Gage. Gage displayed strange decision-making and social behavior characteristics, and contrary to his usual behavior as an industrious and well mannered man, he could now not hold down a job and made risky financial decisions. After Gage's death, his skull was examined by Harlow, and hundreds of years later by Hanna Damasio. The use of modern neuroimaging techniques revealed that the passage of the tamping iron through Gage's skull ablated a portion of the frontal lobe centered around the VMPFC, thus attributing the lesion in this region to be responsible for Gage's impaired decision making and social behavior (Damasio et al., 1994, p. 3 - 32).

A similar example of VMPFC damage came from Elliot (EVR) a patient with bilateral VMPFC lesions due to a brain tumor. As in the case with Gage, EVR develop a severe impairment in real-life decision-making, in spite of otherwise preserved intellect. The impairments were especially marked in the personal and social realms. ERV could not plan for the future and tended to choose unsuitable friends, business partners and activities (Damasio, 1994, 35-39). Even though Damasio could not find anything intellectually wrong with EVR, later investigations revealed that EVR and other patients with damage to VMPFC had a difficulty in expressing emotion and experiencing feelings (Dunn, Dalgleish

& Lawrence, 2006). This was an important key in explaining the deficits in decision making that EVR displayed. Other cases of VMPFC damage that produce equivalent impairment have also been documented (Dimitrov, Phipps, Zahn, & Grafman; Barrash, Tranel & Anderson, 2000).

Neuroimaging studies using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) support the role VMPFC play in decision making (Lawrence, Jollant, O' Daly, Zelaya & Phillips, 2009). A PET study by Ernst et al. (2002) using healthy subjects confirmed the activation of the VM PFC (Brodmann area [BA] 11, 47) in a risky gambling task. Consistent with these findings, Lawrence et al., (2009) also found in an fMRI study that general decision-making in a gambling task elicited activation in the VMPFC. Other studies using fMRI show activation in medial frontal gyrus. A fMRI study on healthy subject conducted by Fukui, Murai, Fukuyama, Hayashi & Hanakawa (2005) examined blood oxygenation level- dependent (BOLD) activity during a gambling task during the decision making phase. The fMRI results confirmed the role of the medial frontal gyrus (BA 10) in the gambling task, and revealed that the activation was positively related to task performance. In line this Windmann, Kirsch, Mier, Stark, Walter, Güntürkün & Vaitl (2006) also found the activation of a medial frontal gyrus in a fMRI study comparing rewarding versus punishing outcomes in a gambling task.

Although bilateral lesion studies have confirmed the role of VMPFC, there are studies that have investigated the effects of unilateral prefrontal lesions on decision making. Tranel, Bechara, & Denburg, 2002) showed in a study that patients with right sided damage to the ventromedial PFC, (Tranel et al., 2002) were just as impaired on a gambling task as patients with bilateral VMPFC damage. On the other hand, patients with left side VMPFC damage displayed an intact task performance on the gambling task. The asymmetrical role of the OFC was further supported in a study by Manes, Sahakian, Clark, Rogers, Antoun, Aitken & Robbins (2002). Manes et al., (2002) found that patients with discrete lesions to left orbitofrontal cortex were not impaired in gambling tasks, whereas patients with large right-sided lesions including the ventral PFC were dramatically impaired. These findings suggest that when only the left-sided sector is damaged, the patient does not display major decision making impairments. Thus, this suggests that it is the right side that may be critical for decision making (Tranel, et al. 2002).

8. 2 The dorsolateral prefrontal cortex

In decision making, it is important to be able to plan the intended action. Planning involves having a logical sequence of the chain of thoughts, and being able to hold them active in working memory. The dorsolateral prefrontal cortex (DLPFC) is known as the main cortical areas responsible for working memory (Gade, 1997, p. 443-448). The DLPFC are located in the Broadmann areas 9 and 46 (Ridderinkhof, van den Wildenberg, Segalowitz & Carter, 2004). The value of working memory in decision making is apparent, as it helps to maintain a focus on goal hierarchies, monitor the status of competing options, and store affective information relevant to attributes and assessment of options (Krawczyk, 2002). Although working memory is crucial in decision making, being able to control the attention toward the specific decision problem is also an important factor. The DLPFC has been found to mediate also this aspect of decision making (Ernst, Bolla, Mouratidis, Contoreggi, Matochik, Kurian, Cadet, Kimes & London, 2002; Fellow, 2004; Ohira, Ichikawa, Nomura, Isowa, Kimura, Kanayama, Fukuyama, Shinoda & Yamada, 2010). In addition to working memory and attention span, the DLPFC has also been implicated in inductive reasoning (Krawczyk, 2002), and response inhibition (Ernst et al., 2002)

Lesion to the DLPFC may disrupt cognitive functions, working memory and attention which are important for decision making (Krawczyk, 2002). Research on patients with DLPFC damage has confirmed the important role DLPFC play in decision making. Manes et al. (2002), found that patients with DLPFC damage were impaired on a gambling task. They further found that patients with DLPFC lesion displayed deficits across a range of tasks requiring working memory, planning and attention shifting. In line with this, Fellows & Farah (2005) also found that subjects with unilateral DLPFC damage were just as impaired on a gambling task as VMPFC damaged subjects. A PET study by Ohira et al. (2010), also found activation of DLPFC in healthy subjects on a decision making task. Ohira et al., (2010) further claims that DLPFC seemed to be more involved in decision-making in uncertain situations, where people have to seek rules or laws by memorizing past experiences of their own actions.

The DLPFC also show laterality effects. Gomez-Beldarrain, Harries, Garcia-Monco, Ballus & Grafman (2004) stress that the right DLPFC seems to be a key structure for processing novel information that requires a response from memory and previous

experience, to resolve ambiguous situations independent of explicit cues, for using previously learned information, and for deciding under uncertain situations. The right DLPFC has also been reported to play a crucial role in the suppressive control of superficially seductive options (Fecteau, Knoch, Fregni, Sultani, Boggio, Pascual-Leone, 2007). The left DLPFC on the other hand, is a key region in producing responses to stimuli from environmental cues, for choosing between similar options, for processing problems with explicit contextual cues (Gomez- Beldarrain, et al., 2004). Thus, although both sides of the DLPFC are involved, they contribute to different aspects of the decision making process.

8. 3 Anterior cingulate cortex

In making decisions it is important to control and select the appropriate behavior for a specific decision making problem. Thus, being able to monitor information processing for errors and outcome expectations are crucial in this area. One central brain region that is responsible for error monitoring, sorting out conflicting options, and signaling outcome relevant information is the anterior cingulate cortex (ACC) (Fishbein, Eldreth, Hyde, Matochik, London, Contoreggi, Kurian, Kimes, Breeden & Grant, 2005; Botnivik, 2007). The ACC is located in the Broadman areas 24 and 32 (Lawrence et al., 2009). The involvement of ACC in decision making was confirmed in a PET study by Ernst et al., (2002) who demonstrated that ACC was one of the brain areas becoming active in a risky card game. The ACC is likely to be involved in several stages in decision making, both before and after the decision outcome is known. Thus, there are various subdivisions of the ACC that serve different functions in decision making. The dorsal region of the ACC may be involved in the cognitive aspects of decision making, including reward based decision making, error monitoring, anticipation, working memory, motor response, and novelty detection. The rostral ACC, has been implicated in emotional processing and error monitoring perhaps this is due to its interconnections with the orbitofrontal cortex, limbic structures, motor cortex and autonomic and endocrine systems (Fishbein et al., 2005).

When a poor decision outcome occurs, the ACC signals that changes will be necessary to avoid future judgment errors (Krawczyk, 2002). Thus, when making decisions the ACC guides action selection on the basis of a cost–benefit analysis, and integrates information about past action outcomes (Rushworth, Walton, Kennerley & Bannerman (2004). The

role ACC plays in decision making was demonstrated in a study by Kennerley, Walton, Behrens, Buckley, and Rushworth (2006). The study found that ACC lesions produced dramatic departures from optimal behavior in a reward based decision-making task. Kennerley et al., (2006) concluded that the "ACC has an essential role in both learning and using extended action-outcome histories to optimize voluntary choice behavior" (p. 940). Critchley, Mathias & Dolan (2001) also found in a fMRI study that ACC was involved in an outcome anticipation related to gambling decisions. Furthermore, ACC was found to be especially active during periods of increasing outcome uncertainty and high arousal. The ACC then seems to be related to both emotional responses and cognitive appraisal of the chances of a successful decision outcome (Krawczyk, 2002).

8. 4 Amygdala

The amygdala is another structure that has been implicated in the decision-making circuitry (Clark, Cools & Robbins, 2004). The amygdala is located in the medial temporal lobe, and is a key component of the brains emotional system (Phelps, 2004). Emotion is as previously discussed an important element in decision making, and without, it decision making would be impaired (Seymour & Dolan, 2008). Bechara, Damasio & Damasio (2006) stress that the amygdala is crucial for attaching affective attributes to stimuli. Furthermore, the amygdala is especially important in producing negative affects and associative aversive learning (Davidson & Irwin, 1999). This is also stressed by Doya (2008) who claims that the amygdala is important for the processing of aversive stimuli and avoidance learning, both of which are important in guiding behavior. However, the amygdala has also been linked to reward-related associative learning (Seymour & Dolan, 2008).

When pondering a decision, the amygdala is one of the first regions to be involved, but as Ernst et al., (2002) stress, once a decision strategy has been implemented, the amygdala ceases to be active. This confirms that the amygdala is important in processing the affective significance of a stimulus before formulating a strategic approach. Amygdalas role in decision making can further be scrutinized when observing amygdala lesioned patients. Amygdala lesions are known to block emotional responses. This blocking of emotions encompasses both unconditioned or conditioned emotional stimuli, and complex cognitive information that through learning has acquired emotional eliciting responses

(Bechara et al., 2006). In a study by Bechara, Damasio, Damasio & Lee (1999) it was found that patients with amygdala damage were impaired on a gambling task. The study also showed that these patients were unable to generate SCRs when they received a reward or a punishment. Bechara et al. (1999) stressed that decision-making impairment after amygdala damage was an indirect consequence of the patients' inability to experience the emotional attributes of the situation. In another gambling study, De Martino, Camerer & Adolphs (2010) found that amygdale lesioned patients showed a dramatic reduction in loss aversion, and thus showed disadvantageous decision making. In line with this, Ghods-Sharifi, Onge & Floresco (2009) highlighted that patients with amygdale damage were found to be impaired on decision making tasks involving risk and rewards. Clearly, the amygdala plays a central role in decision making by providing an emotional ground to guide our actions.

8. 5 Nucleus Accumbens/ ventral Striatum

One major aspect of decision making is the motivation to choose an option. The motivation to choose is further strengthened by the expectancy of a rewarding outcome. Thus, many of our decisions and actions are driven by the combination of expectation of reward and internal motivational factors. One central structure that plays a role in reward and motivation is the nucleus accumbens (NAcc) which is part of the ventral striatum, and is a key node in the limbic corticostriatal loop. Thus, the involvement of the NAcc/ventral striatum in anticipation and detection of rewarding goals is important for preparing, directing, and adapting the decision-making process (Tremblay, Worbe & Hollermann, 2009, pp 51, 52). Several studies have confirmed the role NAcc/ventral striatum play in rewards and the motivational aspect of actions. In an fMRI study by Knutson, Adams, Fong & Hommer (2001) it was found that anticipation of reward elicited both NAcc activation and happiness, whereas anticipation of punishment did not elicit NAcc activation. In a gambling study by Abler, Walter, Erk, Kammerer & Spitzer (2006) it was found that activation in the ventral striatal increased as a function of elevated reward magnitude and probability. The NAcc/ventral striatum involvement in the representation of expected reward and motivation has further been supported by a great body of research (Zink Pagnoni, Martin-Skurski, Chappelow Berns, 2004; Ernst, Nelson, McClure, Monk, Munson, Eshel, Zarahn, Leibenluft, Zametkin, Towbin, Blair, Charney & Pine (2004); Knutson & Bossaerts (2007).

The NAcc/ ventral striatum also seems to have a prediction-error computation function of reward. This was showed in a fMRI study by Pagnoni, Zink, Montague & Berns (2002) that found differentiation of activity in the NAcc/ ventral striatum when withholding a reinforcer at the expected time of delivery. Pagnoni et al., (2002) attributed the activation in the NAcc/ventral striatum to the calculation of an error signal between an expected and received reward. Although most studies of NAcc/ventral striatum show that is has a central role in reward expectation, it has also been found to be involved in processing of aversive information. In a study by Schoenbaum & Setlow (2003) it was demonstrated that rats with NAcc lesions displayed disrupted learning about aversive outcomes. Given that the NAcc/ventral striatum has been implicated in integrating motivational information to guide behavior, Schoenbaum & Setlow (2003) suggests that NAcc/ventral striatum integrates the motivational value of both appetitive and aversive cues to modulate the vigor of the response. Lesions in the NAcc/ventral striatum have also been associated with impulsitivity. In a study by Cardinal, Pennicott, Sugathapala, Robbins & Everitt (2001) it was found that lesions of the NAcc/ventral striatum induced profound and persistent impulsive choices in rats. The rats consistently chose small or poor rewards that were immediately available in preference to larger delayed rewards. This shows that the NAcc/ventral striatum is crucial in regulating impulsive and reward seeking behavior, which are crucial factors in decision making.

9. The somatic marker hypothesis

9. 1 The somatic marker hypothesis

Antonio Damasio developed the Somatic marker hypothesis (SMH) based on work with ventromedial prefrontal cortex (VMPFC) lesioned patients. The SMH was postulated as an explanation for decision making behaviour, and accounted for reasons why VMPFC patients had difficulties in emotional and everyday decision making. The SMH is therefore an intriguing model of how emotions and feedback from the body may successfully guide decision-making in complex and uncertain situations (Dunn, Dalgleish & Lawrence, 2006).

Damasio explained that the "Soma" refers to the body, and includes the body's internal milieu, visceral and musculoskeletal systems. Because emotion and feelings are expressed through changes in the body, the term somatic is an appropriate term as it refers to changes that occur at different levels of the brain and body in different situations. The term "marker" is defined as the image that becomes marked, a representation of what may happen next (Damasio, 1994, p. 173). A somatic state is activated by a chain of physiological events in the body, which are then relayed back to cortical and subcortical structures, a system known as the body loop. Although the somatic signal originates from bodily structures such as the brain stem, hypothalamus and cerebral cortex, the somatic signals do not necessarily need to begin in the body in every instance. Somatic states can in fact be "simulated" intra-cerebrally in the "as if body loop". Instead of having somatic states expressed directly in the body, representations of the somatic state can be activated in the brainstem and/or cortex, and thereby induce changes in neurotransmitter release without engaging the body (Bechara, Damasio, & Damasio, 2000a). These somatic marker signals can also work on both overt and covert level. When they function at an overt level, the individual is consciously aware of the emotions and bodily changes associated with a particular response option. If, on the other hand the somatic markers function at a covert level, the individual is unaware of his/her emotions and bodily activity (Dunn et al., 2006).

When deliberating over decisions, somatic markers rise or are reactivated to indicate our emotional reaction to the various response options. The emotional reactions to response options are based on previous acquired knowledge. Damasio (1994) explains "somatic markers are acquired by experience, under the control of an internal preference system and under the influence of an external set of circumstances and social conventions and ethical rules". (Damasio, 1994, p. 179). In other words, the somatic marker arises as a result of a prior knowledge and experiences of outcome to similar situations previously encountered. Consequently, decision making influenced by these somatic markers depends on the availability of knowledge about previous experiences. Such knowledge is stored in 'dispositional' form throughout higher-order cortices and some subcortical nuclei (Bechara et al., 2000b). The ventromedial sector holds linkages between the facts that compose a given situation, and the emotion previously paired with the experience. The linkages are 'dispositional' in the sense that they do not hold the representation of the facts or of the emotional state explicitly, but hold rather the potential to reactivate an emotion by acting

on the appropriate cortical or subcortical structures (Bechara et al., 2000b). The perception of somatic state information makes us more likely to approach or withdraw from a situation. Consequently, when a negative emotion or somatic marker is linked to a particular future outcome, it serves as an alarm signal telling us to avoid that particular course of action. If instead, a positive somatic marker is linked, it becomes an incentive to make that particular choice (Velásquez 1998).

The somatic markers serve as an indicator of the value of what is represented, and also as booster signal for attention and working memory (Damasio, 1994, s. 198) "Due to somatic markers emotionally signalling effect, they increase the accuracy and efficiency of the decision process" (Damasio, 1994, p.173). In situations of complexity and uncertainty, these marker signals help to narrow down the problem by marking response options with an 'emotional' signal. Only those options that are marked as good, are processed in a full cognitive fashion (Dunn et al., 2006)

9. 2 Iowa Gambling Task

Bechara, Damasio, Damasio & Anderson (1994) developed a card task known as 'the gambling task' in order to detect and measure the decision making problems in patients with VMPFC lesions. The gambling task was designed to mimic real-life situations in the way that it factors uncertainty, reward and punishment. The gambling task requires participants to select from one of four decks of cards; A, B, C, D that are identical in physical appearance. The subjects get a loan of play money where the goal is to maximize the profit. Subjects are required to make a series of 100 card selections, but are not told ahead of time how many card selections they have to make. Cards can be selected from any deck, and subjects are free to switch from any deck to another whenever they like to. Each card choice leads to either a variable financial reward, or a combination of a variable financial reward and penalty. Unknown to the participants, the various rewards and punishments on the decks have been fixed by the experimenter. The cards are arranged in such a way that every time the subject selects a card from deck A or B he or she gets $100, and every time deck C or D is selected, the subject gets $50. However, in each of the four decks, subjects encounter unpredictable money loss. The financial punishments are higher in the high-paying decks A and B, and lower in the low-paying decks C and D. In decks A

and B the subject encounters a total loss of $1250 in every 10 cards, whereas in decks C and D the subject encounters a total loss of $250 in every 10 cards. Consequently, in the long term, decks A and B are disadvantageous because they cost more, whereas decks C and D are advantageous because they result in an overall gain in the end. Thus, successful task performance relies on sampling more from decks C and D than from decks A and B. Participants are told that even though there is no way for them to work out when they will lose money, they will find that some decks are worse than others, and that to do well they need to stay away from the worst decks. To do well participants must rely on more 'intuitive' decision-making processes, or more precisely, rely on the activation of somatic marker signals (Bechara et al., 2000a).

9. 3 Empirical evidence for SMH

The empirical work based on IGT gives support to the SMH, and the work with VMPFC patients has been a key aspect in this matter. Bechara et al. (1994) examined the performance of patients with damage to the VMPFC on the IGT task. The results revealed that the VMPFC patients were significantly worse at the IGT than healthy control volunteers. The control group learned over time to select more from the advantageous decks (C and D) than the risky decks (A and B), thereby showing that they developed an estimation of which decks were risky and which were profitable. The VMPFC group on the other hand continued to prefer the disadvantageous decks for the duration of the task. Interestingly, a patient EVR was tested on multiple occasions of the task and failed to learn. Thus, this impaired performance profile reflects VMPFC patients real-life inability to decide advantageously. This is especially true in personal and social matters, where an exact calculation of the future outcomes is not possible and choices must be based on approximations (Bechara et al., 1994).

Another key evidence for the role of somatic markers in performance on the IGT came from Bechara, Tranel, Damasio & Damasio (1996) when they discovered how skin conductance response (SCR) correlated with success on the decision-making task. Bechara et al. (1996) measured SCRs in seven patients with frontal lobe damage encompassing VMPFC and 12 normal controls during task performance. Both patients and controls showed SCR to both reward and punishment. However, the control group started to develop anticipatory SCRs to imagined outcome of reward and punishment after a short

period of time. The SCRs were larger for selections from the 'risky' decks than the 'safe' decks. Interestingly, the VMPFC group failed to show anticipatory SCRs, suggesting that somatic markers were not activated to help them distinguish between good and bad outcomes in uncertain situations. Failure to activate a negative marking signal for the disadvantageous decks would explain why the VMPFC lesion patients were insensitive to the possibility of future punishment on these decks (Bechara et al., 1996).

Another experiment by Bechara, Damasio, Tranel & Damasio (1997) sought to discern when subjects develop an understanding of which decks are advantageous and which are disadvantageous in the IGT. The reward/punishment schedule of the IGT is believed to be opaque, hence the learning of which decks are good and bad is taking place at a implicit level. Bechara et al. (1997), tested therefore ten normal subjects and six VMPFC patients on the gambling task, while their SCRs were being recorded. In this experiment the game was briefly stopped after every 10^{th} trial, and the subject were asked to describe if they consciously knew what was going on in the game. The analysis showed that they went through four distinct periods across the task. The first was a pre-punishment period, when subjects simply sampled the decks, before they encountered any punishment. The second was a pre-hunch period, when subjects began to encounter punishment, but had no understanding of what was going on in the game. The third was a hunch period, when subjects began to express a hunch about the decks that were riskier, even if they were not sure about their guess. The fourth was a conceptual period, when subjects understood the contingencies in the task, and could distinguish which decks were good and bad. Anticipatory SCR activity and increased selection from the good decks began to take place for the control subjects in the pre-hunch period and was sustained throughout the task. Interestingly 30% of the control subjects did not reach the conceptual period, yet they performed normally on the gambling task. This suggests that non conscious biases guide behavior before conscious knowledge does. Most of the VMPFC patients on the other hand, did not report a hunch, nor did they develop anticipatory SCRs, hence they continued to choose from deck A and B. However, 50% of VMPFC patients did reach the conceptual period and recognized the bad decks. Despite their knowledge of the correct strategy, they still performed disadvantageously (Bechara et al, 1997). Although frontal patients may be fully aware of what is right and what is wrong, they still fail to act accordingly. These patients may 'say' the right thing, but 'do' the wrong thing (Bechara et al. 2000). However, this result gives strength to the SMH as it shows that merely conscious knowledge without

the help of nonconscious biases are insufficient to ensure advantageous behavior (Bechara et al., 1997).

Puzzled by the decision making pattern of VMPFC patients, Bechara, Tranel & Damasio (2000b) designed a variant of the original gambling task to explore reasons behind this disadvantaged decision making pattern. In this variant of the gambling task, the advantageous decks yielded higher immediate punishment but greater delayed reward. The disadvantageous decks on the other hand, gave low immediate punishment but even lower future reward. The results showed that the VMPFC patients opted for the disadvantaged decks. The second experiment investigated whether increasing the delayed punishment in the disadvantageous decks, or decreasing the delayed reward would shift the behavior of the VMPFC patients towards a more advantageous strategy. The results showed that the VMPFC patients failed to shift their behavior, and persisted in choosing from the disadvantaged deck contrary to the behavior of the control group. This suggests that VMPFC patients seem to have a "myopia for the future", meaning that VMPFC patients are primarily guided by immediate prospects, and seem to be persistently insensitive to future consequences (Bechara et al., 2000b).

9. 4 Criticism of the IGT

The results of the IGT strongly support the SMH, suggesting that biasing somatic markers are responsible for advantageous decision making strategies both at a conscious and unconscious level. Even though studies have shown that IGT is a robust, validated and highly sensitive test of decision making, issues have been raised concerning the use of IGT as evidence for SMH (Dunn et al., 2006).

One main criticism made by Maia & McClelland (2004) is that the IGT is cognitively penetrable to the reward/punishment schedule during the early stages of the test (Dunn et al., 2006). Therefore Maia & McClelland (2004) did a replication study of Bechara et al. (1997), using more detailed and focused questions after each block of 20 trials. The study found that participants had explicit reportable knowledge that guided advantageous decision making on the IGT. Maia and McClelland (2004) argued therefore that IGT seems to promote explicit reasoning rather than implicit reasoning, and emphasized two main points as a basis for this criticism. First, the IGT is self paced, thereby allowing the

participant time to reason. Second, it is relatively easy to keep track of the characteristics of the decks, as there is little variation in the reward and punishment that is used. Maia & McClelland therefore concluded that it is inaccurate to claim that the IGT requires the generation of nonconscious somatic marker signals in order to make decisions, and stress that the IGT can be performed through access to conscious, explicit knowledge. This issue constitutes a problem for using the IGT as support for SMH. According to the SMH, learning via emotion based somatic markers is believed to precede explicit insight on the IGT. The claim that the reward/punishment schedule of the IGT is consciously comprehended before somatic markers develop, leaves doubt as to whether decision making is the result of cognition or somatic markers. Maia & McClelland (2004) further argued that the methods that Bechara et al. (1997), used to discern the knowledge the participants had about the game were not sufficiently powerful.

In line with this criticism, Bowmann, Evans & Turnbull (2005) also showed in a study with different variations of the IGT, that participants rated the goodness and badness of the decks at above chance level as early as after the 20 first trials. Maia & McClelland (2004) do not rule out that somatic markers may be involved in IGT, but simply state that there is no need to include it for explaining decision making. In response to the criticism of cognitive impenetrability by Maia & McClelland (2004), Bechara, Damasio, Tranel & Damasio, (2005) argued that it is not problematic for the SMH if the IGT is more transparent than previously thought, as it is emotional signals and not the implicit nature of signals that is the core of the SMH. Bechara et al., (2005) stress that ”The central feature of the SMH is not that non-conscious biases accomplish decisions in the absence of conscious knowledge of a situation, but rather that emotion-related signals assist cognitive processes even when they are non-conscious.” (Bechara et al, 2005 p. 159). In Maia & McClelland’s (2004) defense, Dunn et al., (2006) pointed out that this seems to be a retreat from Bechara & Damasios earlier arguments which emphasize the frequently implicit nature of somatic markers. Dunn et al., (2006) further stressed that this makes the SMH hard to distinguish from other accounts of decision making.

It appears that participants have at least some conscious awareness of the reward/punishment schedule in the task. However, the nature of this awareness remains unclear, and Dunn et al., (2006) stress that this conscious awareness could be due to either a full rational understanding of the reward/punishment schedule, or simply a heuristic

understanding of the schedule. Dunn et al., (2006) continue to argue that a full rational understanding of the IGT would undermine the utility of the SMH. However, a heuristic interpretation of the valence of the decks as either good or bad would be consistent with the broader claim of SMH that emotion guide decision making.

A second criticism concerns the anticipatory SCR as support for the SMH. Bechara et al. (1996), stress that anticipatory SCRs differentiate between the advantageous and disadvantageous decks over time, where SCRs to disadvantage decks are higher than for the advantageous decks. The higher anticipatory SCRs on the IGT reflect growing awareness of the negative long term consequences of the risky decks (Dunn et al., 2006). Although SCR is a reliable measure, there are disagreements on how to interpret the different level of SCR to the different decks. Crone, Somsen, Van Beek & Van der Molen (2004) found in a modified study of the IGT that normal participants split into equal size groups of bad, moderate and good performance based on their total selection of the advantageous decks. Anticipatory SCR and heart rate (HR) were greater for the disadvantageous decks than for the advantageous decks in the group of good performers. Interestingly however, the moderately performing group did not show any difference on anticipatory SCR and HR between the advantageous and disadvantageous decks. These findings can be problematic for the SMH as they show that a number of participants can successfully accomplish the task, without needing to generate anticipatory HR and SCR signals (Dunn et al., 2006).

There also appear to be other ways to explain the elevation of the SCR to the disadvantageous decks. Tomb, Hauser, Deldin, Caramazza (2002) found in a modified version of the IGT where the good decks were associated with higher magnitude of both reward and punishment, that participants showed higher anticipatory SCR to the good decks. The authors attributed the elevated SCR to the high magnitude of reward and punishment on the good decks, and not the goodness or badness of the decks. Tomb et al. (2002) suggested that the higher SCR in the original IGT may be explained by the participants' expectations of an immediate higher- magnitude decision, and not as a result of the badness of the decks.

Other authors have argued that the anticipatory SCR to deck response selection is not as important as the feedback response in the IGT (Dunn et al., 2006). Suzuki, Hirota,

Takasawa & Shigemasu (2003) explored the influence of anticipatory and feedback SCRs on a Japanese version of the IGT. Although they found that 'risky' decks produced a greater anticipatory SCR than the non risky decks, they did not find any difference in anticipatory SCRs for early and late trials. Suzuki et al. (2003) further found that feedback SCRs were greater following punishment than reward on selections from risky decks. Participants who showed greater feedback SCRs, tended to have a steeper learning curve in that they selected fewer times from the 'risky' decks in late versus early trials. Suzuki et al. (2003) therefore suggested that feedback SCRs rather than anticipatory SCRs may be more important for task performance. A further claim that the anticipatory marker generated on the IGT may not be directly involved in the decision making process comes from a study by Amiez, Procyk, Honore, Sequeira & Joseph (2003). They found in a simplified decision making study with monkeys, that SCRs were associated with anticipation of reward after a response had been made rather than before a decision had been made. The findings of both Suzuki et al. (2003) and Amiez et al. (2003) represent a great challenge for the SMH, since it suggests that the 'anticipatory' signals may not play a causal role in shaping decision making behavior (Dunn et al., 2006).

Another issue concerning psychophysiological measures such as SCR as evidence for somatic markers is that they are only correlational with test performance, meaning that no causal conclusions can be drawn. Even though healthy participants show anticipatory SCR activity when performing well on the task, it does not necessarily indicate somatic marker development, it could also reflect the end product of the decision making process (Dunn et al., 2006).

Another criticism is based on the fact that there is a high variability in decision making behavior of control participants, which raises doubt about the ecological validity of the IGT (Dunn et al., 2006). Bechara & Damasio (2002) found that around 20% of all control participants performed disadvantageously on the IGT. Interestingly there was a high variance in SCR among these subjects, with some subjects showing SCR within the normal range, and others showing the same SCR patterns as the VMPFC lesioned patients. Participants with normal anticipatory SCRs and impaired behavioural performance were characterized as risk takers, as they chose to override the somatic marker information to make conscious risky decisions. In line with this, Adinoff, Devous, Cooper, Best, Chandler, & Harris, (2003) also found in an IGT study that there were subgroups of

healthy control participants who did not show a preference for the advantageous deck at the end of the task. These findings make the interpretation of IGT data complex, and question the ecological validity of the IGT (Dunn et al., 2006).

Further, IGT studies of patients with altered body feedback have not provided support for the SMH. Feedback from the body can arise from multiple routes, including spinal cord, vagus nerve, endocrine system, feedback from facial muscles, and from the physiochemical environment of the brain (Dunn et al., 2006). In a study by Heims, Critchley, Dolan, Mathias & Cipolotti (2004) IGT performance was examined in patients with pure autonomic failure (PAF), a condition that leads to peripheral denervation of autonomic neurons, and therefore an absence of peripheral autonomic responses. Considering that longstanding PAF leads to changes in the morphology of brain regions involved in the representation and regulation of the body state (Critchley, Good, Ashburner, Frackowiak, Mathias, & Dolan, 2003), it was predicted that PAF patients would be impaired on the IGT. Contrary to the prediction, PAF patients performed better on the IGT than the control group. This was very surprising considering that PAF patients have both body state feedback and regions of the as if body loop compromised. Another study of patients with spinal cord injury also failed to support the SMH. Patients with spinal cord injury at the 6th cervical vertebrate which blocked somatic feedback, displayed no deficit on the IGT (North & O'Carroll, 2001). This is despite the fact that spinal cord injury has been shown to reduce the intensity of emotion (Hohmann, 1996). North & Carroll (2001) suggested that their data can be reconciled with Damasios model if it is assumed that feedback from the hormonal route and nerves outside the spinal cord is more important than the afferent feedback sent via the spinal cord.

9. 5 Task design issues

A number of methodological features of the task design and psychophysiology analysis of the IGT also complicate interpretation of the IGT. The first issue concerns the use of SCR to designate the anticipatory somatic marker to a given deck selection. Considering that participants are free to shift their attentional focus across all the decks before choosing one, the physiological marker generated may not reflect attention to a single deck, but may represent shifting attentional focus across all decks before arriving at a choice. The second issue concerns the transparent reward/punishment schedule of the IGT. Considering that

the magnitude of rewards is predictable and the only variance concerns the punishment schedule, subjects only have to focus on the punishment schedule to perform well on the task. A third issue concerns the deck position of the IGT. The decks are not counterbalanced, meaning preferential selection could reflect a location bias rather than a genuine decision making deficit. A forth potential issue has to do with the classification of the cards as good or bad. In the early trials of the IGT the bad decks are actually the most advantageous, and it is only later that they become disadvantageous. Early selection from the disadvantageous decks can therefore be interpreted as rational exploratory behavior rather than impaired decision making. A way to control for this issue is to exclude the first 20 trials from the analysis, and see if a similar behavioral pattern emerges (Dunn et al., 2006).

9. 6 Alternative explanations for impaired test performance on the IGT

There are alternative explanations other than the SMH that may explain impaired performance on the IGT. One alternative mechanism that may explain impaired performance on IGT is a difficulty in reversal learning. In order to perform successfully on the IGT, participants have to shift their preferences away from the initially rewarding decks that turn out to be disadvantageous later on (Dunn et al., 2006). Rolls, Hornak, Wade, McGrath (1994) found that patients with ventral PFC damage had difficulties in reversal learning. Consistent with this, Fellows & Farah (2003) also found that patients with lesions restricted to VMPFC were impaired on a simple reversal learning task. To directly test the possibility that a reversal deficit explains impaired IGT performance, Fellows & Farah (2005) rearranged the initial reward/punishment schedule on the task such that the two disadvantageous decks no longer had an initial advantage in the opening trials. The results showed that the task performance of the VMPFC patients were the same as that of control volunteers. This suggests that difficulty in reversal learning may account for the disadvantageous decision making in the IGT. The inability to show reversal learning may also be closely related with impairment in response inhibition where VMPFC patients are unable to inhibit the immediate high payoff of the disadvantageous decks. The characteristic decision making behavior of VMPFC patients may therefore reflect a pattern where their responses are driven by feedback in the moment, rather than on long term profitability (Dunn et al., 2006).

Another possible explanation for impaired decision making could be that VMPFC patients have a deficit in future time perspective (Dunn et al., 2006). This is exactly what Fellows & Farah (2005b) found in a study of VMPFC patients. They discerned different aspects of future directed thinking, and found that VMPFC patients had temporal discounting intact, but had an impaired future time perspective. Crucially, this deficit in future time perspective was found to correlate with symptoms of apathy rather than impulsitivity (Dunn et al., 2006).

Another explanation of impaired performance on the IGT could simply reflect individual differences in risk preference, rather than good/bad decision making behavior. Sensation seeking individuals may for instance prefer decks that generate the most arousal or interest instead of decks that are more profitable in the long run. Thus, selection from the disadvantageous decks can be perfectly rational depending on individuals risk preference. Difference in risk preference may therefore explain the variation found in the control group performance and also account for impaired decision making (Dunn et al., 2006)

10. Disadvantageous decision making

In the famous longitudinal study by Mischel, Shoda & Peake, (1988) it was showed that preschoolers who were able to delay gratification became adolescents who coped better with stress and frustration. In addition, they demonstrated better abilities to concentrate and maintain attention, responded better to reason and scored higher on the SAT than their more impulsive peers. Thus, the ability to control and regulate impulses has long been linked with prosperity and good outcomes. In contrast, being unable to resist impulses, drives or temptations may be harmful to oneself or others, and is consequently considered to be one of the core features of disadvantageous decision making. History is full of examples that poor decision making results from the failure to inhibit responses to immediately attractive but suboptimal alternatives. As decision making is subjected to the law of cause and effect, the decisions people make will always have consequences. Whether the consequences will be good or bad depend to a greater degree on the choices people make. Choosing attractive suboptimal alternatives, may give advantages in the short

term, but may not pay off in the long term. In everyday life, individuals are often faced with the complex and conflicting decisions of having to choose between options with long term payoff or options yielding immediate gratification (Rivalan, Ahmed & Dellu-Hagedorn (2009). Making good decisions are therefore not always easy. Furthermore, decision making may pose an even greater challenge in situations of emotional distress and for impulsive individuals.

10. 1 Impulsivity and decision making

The diminished ability to delay gratification is one of the core features of impulsivity. Personality type ratings of impulsivity typically focus on people's ability and willingness to decide and act rapidly, as opposed to preference for careful consideration, planning and security (Patton, Stanford, Barratt, 1995). Impulsivity is not only characterized by an inability to delay gratification, but has been described as a multidimensional construct with several features. Petry & Madden (2010, p. 276) suggests that the construct of impulsivity also include an increased orientation toward the present, behavioral disinhibition, risk taking, sensation seeking, carelessness, underestimating harm, reward sensitivity, pleasure seeking, and poor planning. Based on the negative characteristics of impulsivity, it is not surprising that impulsivity has been linked with poor decision making (Zermatten, Van der Linden, d'Acremont, Jermann, & Bechara, 2005).

Impulsive individuals have a tendency to be sensation seekers, and have an increased search for new, exciting and risky experiences. Risk taking behaviors may therefore be the price people pay for certain kinds of activities that satisfy their need for novelty, change and excitement (Zuckerman, 2000). Suboptimal decision making may consequently be found in individuals who are high sensation seekers. Zuckerman (2000) stress that sensation seeking individuals are more likely to use drugs than people without this trait. Furthermore, sensation seeking individuals have also been found to increase alcohol use over time (Newcomb & McGee, 1991), participate in high risk sports, and engage in risky antisocial behaviors (Horvath & Zuckerman, 1993).

10. 1 .1 Neurobiology of impulsivity

The field of impulsive and disadvantageous decision making has also received neurobiological attention. McClure, Laibson, Loewenstein & Cohen (2004) reported that

ventral striatum activity were significantly higher when participants were unable to delay gratification. Bechara (2005) attribute impulsivity to be a result of a hyperactive amygdala-ventral- striatal neural circuit that weakens and takes control over the reflective prefrontal system. Weaker prefrontal system in impulsive individuals has also been reported by Dolan, Deakin, Roberts & Anderson (2002). This is also in line with Hollander & Evers (2001) who stress that frontal lobe abnormalities are associated with an inability to delay or inhibit acting on impulse, and an inability to calculate odds of negative risk or outcome. Furthermore, Hollander & Evers (2001) emphasizes that aspects of impulsivity are core symptoms of several frontal lobe syndromes, and that frontal-lobe hypo-function has been observed in impulsive individuals.

10. 2 Decision making under emotional distress

Everyone will from time to time have problems with delaying gratification, and make disadvantageous and risky choices. Although there could be many reasons for this, one central factor concerns the influence of emotion, and emotional distress. Leith & Baumeister (1996) argues that emotional distress marked by high arousal may impair people from thinking through the implications of their actions, resulting in risky and potentially self-defeating actions. Consistent with this, it was found in a study by Tice, Bratslavsky & Baumeister (2001) that emotional distress made people's impulse control break down, suggesting that emotionally distraught individuals may act impulsive and risk-oriented. Furthermore, negative current emotional states may shift people's priorities toward the immediate present, causing people to make shortsighted, irrational decisions. When people are emotionally distressed they generally have an urgent wish to feel better, which in turn, may increase the subjective intensity or urgency of hedonistic desires and impulses. Thus, emotionally distraught people indulge their impulses because they hope that indulgence will bring pleasure that may in turn repair their mood, and dispel their distress. Consequently, people may indulge in drugs, alcohol, or gambling when emotionally distressed. This may produce a temporary relief from the negative affective state. However, the short term gains will be outweighed by the eventual outcomes of the actions such as addiction, arrest, or financial ruin. Thus, the tendency to give priority to affect regulation is therefore detrimental to behavioral self-control and can be costly in the long run (Tice et al., 2001).

10. 2.3 Emotional distress and coping mechanisms

However, not everyone faced with emotional distress will give in to overindulgence of hedonic impulses. People's reactions to stressful events differ widely. Hence, it is not stressful life conditions per se, but the perceived inability to manage them that is debilitating (Bandura, 1994, p. 75). One way to get a clearer picture of why impulse control breaks down under stressful events for some individuals, whereas others seem to be unaffected by the same stressful events, is to considering the various coping mechanisms used in stressful situations. The use of effective coping mechanisms such as problem focused coping may lead to functional decision making and healthy outcomes, whereas the use of ineffective coping such as denial, avoidant coping may lead to dysfunctional outcomes (Carver, Scheier & Weintraub 1989).

Personal dispositions like impulsivity may also influence the coping mechanisms people use. Thus, having an impulsive disposition may result in ineffective coping mechanisms such as gambling (Nower, Gupta & Derevensky,2000) and drug addictive behaviors (Belding, Iguchi , Lamb, Lakin &Terry, 1999). Lightsey & Hulsey (2002) investigated the relationship between impulsivity, coping, stress, and problem gambling, and found that ineffective coping responses among impulsive men were related to gambling. Impulsive individuals may behave with a lack of restraint or reflectiveness, and may be less likely to use planning and other forms of adaptive coping. Furthermore, the use of dysfunctional coping mechanisms such as social diversion, anger, or blame often leads to stress exacerbation and in theory, to gambling or other addictive behaviors (Lightsey & Hulsey, 2002).

Considering the dysfunctional decision making pattern characterized by some impulsive individuals, leading to both increased risk taking and dysfunctional stress coping, it is not surprising that impulsivity has been regarded as a central component in a wide range of pathological behaviors and disorders, such as substance abuse, pathological gambling, borderline personality disorder and suicidal tendencies (Hollander & Evers, 2001). Given the range of problematic behavior associated with impulsivity, it would be interesting to discern some of the neurobiochemical underpinnings of impulsivity. Studies of impulsivity have suggested that serotonergic and dopaminergic systems might play an important role in impulsivity (Carver & Miller, 2006; Hollander &Evers, 2001).

10. 4. Serotonin

Serotonin (5-hydroxytryptamine, 5-HT) is an important neurotransmitter in the human central nervous system (CNS), and has been shown to play a central role in the neurobiology of decision making, emotional learning and social behavior (Crisan, Pana, Vulturar, Heilman, Szekely, Druga, Dragos & Miu, 2009). Furthermore, 5-HT has also been linked with impulsivity (Carver & Miller, 2006), and several physiological and behavioral disorders such as depression, anxiety, addictions, personality disorders (Fillip & Bader (2009). Impulsive behaviors leading to poor decision-making may be a common symptom of several neuropsychiatric diseases that are related to disturbed 5-HT homeostasis (Brand, Labudda, Markowitsch, 2006).The association between impulsive behavior and low capacity of the serotonergic system has been demonstrated in both rodents (Evenden, 1999) and primates (Fairbanks, Melega, Jorgensen, Kaplan & McGuire, 2001). Low 5-HT levels have also been implicated with the inability to delay gratification and detect changes in reward (Denk, Walton, Jennings, Sharp, Rushworth & Bannerman, 2005). Reduced baseline activity of the serotonergic activity has also been associated with impulsive behaviors in alcoholics (Fils-Aime, Eckardt, George, Brown, Mefford & Linnoila, 1996) violent offenders (Linnoila, Virkkunen, Scheinin, Nuutila, Rimon & Goodwin, 1983), patients with personality disorders (Brown, Ebert, Goyer, Jimerson, Klein,Bunney, Goodwin,1982), and healthy volunteers with impulsiveness as a personality trait (Roy & Linnoila, 1988). Clearly, 5-HT may be seen as an influencing factor in the impulsive choices people make. It would therefore be beneficial to take a closer look at how 5-HT is regulated, and how the modulations of the regulating factors influence the 5-HT level in the brain.

10. 4.1 Regulation of serotonin in the brain

The neurotransmitter 5-HT is synthesized from the amino acid tryptophan which is obtained in the diet (Cooper & Melcer, 1961). The 5-HT-containing neurons are mainly collected in the raphe nuclei (Fillips & Bader, 2009). Collectively, the raphe nuclei innervates almost all brain areas, but each nucleus is also known to have specific projections to particular brain areas and structures (Fillips & Bader, 2009) Consequently, the 5-HT system innervate many brain areas related to decision-making, including the amygdala, the prefrontal cortex, and the striatum (Stoltenberg,Vandever, 2009). The brain's 5-HT activity is regulated by the 5-HT transporter (5- HTT). The 5-HTT is a

sodium chlorine-dependent transporter located in the plasma membrane of the cell. Under normal physiological circumstances, the 5-HTT's major purpose is the efficient removal of 5-HT from extracellular areas. When 5-HT is released in the synaptic gap the presynaptically located 5-HTT will return 5-HT to the cell for recycling and metabolic decomposition. Other neurotransmitters and their respective reuptake transporters are mediated by the same functional principle (Stahl, 2008 s. 95-97). 5-HT may also be catabolized and inactivated by the enzyme monoamine oxidase. Manipulating the 5-HT level will alter the duration and intensity of 5- HT communication with its receptors and postsynaptic targets (Fillip & Bader, 2009).

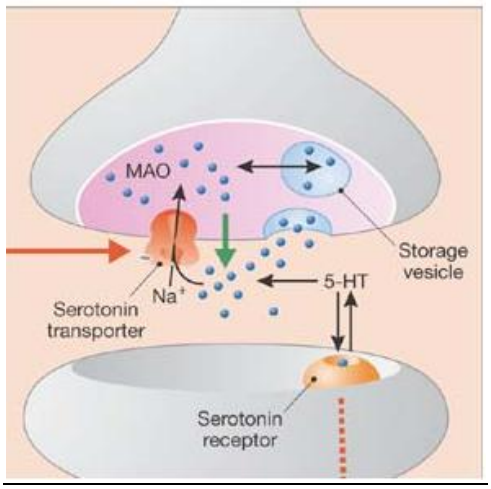

Figure 3: Illustration of serotonergic neurotransmission (Adapted from Canli & Lesch, 2007)

10. 4.2 Serotonin and decision making

One accepted method of studying behavioral and cognitive effects of reduced 5-HT availability is through acute tryptophan depletion (ATD). This procedure transiently lowers central nervous system 5-HT levels, by reducing serum and central nervous system levels of its precursor tryptophan by the intake of a tryptophan-free amino acid mixture (Krakowski, Czobor, Carpenter, Libiger, Kunz, Papezova, Parker, Schmader, Abad, 1997; William, Shoaf, Hommer, Rawlings & Linnoila, 1999). Interestingly, ATD has been found to increase impulsiveness (Walderhaug, Lunde, Nordvik, Landrø, Refsum & Magnusson, 2002), impair decision making (Rogers, Everitt, Baldacchino, Blackmore, Swainson & London, 1999), and reduce punishment processing (Blair, Finger, Marsh, Morton, Mondillo, Buzas, Goldman, Drevets & Blair, 2008) in healthy individuals. The findings

that ATD has been reported to impair decision making have been attributed to a neuromodulatory effect of reduced 5-HT on the ventral prefrontal cortex (Talbot, Watson, Barrett & Cooper, 2006). Interestingly, 5- HT is known to influence the specific parts of decision making that relies on conscious knowledge. This was illustrated in an IGT study by Bechara, Damasio & Damasio (2001) where both the blockade and stimulation of 5- HT affected decision making. This was exclusively on the latter part of the task, when decision making was under conscious knowledge. These results imply that the specific part of decision making that relies on conscious thought might be under serotonergic influence (Bechara, 2003).

10. 4.3. Genetic variations in the serotonergic system and decision making

Regulations in the available 5- HT level may be influenced by different genotypes in the serotionergic system. One such genetic factor may be related to the tryptophan hydroxylase (TPH) enzyme. Tryptophan hydroxylase (TPH) is the rate-limiting enzyme in 5-HT biosynthesis. TPH exists in two isoforms, TPH1 and TPH2. Variations in the TPH-1 has been associated with a number of psychiatric disorders including mood disorders, violent behavior, and suicide (Mann, Malone, Nielsen, Goldman, Erdos & Gelernter, 1997; Skodol, Siever, Livesley, Gunderson, Pfohl & Widiger, 2002; Arango, Huang, Underwood & Mann 2003). Furthermore, variation in the neuronally expressed tryptophan hydroxylase gene (TPH2), is associated with individual differences in amygdala activation (Brown, Peet, Manuck, Williamson, Dahl, Ferrell & Hariri, 2005) response inhibition (Stoltenberg, Glass, Chermack,, Flynn, Li, Weston & Burmeister, 2006) and decision-making (Jollant, Buresi, Guillaume, Jaussent, Bellivier, Leboyer, Castelnau,Malafosse & Courtet, 2007).

Another genotype in the serotonergic system is related to the 5-HTT. The 5- HTT has a common polymorphism in the promoter region comprising of a long (ll) and a short (ss) variant (Lesch, Bengel, Heils, Sabol, Greenberg, Petri, Benjamin, Müller, Hamer & Murphy,1996). This polymorphism is referred to as the 5-HT transporter protein gene-linked polymorphic region, or the 5-HTTLPR. Heils, Teufel, Petri, Stöber, Riederer & Bengel (1996) found that the (ll) variant was associated with approximately three times higher transcriptional activity compared to the (ss) variant. Thus the rate of 5-HT uptake was double in (ll) cells compared to (ss) cells. When the association between 5-HTTLPR

and its role in the brain's 5-HT function was discovered by Lesch et al., (1996), individuals with the (ss) allele was found to show increased trait anxiety, neuroticism and harm avoidance, compared with individuals homozygous for the long variant. Evidence suggests that allelic variation in functional 5-HTT expression, plays a crucial role in synaptic plasticity, and consequently set the stage for expression of complex traits and their associated behavior (Lesch & Mössner, 1998).

The genetic variation in the 5-HT transporter has been associated with individual differences in VMPFC and amygdala activation (Hariri, Drabant, Munoz, Kolachana, Mattay, Egan &, Weinberger, 2005; Heinz, Braus,Smolka, Wrase, Puls,Hermann, Klein, Grusser, Flor, Schumann, Mann, & Buchel, 2005). Research shows that individuals with one or two copies of the (ss) allele, exhibit greater amygdala neuronal activity to fearful stimuli compared to individuals homozygous for the (ll) allele (Hariri, Mattay, Tessitore, Kolachana,, Fera & Goldman, 2003). In the same vein, a fMRI study by Rao, Gillihan, Wang, Korczykowski, Sankoorikal, Kaercher, Brodkin, Detre & Farah (2007) showed that individuals homozygous for the short variant, demonstrated increased cerebral blood flow (CBF) in the amygdala and decreased CBF in the ventromedial prefrontal. Interestingly, it was also found in a study by Pezawas, Meyer-Lindenberg, Drabant, Verchinski, Munoz,Kolachana, Egan, Mattay, Hariri & Weinberger (2005) that individuals with the short allele had a decreased functional connectivity between the amygdala and the rostral anterior cingulate cortex, whereas individuals with the long allele were found to have an increased coupling between the anterior cingulate cortex and the amygdale. Considering that these brain regions are important in decision making, it is not surprising that 5-HTTLPR also have been associated with performance on decision-making tasks (Roiser, Rogers, Cook & Sahakian, 2006). In a IGT study by Homberg, van den Bos, den Heijer, Suer, & Cuppen (2008) it was found that women homozygous for the short allele of the 5-HTTLPR, choose more disadvantageously than women homozygous for the long allele as the IGT progressed. Homberg et al. (2008) stresses that reasons for the poor decision making of (ss) subjects may be related to the increased amygdala activation which may hijack the cognitive resources of the PFC. Furthermore, is it also possible that the reduced functional coupling between the ACC and amygdala which is found in (ss) individuals makes it difficult for them to change their selection, and use the choice outcome to guide the next choice. Consequently, they may persist with the choice that they selected during the first phase of the task (Pezawas et al., 2005).

10. 5. Dopamine

The neurotransmitter dopamine (DA) has also been implicated in risk seeking and impulsive behaviors (Heilbronner, Hayden & Platt, 2010,p .180). Reasons for this becomes apparent when considering the important role DA plays in reward related behaviors and decision making. DA mediates the 'binding' between the hedonic evaluation of stimuli and the assignment of these values to objects or acts. Thus, DA release and binding provides therefore a necessary link between the evaluation of potential future rewards, and the sequence of actions that acquires the rewards (Montague, Hyman & Cohen, 2004, Berridge & Robinson, 1998). Studies have confirmed the role of DA in motivation (Salamone, Correa, Farrer & Mingote, 2007), and action (Daberkow, Kesner & Keefe, 2005). When considering that DA mediates both reward seeking behavior and impulsive behaviors, it is not surprising that it also has been found to play a major role in addictions (Montague, Hyman & Cohen, 2004, Kalivas and Volkow 2005).

DA is synthesized in dopaminergic nerve terminals from the amino acid tyrosine in two subsequent steps. Tyrosine is first converted to dihydroxyphenylalanine (DOPA) by the rate limiting enzyme tyrosine hydroxylase and then converted to DA by the enzyme dopa decarboxylase. After DA has been released from the presynaptic synapse and further activated the postsynaptic receptors, the remaining DA is removed from the synapse by the DA transporter (DAT) (Rolls, 1999, s. 168-169) However, due to the low level of DA transporters in the PFC, DA is inactivated by the enzyme COMT in this region (Mazei, Pluto, Kirkbride, & Pehek, 2002; Moron, Brockington, Wise, Rocha, & Hope, 2002). The dopaminergic neurons from the ventral tegmental area and the substantia nigra influence an array of cortical and subcortical structures, including the VM cortex, amygdala and nucleus accumbens (Bechara, Damasio & Tranel, 2000)

10. 5.1 Dopamine and decision making

Several studies have shown that DA may influence decision making and impulsivity. Van Gaalen, van Koten, Schoffelmeer & Vanderschuren, (2009) confirmed that dompaminergic neurotransmission plays an important role in impulsive decision making. Reduced dopaminergic activity has further been associated with poor emotion based decision making, characterized by shortsightedness, and difficulties resisting short-term reward, despite long-term negative consequences. Furthermore, a deficiency in dopaminergic

activity may result in heightened affective reactions leading to impaired decision making (Sevy, Hassoun, Bechara, Yechiam, Napolitano, Burdick, Delman & Malhotra, 2006). This is in line with Scarna, McTavish, Cowen, Goodwin & Rogers (2005) who suggests that DA may play a more general role in the processing of emotional signals in risky decision-making. Consistent with this, it was found in an IGT study of Sevy et al., (2006) that acutely decreasing central DA levels in healthy subjects, impaired decision making. Bechara, Damasio, & Damasio (2001) suggest that DA may influence specific aspects of decision making. In their study, they found that blocking of DA, interfered with the selection of advantageous choices on the earlier parts of the IGT, when decisions were guided by covert knowledge. However, stimulating DA improved decision making, but only on the early parts of the task when knowledge were covert, suggesting that decisions under covert knowledge may be under dopaminergic influence.

However, not all studies support that low levels of DA are associated with poor decision making. In contrast, Zeeb, Robbins & Winstanley (2009) argues that an elevated DA level may be related to poorer decision making. This has also been supported in studies of the COMT enzyme. A study by Roussos, Giakoumaki, Pavlakis & Bitsios (2008) found that individuals with low activity of the COMT enzyme, giving high level of DA in the PFC, displayed poor decision making on the IGT. Roussos et al. (2008) suggests that even though individuals with high PFC DA levels may be impaired on emotion based decision making, they may be skilled in non emotional problem solving. In line with this study, Van den Bos, Homberg, Gijsbers, den Heier & Cuppen (2009) also found that low activity of the COMT enzyme resulting in high levels of DA in the PFC, lead to impaired emotional decision making on the IGT. Although there could be many reasons for the divergent findings of the effect of DA on decision making, Zeeb et al., (2009) suggests that the optimal level of DA may follow an inverted U-shaped curve, where both reduced and excess levels of DA may lead to poor decision making.

10. 6. Substance use disorder

Considering the chief role that DA plays in reward seeking behaviors, it is not surprising that dopaminergic functions have been implicated in substance use disorders (SUDs) (Volkow, Fowler, Wang & Swanson, 2004). Drug users are known to display reward seeking behaviors and seem to have reduced sensitivity for punishment (Verdeja et al.,

2008). Furthermore, there is also a robust association between the construct for impulsivity and SUDs. It has even been proposed that high impulsivity and risky decision making are factors that might lead to drug use (Bechara and Damasio 2002; Bechara, Dolan, Denburg, Hindes, Anderson & Nathan, 2001; Ernst, Grant, London, Contoreggi & Kimes & Spurgeon, 2003; Verdejo- Garcia, Lawrence & Clark, 2008; Schilt, Goudriaan, Koeter, van den Brink & Schmand, 2009). Substance abuse is characterized by maladaptive and recurrent substance use resulting in physical, legal, and/or interpersonal problems (Yi, Mitchell & Bickel, 2010, p. 191). Poor decision making skills are an important factor in explaining the negative outcomes often associated with SUD. Individuals with SUDs are constantly faced with a choice between another drug episode and the potential of losing a job, family breakdown and financial ruin. Individuals who show little or no reflection on the consequences of their decisions may be similar to individuals with the personality trait of 'non-planning' impulsivity, a tendency to live for the moment with no regard for the future, or individuals that lack the trait of 'premeditation', a tendency to think and reflect on the consequences before acting (Behara, 2005).

10. 6.1 Decision making deficits in substance use disorder groups

Research confirms poor decision making skills in the SUD population (Allen, Moeller, Rhoades, & Cherek, 1998) Coffey, Gudleski, Saladin & Brady (2003) compared discounting of hypothetical monetary outcomes in people dependent on crack cocaine and control participants. Crack dependent participants discounted the money more steeply than control participants. Other studies have found similar results (Heil, Johnson, Higgins & Bickel, 2005; Kirby & Petry, 2004). Poor decision making skills have also been found in subjects with alcohol dependence (Bechara et al., 2001; Bjork, Hommer, Grant & Danube, 2004; Petry, 2001), Cannabis (Verdejo-Garcia, Benbrook,Funderburk, David, Cadet & Bolla, 2007), methamphetamine (Hoffman, Moore,Templin, McFarland, Hitzemann & Mitchell, 2006), MDMA (Morgan, Impallomeni, Pirona & Rogers, 2006) and in polydrug use (Grant, Contoreggi, & London, 2000). Heroin users have also been found to show poor decision making and to show steep discounting of both hypothetical and real delayed monetary rewards (Kirby and Petry, 2004). The high discounting rate by heroin users combined with the route of administration of the drug may pose an alternative health hazard to this drug user group. This was illustrated in a study by Odum, Madden, Badger & Bickel (2000) who found that 50 per cent of heroin abusers would share a needle rather

than wait to obtain a clean needle. Decision making deficits in the SUD population has also been confirmed in measures of emotional decision making such as the IGT (Bechara and Damasio, 2002; Bechara, Dolan, Denburg, Hindes, Anderson &,Nathan 2001). Furthermore, it has also been demonstrated that adverse real life consequences of substance use, including medical and legal problems, are associated with poor performance on the IGT among SUD treatment patients (Dom, D'haene, Hulstijn, & Sabbe, 2006).

Interestingly, SUD participants have been found to perform poorly on the IGT regardless of the specific substance used or the duration of regular substance use (Barry & Petry, 2008). This suggests that poor decision making may be attributed to addiction in general, rather than to the effects of a specific type of drug (Bechara, 2005). However, even though IGT performance is irrespective of the specific substance, the decision making deficits of the SUD group is not uniform across all individuals belonging to this group (Bechara, 2003). Bechara et al., (2001) showed in a comparison of decision making impairments in addicts and patients with VMPFC damage, that 63 per cent of the addicts displayed gambling task deficits consistent with VMPFC group. The remaining 37 per cent performed like normal controls. It is difficult to determine whether decision making deficits displayed by SUD groups are the consequences of drug use or if they were present before the initiation of drug use. Two perspectives have been proposed as an explanation for the poor decision making skills of SUD: The neurotoxic attrition model and the diathesis model (Verdejo- Garcia et al., 2008).

10. 6.1.1 The neurotoxic perspective of drug abuse

The neurotoxic attrition perspective, stresses that heavy substance use could cause chronic neurobiological attrition effects, and lead to a gradual impairment of behavioral self control mediated by structural changes in the prefrontal cortex (Verdejo- Garcia et al., 2008). Neurobiological attrition may occur via direct and enduring neurotoxic damage and consequently tissue shrinkage. This is supported by the finding that MDMA induce selective 5-HT neurotoxicity (McCann, Ridenour, Shaham, Ricaurte, 1994). Furthermore, imaging studies have also revealed reduced grey matter volume in the prefrontal cortex of drug abusers (Liu, Matochik, Cadet, & London, 1998), particularly in the orbitofrontal cortex (London, Ernst, Grant, Bonson, & Weinstein, 2000). Several voxel-brain-morphometry studies of brain scans of addicts have also found varying degrees of

structural abnormalities in several brain regions including the VMPFC, anterior cingulate (Franklin, Acton, Maldjian, Gray, Croft, Dackis, O'Brien & Childress, 2002), and dorsolateral prefrontal cortex (Matochik,London, Eldreth, Cadet & Bolla, 2003) areas known to affect decision making process. It is difficult to determine whether these abnormalities were the consequences of drug use, or if they existed before the subjects started their drug use. It is possible that an excessive and chronic drug use may lead to these abnormalities. However, it is also possible that a degree of abnormality pre-existed the addiction, predisposing them to drug experimentation and addiction (Bechara, 2005).

10. 6.1.2.The diathesis model of drug addiction

Decision making deficits associated with SUD may also be explained by a diathesis model, where developmental or genetic abnormalities in the brain decision-making circuitry predispose the individual to addictive behaviors (Clark & Robbins, 2002). Cross-sectional studies in adolescent samples have shown that elevated trait impulsivity and higher rates of delay-discounting were associated with earlier age of alcohol and drug experimentation (Kollins, 2003; Martin, Kelly, Rayens, Brogli, Himelreich, Brenzel, Bingcang & Omar, 2004). There are also indications that the prevalence of SUDs is elevated in the offspring of parents with SUDs including alcohol-dependency and stimulant use (Kendler, Prescott, Myers & Neale, 2003;). In line with this, Kreek, Nielsen, Butelman & Laforge (2005) argued that there is a high genetic contribution to SUDs ranging from 30–60 per cent.

10. 6.2. Neurobiological basis for drug addiction

In addition to the genetic predisposition explanation for SUDs, it has been suggested that SUD typically starts in adolescence (Verdejo- Garcia et al., 2008). Chambers, Taylor, Potenza (2003) proposed a neurobiological explanation for this, and attributed the increased risk taking behavior in adolescents to the greater maturity of the subcortical system coupled with the relative immaturity of the prefrontal cortical system. The fact that the functions of the prefrontal cortex may not fully develop before the age of 21 further lends support these explanations (Bechara, 2005). Thus, the imbalance between the reward and control system found in adolescents, where the activity of the reward system prevails over the systems governing inhibition and self-control, might be one explanation for why

adolescence is a high risk period for drug experimentation, which subsequently could lead to SUDs (Verdejo- Garcia et al., 2008).

The view that SUD may result from the imbalance between the reward and control system is also shared by Bechara (2005), who also suggests that this imbalance may also be genetically induced. Bechara (2005) stress that there are two separate, but interacting, neural systems that controls decision making. The impulsive amygdala system is involved in triggering the affective/emotional signals of immediate outcomes, whereas the reflective prefrontal cortex system is involved in triggering the affective/emotional signals of long-term outcome. The dynamic interaction between the two systems is linked with willpower, thus there is always a decision whether to use drugs or not. In most cases, the reflective system controls the impulsive system via several mechanisms. However, this control is not absolute; hyperactivity within the impulsive system may override the reflective system leading to dysfunctional decision making and consequently SUDs. Although most people resist losing control and succumbing to addiction, some individuals have a dysfunctional inhibitory system, leaving them vulnerable to immediate impulses and consequently addictions. Furthermore, drugs may trigger bottom-up, involuntary signals originating from the amygdala, and bias or even hijack the goal-driven cognitive resources that are needed for the reflective system (Bechara, 2005).

The vulnerability and the neurotoxic attrition accounts are by no means mutually exclusive. Substance users may have impulsive personalities pre-morbidly and display decision making deficits, leading them to ignore long- term consequences in the interest of immediate gratification or relief from uncomfortable states. This poor and impulsive decision making style may be further exacerbated via chronic substance administration (Verdejo- Garcia et al., 2008). When substance abuse arises, cognitive control functions such as the PFC and ACC may diminish (Van Holst, van den Brink, Veltman, & Goudriaan, 2010). Furthermore, as a consequence of continued drug use, the salience of drug-related stimuli increases, and drug craving mediated by DA function emerges (Kalivas and Volkow, 2005). Repeated exposure to drugs or drug-related cues enhances the memory of the expected reward, resulting in decreased influence of the cognitive control circuit, leading to an inability to inhibit the drive to seek and consume drugs (Van Holst et al., 2010).

10. 7. Pathological Gambling

Pathological gambling (PG) has been considered to be a form of 'behavioural addiction', and shares many of the etiological mechanisms and vulnerability factors with SUDs. However PG represents a unique addiction, because it does not involve the administration of substances to cause harmful effects in the brain. Nevertheless, pathological gamblers are similar to the SUD population in many ways, and show the same pattern of impulsivity, delay discounting, risky decision making as SUD individuals do (Verdejo- Garcia et al., 2008). PG is characterized as repeated unsuccessful efforts to control, cut back, or stop gambling, committing illegal acts to finance gambling, and jeopardizing a job or significant relationship due to gambling (Goudriaana, Oosterlaanb, Edwin de Beursc & van den Brink, 2005). In addition to functional impairments in occupational, financial and interpersonal capacity as a result of continued gambling, there is empirical evidence that PG individuals also display cravings (Tavares, Zilberman, Hodgins,& el-Guebaly, 2005), withdrawal symptoms (Wray and Dickerson, 1981) and frequent relapse (Ledgerwood and Petry, 2006). Clearly, the persistent gambling behavior is destructive to both the individual and the society in the long run, and may therefore be seen as a serious public health problem.

10. 7.1 Decision making deficits in pathological gamblers

The poor decision making skills showed by PG have found robust empirical support (Petry, 2001, Dixon, Marley & Jacobs, 2003, Lakey, Goodie & Campbell, 2007). A study by MacKillop (2006) found that PG displayed a higher delay discounting rate than healthy controls, and that the degree of discounting was related to gambling severity. In an IGT study by Cavedini et al. (2002) comparing PG and healthy controls, it was found that the PG group selected significantly more cards from the risky decks than from the safe decks, and showed increased preference for the risky decks over the course of the task. Goudriaan, Oosterlaan, de Beurs, and van den Brink (2005) reported that pathological gamblers with no history of drug or alcohol dependence chose from the IGT's disadvantageous decks significantly more often than non-disordered gambling controls. Similar findings was repeated in an IGT study by Roca, Torralva, Lopez, Cetkovich, Clark & Manes (2008) using a small group of pathological gamblers from a casino hall. Consistent with other PG studies using the IGT, Brand, Kalbe, Labudda, Fujiwara, Kessler

& Markowitsch (2005) showed that pathological gamblers had a significant preference for disadvantageous choices compared to controls on the game of dice task. In addition to these findings, Van Holst et al. (2010) argued that the decision making impairments by pathological gamblers are characterized by a diminished switching behaviour after punishment trials.

10. 7.2 The biopsychosocial model of gambling

Several models have been developed to explain PG behavior. The biopsychosocial model by Sharpe (2002) suggests that genetic predisposition such impulsive personality traits or changes in the neurotransmitter system or are likely to contribute to the vulnerability for developing gambling problems. Studies investigating the heritability and genetic contribution of PG have found the involvement of allelic variations in both the dopaminergic and the serotonergic neurotransmitter systems (Eisen, Slutske, Lyons, Lassman, Xian, Toomey, Chantarujikapong & Tsuang, 2001; Ibanez, Blanco, Perez de Castro, Fernandez-Piqueras, Saiz-Ruiz, 2003). In the biopsychosocial model two subgroups of gamblers have been identified; slot machine players and casino/horse race gamblers. Slot machine players are thought to gamble as a response to negative life circumstances. They frequently use gambling as a coping mechanism to escape stressful situations and to reduce arousal. Casino and horse race gamblers on the other hand are often described as high sensation seekers. This subgroup of gamblers is therefore thought to resolve feelings of boredom with exciting gambles as a means to increase their arousal level. In an fMRI study by Reuter, Raedler, Rose, Hand, Glascher & Buchel (2005), it was found decreased ventral striatum activation in pathological gamblers, indicating a reduction in the sensitivity of the reward system. This reduction in reward sensitivity may induce pathological gamblers to seek more rewarding events to compensate for a pre-existing anhedonic state, hence displaying an increased reward seeking behavior. Furthermore, it has also been found that pathological gamblers are characterized by diminished punishment sensitivity (de Ruiter, Veltman, Goudriaan, Oosterlaan, Sjoerds & van den Brink, 2009). All these factors may contribute to persistent gambling behavior (Van Holst et al., 2010).

10. 7.3.The pathway model of gambling

In the pathway model by Blaszczynski & Nower (2002) it is argued that gambling behavior is influenced by classical and operant conditioning, leading to development of habitual patterns of gambling. Casino gamblers often report euphoric feelings during a gambling episode, which may be comparable to the ‘‘high’’ drug users experience. This euphoric feeling may make them more prone to continue gambling. As the urges for gambling develop, the capacity for behavioral self control weakens, leading to increased gambling and negative outcomes. This vicious cycle is thought to perpetuate gambling problems (Van Holst, et al. 2010). In addition, gamblers may also start to use gambling as a coping mechanism, making the patterns of gambling behavior even more entrenched and maladaptive.

10. 7.4. *Cognitive distortions in gamblers*

In addition to the previously mentioned factors accounting for gambling behavior, gambling propensity may further be stimulated by the cunning nature of gambling games. The games often foster an illusion in the gambler that the chances for winning are high. Furthermore, cognitive distortions, such as the erroneous beliefs that chances to win are influenced by external factors, may further increase the gambling behavior (Van Holst et al., 2010)

11. Empirical part

This part of the thesis consists of two studies concerning how modulation of the serotonergic system may influence decision making. The two studies in this thesis are part of two major research programs; Cimbi (Erritzoe, et al., 2010, in preparation) and Agenda (Knorr, Vinberg, Klose, Feldt-Rasmussen, Hilsted, Gade, Haastrup, Paulson, Wetterslev,; Gluud, Gether & Kessing,Lars, 2009). I would therefore especially like to thank David Erritzøe, Gry Zornhagen and my supervisor Anders Gade in the cimbi research program, and Ulla Knorr in the Agenda research program for giving me permission to use their collected data material in my thesis. The first study, which is part of the Cimbi research program, compare MDMA users and healthy controls to investigate whether serotonergic

downregulation due to MDMA abuse may affect decision making. The second study, which is part of the Agenda research program, compare the effect of SSRI treatment, which may lead to serotonergic upregulation, on decision making in healthy first degree relatives of patients with depression.

11.1 The effect of MDMA on decision making in healthy subjects

11. 1.2 Theoretical overview

The lack of inhibition and impulse control is a highly associated with drug abuse (Clark, Roiser, Robbins, Sahakian, 2009), including the groups that regular make use of 3,4 methylenedioxymethamphetamine (MDMA) (Halpern, Pope, Sherwood, Barry, Hudson & Yurgelun- Todd (2004). Furthermore, lower cognitive performance such as working memory impairments have also been reported in repeated users of MDMA (Curran & Travill, 2006). MDMA is a ring-substituted amphetamine derivative whose structure is similar to both amphetamine and the hallucinogen mescaline. MDMA is the main psychoactive compound in 'ecstasy' tablets and is a popular drug of abuse for their effects of increased energy, euphoria and extroversion (Hoshi, Mullins, Boundy, Brignell, Piccini & Curran, 2007). MDMA binds to the serotonin transporter (5-HTT), preventing reuptake and stimulating release of serotonin (5-HT), and causes long-term changes to the 5-HT system (Roiser, Cook, Cooper, Rubinsztein & Sahakian, 2005). It has been suggested that MDMA elicits an initial upsurge in brain serotonin (5-HT) release and blocks reuptake, followed by a period of diminished release after prolonged use (Hanson, Luciana & Sullwold (2009).This is in line with Green, Mechan, Elliott, O'Shea & Colado (2003) who stresses that MDMA cause extensive serotonin (5-HT) depletion when administered in high doses to experimental animals. Furthermore, a number of studies have reported that human users of ecstasy show signs of serotonergic downregulation, including reduced 5-HT transporter (5-HTT) binding (Buchert, Thomasius, Wilke, Petersen, Nebeling, Obrocki, Schulze, Schmidt, Malte, 2004; McCann, Szabo, Seckin, Rosenblatt, Mathews, Ravert, Dannals, & Ricaurte, 2005; Semple, Ebmeier, Glabus, O'Carroll & Johnstone,E.C, 1999), and reduced concentration of 5- HT metabolites in cerebrospinal fluid (McCann, Ridenour, Shaham & Ricaurte, 1994).

Considering that MDMA has such profound effects on the serotonergic system, it is not surprising that is has been found to have selective neurotoxic effects on serotonin (5-hydroxytryptamine, 5-HT) neurons (Clark, et al., 2009). Several studies have demonstrated that the MDMA induced damage on serotongergic nerve endings in the forebrain is of long duration (Green et al., 2003; Hatzidimitriou, McCann, Ricaurte, 1999). However, other studies have found that serotonergic deficits in 'ecstasy' users can recover after prolonged abstinence (Reneman, Booij,de Bruin, Reitsma, de Wolff, Gunning, den Heeten & van den Brink,Wim, 2001; Buchert et al, 2004; Thomasius, Petersen, Buchert, Andresen, Zapletalova, Wartberg, Nebeling, Schmoldt, 2003). It is however important to note the concept of toxicology when considering the effect MDMA has on humans. The dose-response relationship states that there is a direct relationship between the amount of intake of a toxic substance and the effect it will have on individuals. Indicating that when the drug reaches a certain dosage, it will produce toxic effects (Quednow, Kühn, Hoppe, Westheide, Maier, Daum & Wagner, 2007). This might indicate that high or frequent doses of MDMA might be required to produce neurotoxic damage (O'Shea, Granados, Esteban, Colado & Green, 1998) and impulsivity (De Win, Schilt, Reneman, Vervaeke, Jager, Dijkink, Booij, van den Brink, (2006). Indication of neurotoxicity may be manifested as deficits in cognitive functions (Quednow et al., 2007) and emotional changes (Hanson et al.,2009). Consistent with this, Yip and Lee (2005) also found that MDMA users were impaired on several cognitive tests. Furthermore, Clark et al., (2009) stresses the longstanding association between reduced serotonin neurotransmission and behavioral impulsivity, and argues that neurotoxicity and 5- HT depletion of MDMA may cause or exacerbate impulsivity in human users. This has been confirmed in a study by Butler & Montgomery (2004) showing that MDMA users had higher levels of impulsivity than non drug users.

Considering that MDMA users have been found to both have reduced 5- HT level and increased impulsivity (Quednow, et al.,2007), it would be expected that they would also show decision making impairment. Interestingly, although impairments have been reported, findings remain equivocal. Morgan, Michael, Impallomeni, Pirona & Rogers (2006) found risky decision-making among MDMA users compared with polydrug and controls. Butler & Montgomery, 2004) found that high MDMA users scored higher on risk taking measures than non drug users. Furthermore, Quednow et al., (2007) found that MDMA users made more disadvantageous choices on the IGT relative to marijuana and

nondrug controls. Conversely, other studies have not reported decision making deficits in MDMA users. Fox , McLean, Turner, Parrott, Rogers & Sahakian (2002) did not find any differences in decision making between ecstasy users and controls after a minimum abstention period of two weeks. Similarly, Lamers, Bechara, Rizzo & Ramaekers (2006) did not find any differences between MDMA users and controls. The conflicting findings may reflect methodological problems. Furthermore, considering that many MDMA users are polydrug users may make it difficult to attribute deficits specifically to MDMA (Hanson et al., 2009). Another artifact could be the intake dose of MDMA. Quednow et al. (2007), suggests that impulsivity of MDMA users and disturbed decision-making may be associated with the lifetime peak dose of MDMA and the years of MDMA intake.

This aim of this study is to examine the effect of MDMA on decision making in an IGT paradigm. Considering that MDMA may produce neurotoxic effects on the serotonin system, which is known to be involved in impulsivity and decision making, it would be plausible to think that MDMA would impair decision making. This study therefore hypothesizes that there will be a difference between the MDMA group and the healthy controls, and that the MDMA group will show impaired decision making compared to the healthy controls.

11. 1.3 Method

(Erritzoe, et al., 2010, in preparation)

11. 1.3.1 Subjects

42 subjects participated in the study (37 males and 5 females) in the age range from 19- 34 years (mean age = 28,8 ± 3,8 (SD) years). Participants were recruited through advertisement in fliers and via internet. All the participants were ethnic white, and were Danish citizens. Out of the 42 participants, 23 subjects were MDMA users and users of other hallucinogenic drugs. The whereas 19 subjects were healthy controls. The two groups were matched for age and sex. Participants were screened using blood sampling in order to rule out somatic illness. Participants with somatic or psychiatric illness were not included in the study.

11. 1.3.2. Procedure

Decision making was tested using the computerized version of the Iowa Gambling task, (IGT). The participants were tested in individual sessions in KU, institute of psychology, where they also were tested in a range of other cognitive and social cognition tests. The procedure has been described in detail by Bechara, Damasio, Damasio & Lee, (1999). Subjects were presented with four decks of cards on a computer screen. The decks were labeled A, B, C, and D. The subjects were then requested to click on a card on any of the four decks using a mouse. Each choice resulted in winning or losing money. The decks A and B were disadvantageous. They gave high rewards, but also high losses, and resulted in a net loss in the long run. The two other decks, C and D were advantageous. They gave low rewards, but also low losses, resulting in a net gain in the long run. The computer tracked the sequence of the cards selected from the various decks. Every time the subject clicked on a deck "to pick a card," the computer generated a distinct sound. A message on the screen displayed the amount of money the subject won or lost. Unbeknown to the subject, each deck consisted of 60 cards, and the task ended after 100 trials. The goal of the gamble was to make as much profit as possible. Standard test instructions were used (Bechara et al. 1999). Subjects were instructed to win as much money as possible, and they were told that some decks were worse than others, and that in order to do well they needed to stay away from those decks.

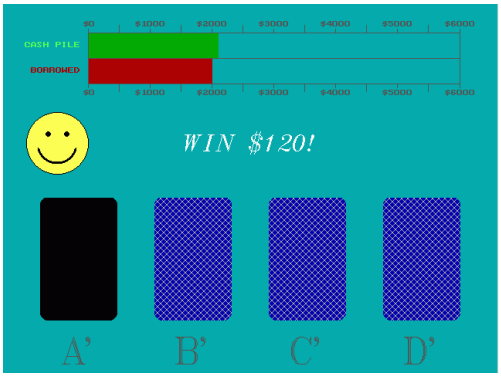

Figure 4: Screen shot of the Iowa Gambling Task (Adapted from Anestis, 2010)

11.1.3. Results

11. 1.3.1. Selection of the risky cards in blocks of 20 trials

The means and standard deviations of the selection of risky decks in blocks of 20 trials are illustrated in table 1.

Table 1: *Means and standard deviations (SD) expressed as percentages of risky deck choices in blocks of 20 trials for the MDMA group and healthy controls*

Blocks	MDMA (percent)	SD (percent)	Healthy controls (percent)	SD (percent)
(1-20)	67,35	13,95	65,25	13,55
(21-40)	51,05	19,95	43,95	20
(41-60)	45,5	21,85	47,1	17,5
(61-80)	44,75	24,95	36,6	18,9
(81-100)	42,6	28,65	35,5	22,8

The two – way repeated measures ANOVA found no significant difference between the MDMA group and the healthy control group (F=1,048, p= 0,313), but there was a significant main effect for blocks (F= 35, 185, p=0,001). The analysis did not find any significant interaction between blocks and groups (F=0,286, p=0,596). The selection of risky cards in blocks of 20 trials for the MDMA group and healthy controls are displayed in figure 5.

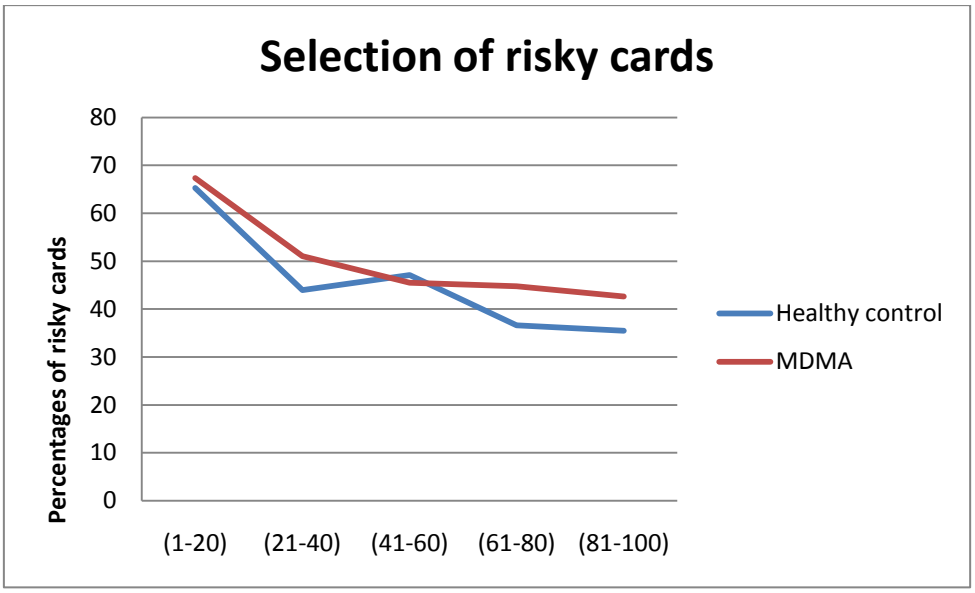

Figure 5: Risky card selection in blocks of 20 trials expressed in percentages for the MDMA group and the healthy controls.

11. 1.3.2. Selection of the risky cards in the last 60 trials

The means and standard deviations of the selection of risky decks in the last 60 trials are presented in table 2. The one- way ANOVA revealed no significant difference between the MDMA group and healthy controls (F= 0,638, p=0,430).

11. 1.3.3. Total selection of the risky cards

The means and standard deviations of the total selection of risky decks are presented in table 2. The one- way ANOVA found no significant difference between the MDMA group and healthy controls (F= 1,048, p=0,313).

Table 2: *Means and standard deviations of the risky card selection in the last 60 trials and the total risky card selection for the MDMA group and healthy control group*

Condition	MDMA	SD	Healthy control	SD
Last 60 (percentages)	44	25,1	39,7	19,7
Total AB (1-100) (percentages)	50,26	15,39	45,68	11,96

11. 1.4 Discussion

This study sought to examine the effect of MDMA on decision making. More specifically, it wanted to examine whether MDMA users would have impaired decision making on the IGT compared to healthy controls. The results showed that there were no overall significant difference between the two groups (F=1,048, p= 0,313). Furthermore, no significant difference were found in the last 60 trials selection of risky decks (F= 0,638, p=0,430) and no significant difference were found in the total selection of risky decks (F= 1,048, p=0,313). However, there was a significant main effect in the blocks of 20 trials condition (F= 35, 185, p=0,001). When comparing the means in percentages for the first block of the two groups (MDMA 67,35±13,95 and healthy control 65, 25±13,33) with the last block (MDMA 42,60±28,65 and healthy controls 35,5 ± 22,80) the selection of risky cards decreased. Although, not included in this specific study, a comparison between the MDMA group and a larger sample of healthy control has also been analyzed. However, no significant differences were found. This indicates that both the MDMA group and the healthy controls showed improvement over the course of the task. Based on these results, the hypothesis that the MDMA users would have impaired decision making compared to the healthy controls was not confirmed.

The findings of this study is in line with Fox et al. (2002), and Lamer et al. (2006), suggesting that MDMA does not impair decision making. Thus, it could be that MDMA may not have an effect on decision making. However, several studies have found decision making impairment in MDMA users (Morgan et al., 2006; Butler & Montgomery, 2004; Quednow et al., 2007). This discrepancy may be due to a publication bias, suggesting that there is an over representation in the literature showing the adverse effects of MDMA. Hence, it is possible that the failure to find evidence of MDMA's detrimental effects may be under-reported due to the reluctance of scientific journals to publish nonsignificant results (Dafters et al., 2004). Researchers consistently suggest that cognitive and impulse control deficits found in ecstasy users may be caused by neurotoxic effects of MDMA on 5-HT neurons (Hoshi et al., 2007). This may still be true, however, the disruption of cognitive and inhibitory mechanisms may first occur at a later stage in the neurodegenerative process (Fox et al. 2002). Consequently, even though MDMA has been found to deplete 5- HT and increase impulsivity (Clark et al., 2009) leading to disadvantageous decision making (Morgan et al., 2006) it could be that the drug use of the

MDMA users were not sufficiently high to produce these effects. MDMA induced impulsivity which may lead to impaired decision making may only become apparent after high cumulative doses (De Win et al., 2006). This is consistent with the toxicology perspective, stating that a drug will produce toxic effects only after a certain dose of the drug (Quednow et al., 2007). It is therefore possible that the MDMA use was not sufficiently high or frequent to produce adverse decision making effects. It could also be that some of the MDMA users had been abstinent for a while, which may also have reduced the impact of MDMA to the sertonergic system.

Although this study did not find any impairments of MDMA on decision making, further studies examining the effect of MDMA on decision making should be conducted. It would be interesting to see whether the inclusion of a bigger sample size of MDMA users might reveal decision making impairments. Furthermore, in order to elaborate on the understanding of MDMA and decision making, it would be useful to map the exact drug use of the MDMA users. Given that the neurotoxic effect of MDMA on the serotonergic system may be dose dependent, it would be valuable to examine whether different doses or frequencies of MDMA use might affect decision making.

11. 2 The effect of SSRI on decision making in healthy first-degree relatives of persons with depression

11. 2.1. Introduction

Depression has been associated with a range of cognitive deficits, such as deficits in attention, working memory, verbal fluency, inhibition of prepotent responses, cognitive flexibility, visual recognition, memory recall of verbal material, planning (Savitz, Solms & Ramesar, 2005). Furthermore, depressed individual have also been found to have deficits in decision making (Murphy, Rubinsztein, Michael, Rogers, Robbins, Paykel & Sahakian, 2001). Must, Szabó, Bódi, Szász, Janka, & Kéri (2006) reported that patients with major depression were impaired on the IGT, and suggested that depressed individuals have an altered sensitivity to reward and punishment. It is unclear whether cognitive deficits develop in depression, or if they are present in the premorbid state and possibly influenced by a genetic marker (Chowdhury, Ferrier & Thompson). Interestingly, it has been found that depression tends to run in families, suggesting that depression might be linked to a genetic or biological marker (Cannon & Keller, 2006). It has been argued that close relatives of depressed individuals also experience some of the same cognitive deficits as depressed people do. Christensen, Kyvik & Kessing (2006) found that healthy twins of depressed persons showed significant impairment on selective and sustained attention, executive function, language processing and working and declarative memory. Furthermore, it was also reported in a study by Clark, Sarna & Goodwin (2005) that first degree relative of patients with bipolar disorder and euthymics patients with unipolar disorder showed impairments of executive functions.

The search for biological markers associated with specific genes amounts to the study of endophenotypes. Endophenotypes link lower level biological processes to observable syndromes of a disorder, thus providing insight into which mechanism may be dysfunctional for a given disorder (Cannon & Keller, 2006). Although there may be various genetic markers related to depression, it has been suggested that one of the genetic markers might be related to the serotonin system (Ely, Sudgen, Corsico, Gregory, Sham, McGuffin, Plomin & Craig, 2004), where the s allele of the 5HTTLPR gene has been associated with a "low mood endophenotype" (Gonda, Juhasz, Laszik, Rihmer & Bagdy, 2005). Interestingly, the individuals carrying the s allele have found to show poorer

response to the antidepressant effects of the selective serotonin reuptake inhibitors (Serretti, Mandelli, Lorenzi, Pirovano, Olgiati, Colombo & Smeraldi, 2007)

SSRIs are used in the treatment of depression and a range of anxiety disorders (Murphy, 2010). Although it has shown to be effective, it is still unknown how they work to normalize abnormal cognitive and emotional processes (Arce, Simmons, Lovero, Stein & Paulus(2008). One of the actions of SSRI is to bind to the 5- HTT and block the reuptake of the secreted serotonin into the presynaptic neuron. This increases the synaptic availability of 5- HT and prolongs its action on postsynaptic receptors. Consequently, this leads to an increase in serotonergic function within the central nervous system (Owen, Knight & Nemeroff, 2010). Although acute effects of SSRIs have been found to be pharmacologically active, their clinical antidepressant therapeutic effects are thought to have a delay of several weeks. The therapeutic efficacy of SSRI's has been suggested to result from adaptive neurobiological changes in the 5- HT system, such as the desensitization of serotonin 1A receptors and increases in the expression of neurotrophic factors (Murphy, 2010). Increase in 5- HT has been found increase cooperation and reduced ratings of negative effect in healthy subjects (Knutson, Wolkowitz, Cole, Chan, Moore,Johnson,Terpstra,Turner & Reus (1998) and to increase assertive behaviors Moskowitz, Pinard, Zuroff, Annable & Young, 2001).

The serotonin receptors are widely expressed within the amygdala (Kent, Coplan & Gorman, 1998), and it has been suggested that the amygdala may be the most important site for antidepressant action. Imaging studies have found a reduction in glucose metabolism and functional activation of the amygdale has been found following SSRI treatment in depressed patients (Murphy, 2010). Sheline, Barch, Donnelly, Ollinger, Snyder & Mintun (2001) reported that the amygdala response to fearful faces was reduced after eight weeks treatment with SSRI. In addition, there is increasing evidence suggesting that SSRIs may have more distributed effects across the corticolimbic neural circuitry involved in emotional processing (Murphy, 2010). In a PET study by Mayberg, Brannan, Tekell, Silva , Mahurin, McGinnis & Jerabek (2000) investigating the effect of SSRI on unipolar depressed patients after six weeks of treatment, it was found that brain glucose was reduced in the limbic areas and increased in the cortical areas. Furthermore, a study by Chen, Suckling, Ooi, Fu, Williams,Walsh, Mitterschiffthaler, Pich & Bullmore (2008)

reported that individuals treated in eight weeks with SSRI had a increased degree of coupling between the amygdale, the prefrontal and the anterior cingulate cotex. This raises the interesting possibility that antidepressants may exert their effects by redressing the hyper-responsivity of the amygdala and the relatively reduced prefrontal control that has been implicated in the pathophysiology of depression and anxiety (Murphy, 2010).

The effect of SSRIs has also been studied in healthy volunteers. The acute effect of SSRI has been found to increase recognition of fearful faces (Browning, Reid, Cowen, Goodwin & Harmer, 2007; Harmer, Bhagwagar, Perrett, Vollm, Cowen & Goodwin, 2003), whereas the long term effects have been found to reduce sensitivity to negatively valenced information (Harmer, Shelley, Cowen & Goodwin, 2004). In a fMRI study by Arce, Simmons, Lovero, Stein & Paulus (2007) it was found that a sub chronic escitalopram treatment attenuated BOLD activity in the bilateral insula and the amygdale during emotional processing in healthy subjects. Interestingly, McCabe, Mishor, Cowen & Harmer (2010) investigated the effect of SSRI on healthy volunteers, and found that SSRIs can diminish the neural processing of both rewarding and aversive stimuli. Considering that SSRI increase the serotonergic function within the central nervous system (Owen, et al.,2010), it is interesting to see how increased 5-HT may influence decision making. A study by Murphy, Longhitano, Ayres, Cowen, Harmers & Rogers (2009) investigated the role of increased serotonergic activity in decision-making under conditions of uncertainty in healthy individuals. The results showed that two week tryptophan treatment altered the way subjects combined information about possible gains and losses when making risky choices. The increased 5- HT activity reduced loss aversion, thus increasing gambling behavior in options with low or moderate negative expected value.

The goal of this study is to investigate whether the effects of SSRI will have any effect on decision making in individuals who are first degree relative of patients with depression. Considering that close relatives to depressive individuals have found to have many of the cognitive impairments as depressed individuals, it would be interesting to see whether the effect of SSRI would have any effect on decision making in these specific individuals. Consequently, if there is an effect, will it improve, impair, or leave decision making

unaltered? Based on the observed cognitive differences in close relatives of depressed persons, this study hypothesize that there will be a difference in decision making.

11. 2.2 Method

The rationale and design of the study has been described in detail in Knorr et al. (2009), thus the method description is adopted from this article.

11. 2.2.1. Subjects

80 subjects participated in the study (51 males and 29 females) in the age range 18-59 years (mean age = 31,5±10,3 (SD) years). Participants were recruited as healthy first-degree relatives of patients with a diagnosis of depression given at discharge from psychiatric hospital in- or out-patient contact. The participants were offspring or sibling of an ethnic Dane, with a history of psychiatric in- or outpatient care with the diagnosis of depression and who later had the diagnosis verified in a SCAN interview at the Department of Psychiatry Rigshospitalet, Denmark 2004–2009. In order to decrease confounding factors, subjects who met any of the exclusion criteria were not enrolled in the study.

Exclusion criteria

- Somatical illness or other handicap, which make participation in the trial impossible.
- Daily intake of drugs interfering with corticosteroids or escitalopram, including birth
  control pills or any kind of corticosteorids
- Hypersensitivity to escitalopram, dexamethasone,or human corticotrophin-releasing hormone
- Former medical or psychological treatment for diseases in the affective or schizophrenic spectrum.
- Abuse of alcohol or psychotropic medication.
- For women: pregnancy or breastfeeding.

11. 2.2.2. Interventions

The participants were randomized to receive either a single dose of escitalopram (10 mg) or placebo by oral administration each evening as self-medication at home for four weeks. On completion of four weeks of double-blind intervention, participants entered a five-day blinded down-titration period to nil medication. Escitalopram 10 mg was selected due to its specific serotonergic selectivity. Escitalopram and placebo tablets were identical in appearance, colour, smell, and solubility allowing for blinding of treatment assignment. H. Lundbeck A/S provided identically appearing blister packages containing escitalopram or placebo. An independent pharmacist then packed, sealed and numbered the drug packages according to a randomization list provided and concealed by the Copenhagen Trial Unit (CTU), Centre for Clinical Intervention Research, Rigshospitalet

11. 2.2.3. Study design

The study was conducted as randomized double blind placebo controlled trial. Subjects were randomized into one of the two intervention groups immediately after the subject had been screened for the exclusion criteria and was accepted to participate in the study. Randomization was stratified by age (18 – 31 years and 32 – 60 years) and sex in order to get an equal distribution in the intervention groups. Participants were randomized in a 1-to-1 ratio to receive escitalopram 10 mg or placebo. The sponsor-investigator (UK) provided information of the participants to the Copenhagen Trial Unit (CTU) Centre for Clinical Intervention Research, Rigshospitalet during the entry assessment as soon as participation in the study had been decided. The CTU performed the centralized randomization, and only the IT Manager of the CTU was informed about the block size used for stratification.

11. 2.2.4. Procedure

Decision making were tested using the computerized version of the Iowa Gambling task, (IGT). The participants were also tested in a range of other cognitive and social cognition tests. The tests were administered by the same psychologist student both at the pre and post test. The procedure was identical to the one used in the Cimbi study.

11.2.3. Results

11. 2.3.1.Selection of the risky cards in blocks of 20 trials in the pre- and post intervention condition

The means and standard deviations of the pre intervention condition for the selection of risky decks in blocks of 20 trials are presented in table 3. The means and standard deviations for the post intervention condition are presented in table 4.

Table 3: *Means and standard deviations expressed as percentages of the risky decks in blocks of 20 trials for the escitalopram group and the placebo group in the pre intervention condition.*

Blocks	Escitalopram group	SD	Placebo group	SD
(1-20)	56,45	14,15	58,6	9,55
(21-40)	48	18,7	50,6	15,5
(41-60)	39,15	22	45,25	21,75
(61-80)	39,75	23,05	42,3	23,55
(81-100)	40,95	23,65	37,65	22,35

Table 4: *Means and standard deviations expressed as percentages of the risky decks in blocks of 20 trials for the escitalopram group and the placebo group in the post intervention condition.*

Blocks	Escitalopram group	SD	Placebo group	SD
(1-20)	41,95	24,65	49,1	20,5
(21-40)	33,9	25,8	39,6	18,9
(41-60)	31,05	28,85	32,65	22,35
(61-80)	25,1	27,35	30,9	22,5
(81-100)	30,45	28,5	33,55	25,45

The two-way repeated measures ANOVA found no overall significant difference between the escitalopram group and the placebo group (F= 1,209, p= 0,275). There was a significant main effect for the pre-post conditions (F= 20, 362, p=0,0001), but no interaction between the two groups and pre-post condition (F= 0,293, p= 0,590). The analysis showed a significant main effect for blocks of 20 trials (F= 26,540, p= 0,0001), but there was no interaction between the blocks and groups (F= 0,502, p= 0,734). Further, there was no significant interaction between pre-post conditions and blocks (F=1, 026, p=

0,394). There was also no significant three- way interaction between pre-post condition, blocks and groups (F= 0,841, p= 0,500).

11. 2.3.2. Selection of the risky cards for the last 60 trial condition

The means and standard deviations of the selection of risky decks for the last 60 trials are presented in table 5. The mixed design repeated measure two- way ANOVA did not find any significant difference between the escitalopram group and the placebo group (F=0,015, p=0,901). The analysis revealed a significant main effect for pre-post condition (F=11,593, p=0,001), but there was no interaction between the last 60 trials and the two groups (F=0,167, p=0,684).

11. 2.3.3. The total selection of risky cards condition

The means and standard deviations of the total selection of risky decks are presented in table 5. The analysis showed no significant difference between escitalopram group and the placebo group (F=1, 040, p=0,311). The analysis revealed a significant main effect for pre-post condition (F=20, 17, p=0,001), but there was no interaction between the total AB (1-100) trials and the two groups (F=0,265, p=0,608).

Table 5: *Means and standard deviations in percentages of the last 60 trials and total risky deck selection for the escitalopram and placebo group*

Condition	Escitalopram group	SD	Placebo group	SD
Last 60 trials (percent)	37,2	21,6	36,7	7,8
Total risky decks (1-100) (percent)	38,7	18,7	41,8	4,3

11. 2.3.4.Test- retest correlations for the selection of risky cards

The test re- retest correlation coefficients for the escitalopram group between the pre and the post test are presented in table 6. Whereas the test re- retest correlation coefficients for the placebo group between the pre and the post test are presented in table 7.

The analysis found a significant test retest correlation between the pre and the post test for the last 60 trials condition (p<0,05). There test- retest correlations for the other conditions

were not significant. In the placebo group all the blocks from (41-60), (61-80) were highly significant (p<0,01), whereas also the block (81-100) was significant (p<0,05). The test-rest correlations were also highly significant in the last 60 trials condition and in the total selection of risky cards (p<0,01).

Table 6: *Test- retest correlation coefficients between pre and post test for risky card selection for the escitalopram group*

Escitalopram group	AB (1-20)	AB (21-40)	AB (41-60)	AB (61-80)	AB (81-100)	AB (last 60)	AB (total)
AB (1-20)	-0,039	-0,319*	-0,385*	-0,517**	-0,352*	-0,463**	-0,394*
AB (21-40)	-0,055	0,089	0,241	0,091	0,098	0,124	0,116
AB (41-60)	-0,093	0,143	0,230	0,074	0,105	0,212	0,156
AB (61-80)	-0,038	0,090	0,318*	0,122	0,175	0,290	0,167
AB(81-100)	0,058	0,038	0,197	-0,022	-0,023	0,091	0,060
AB(last 60)	0,128	0,238	0,399**	0,227	0,242	0,403*	0,300
AB (total)	0,013	0,044	0,217	-0,023	0,036	0,119	0,07

Note: *p<0,05, **p<0,00

Table 7: *Test- retest correlation coefficients between pre and post test for risky card selection for the placebo group*

Placebo group	AB (1-20)	AB (21-40)	AB (41-60)	AB (61-80)	AB (81-100)	AB (last 60)	AB (total)
AB (1-20)	-0,006	-0,057	-0,068	0,003	-0,218	-0, 103	-0,101
AB (21-40)	-0,038	-0,028	0,406*	0,559**	0,361*	0,489**	0, 363*
AB (41-60)	-0,084	0,206	0,524**	0,682**	0,456**	0, 602**	0,501**
AB (61-80)	-0,100	0,107	0,366*	0,597**	0,295	0, 452**	0,357*
AB(81-100)	-0,055	0,158	0,458**	0,537**	0,374*	0,492**	0,414**
AB(last 60)	-0,089	0,176	0,474**	0,655**	0,399*	0,550**	0.454**
AB (total)	-0,083	0,131	0,492**	0,680**	0,394*	0,566*	0,455**

Note: *p<0,05, **p<0,001

11. 2.4. Discussion

The goal of this study was to investigate whether the effect of SSRI would have any effect on decision making in individuals who are first degree relative of patients with depression. The test- retest correlations for escitalopram group comparing the pre and post test were only significant in the last 60 trials condition ($p<0,05$), whereas the test retest correlations for the placebo group was significant in almost all conditions. This indicates that the performance on the IGT was approximately the same pre and post intervention for the placebo group, while the test-retest correlations for the escitalopram group diverged. Although test-retest differences was found, the two-way repeated measures ANOVA found no overall significant difference between the escitalopram group and the placebo group ($F= 1,209$, $p= 0,275$). There was a significant main effect for the pre-post conditions for the groups ($F= 20, 362$, $p=0,0001$), suggesting a significant better performance in the post condition for both groups. Furthermore, there were no significant difference between the two groups in the pre-post condition ($F= 0,293$, $p= 0,590$). When examining the results in more detail, the analysis did not find a significant difference between the two groups in the blocks of 20 trials ($F= 0,502$, $p= 0,734$), and there were no further significant 3-way interaction between the pre-post condition, blocks of 20 trials and groups ($F= 0,841$, $p= 0,500$). However, a main effect was found in the blocks of 20 trials condition ($F=26,54$, $P= 0,0001$) suggesting that both groups performed better as the task proceeded. The ANOVA did not reveal any significant difference between the two groups in the last 60 trials condition ($F= 0,015$, $p= 0,901$). Similarly, the analysis did not find any significant differences between the two groups in the total selection of risky cards ($F=1, 040$, $p=0,311$). Based on the results of this study, the hypothesis that there would be a difference in decision making between the SSRI group and the placebo group was not confirmed.

The effect of SSRI on decision making in healthy first degree relatives of depressed persons has, as far as I know, not been tested before. Based on the finding of this study, it appears that SSRI does not influence decision making in first degree healthy individuals. Both the escitalopram and the placebo group performed equally well on the IGT. Although previous studies of healthy individuals have found that increased levels of 5-HT diminish the neural processing of rewarding and aversive stimuli (McCabe et al., 2010), and alters the way subjects combine value based information leading to riskier choices (Murphy et

al., 2009), the subjects in the present study represent a specific group. Although they were healthy, they were first degree relatives to persons with depression. It is therefore likely that they may share some of the same genetic markers as depressed individuals (Cannon & Keller, 2006). It has been found that people with the s allele of the 5- HTTLPR, a possible genetic marker for depression, show poorer response to SSRI (Serretti et al., 2007). Perhaps, other genetic markers of depression also influence the response to SSRIs. Although speculative, it could be that these participants, assumed to have heritable makers for depression, showed a poor response to escitaloptam. Further studies are therefore necessary to examining the response and effect of SSRIs on healthy first degree relatives to depressed persons, and identifying how various genetic markers of depression may respond to SSRIs.

12.General conclusion

The main scoop of this thesis was to investigate the cognitive, emotional and neurobiological basis for decision making, and to examine how impulsivity may lead to inferior choices. Cognition and emotion both play important roles in guiding decision making. However, emotion and cognition do not operate in isolation, but work in concert to guide decision making (Loewenstein et al., 2001). Although the cognitive and emotional system works together, they may be engaged to a different degree depending on the situation. In some situations, people cognitively and systematically contemplate various options before making a decision, whereas at other times, people follow their emotions when deciding. Both strategies may yield equally good results, but then again, both strategies may also lead to less optimal outcomes due to the various biases affecting emotion and cognition. In many cases, our decisions are based on rational and analytical deliberations where intentions, attitudes and subjective norms are scrutinized. However, even the most rational and analytical deliberations may be prone to biases and undergo systematic changes and cognitive distortions. Emotions also have a great impact on the decisions we make. Emotions may both facilitate decision making but also interfere with decision making. Both anticipated and current emotions may color and shape people's decisions. Current negative emotions may interfere with decision making. When experiencing current negative emotions, people generally wish to feel better, and may engage in rash and impulsive actions in order to repair or distract them from their current negative emotions. Consequently, negative emotions may lead people to make shortsighted and irrational decisions, and abandon their long term priorities for immediate gratification (Tice et al., 2001).

The crucial role emotions plays in decision making has also been acknowledged by Damasio (1994), who, based on his work with ventromedial prefrontal cortex (VMPFC) lesion patients, developed the somatic marker hypothesis. VMPFC plays an important role in adapting emotional associations between objects and bodily feedback, and is believed to moderate emotions and emotional reactions. Thus, lesion in this area is known to produce severe decision making impairments. The somatic marker hypothesis therefore emphasizes the important role emotions have in guiding decision making in complex and uncertain situations. Bechara et al. (1994), developed the IGT as an measurement of the impaired

decision making demonstrated by VMPFC patients. Interestingly, other individuals have also been found to show impaired performance on the IGT and decision making. Individuals with other neurological lesions such as lesions in the amygdala, a structure known to be involved in the decision making circuit, have found to been impaired decision making. Considering the many processes involved in decision making, it is not surprising that other neurological structures are involved as well. Structures such as the dorsolateral prefrontal cortex, the anterior cingulated cortex and the nucleus accumbens have all been implicated in the decision making process.

The IGT has also been expanded to measure decision making deficits in other groups. Interestingly, impaired decision making has been found in normal individuals as well. Inferior decision making has frequently been displayed in sensation seeking and impulsive individuals, who reflect an increased need to search for risky experiments and display an inability to delay reward. Disorders believed to be related to impulsivity, such as substance abuse and pathological gambling, have also found to be associated with disadvantageous decision making. Biological underpinnings for impulsive behaviors may relate from abnormalities in the serotonergic and dopaminergic system, where especially low levels of 5- HT have been believed to impair decision making.

Considering that the serotonergic system has been implicated in decision making, it was interesting to investigate in two empirical studies whether the manipulation of the serotonergic system affected decision making performance in the IGT. Although, neither of the studies found significant effects of the serotonergic manipulation, it is important to keep in mind that decision making is complex. There will always be several interacting factors when making a decision. Even though biology plays a great role in decision making, other factors such as environment and life experiences are also important. It is therefore crucial to take into account the interplay between biological and environmental factors when considering the basis for decision making.

13.References

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