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Functional and neural mechanisms of intertemporal choice

Presentata da: ***Dott.ssa Manuela Sellitto***

Coordinatore Dottorato
Prof.ssa Elisabetta Làdavas

Relatori
Prof. Giuseppe di Pellegrino
Prof. Paul E. Downing

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Abstract

People are daily faced with intertemporal choice, i.e., choices differing in the timing of their consequences, frequently preferring smaller-sooner rewards over larger-delayed ones, reflecting temporal discounting of the value of future outcomes. This dissertation addresses two main goals. New evidence about the neural bases of intertemporal choice is provided. Following the disruption of either the medial orbitofrontal cortex or the insula, the willingness to wait for larger-delayed outcomes is affected in odd directions, suggesting the causal involvement of these areas in regulating the value computation of rewards available with different timings. These findings were also supported by a reported imaging study. Moreover, this dissertation provides new evidence about how temporal discounting can be modulated at a behavioral level through different manipulations, e.g., allowing individuals to think about the distant time, pairing rewards with aversive events, or changing their perceived spatial position. A relationship between intertemporal choice, moral judgements and aging is also discussed. All these findings link together to support a unitary neural model of temporal discounting according to which signals coming from several cortical (i.e., medial orbitofrontal cortex, insula) and subcortical regions (i.e., amygdala, ventral striatum) are integrated to represent the subjective value of both earlier and later rewards, under the top-down regulation of dorsolateral prefrontal cortex. The present findings also support the idea that the process of outcome evaluation is strictly related to the ability to pre-experience and envision future events through self-projection, the anticipation of visceral feelings associated with receiving rewards, and the psychological distance from rewards. Furthermore, taking into account the emotions and the state of arousal at the time of decision seems necessary to understand impulsivity associated with preferring smaller-sooner goods in place of larger-later goods.

To Cecilia and Matteo

"Hard work pays off in the future; laziness pays off now!"

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Introduction

Every day of their life people make decisions. From the moment they wake up until they go to sleep again, people make choices that give a direction to the course of their day, also affecting the general course of their life. On the one hand, some choices will apparently have an impact only on the short-term (e.g., ‘Do I clean my bedroom or do I order the books in the bookcase in the lounge, today?’). On the other hand, other choices will affect what people will become or do in the future (e.g., ‘Do I study for my upcoming exam or do I go out with friends, today?’). Even though we have evolved from prehistoric mankind, making optimal choices is still necessary for people to survive. Of course, this will depend on how good or bad one defines an outcome; what are one’s emotions about it; what were one’s previous experience with it; how much effort it requires to be obtained; what one forecasts about it, and so on. When people have to make a decision between two outcomes achievable at different points in time (e.g., going out with friends today means spending fun time in a few hours, whereas studying today for the exam means gaining a much more important reward, a good score, in a few days, but with a present effort), they are making an *intertemporal choice*. Basically, the more people tend to prefer the sooner smaller reward over a larger delayed one, the more they are considered impulsive, assigning a smaller value to the future outcome (i.e., *temporal discounting*).

This type of decision-making has been widely studied both in behavioral economics and, more recently, in *neuroeconomics*. As compared to the former, by combining paradigms and concepts derived from neuroscience, psychology, genetics, and economics, neuroeconomics investigates how the brain represents, computes, stores, and acts upon value (Monterosso et al., 2012): Instead of inferring value from the behavioral choices (Bickel et al., 2007), it uses the neuronal value signal to predict those choices. Neuroeconomics has primarily challenged the standard economic assumption that decision making is a unitary process — a simple matter of integrated and coherent utility maximization — suggesting instead that it is driven by the interaction of several mechanisms, including automatic and controlled processes, resulting in patient or imprudent behaviors (Loewenstein et al., 2008).

In Part I of this dissertation, current behavioral and neural knowledge about decision-making and intertemporal choice will be reviewed. The starting point will be neuroeconomics and recent imaging findings to highlight the role of neuroscience in understanding the way in which people encode decisions. Then, a general overview on value-based decision-making will be made to introduce the main topic of intertemporal choice, on which this dissertation will extensively further focus. Here, behavioral and neural findings about the phenomenon of temporal discounting will be outlined, as well as its relationship with levels of impulsivity (Sellitto et al., 2011).

Part II of this dissertation is dedicated to new neural evidence we provided about intertemporal choice. By the means of using a lesional approach, the first two studies will outline opposite altered intertemporal choice patterns deriving, on the one hand, from damage to the medial orbitofrontal cortex, and, on the other hand, from damage to the insular cortex. While the first group of patients showed an increase in impulsive choices along different commodities (Sellitto et al., 2010), the second group of patients showed decreased imprudent decisions when both an immediate option was available in the pair and when it was not (Sellitto et al., under submission). The third study will provide preliminary evidence about the neural substrate of the carry-over effect in intertemporal choice. That is, we started to investigate, in a fast and counterbalanced series of intertemporal decisions, the influence that a previous monetary intertemporal choice can have on the subsequent one at neural level. The idea was that stimuli perceived to be similar were represented by similar neural states, so that, during stimulus repetition, a reduced firing rate of cells can be observed (Henson and Rugg, 2003; Aguirre, 2007). The reduction in the magnitude of neurons response that can be seen toward stimuli sharing a particular property is considered the proof that the identified voxel contains a population of neurons that code that specific dimension (Aguirre, 2007; Grill-Spector and Malach, 2001). Also, both univariate and multivariate techniques have been used.

Part III of this dissertation will go through several behavioral manipulations of intertemporal choice we carried out to lessen impulsive preferences for smaller sooner rewards over larger later ones. In Study I we trained participants to mentally time travel before making decisions, in order to activate representations of the distant time. In Study II we showed correlations between the degree to which people tended to prefer sooner smaller options and the degree they tended to accept violations during moral judgments forgoing long-term gains (e.g., larger monetary amounts and no remorse for having broken a social norm). In Study III we changed the perceived spatial position of monetary outcomes to decrease impatient choices: Highlighting abstract features of the options at stake or increasing the salience of the larger later outcome affected participants mental representations about rewards. In Study IV we showed a way to influence intertemporal choices toward foods, suggesting the use our method as training for people suffering from obesity and binge eating disorders. In Study V we will provide evidence about discounting trajectories in intertemporal decision-making at different ages.

Both lesional studies, preliminary imaging evidence, and behavioral manipulations of individual intertemporal decisions provide support to a proposed unitary model in which different brain structures are supposed to work together, with special attention to the medial orbitofrontal cortex, to result in the subjective value one assigns to different outcomes available at different delays, driving her to pick her preferred option up when making an intertemporal judgement.

PART I – Intertemporal decision-making: Current knowledge

Précis

How can species, whether they be humans or other animals, survive? The ‘trick’ is to make advantageous choices that foster them to adapt to several conditions. It is also a consolidate matter of fact that now people cannot be seen as simple *Homo oeconomicus*, namely rational actors who ponder their choices to maximize their individual satisfaction. In fact, humans have reached a level of brain organization that allows them to live in a complex social and technological environment, even simulated ones, where they do not simply calculate their advantage rationally, but are more often than not influenced by their emotions, by the way in which they represent outcomes and gains, by their present inner state, and by the presence of other individuals. All these factors combine to generate the overall utility derived from a specific decision, with an impact on their immediate present and/or the near or far future.

Chapter I – Decision-making: A general overview

Neuroeconomics and the irrational decision-maker

The recent field of *neuroeconomics* (e.g., Glimcher and Rustichini, 2004; Glimcher et al., 2009) is trying to put together, since the late 1990s (Loewenstein et al., 2008), all we know about how human beings act upon the value they individually assign to rewards to choose (i.e., biological mechanisms of decision-making, Levallois et al., 2012), to construct a general neural model of 'behavior of markets' (Glimcher, 2011) that could be applied on a large scale. A common neural base for all individuals is a necessary presumption for all those attempts toward problem solving of all kinds, from goods availability and distribution, to wealth and health. This implies that neuroscientific techniques are nowadays able to overcome the pessimism associated with seeing the brain as a 'black box' (Jevons, 1871, Camerer et al., 2005).

Neuroeconomics research is focused principally in three domains of interest common to both economists and psychologists: decision-making under risk and uncertainty, social decision-making, and intertemporal choice (Loewenstein et al., 2008). While it was convenient for economists to think that decision-makers are rational, namely, they make choices to maximize the utility of rewards (i.e., its desirability) or actions allowing them to obtain that reward (expected utility model, EUD, Bernoulli, 1738), people have been demonstrated by 'psychological realism' (Loewenstein et al., 2008) to act irrationally, under the influence of several variables.

Decision-making under risk and uncertainty. Consider you are playing a lottery. You have to choose between a sure option of £ 5 and the 50% of chance of winning £ 10 or the 50% of chance of losing everything (gamble option). Both gamble options are equipollent in the expected value (i.e., the probability of receiving an amount multiplied by the amount itself, $EV = px$, where EV = expected value, p = probability, x = amount), however, people do not choose equally when faced with the first and the second type of offer (based on the different gamble option). Indeed, as demonstrated by Tversky and Kahneman ('prospect theory', 1981), under the 'framing effect', people are biased to think (i.e., the perspective) that there is a greater risk associated with the alternative implying a loss, rather than equal to the risk associated with the option where a win is hypothesised. The framing effect, indeed, accounts for how people tend to be description-sensitive, preferring gains and displaying loss aversion when faced with an uncertain outcome (Fig. 1; Tversky and Kahneman, 1981).

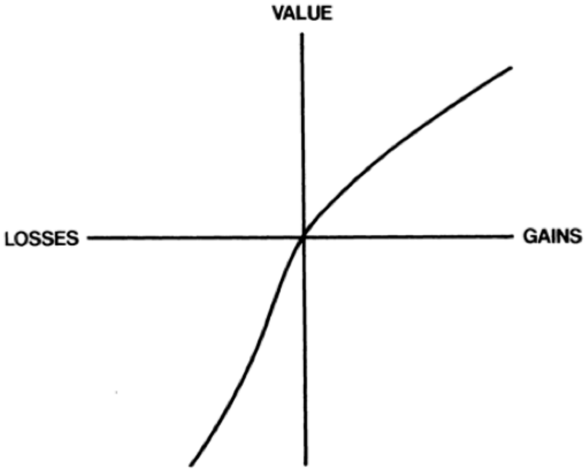

Figure 1. A typical value function, based on losses and gains (Adapted from Tversky and Kahneman, 1981).

Moreover, judgement under uncertainty is also modulated by other variables like the amount of money at stake (inducing people to accept the risk with different degrees), their insensitivity to prior probability of outcomes, the sample size, their need of 'narrow bracketing' (i.e., the evaluation of risky decisions separately, Tversky and Kahneman, 1974) and so on, suggesting a revision of the EUD. Thus here it is the turn of neuroscience. This new discipline is helping to understand how humans act differently, driven by emotions when faced with uncertain decisions. Several imaging studies (e.g., those using functional magnetic resonance imaging, fMRI), highlighted how the brain tends to encode gambles as gains or losses based on the deviations from expectations (Loewenstein et al., 2008). Areas like the medial prefrontal cortex (mPFC) or the Nucleus Accumbens (NAcc), both targets of dopaminergic projections, responded differently between anticipated and unanticipated reward delivery (e.g., Berns et al. 2001; Knutson et al., 2003; McClure et al. 2003). Furthermore, amygdala and NAcc responded accordingly to the anticipated emotion elicited by the prospect of a risky outcome (e.g., Knutson et al., 2001a; Kahn et al., 2002). More recently, De Martino and colleagues (2006) found that those subjects who acted more rationally exhibited greater activation in the medial and the orbitomedial portions of the prefrontal cortex (OMPFC) associated with the frame effect, supporting a model in which the OMPFC evaluates and integrates emotional and cognitive information, thus underpinning more rational (i.e., description-invariant) behavior (Fig. 2; De Martino et al., 2006; Loewenstein et al., 2008; for a complete review, see Platt and Huettel, 2008).

Social decision-making. As we saw for risky decisions and as we will later see for intertemporal choices, social decision-making, namely, the type of choices where we do not care only about our self-interests, but also about the welfare of others, cannot be explained by simple sum and the difference between our weighted payoffs and those of other people. In fact, not only in our daily life do we make a lot of decisions that are dependent on the concomitant choices of others (Sanfey 2007), affecting others and not only ourselves (Fehr and Camerer 2007), but also, once again, emotions come into play (e.g., Loewenstein et al., 1989; 2008).

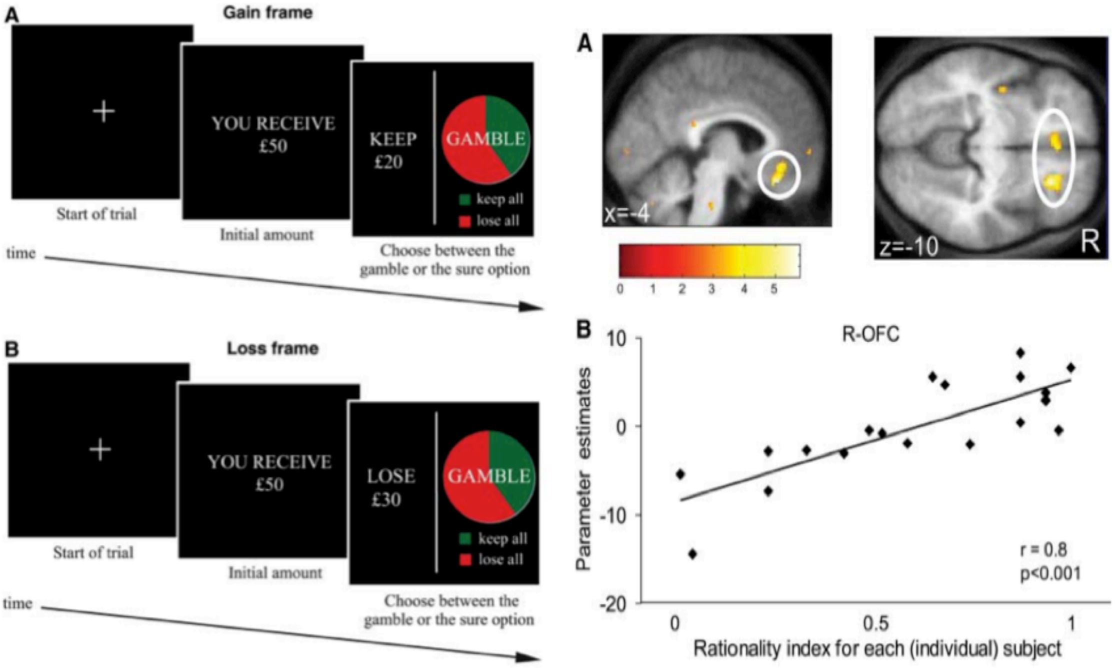

Figure 2. On the left, example of a gambling task with (A) the gain frame and (B) the loss frame. On the right, rationality across participants: fMRI correlational analysis. (A) OMPFC and vmPFC activations; (B) correlation between the susceptibility to the framing manipulation (rationality index) and the parameter estimates (Adapted from De Martino et al., 2006).

Social emotions often help us to reach more adaptive decisions than would be possible by reasoning alone (Damasio 1994, Frank 1988), for example feeling guilty can dissuade us from harming a friend, whereas sometimes we need to override emotions through cognitive control, e.g., when suppressing indignation over unfair treatment by a more powerful other (Rilling and Sanfey, 2011). What does happen when, interacting with other individuals, we make decisions that deviate from the predicted rationality? Why do subjects prefer to punish at their own cost peers who have previously treated them unfairly (e.g., Singer et al. 2006)? When making a moral judgment, namely when deciding if an act can be considered appropriate or not taking in consideration both that it can harm other people and that it can be due to the subject's intentionality or not (e.g., Greene et al., 2001), patients with a lesion in the ventromedial prefrontal cortex (vmPFC) have been found to be more likely to make utilitarian judgments (i.e., they were more willing to accept a moral violation) then control participants (Ciaramelli et al., 2007; Koenigs et al., 2007), failing to generate anticipatory skin conductance responses before endorsing personal moral violations (Moretto et al., 2010). Sanfey and colleagues (2003; Fig. 3) found that whether players rejected unfair offers from human proposers or from a computer could have been reliably predicted by the level of their anterior insula activity, the same as when watching a loved one receiving a painful stimulus (Singer et al. 2004). Furthermore, Knoch et al. (2006) provided evidence of the right dorsolateral prefrontal cortex (dlPFC)'s key role in overriding or weakening self-interested impulses, allowing people to implement their taste for fairness, by selectively disrupting either the right or the left portion of the dlPFC by the means of using repetitive transcranial magnetic stimulation (rTMS) (Loewenstein et al., 2008; for a complete review, see Rilling and Sanfey, 2011).

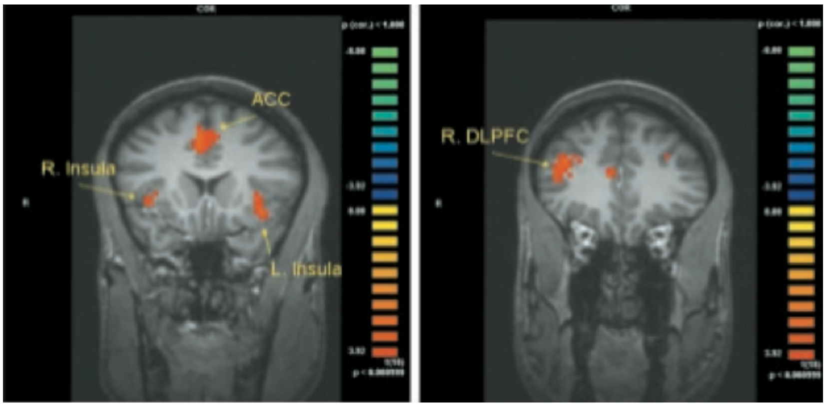

Figure 3. Activations in the PCC, insula, and dlPFC when receiving unfair offers from other humans (Adapted from Sanfey et al., 2003).

The above evidence, together with evidence of intertemporal choice (outlined later), comes a long way to support the view that it is currently pointless to study how people behave toward outcomes regardless of the brain. Indeed, we know that neurochemical factors drive our preferences and then our decisions. Functional studies, brain stimulation techniques, real and virtual lesional evidence are the way to follow for a complete understanding of how we adapt to the environment by making decisions, sometimes apparently against our evident interests, which is continuously outlined by behavioral experiments. The integration of these disparate theoretical approaches and methodologies in a unified perspective offers exciting potential for the construction of more accurate models of decision-making (Sanfey et al., 2006).

Reward and value-based decision-making

What we have assumed here is that, in order to adapt, people (and other animals) have to make good choices. What we are referring to specifically is the way in which we all direct our behaviors towards a reward (i.e., 'economic choice'; Padoa-Schioppa, 2011).

In 1927, Pavlov defined the reward as an object that produces an observable change in behavior, serving as a positive reinforcer by increasing the frequency of that behavior resulting in that outcome, also called learning (Schultz, 2006). On the one hand, there are rewards that elicit approach and consumption due to their appetitive value, being under the control of innate mechanisms (e.g., primary rewards) or of classical or instrumental conditioning (e.g., Wise, 2002). For instance, if one is thirsty and she sees a bottle of water, this object will suddenly reach a high value since it is able to reduce her state of need. On the other hand, rewards can also have a negative valence, functioning as punishments, inducing withdrawal behavior, thereby increasing the frequency of behaviors that can decrease the aversive outcome frequency (Schultz, 2006).

In the model proposed by Rangel and colleagues (2008), value-based decision-making, namely the kind of choice that occurs whenever an animal decides between several alternatives, can be synthesized in five basic steps. The first process (1) is the representation of the decision problem, that is, the comparison of internal and external states, and the identification of potential courses of action. Second (2), one will compute the value of each action, and, based on this, (3) she will select the optimal action. Finally, (4) the evaluation of the outcome will define how desirable is the chosen outcome, depending on the resulting states, and then (5) she will update the initial representation of states and actions based on satisfied or not conditions and expectations (i.e., learning).

The starting point for value-based decision-making, whatever the domain in which the choice is applied, is the subjective value.

Neural bases of subjective value. The subjective value (i.e., desirability) of a reward is computed in the brain in order for choices to be guided by preferences (Grabenhorst and Rolls, 2009). What we have to calculate is the expected value of a reward, namely the weighted probabilistic average of all possible values for an uncertain reward (Schultz et al., 1997). To express preferences, people have to consider different dimensions of options at stake (i.e., magnitude and delay) that, even though different and incommensurable, are valued and compared on a common scale (Chib et al., 2009; Padoa-Schioppa, 2011). Although many cells in the brain respond to reward, the cortical-basal ganglia circuit [i.e., principally the orbital part of the prefrontal cortex (i.e., orbitofrontal cortex, OFC), the anterior cingulate cortex (ACC), NAcc, the ventral striatum (VS), the ventral tegmental area, substantia nigra)] is the core of the reward system. Recent studies demonstrated that human frontal functional and structural imaging evidence map close to nonhuman primate anatomy (Schultz, 2006; Luhmann, 2009; Montague and Berns, 2002; Haber and Knutson, 2010). Specifically, in both humans and sanimals, neurons in OFC seem to be pivotally designated to encode the subjective value assigned to different reward stimuli, more active when the situation does require a choice, and is not attached to specific goods, actions or spatial locations (for review, see O'Doherty, 2004; Padoa-Schioppa and Cai, 2011; Cai and Padoa-Schioppa, 2012). In humans, the OFC (Schoenbaum et al., 1998, 1999, 2006; Rangel et al., 2008) and its relative medial portion (i.e., medial orbitofrontal cortex, mOFC) [paralimbic Brodmann's areas (BAs) 25, 13, and medial portion of BA 11, 12 and 10 (Brodmann, 1909; Kringelbach and Rolls, 2004; Bechara, 2005)], together with striatal and midbrain areas, such as the entire VS (including the NAcc), the medial amygdala, and the substantia nigra (Fig. 4; Haber and Knutson, 2010) were activated during the anticipation of expected rewards (e.g., Mainen and Kepecs, 2009), coding the incentive value of both real and abstract rewards (Damasio, 1994; Rolls et al., 1999; Elliott et al., 2000b; O'Doherty et al., 2001; O'Doherty, 2004; Kringelbach, 2005; Schoenbaum et al., 2006), monitoring the value of different reinforcers (Kringelbach and Rolls, 2004), and responding to changes in outcome predictions (e.g., Gottfried et al., 2003; O'Doherty et al., 2002). Moreover, while neurons in the caudate nucleus (dorsal striatum) encode the difference in the temporally discounted value of two alternative rewards more reliably than neurons in the VS, these latters encode the sum of temporally discounted values, that is, the overall goodness of available options (Cai et al., 2011).

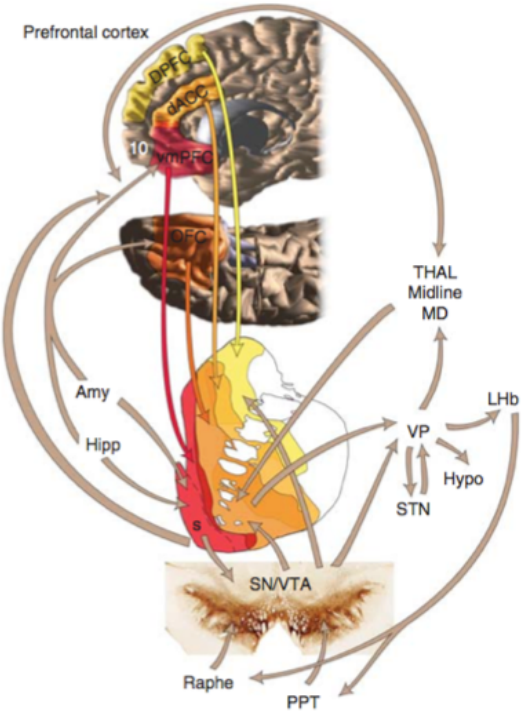

Figure 4. Human key structures and pathways of the reward circuit. Red arrow = input from the vmPFC; dark orange arrow = input from the OFC; light orange arrow = input from the dACC; yellow arrow = input form the dPFC; brown arrows other main connections of the reward circuit. Amy = amygdala; dACC = dorsal anterior cingulate cortex; dPFC = dorsal prefrontal cortex; Hipp = hippocampus; LHb = lateral habenula; hypo = hypothalamus; OFC = orbital frontal cortex; PPT = pedunculopontine nucleus; S=shell, SNc=substantia nigra, pars compacta; STN = subthalamic nucleus; Thal = thalamus; VP=ventral pallidum; VTA=ventral tegmental area; vmPFC=ventral medial prefrontal cortex (Adapted from Haber and Knutson, 2010).

The orbitofrontal cortex. As we highlighted above, frontal and prefrontal neural circuits (both cortical and subcortical) are the principal candidates as areas encoding the subjective value of different goods. However, the OFC and its involvement in dopamine transmission seem to play a prominent role in reward processing, both in nonhuman (e.g., Tremblay and Schultz, 1999; Padoa-Schioppa and Assad, 2008) and human primates (O'Doherty et al., 2003; Plassmann et al., 2007; Chib et al., 2009; Fitzgerald et al., 2009).

OFC is part of the human prefrontal cortex, lying in the ventral surface of the frontal lobe, over the orbits, and consists of five cytoarchitectonic subregions: frontal polar Brodmann Area (BA) 10, BA 11 anteriorly, BA 13 posteriorly, BA 14 medially, and BA 47/12 laterally (Fig. 5; see Carmichael and Price, 1994, Petrides and Pandya, 1994, Wallis, 2007). Fuster (1997, 2001) defined it as the part of the prefrontal cortex that, differently from the others, receives projections from the magnocellular, medial nucleus of the mediodorsal thalamus (Kringelbach and Rolls, 2004), conveying information from the object-processing visual stream, and taste, olfactory and somatosensory inputs (see Öngur and Price, 1998, 2000; Rolls, 2000), projecting back principally to the temporal lobe and the cingulate cortex (see Carmichael and Price, 1994, Petrides and Pandya, 1994, Rolls, 2004). OFC is indeed special because it is the only portion of the frontal cortex that receives information from all sensory modalities; it has only weak motor connections, and extensively links with the limbic system, amygdala, cingulate gyrus and hippocampus (e.g., Carmichael and Price, 1995; Walliss, 2007), making it a region that integrates multiple sensory properties with affective information (Wallis, 2007).

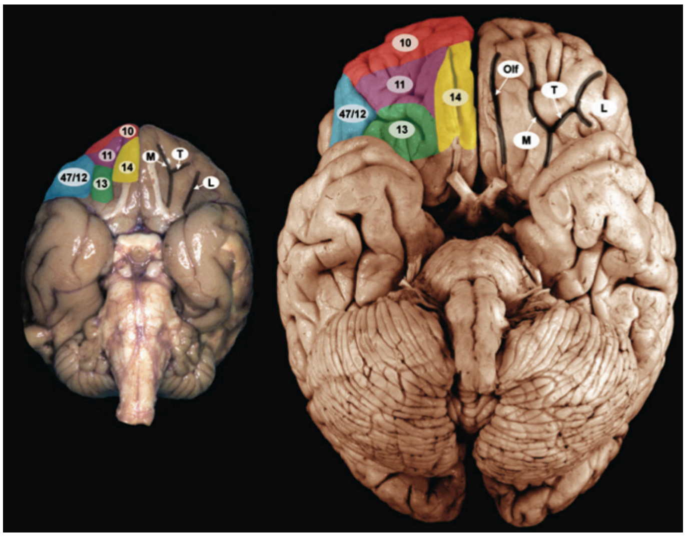

Figure 5. Ventral view of macaque (left) and human (right) brains illustrating the major cytoarchitectonically distinct regions of OFC (Petrides & Pandya 1994) and the main sulci. Olf = olfactory sulcus, M = medial orbital sulcus, T = transverse orbital sulcus, L = lateral orbital sulcus. In the macaque brain preparation, the olfactory tubercle obscures the olfactory sulcus. (Adapted from Wallis, 2007).

Specifically, OFC anterior part, characterized by granular cells, is thought to be more phylogenetically and ontogenetically recent than posterior and medial parts, consisting in agranular and dysgranular cortices (Öngur and Price, 2000; Wise, 2008). While the anterior part seems to respond to secondary rewards, the posterior preferentially processes primary outcomes (Kringelbach and Rolls, 2004). Recently, Sescousse and colleagues (2010) demonstrated that, while the anterior lateral OFC (BA 10) processes monetary gains, the posterior lateral OFC (BA 11) processes more basic erotic stimuli, considered as primary outcomes as food. Importantly, all rewards in the above study were hypothetical, suggesting that OFC processes representations of both abstract and real outcomes (see also Johnson and Bickel, 2002; Bickel et al., 2009). Moreover, it has been demonstrated (Elliott et al., 2000a; Liu et al., 2007; Mainen and Kepecs, 2009; O'Doherty et al., 2001) that mOFC is specifically sensitive to benefits and positive outcomes, whereas the lateral portion of the OFC is more modulated by costs (i.e., losses or punishments), and that that more medial-caudal regions encode reward-identity representations that are invariant to predictive stimuli, whereas more rostro-lateral regions contain reward representations paired to specific stimuli (Klein-Flugge et al., 2013).

OFC is the target of dopamine projections (e.g., Haber et al., 2000; Roesch et al., 2007; Winstanley, 2007; Takahashi et al., 2009; Winstanley et al., 2010), as demonstrated to be dysfunctional, for instance, in abstinent cocaine users (e.g., Volkow et al., 1996) and patients with Parkinson disease (Moustafa et al., 2008), both pathological populations in which dopamine dysregulation has a prominent role. The involvement of OFC in the dopamine system, and so in the 'reward prediction error' (i.e., the ability to learn stimulus-reward associations depending on the discrepancy between the predicted reward and the actual occurrence of reward; e.g., Rescorla and Wagner, 1972), helps to explain why OFC is involved in processing reward value. Some neurons in OFC are able to distinguish between rewarding outcomes and punishments (Thorpe et al., 1983) and between rewarding and non-rewarding outcomes (Tremblay and Schultz, 2000), namely, the relative motivational value of a good at that moment (Schultz, 2000), as well as in coding the economic value of an outcome independently of other goods available at the same time (i.e., 'transitivity'; Padoa-Schioppa and Assad, 2008). OFC lesioned patients were indeed found to be impaired in reversal learning, producing more perseverations (Fellows and Farah, 2003), as well as in the Iowa gambling task where they failed to adjust their choices according to money losses (Bechara et al., 1998).

More broadly, damage to the mOFC in humans results in motivational, emotional, affective and behavioral deficits, such as dysregulated social behavior (Damasio et al., 1991; Damasio and Anderson, 1993), inability to inhibit simple responses, short-term goals preference instead of long-term goals, inability to make advantageous decisions (poor choice pattern), inefficient coping with risk, abolished physiological responses in anticipation of punishment or before endorsing harmful actions that maximize good consequences (Moretto et al., 2010), all in the presence of well-preserved basic intellectual abilities (Bechara et al., 1997). Moreover, early signs of fronto-temporal dementia (e.g., eating disorders), a pathology affecting also the OFC (Glimcher et al., 2009), may reveal deficits in assigning the correct value to appetitive stimuli (Pasquier and Petit, 1997).

A suggested model (Schultz, 2000) is that, while ACC is involved in matching the actual outcome with the expected one to guide movements and execution activity, OFC seems to be engaged in the details of detection, perception and expectation of rewards, encoding the value of a choice outcome based on current needs and trade-offs, comparing the present reward with other potential outcomes. All this information will be held in working memory, passing then to the dlPFC, which uses them to control behavior and prepare plans toward the acquisition of rewarding goals based on cost-benefits analysis (Fig. 6; Schultz, 2000; Wallis, 2007; Kennerly and Wallis, 2009).

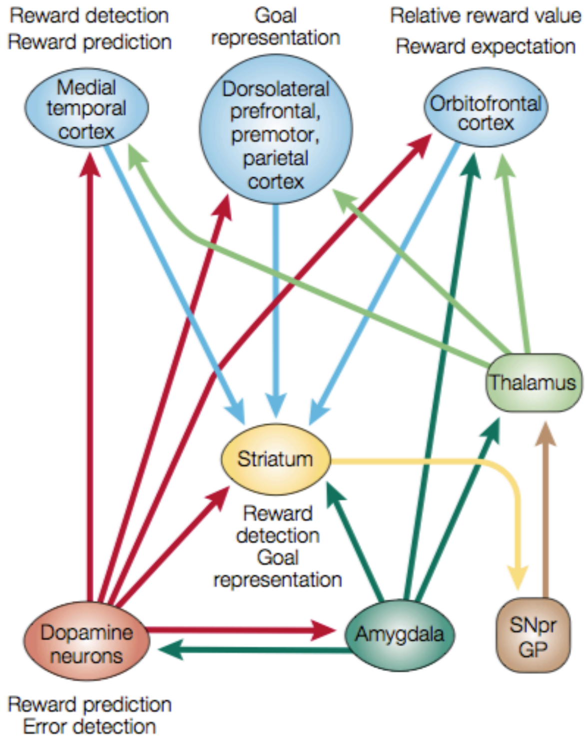

Figure 6. Model of reward processing related to brain regions. Many reward signals are processed by the brain, including those that are responsible for the detection of past rewards, the prediction and expectation of future rewards, and the use of information about future rewards to control goal-directed behaviour (SNpr, substantia nigra pars reticulata; GP, globus pallidus) (Adapted from Schultz, 2000).

Chapter II – Intertemporal choice and temporal discounting

[This review has been published in Sellitto et al., 2011]

Intertemporal choice

Individuals are often faced with choices whose consequences are spread over time. Such decisions, involving trading off between benefits and costs differing in the time of their occurrence, are commonly referred to as *intertemporal choices*. Making advantageous choices is crucial for survival and adaptation to the environment. People may have to choose, for example, between saving money or spending it immediately, quitting smoking to reduce the risk of future disease or continuing to smoke, forgoing a walk with friends to remain at home to study for an upcoming exam or giving up studying and going out. In all these cases, the question is: in order to reach the greatest advantage, is it best for me to indulge in the present or postpone the gain? By taking into account what they prefer and how long they are willing to wait to obtain it, all intertemporal choices affect people's health, wealth and mood (Frederick et al., 2002), with an impact on the immediate present or on the near or far future. In a more general view, individual intertemporal choices also affect others lives and the overall economic prosperity of nations (Smith, 1776).

Humans and other animals' preferences for one option over another reflect not just the amount of expected reward, but also the time at which the reward will be received. Economic models usually explain this in terms of maximization of achieved utility (Kalenscher and Pennartz, 2008). In order to choose the most rewarding course of action, people consider the utility of the temporally proximal outcome against the utility they assign to a temporally distant outcome. To explore such issue in the laboratory (both from an economic and psychological point of view), these decisional situations are usually recreated manipulating the amount of the offered rewards (e.g., money for humans), and the time at which these rewards are delivered, along a series of binary choices (e.g., Kirby et al., 1995; Mazur et al., 1997; Frederick et al., 2002). As an example, a subject might choose between \$5 now and \$15 in one week. However, a wide range of goods has been tested during years, not only at a behavioral level[1], but also with neuroimaging techniques (e.g., McClure et al., 2007; Prévost et al., 2010), with important implications on both the understanding of the neural bases of intertemporal choice, and of the computation of the subjective value for all goods. I will further examine this issue later.

Temporal discounting

Economics and psychology have long established that humans and other animals frequently prefer smaller rewards with short-term availability over larger rewards that become available in the long run, even when waiting would yield larger payoffs than pursuing immediate feelings (Ainslie, 1974; Rosati et al., 2007). Preferring closer reward implies that the subjective value (i.e., utility depending on specific characteristics of a subject) of a future reward is weakened (discounted), as a function of the time until its delivery (e.g., Cardinal et al., 2001; Kalenscher et al., 2005; Myerson and Green, 1995). This phenomenon is known as delay or *temporal discounting* (TD, Ainslie, 1975; Samuelson, 1937).

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[1] e.g., traffic tickets, Thaler, 1981; pain, Loewenstein, 1987; salary, Hsee et al., 1991; discomfort, Varey and Kahneman, 1992, dinners and vacation trips, Loewenstein and Prelec, 1993; health, Dolan and Goodex, 1995; life years, Johannesson and Johansson, 1997; corn, Holden et al., 1998; for a complete review, see Frederick et al., 2002.

In economics, the discounted utility (DU) model (Samuelson, 1937) provided for many years a theory framework for intertemporal choices, taking into account that all reasons or drives to make such choices can be described by a single parameter, the discount rate (usually referred to as *k*; Frederick et al., 2002). Discount rate refers to the subjective value of rewards that decreases by a fixed percentage for each unit of time that those rewards are delayed (Luhmann, 2009). This drop is described, within the DU model, by a curve represented by the exponential function $SV = e^{kD}$ (Ainslie, 1992; Mazur, 1987)[2]. This model however, implies that a given temporal delay leads to the same degree of discounting regardless of when it occurs (Loewenstein et al., 2008), that is, the discount rate is a weighted sum of utilities, constant over time (Kalenscher and Pennartz, 2008). For instance, delaying the availability of a reward by one day from now leads to the same degree of discounting of delaying the availability of the same reward by one day from one year (Frederick et al., 2002).

More recently, research has pointed out that intertemporal behavior may be not linear, and that deviations from rationality in estimating present and future consequences of actions cannot be well captured by an exponential function (Frederick et al., 2002). Both humans and animals care in fact, more about a delay if it is proximal than if it is distal in time (Loewenstein et al., 2008), so that reward discounting is initially more prominent, and then as more time passes, it becomes less steep (Kirby and Marakovich, 1995; Johnson and Bickel, 2008). For instance, one may prefer $110 in 31 days over $100 in 30 days, but $100 now over $110 tomorrow (Frederick et al., 2002).

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[2] where SV = subjective value (expressed as a fraction of the delayed amount), D = delay (in days), and *k* = discounting coefficient.

These so called ‘preference reversals’ or ‘time inconsistencies’ (Frederick et al., 2002) are better explained by a *hyperbolic model* described by an hyperbolic function (Ainslie, 1992; Mazur, 1987)

$$SV = 1/(1+kD)$$

than by an exponential model, which accounts for non-constant discounting (Cardinal, 2006; Kalenscher and Pennartz, 2008; Mazur, 1987)[2]. Other anomalies in discount rates are detectable when people have to decide, between gains vs. losses, or between small vs. large outcomes. As for the former, losses are usually less discounted in time than gains are. People are eager to receive gains as soon as possible, not so to obtain losses, even if these would be less conspicuous than future losses. (‘sign effect’, Thaler, 1981; Loewenstein, 1987). Second, large quantities of an outcome are discounted less than smaller quantities: larger outcomes are valued more, making people more willing to wait for them (‘magnitude effect’, Fig. 1; Myerson and Green, 1995;Green et al., 1997).

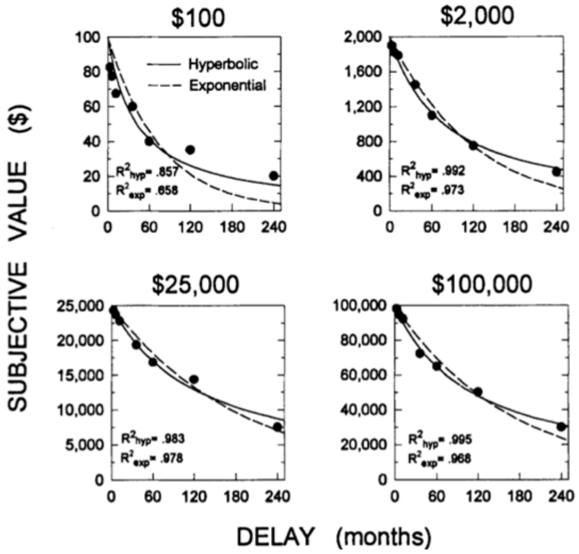

Figure 1. Example of ‘magnitude effect’: present, subjective value of the delayed reward as a function of the time until its receipt. Data for four different future amounts are shown in separate panels. Data points represent the median amount of immediate reward judged equal in subjective value to the delayed reward. Solid and dashed curves represent the best fitting hyperbolic and exponential discounting functions, respectively (Adapted from Green et al., 1997).

Impulsivity, state and trait factors

TD is usually considered a good measure of impulsivity (e.g., Takahashi, 2005). Individuals with greater discounting, are described as unable to wait for delayed rewards (impatience choices, Takahashi et al., 2007; Frederick et al., 2002) and may have impaired self-control (e.g., Takahashi et al., 2007), which is necessary to favour distant, more important goals (Shamosh and Gray, 2008). Suboptimal intertemporal choices can be observed in conditions characterized by poor self-control, including drug addiction (heroine or cocaine), cigarette smoking and binge drinking (e.g., Vuchinich and Simpson, 1998; Bickel et al., 1999, 2007; Kirby et al., 1999; Dalley et al., 2011; Vassileva et al., 2011; Klapproth, 2012; MacKillop et al., 2012; Yi and Landes, 2012), attention deficit/hyperactivity disorder (ADHD), oppositional defiant disorder and autism spectrum (e.g., Barkley et al., 2001; Demurie et al., 2012; Scheres et al., 2013), bipolar disorder and schizophrenia (Ahn et al., 2011), depression (Takahashi et al., 2011), compulsive gambling (Holt et al., 2003; Dixon and Holton, 2009) and obesity (Weller et al., 2008; Takahashi, 2010). Substance users (Kirby and Petry, 2004) show increased discount rates compared to healthy controls, consistent with their inability to make prudent choices forgoing instant gratifying rewards (e.g., drug) to favor later rewards of larger value (e.g., health). Moreover, this is true not only for the object of their desire, the drug itself, but also for other rewards, for example monetary rewards in alcoholics (e.g., Petry, 2001) and opioid-dependent individuals (e.g., Madden et al., 2007; Fig. 2).

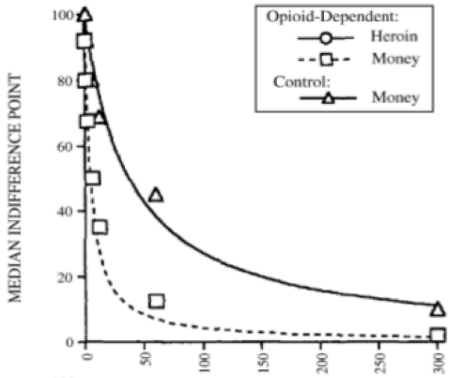

Figure 2. Hyperbolic delay discounting function curve, representing median *k* values, reported for heroin users and healthy individuals (Adapted from Madden et al., 2007).

Related to both poor self-control and higher delay discounting also performance on measures of intelligence, working memory and cognitive abilities has been found impaired (Shamosh and Gray, 2008; Shamosh et al., 2008). For instance, it has been observed that children who were able to wait longer to obtain more marshmallows at age 4 or 5 became adolescents more academically and socially competent, rational, planful and able to deal well with frustration and stress (Mischel et al., 1988; Eigisti et al., 2006), indicating that individual differences in delay gratification are stable in time. Moreover, the ability in delay gratification at age 4 correlated with the risk of being overweight as an adolescent (Seeyave et al., 2009; Tsukayama et al., 2010). It is not surprising, then, that even in non-obese women, the delay discounting linearly moderated the total energy intake (Rollins et al., 2010), as well as with a relationship with the Body Mass Index (Borghans and Golsteyn, 2006). Hinson and colleagues (2003) found that the more the cognitive load, the greater the discount rate (but see Franco-Watkins et al., 2010), together with an increased number of disadvantageous choices during a reversed Iowa gambling task (Dretsch and Tipples, 2008). Moreover, evidence for a functional relationship between delay discounting and working memory has also been provided in addicted individuals:

neurocognitive training of working memory significantly decreased delay discounting (Bickel et al., 2011).

Large delay discounting rates in adults have been found to correlate with a number of personality traits, such as extraversion (Ostaszewski, 1996), empathy (e.g., Kirby et al., 1999), agreeableness (Miller et al., 2008), sense of powerlessness over the future (i.e., fatalism, Johnson et al., 2010) and religious beliefs (Paglieri et al., 2013), as measured by personality scales. Gender differences have been found in time consistency, for example females are less impulsive than males under several conditions (Prince and Shawhan, 2011; Diller et al., 2011). Education level influenced the discount rate (the higher the education, the lower the discounting; de Wit et al., 2007). Age is also a factor, teenagers are indeed more impulsive than adults (Reimers et al., 2009; Whelan and McHugh, 2009; Löckenhoff et al., 2011; but see also Study V-Part III). Intelligence quotient (Shamosh and Gray, 2008) and culture also influence time consistency (e.g., Western people are more impulsive than Eastern people; Markus et al., 1991; Du et al., 2002, de Wit et al., 2007; Takahashi et al., 2009; Ma-Kellams et al., 2012). In this regard, it is worth reporting that recently genetic investigations highlight how TD rates could be predetermined at an innate level. For instance, different polymorphisms of the catechol-*O*-methyltransferase (COMT) gene, which is important in regulating frontal dopamine (e.g., Chen et al., 2008; Pine et al., 2010), were found to predict discounting behavior and brain activity during intertemporal choice (e.g., Boettiger et al., 2007; Paloyelis et al., 2010; Gianotti et al., 2012; Lancaster et al., 2012; Smith and Boettiger, 2012). Recently, also variations of the DRD2 gene, a D2 subtype of dopamine receptors, have been associated with impulsivity in delay discounting (Kawamura et al., 2013).

However, as a multicomponent construct, intertemporal choice and TD are sensitive to both state and trait influences (Odum and Baumann, 2010). That is, individual differences in discount rate can be attributable not only to traits (i.e. differences between subjects, such as genetic factors or personality), as just reported above, but also to internal state features (i.e. differences within the same subject, such as stress or hunger) and aspects of the situation, such as reward type (Kirby 2009; Peters and Büchel, 2011). On the one hand, a trait factor drives overall a choice by determining the degree at which a good is discounted generally. On the other hand, a state factor influences behavior on the relatively short-term. Indeed, a difference in the ability to resist to immediate gratification can be observed when people are faced with primary or secondary rewards (‘domain effect’, e.g., Madden et al., 1997; 2007; Frederick et al., 2002; Odum and Rainaud, 2003; McClure et al., 2007). Primary rewards, such as, food, drugs and alcohol, due to their perishability, depending upon internal states (e.g., hunger, stress, mood) and desires (Catania, 1998; Odum et al., 2006; Charlton and Fantino, 2008), as well as their ability to rapidly bring to satiety, are discounted at a higher rate than secondary rewards. Compared to primary rewards, money and gift certificates tend to elicit a less strong desire for immediate reward consumption (e.g., Odum et al., 2006; Estle et al., 2007; see Evans et al., 2012 for a comparison with animals). Metabolism is a powerful determinant of humans’ choice behavior, exerting an effect also on secondary rewards (Wang and Dvorak, 2010): increased blood glucose levels led to an increase in the value placed on future rewards; vice versa, drinking a beverage without sugar led to an increase in the value placed on current rewards. Moreover, if a reward implies a gain, a loss, or a punishment, the context in which the choice is made (Dixon et al., 2006), the effort required, and so on, will have an impact on the decision at stake.

Chapter III – The neurobiology of intertemporal choice: insight from imaging and lesion studies

[This review has been published in Sellitto et al., 2011]

Functional studies

Since about ten years (see Appendix A), neurobiological research has focused on the neural underpinnings of value encoding of competing rewards, necessary to guide optimal choice behavior among alternatives differing in the time of their consequences.

Animal studies. Due to evolutionarily similarities, relying on animal evidence is always a useful starting point for neural and behavioral research in humans, both healthy and pathological individuals (e.g., Chang et al., 2012). Overall, animal studies (mostly conducted with single unit cell recording) suggest a role of mOFC in intertemporal decision-making (Winstanley et al., 2004). In both rodents (Roesch et al., 2006; da Costa Araùjo et al., 2010) and monkeys (Wallis and Miller, 2003; Padoa-Schioppa and Assad, 2006; Roesch et al., 2006), mOFC neurons have been found to encode the subjective value of different foods when choosing between them, and to be sensitive to the reward amount and to the duration of a delay intervening before food delivery, responding more strongly to short delays predicting cues and before larger rewards. Disruption of both rats' (Cardinal et al., 2001; Mobini et al., 2002; Winstanley et al., 2004; Rudebeck et al., 2006; Mar et al., 2001; Jo et al., 2013) and monkeys' (Tremblay and Schultz, 1999; Izquierdo and Murray, 2004) mOFC was found to alter discount rates differently (e.g., in odd directions based on wether the lesion occurred before learning the task or not), sensitivity (preferences) to size of reward and time to wait for it, and to produce abnormal responses to changes in reward expectations. Moreover, the inactivation of the OFC has been found to increase impulsive choices in less impulsive rats when the delay of the outcome was cued, but decrease impulsive choices in highly impulsive rodents in an uncued condition, suggesting differential changes in the dopamine system activation (Zeeb et al., 2010). Similarly, a disruption of NAcc in rodents (da Costa Araùjo et al., 2009; Valencia-Torres et al., 2012) has been found to decrease indifference points between sooner and later rewards, as well as a disconnection of OFC from NAcc (Bezzina et al., 2008). Also, single-cell recordings in pigeons' analogue of the mammalian prefrontal cortex revealed that neural response was modulated by reward amount and delay, according to the hyperbolic equation (see Part I; Kalenscher et al., 2005).

Humans have been deemed to be evolutionarily more patient than animals, despite both exhibit TD of future delays (e.g., Green and Myerson, 2004; Woolverton et al., 2007; Hwang et al., 2009; Andrade and Hackenberg, 2012). However, several studies (Rosati et al., 2007; Addessi et al., 2011) demonstrated recently that humans share similar levels of patience with bonobos and chimpanzees in some contexts, for example when food rewards are at stake, but also with capuchins, due to their tool use ability. Under some conditions, humans were even less willing to wait for food than chimpanzees. Moreover, Jimura and colleagues (2009) found that, like animals, humans exhibited TD also with rewards delayed by seconds.

Human studies. In humans, VS, mOFC, PCC, and lateral prefrontal cortex have been identified as other critical neural substrates of intertemporal choices (McClure et al., 2004, 2007; Kable and Glimcher, 2007, 2010). Their specific role, however, is still unclear.

Imaging studies by McClure and colleagues (2004, 2007) emphasize the view that discounting behavior reflects the differential activation of two distinguishable neural systems (see also Elster, 1979; Loewenstein, 1996; Loewenstein et al., 2008; Shefrin and Thaler, 1988). One system is responsible for impatient choices, driven by the desire for present outcomes (the 'myopic doer', Thaler and Shefrin, 1981; Elster, 1985, 1986; Graham and Isaac, 2000). The other is responsible for prudent choices, emphasizing more the consequences of choosing delayed outcomes (the 'farsighted planner', Thaler and Shefrin, 1981). These two systems are commonly defined ß, the more impulsive system, and ∂, the more rational system (e.g., Laibson, 1994, 1997; Loewenstein, 1996). From this perspective, the balance between the activation of these two systems is responsible for the impulsivity or the patience exhibited by people during intertemporal choices (e.g., Laibson, 1994, 1997; Loewenstein, 1996; Peters and Büchel, 2011). McClure and colleagues (2004; Fig. 1) found that VS, mOFC and mPFC were preferentially activated when an immediate monetary option was available; therefore, they deemed these structures as the neural bases of the ß-system. Conversely, lateral prefrontal cortex and the posterior parietal cortex (PPC) were not preferentially activated by the presence of a particular option, but activated by all types of choice (between immediate versus delayed options, or between two delayed options); therefore, the authors related these areas to the ∂-system. When the ß-system is engaged, it favors the immediate option, whereas when a greater activation in the ∂-system overcomes that in the ß-system, a delayed option is favored (McClure et al., 2004). These activations (McClure et al., 2004) were not found solely using monetary rewards, but also with primary rewards available immediately after each decision (McClure et al., 2007).

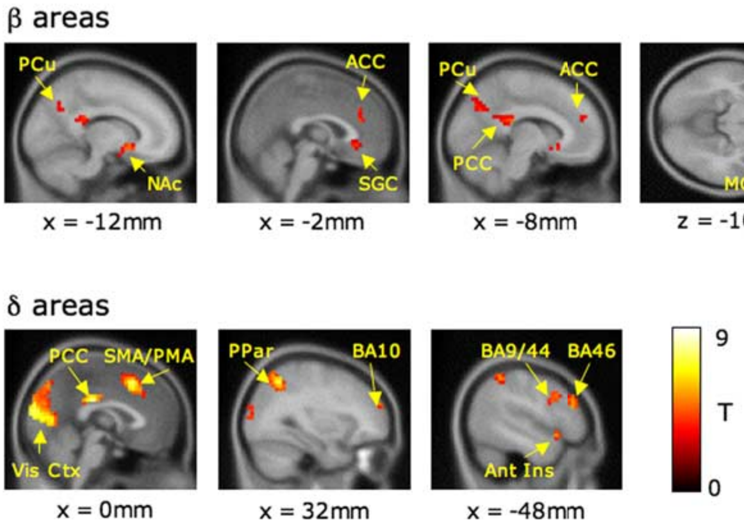

Figure 1. ß and ∂ brain regions in the context of the dual model (Adapted from McClure et al., 2007).

Another approach to relate neural activity to intertemporal choices is by linking neural states to subjective value directly (Kable and Glimcher 2007, 2010). In Kable and Glimcher (2007)'s study, participants were submitted to monetary choices between a fixed option, always immediately available, and a variable option, offered at different delays. Based on behavioral choices, they derived an individual preference curve for each participant, to estimate how the subjective value changed as a function of delay and amount. Brain activity during subsequent intertemporal choices was then examined that covaried with this parameter. It was found that activity in VS, mPFC and posterior PCC tracked subjective value, regardless of whether the delayed reward could be obtained in hours or in months. Despite marked differences in the discount curves of each subject (ranging from most patient to most impulsive), subjective preferences were mirrored in the pattern of activity in VS, mPFC and PCC (Kable and Glimcher, 2007). This activity varied with the delayed option (the immediate option was fixed and never presented on the screen during the experiment) demonstrating that these regions do not value immediate rewards only, but represent the subjective value of delayed rewards (Kable and Glimcher, 2007). According to Kable and Glimcher (2007); therefore, findings from McClure and colleagues (2004) that limbic activity was greatest for immediate rewards, could merely reflect the fact that immediate options generally have a greater subjective value than delayed ones (Kable and Glimcher 2007).

To strengthen their point further, Kable and Glimcher (2010) conducted a second experiment including a condition in which two delayed options were offered, testing for preference reversals in the context of a model called 'As Soon As Possible' (ASAP). While the hyperbolic model accounts for a hyperbolic decline of the subjective value with regard to the present, the ASAP model accounts for a hyperbolic decline of the subjective value relative to the soonest possible reward, which may not necessarily be available immediately. The most evident difference between these two models is the expected occurrence of preference reversals. While in McClure and colleagues (2004, 2007) discounting function predicts that people will sometimes make preference reversals between two delayed options (i.e., choosing the larger later reward, while this same option was previously refused when paired with an immediate one), the ASAP model predicts that people will make the same choice in both conditions, and that possible changes are just stochastic (Kable and Glimcher 2010). Indeed, Kable and Glimcher (2010) found that when subjects chose between two delayed options, they were, in some cases, even more impulsive than when an immediate reward was available. At a neural level, the activity in VS, mPFC and PCC was found to track the subjective value of both immediate and delayed rewards. This (absolute) subjective value varied as a function of the delay to the soonest possible reward. Once again, Kable and Glimcher (2010, Fig. 2) did not find a greater activation of VS, mPFC and PCC in the immediate condition compared to the delayed condition, showing that these areas do not carry an impulsive signal that primarily values immediate rewards, but rather a value signal for delayed rewards. At any rate, marked differences in the analysis of the above-described studies (McClure et al., 2004, 2007; Kable and Glimcher, 2007, 2010) make direct comparison of the two diverse findings difficult.

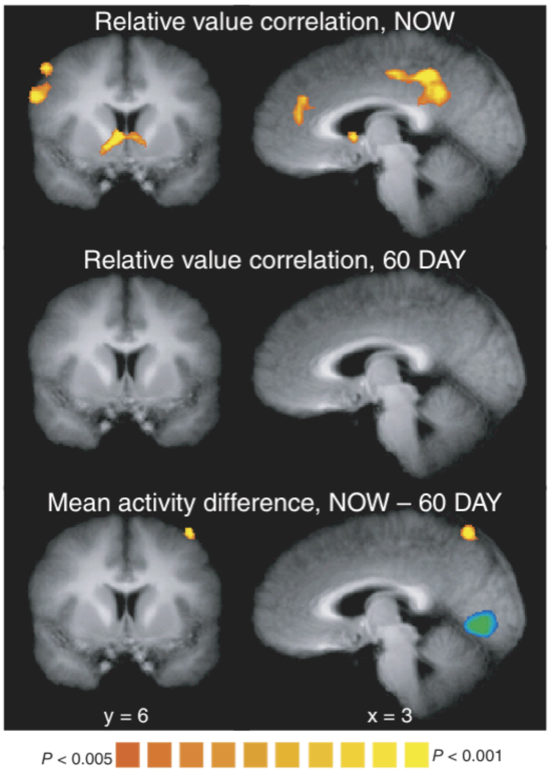

Figure 2. Activations correlating with subjective value for money, both whenn an immediate option was available (NOW), and when it was not (60 DAY) (Adapted from Kable and Glimcher, 2010).

More recently, the study of Ballard and Knutson (2009) provided further evidence for the involvement of mesolimbic and lateral brain regions in future rewards evaluation, but differentially according to magnitude and delay. Across subjects, activity in the NAcc, mPFC, and PCC positively correlated with the magnitude of future rewards, while that in the dorsolateral prefrontal cortex, temporo-parietal junction cortex and PCC negatively correlated with the delay of future rewards. Neural activity in response to magnitude and delay was then correlated with discount rates for each participant. More impulsive subjects showed diminished activation of NAcc to future rewards magnitude (they were even less sensitive to large magnitudes of future rewards), and increased deactivation of dorsolateral prefrontal and parietal cortices to future rewards (Ballard and Knutson, 2009). This functional dissociation is in fact reminiscent of the dual-system model of McClure and colleagues (2004, 2007). However, the finding mPFC and PCC responded to both immediate and delayed rewards (Ballard and Knutson, 2009) better fits with the unitary model proposed by Kable and Glimcher (2007, 2010; Peters and Büchel, 2010b).

Moreover, it is worth highlighting that very recently new imaging techniques have been used to explore intertemporal choice. On the one hand, two studies applied the multi-voxel pattern analysis to fMRI data (Clithero et al., 2009; Murawski et al., 2012; but see also Study III-Part II). This technique, by the means of support learning vector machines, investigates if the stimulus encoding depends on patterns of high and low activation across voxels, instead of averaging across voxels within an area thus concluding that if that area responds more to that stimulus it means that it encodes that stimulus, as in traditional univariate analysis (Huettel et al., 2009). Local voxel patterns in the left PPC have been found to contain unique information to differentiate probabilistic (when outcomes occur only with some probability; Frederick et al., 2002) and intertemporal valuation (Clithero et al., 2009), while regions included in the mPFC, where the subjective value during intertemporal choices is encoded, were modulated by incidental contextual information (Murawski et al., 2012). On the other hand, functional connectivity during resting state allows investigating abnormalities in specific interacting neural networks without confounding like stimulus presentation or task performance (Friston et al., 2003). Using this technique, Camchong and colleagues (2011) found that hyperconnectivity within the ACC network involved in ‘mentalizing’ (i.e., the ability to understand the thoughts and the intentions of oneself and others) in chronic drug addicted was associated with difficulties during intertemporal choice and adaptive learning. Also, Li and colleagues (2013) found that resting-state functional connectivity of regions involved in valuation and choice processes (i.e., VS, PCC, mPFC, dlPFC, ACC, and insula) predicted impulsivity in a monetary TD task. More recently however, functional connectivity has been recorded also while making on-line intertemporal choices (Jimura et al., 2013). This study showed that vmPFC exhibited a specific pattern of activity during the delay periods and during choice. The same pattern was found in VS, but only in impulsive individuals, and activity in the anterior PFC (aPFC) was present only in patient subjects. vmPFC and aPFC had an opposite modulatory influence on VS (Jimura et al., 2013). Furthermore, the dynamic causal modeling (Friston et al, 2003) has also been suggested as an integrative tool for research on intertemporal choice, focusing on both the dynamic properties of the decision process, and on the role of self-control and time framing (e.g., calendar dates or delays) during choice behavior (Scherbaum et al., 2012).

Lesion studies

Fellows and Farah (2005) evaluated for the first time intertemporal choices in brain-lesioned patients. They compared performance of vmPFC patients, dorsolateral frontal patients, in which damage encompassed frontal cortex, but spared vmPFC, non-frontal patients, in which frontal cortex was spared, and healthy controls. Participants were assessed on intertemporal monetary decisions (Kirby and Marakovic, 1995), and on the ‘future time perspective’ test, which assesses several facets of future time representation. VmPFC patients showed discounting rates comparable to those of the other two groups of patients and healthy controls. Concerning ‘future time perspective’, instead, vmPFC patients revealed significant foreshortened personal future time perspective than healthy controls. These results suggest that despite the temporal (future) window of vmPFC patients was shorter than it was in the other groups, this did not have an impact on intertemporal choice. Fellows and Farah (2005) themselves, anyway, did not exclude the possibility that their discounting task was less sensitive than the future time perspective task. Recent studies have evidenced that focal lesions encompassing mOFC, but not necessarily vmPFC affected TD in monkeys by increasing its steepness (Rudebeck et al., 2006), which suggests that mOFC may be the critical region for evaluating different rewards delivered at different times (Noonan et al., 2010). Since in Fellows and Farah (2005)’s study some patients had damage involving mPFC, but sparing mOFC, their results did not clearly shed light on the role of human mOFC during intertemporal choice.

More recently, Sellitto and colleagues (2010, see Study I-Part II) reconsidered intertemporal choices, comparing mOFC damaged individuals with patients whose lesion spared the frontal lobe, and healthy controls. Precisely, the maximal overlap of lesions in the mOFC was in BAs 10 and 11, and the adjacent mPFC (BA 32). All participants performed three TD tasks involving, separately, primary (food) and secondary (money and discount voucher). In the three TD tasks, participants chose between an immediate variable amount of reward and a fixed amount of reward that could be received after a delay (Kirby and Herrnstein, 1995; Myerson et al., 2003; Sellitto et al., 2010). The amount of the immediate reward was adjusted based on the participant’s choices, using a staircase procedure that converged on the amount of the immediate reward that was equal, in subjective value, to the delayed reward (Du et al., 2002; Sellitto et al., 2010).

mOFC patients exhibited greater impatience than healthy and brain-damaged control participants across types of reward. That is, compared to controls, the preference for immediate rewards was increased in mOFC patients, as was the steepness of the hyperbolic function that best described their behavior. Moreover, lesion volume in BA 11 showed a strong correlation with discounting behavior, with larger lesions associated with steep discounting rates. These findings argue for a necessary role for mOFC in the valuation of rewards, regardless of the type of reward at stake. This is consistent with a recent study (Chib et al., 2009) that found that vmPFC (which includes mOFC and mPFC) activity correlated with subjects' value for all types of goods (food, non-food consumable and money), suggesting that a common 'neural currency' (Montague and Berns, 2002), computed via mOFC, underlies the evaluation of different categories of goods. Interestingly, differences in TD were observed despite patients not rating themselves as impulsive in a self-assessed impulsivity scale (Fossati et al., 2001). This finding confirms previous reports of a lack of awareness self-insight in vmPFC patients (Ciaramelli and Ghetti, 2007; Modirrousta and Fellows, 2008; Barrash et al., 2000; Beer et al., 2006; Sellitto et al., 2010), and stresses the need for converging measures. Moreover, the lesion volume in BA 11 strongly correlated with the discounting behavior, further suggesting that mOFC is a crucial area in evaluating reinforcers. A further, recent study (Figner et al., 2010) focused on the role of cognitive control during intertemporal choices, based on the idea that choice does not follow automatically from valuation, as valuation judgments and choice can be discrepant due to the intervention of deliberative processes. Activity in lateral prefrontal cortex, often found during intertemporal choices in previous studies

(McClure et al., 2004, 2007; Kable and Glimcher, 2007, 2010), has long known to be responsible of the implementation of self-control during several types of task (e.g., Miller and Cohen, 2001; Knoch and Fehr, 2007). When we are faced with tempting short-term gratifications, self-control processes must intervene to resist temptation in favor of a farsighted choice (i.e., the future outcome). Figner and colleagues (2010, Fig. 3) described two types of preference reversals: 'self controlled preference reversals', in which, despite the higher valuation of the tempting short-term gratification, the long-term outcome is chosen, and 'impulsive preference reversals', where the long-term outcome has the larger evaluation but the short-term one is chosen. This model predicts more 'self controlled preference reversal' than 'impulsive preference reversal' when self-control mechanisms are normally available. This 'self-control account' (Figner et al., 2010) makes three fundamental predictions. First, lateral prefrontal cortex is involved in choice, but not in explicit evaluation; therefore, a virtual disruption of these cortices should affect the former but leave unaltered the latter. Second, this disruption should affect predominantly choices in which an immediate option is available, not when only delayed options are put up against, since the former are strong and tempting, requiring more self-control. Third, to the extent that disruption of the lateral prefrontal cortex leads to diminished self-control capability, both a reduction in 'self-controlled preference reversals' and an increase in 'impulsive preference reversals', should be expected. Low-frequency repetitive transcranial magnetic stimulation on lateral prefrontal cortex before performing the choice task resulted in an increase in impatient choices, without changing the pattern of choices involving only future options, or valuation ratings of both types of rewards.

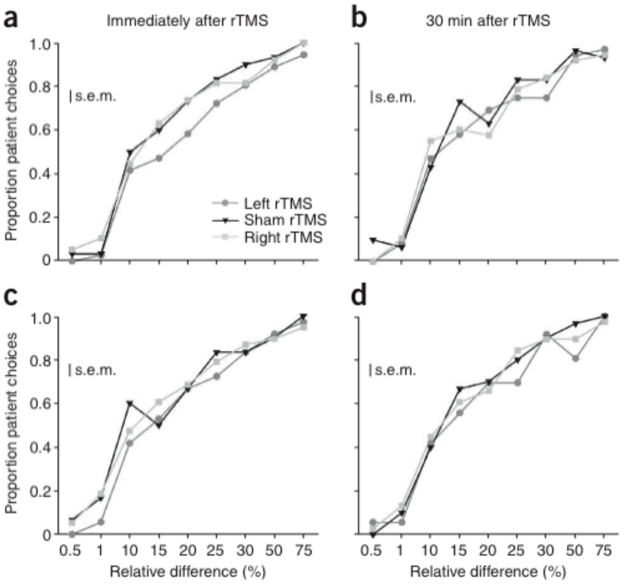

Figure 3. Proportion of prudent choices as a function of the relative difference between magnitude of sooner-smaller and later-larger rewards. Lines indicate the proportion of later-larger choices for left, right and sham rTMS groups. (a) Now trials immediately after rTMS train. (b) Now trials 30 minutes after rTMS train. (c) Not-now trials immediately after rTMS train. (d) Not-now trials 30 minutes after rTMS train. The largest standard error of the mean for difference left versus sham in each panel is shown (Adapted from Figner et al., 2010).

These findings support the idea that lateral prefrontal cortex exerts a modulatory (self-control) role on the activity of regions (e.g., mOFC) involved in intertemporal reward choice (Figner et al., 2010). It is worth noting, however, that very recently Essex and colleagues (2012) found that the posterior parietal cortex had roughly the same role as the dorsolateral prefrontal cortex in favoring long-term choices over immediate gratification, again only when decisions were difficult. Namely, when the subjective value of the two options at stake are close to them, suggesting a wider circuit involved in implementing self-controlled and more rational decisions. Focusing particularly on choice difficulty helps to better understand the role of areas involved in the reward circuit. Indeed, VS, vmPFC, and insula have been found to be activated in trials below and above the indifference point, with the mPFC activated during decisions at the indifference point (Marco-Pallarés et al., 2010). Moreover, vmPFC, ACC, dlPFC, and insula activations have been found to be associated with choosing the larger later option in the pair; during larger later option choices, steeper discounters recruited more larger later option-related activity during larger later option choice (Luo et al., 2012).

To date, following Sellitto and colleagues' evidence (2010), only one study (Wood and McHugh, 2013) examined TD in another category of patients. Individuals who had suffered from traumatic brain injury showed increased discount rates as compared to control participants. TD rates were unaffected by ratings of impulsiveness, intelligence, memory, and everyday executive function. However, no lesion information has been reported in the study, so that these findings cannot be related to a specific focal brain damage. In the first two studies reported in Part II of this dissertation, both lesional findings of Sellitto and colleagues (2010) on mOFC patients and new lesional evidence on insular cortex damaged individuals (Sellitto et al., under submission) will be reported. To follow, preliminary results of an fMRI study will be described.

PART II – Neural basis of intertemporal choice and temporal discounting: New evidence from lesional and imaging studies

Précis

Functional imaging studies in humans are useful to observe and detect activity in brain regions during cognitive processes a subject is engaged in, as in the present case, when it comes to make a choice between goods available at different delays. However, these methods in isolation can account only for mere statistical correlations, while a causative explanation is required. Lesion studies can overcome this inferential limitation.

Of course, we are aware that also lesional studies have their limitations. Indeed, as highlighted by Molenberghs and colleagues (2008), even if lesions are restricted to a specific brain region of interest, fibres connections could also be impaired (Corbetta et al., 2005), and, ways commonly used to dichotomize patient groups for the purpose of lesion mapping (Karnath et al., 2001; Mort et al., 2003; Hillis et al., 2006) do not map rigorously onto the specific processes that are isolated by the subtraction method in fMRI in the intact brain (Husain and Rorden, 2003; Nachev and Husain, 2006). For this reason, here we assume that lesion studies can add important information to the knowledge of cognitive processes of interest, but not regardless of imaging evidence.

Here I will provide new neural evidence about intertemporal choice along two lesion studies carried out on brain lesioned patients, demonstrating the causal involvement of both mOFC and insular cortex during the computation of intertemporal decisions about hypothetical rewards. In a third study, I will provide preliminary evidence about brain areas active during intertemporal choice, specifically those involved in the carry-over effect on TD, by the means of using also both univariate and multivariate fMRI analyses.

Study I - Medial Orbitofrontal Cortex damage increases myopic discounting of future rewards in humans

[These data have been published in Sellitto et al., 2010]

Introduction

As highlighted before (see Part I; Sellitto et al., 2011), research in cognitive neuroscience has begun to investigate the neural mechanisms governing TD (Luhmann, 2009). On the one hand, fMRI studies in humans have consistently detected activity in brain structures such as the medial orbitofrontal cortex (mOFC) and adjacent mPFC (designated collectively as vmPFC) during intertemporal choices, especially when individuals weighted delayed rewards against immediately available rewards (McClure et al., 2004, 2007; Ballard and Knutson, 2009). Other fMRI studies have shown that activity in the mOFC and mPFC tracked the subjective value of rewards, over both short and long timescales (Kable and Glimcher, 2007; Peters and Büchel, 2009; Pine et al., 2009). Together, these findings identify the mOFC as an important structure for intertemporal choice. On the other hand, while several nonhuman animal studies have shown abnormal TD following lesion to the OFC (Cardinal et al., 2004; Winstanley et al., 2004; Rudebeck et al., 2006), providing evidence for a causal involvement in TD, the only study assessing TD in human patients with lesion to the vmPFC, found no deficit (Fellows and Farah, 2005). Crucially, some patients in that study had damage involving mPFC but sparing mOFC. Thus, whether mOFC plays a necessary role in TD in humans remains unknown.

Here, we investigated TD of hypothetical primary and secondary rewards in patients with lesions in mOFC, control patients with lesions outside the frontal lobe, and healthy individuals. If mOFC plays a crucial role during intertemporal choice, favouring valuation of long-term outcomes (Bechara et al., 1997; Schoenbaum et al., 2009), then patients with lesions involving this brain region should show increased TD of future rewards compared with control groups.

Materials and Methods

Participants

Participants included 16 patients with brain damage and 20 healthy individuals (see Table 1 for demographic and clinical information). Patients were recruited at the Centre for Studies and Research in Cognitive Neuroscience, Cesena, Italy. Patients were selected on the basis of the location of their lesion evident on magnetic resonance imaging (MRI) or computerized tomography (CT) scans.

Seven patients (1 female) had lesions encompassing the medial one-third of the orbital surface and the ventral one-third of the medial surface of the frontal lobe, as well as the white matter subjacent to these regions (Fig. 1). Since lesions predominantly involved the mOFC (see Lesion analysis), we henceforth refer to this group as mOFC patients. Lesions were the results of the rupture of an aneurysm of the anterior communicating artery in 5 cases, and traumatic brain injury in 2 cases. Lesions were bilateral in all cases, though often asymmetrically so.

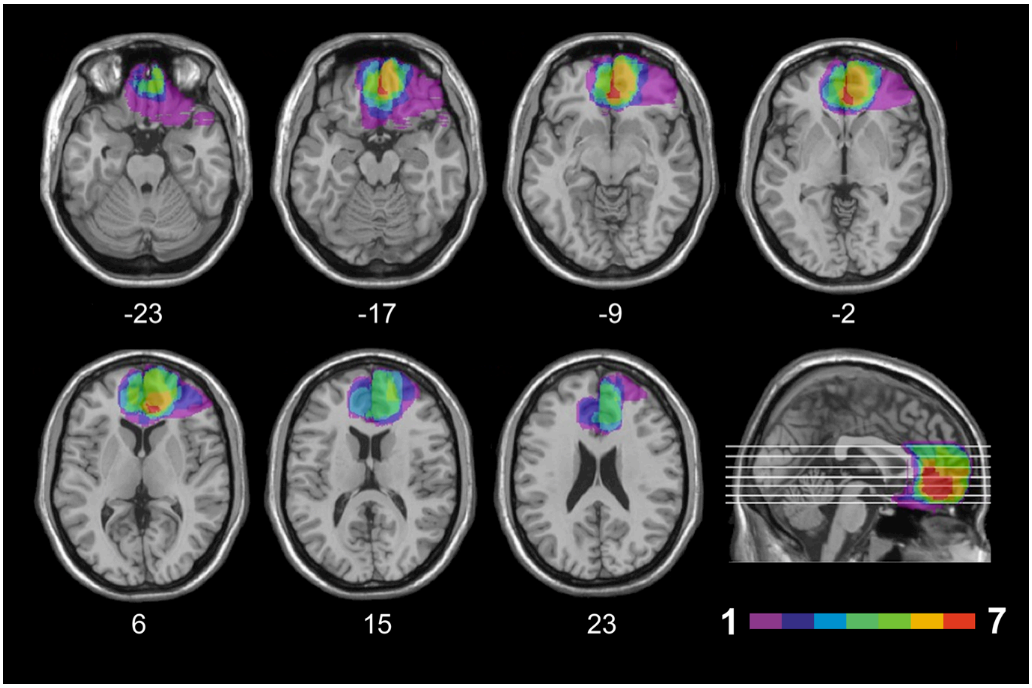

Figure 1. Location and overlap of brain lesions. The panel shows the lesions of the seven patients with mOFC damage projected on the same seven axial slices and on the mesial view of the standard Montreal Neurological Institute brain. The level of the axial slices has been marked by white horizontal lines on the mesial view of the brain. z-coordinates of each axial slice are given. The color bar indicates the number of overlapping lesions. In each axial slice, the left hemisphere is on the left side. Maximal overlap occurs in the medial orbitofrontal cortex (BAs 10, 11), and adjacent mPFC (BA 32).

Nine patients (two females) were selected on the basis of having damage that did not involve the mesial orbital/vmPFC and frontal pole, and also spared the amygdala in both hemispheres. We henceforth refer to this group of non frontal patients as non-FC patients. In this group, lesions were unilateral in all cases (in the left hemisphere in 6 cases, and in the right hemisphere in 3 cases), and were all caused by ischemic or hemorrhagic stroke. Lesion sites included the lateral aspect of the temporal lobe and adjacent white matter (in 5 cases), the inferior parietal lobule (in 1 case), the medial occipital area (in 1 case), and the lateral occipitoparietal junction (in 2 cases).

Included patients were in the stable phase of recovery (at least 12 months postmorbid), were not receiving psychoactive drugs, and had no other diagnosis likely to affect cognition or interfere with participation in the study (e.g., significant psychiatric disease, alcohol abuse, history of cerebrovascular disease). There was no significant difference in lesion volume between mOFC patients and non-FC patients (49.2 vs. 46.9 cc; p = 0.88).

The healthy control (HC) group comprised 20 individuals (two females) matched to the patients on mean age, gender, and education. Control participants were not taking psychoactive drugs, and were free of current or past psychiatric or neurological illness as determined by history. Participants gave informed consent, according to the Declaration of Helsinki (International Committee of Medical Journal Editors, 1991) and the Ethical Committee of the Department of Psychology, University of Bologna.

Patients' general cognitive functioning was generally preserved, as indicated by the scores they obtained in the Mini-Mental State Examination (Folstein et al., 1975), the Raven Standard Matrices, and the digit span test, which were within the normal range in all cases (Spinnler and Tognoni, 1987) (Table 1).

Group	**Sex (M/F)**	**Age (years)**	**Education (years)**	**MMSE**	**BIS-11**	**Lesion volume (cc.)**	**SRM**	**DS**
mOFC (n=7)	6/1	57.7 (10.4)	11.1 (6.4)	27.6 (2.3)	63.4 (6.1)	49.3 (14.6)	30.1 (5.8)	4.9 (0.7)
non-FC (n=9)	7/2	57 (12.8)	12.1 (4.0)	28.1 (1.9)	64.3 (10.9)	46.8 (33.9)	27.6 (4.5)	5.1 (1.4)
HC (n=20)	18/2	58.2 (6.6)	10.6 (4.6)	28.6 (1.44)	57.9 (7.5)	-	-	-

Table 1. Participant groups' demographic and clinical data. Note. mOFC group = patients with lesions in medial orbitofrontal cortex; non-FC group = patients with lesions outside the frontal lobe; HC group = healthy controls; M = male; F = female; MMSE = Mini Mental State Examination; BIS-11 = Behavioral Impulsivity Scale; SRM = Standard Raven Matrices (corrected score); DS = digit span forward (corrected score). The values in parentheses are standard deviations.

Lesion analysis

For each patient, lesion extent and location were documented by using the most recent clinical CT or MRI scan. Lesions were traced by a neurologist with experience in image analysis on the T1-weighted template MRI scan from the Montreal Neurological Institute provided with the MRIcron software (Rorden and Brett, 2000; available at http://www.mricro.com/mricron). This scan is normalized to Talairach space and has become a popular template for normalization in functional brain imaging (Moretti et al., 2009). Superimposing each patient's lesion onto the standard brain allowed us to estimate the total brain lesion volume (in cubic centimeters). Furthermore, the location of the lesions was identified by overlaying the lesion area onto the Automated Anatomical Labeling template provided with MRIcron. Figure 1 shows the extent and overlap of brain lesions in mOFC patients. Brodmann's areas (BA) affected in the mOFC group were areas 10, 11, 47, 32 (subgenual portion), and 24, with region of maximal overlap occurring in BA 11 [mean (M) = 21.0 cc, SD = 8.6], BA 10 (M = 12.6 cc, SD = 4.7), and BA 32 (M = 5.4 cc, SD = 4.0).

Temporal discounting tasks

In each of three computerized TD tasks, participants chose between an amount of a reward that could be received immediately and an amount of reward that could be received after some specified delay (Kirby and Herrnstein, 1995; Myerson et al., 2003). The nature of the reward changed across tasks. One task assessed TD for money, one task assessed TD for food (e.g., chocolate bars; see Procedures), and one task assessed TD for discount vouchers (e.g., discount vouchers for gym sessions; see Procedures). All rewards used were hypothetical. In each task, participants made five choices at each of six delays: 2 d, 2 weeks, 1 month, 3 months, 6 months, and 1 year. The order of blocks of choices pertaining to different delays was randomly determined across participants. Within each block of five choices, the delayed amount was always 40 units (e.g., 40 €, 40 chocolate bars, a 40 € discount voucher for a gym session). The amount of the immediate reward, on the other hand, was adjusted based on the participant's choices, using a staircase procedure that converged on the amount of the immediate reward that was equal, in subjective value, to the delayed reward (Du et al., 2002). The first choice was between a delayed amount of 40 units and an immediate amount of 20 units. If the participant chose the immediate reward, then the amount of the immediate reward was decreased on the next trial; if the subject chose the delayed reward, then the amount of the immediate reward was increased on the next trial. The size of the adjustment in the immediate reward decreased with successive choices: the first adjustment was half of the difference between the immediate and the delayed reward, whereas for subsequent choices it was half of the previous adjustment (Myerson et al., 2003). This procedure was repeated until the subject had made five choices at one specific delay, after which the subject began a new series of choices at another delay. For each trial in a block, the immediate amount represents the best guess as to the subjective value of the delayed reward. Therefore, the immediate amount that would have been presented on the sixth trial of a delay block was taken as the estimate of the subjective value of the delayed reward at that delay.

Self-report impulsivity scales

Participants were administered the Barratt Impulsiveness Scale (BIS-11) (Fossati et al., 2001), a 30-item self-report questionnaire evaluating everyday behaviors reflecting impulsivity on a 4-point Likert scale. The BIS-11 assesses 3 facets of impulsivity:

attentional impulsivity (AI sub- scale, e.g., “I am more interested in the present than the future”), motor impulsivity (MI subscale, e.g., “I do things without thinking”), and impulsive nonplanning (INP subscale, e.g., “I make up my mind quickly”). High BIS-11 scores indicate high levels of impulsivity.

Procedure

To ensure motivation across tasks, before starting the experiment, participants were invited to choose their favourite food and discount voucher among four alternatives, presented on the computer screen. Food alternatives included two sweet snacks (cookie and chocolate bar), and two salty snacks (cracker and breadstick). Discount voucher alternatives included discount vouchers for a museum tour, gym session, hairdresser/ barber session, and book purchase. The favorite food and discount vouchers were used as the reward for the food task and the discount voucher task, respectively.

Participants then underwent the three TD tasks. The tasks were administered separately, and the order of tasks was randomly determined across participants. Participants were told that, on each trial, two amounts of a hypothetical reward would appear on the screen. One could be received right now, and one could be received after a delay. They were informed that there were no correct or incorrect choices, and were required to indicate the option they preferred by pressing one of two buttons (Estle et al., 2007). Figure 2 illustrates the experimental paradigm. Each trial began with a 1 s fixation screen, followed by a screen depicting the two available options. The two options appeared on the left and right side of the screen, and clearly indicated the type of reward, the amount of reward, and the delay of delivery of the reward. After the participants made their choices, the nonpreferred option disappeared, whereas the preferred option remained on the screen for 1 s, with a triangle underneath it. The intertrial interval was 1.5 s.

Figure 2. Experimental paradigm. In each trial, after a 1 s fixation period, subjects chose between a small amount of reward delivered immediately and a larger amount of reward delivered after a delay. The preferred option remained highlighted for 1 s. Separate tasks involved different types of rewards, including money, discount vouchers, and food. All rewards used were hypo- thetical. The picture refers to a choice trial in the money task. See Materials and Methods for a more detailed explanation of procedures.

Data analysis

For each task, the rate at which the subjective value of a reward decays with delay (TD rate) was assessed through two indices: the TD parameter (k) (Mazur, 1987; Rachlin et al., 1991; Green and Myerson, 2004; Fellows and Farah, 2005), and the area under the empirical discounting curve (AUC) (Myerson et al., 2001).

Estimation of k. The hyperbolic function SV = 1/(1+*k*D), where SV = subjective value (expressed as a fraction of the delayed amount), and D = delay (in days), was fit to the data to determine the *k* constant of the best fitting TD function, using a nonlinear, least-squares algorithm (as implemented in Statistica; Statsoft). The larger the value of k, the steeper the discounting function, the more participants were inclined to choose small-immediate rewards over larger-delayed rewards. Subjective preferences were well characterized by hyperbolic functions across groups. There were not significant differences in R2 across participant groups in any of the tasks (money task: HC group = 0.72; mOFC group = 0.72; non-FC group = 0.68, F(2,33) = 0.11, p = 0.89; discount voucher task: HC group = 0.65; mOFC group = 0.70; non-FC group = 0.72, F(2,33) = 0.37, p = 0.68; food task: HC group = 0.71; mOFC group = 0.87; non-FC group = 0.80, F(2,33) = 1.74, p = 0.19).

For comparison purposes, we also assessed the fits to the data of an exponential discounting model. For each TD task, the exponential function $SV = e^{kD}$ was fit to the data to determine the *k* constant of the best fitting TD function. Although both the hyperbolic and the exponential functions fit the data well, the hyperbolic function fit better than the exponential across participant groups and reward types. We entered R2 scores as the dependent variable in an ANOVA with group (mOFC patients, non-FC patients, and HC) and model (hyperbolic, exponential) as factors, for each reward separately. For the money task, there was a significant effect of model (F(1,33) = 10.16, p = 0.003), such that the hyperbolic model fit better than the exponential model (0.71 vs. 0.64; p = 0.001), with no significant effect of group (p = 0.94) or group × model interaction (p = 0.91). Similar results were found for the discount voucher and food tasks. For the discount voucher task, there was a significant effect of model (F(1,33) = 5.83, p = 0.02), such that the hyperbolic model fit better than the exponential model (0.69 vs. 0.63; p = 0.01), with no significant effect of group (p = 0.62) or group × model inter- action (p = 0.61). As well, for the food task, there was a significant effect of model (F(1,33) = 4.43, p = 0.04), such that the hyperbolic model fit better than the exponential model (0.79 vs. 0.73; p = 0.02), with no significant effect of group (p = 0.11) or group × model interaction (p = 0.77). It is worth noting that the superiority of the hyperbolic over the exponential model in describing discounting behavior applied to healthy participants as well as patients with mOFC lesions.

This finding indicates that lesions to mOFC steepened the discounting function, but did not alter it in any other way (e.g., shape). Together with the lack of evidence for inconsistent preference in this patient population (see Results), this finding strongly suggests that mOFC patients' behavior was truly reflective of TD, and not poor task comprehension or idiosyncratic preferences. Given the superiority of the hyperbolic over the exponential model in describing discounting behavior, hyperbolic k values were adopted as measures of TD. The hyperbolic k constants were normally distributed after log-transformation (Kolmogorov–Smirnov $d < 0.14$, $p > 0.2$ in all cases), and therefore, comparisons were performed using parametric statistical tests.

Estimation of AUC. Although hyperbolic functions captured participants' TD behavior relatively well, we also obtained AUC as an additional index of TD rate that, unlike k, does not depend on theoretical models regarding the shape of the discounting function (Myerson et al., 2001; Johnson and Bickel, 2008). Briefly, delays and subjective values were first normalized. Delays were expressed as a proportion of the maximum delay (360 d), and subjective values were expressed as a proportion of the delayed amount (40 units). Delays and subjective values were then plotted as x and y coordinates, respectively, to construct a discounting curve. Vertical lines were drawn from each x value to the curve, subdividing the area under the curve into a series of trapezoids. The area of each trapezoid was calculated as $(x2 - x1)(y1 + y2)/2$, where x1 and x2 are successive delays, and y1 and y2 are the subjective values associated with these delays (Myerson et al., 2001). The AUC is the sum of the areas of all the trapezoids. The AUC varies between 0 and 1. The smaller the AUC, the steeper the TD, the more participants were inclined to choose small-immediate rewards over larger-delayed rewards. The AUC scores were normally distributed (Kolmogorov–Smirnov $d < 0.12$, $p > 0.2$ in all cases), and therefore, comparisons were performed using parametric statistical tests.

Results

Figure 3 shows TD curves by participant group and delay. The *k* value for each curve reflects the geometric mean of the group — which corresponds to mean of the log-transformed values — and thus provides a better measure of central tendency for positively skewed metrics, such as TD rates, than does the arithmetic mean. Figure 4 shows the AUC for each participant group and type of reward. As is evident, TD curves were steeper and the AUC was smaller in mOFC patients compared with non-FC patients and normal controls (HC), suggesting that mOFC patients had an increased tendency to discount future rewards compared with the control groups. For example, on average, 40 € delayed by 1 month were worth ~32 € now for normal controls, but only 12 € for mOFC patients (losing ~70% of their value). Figures 3 and 4 also highlight that TD of food was steeper than TD of money and discount vouchers across groups. These impressions were confirmed by ANOVA analyses.

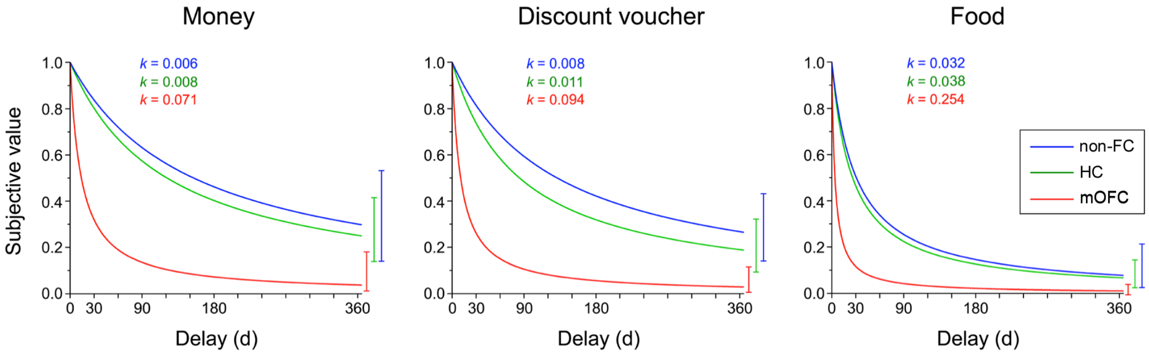

Figure 3. TD functions by participant group (mOFC, non-FC, HC) and type of reward. The hyperbolic curves describe the discounting of subjective value (expressed as a proportion of the delayed amount) as a function of time (days). The discounting parameter *k* reflects the geometric mean of the group (mean of the log-transformed values). Confidence intervals are 95% intervals.

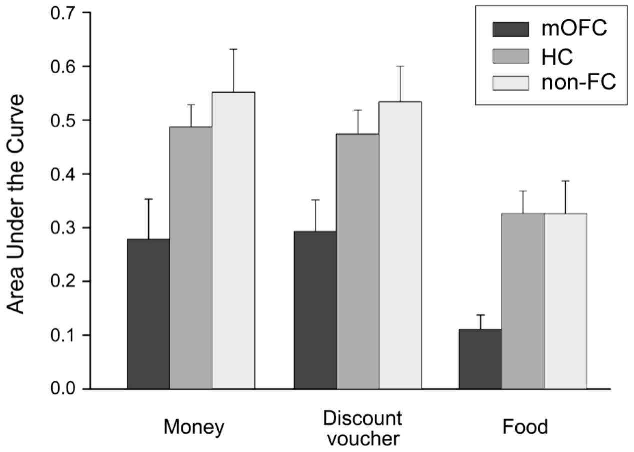

Figure 4. Area under the empirical discounting curve by participant group (mOFC, non-FC, HC) and type of reward. The error bars indicate the standard error of the mean.

k. An ANOVA on log-transformed *k* values with group (mOFC, non-FC, and HC) as a between-subject factor, and task (money, food, discount voucher) as a within-subject factor yielded a significant effect of group (F(2,33) = 8.56, p = 0.001). Post hoc comparisons, performed with the Newman–Keuls test, showed that TD was steeper in mOFC patients compared with non-FC patients (-0.92 vs. -1.93; p = 0.0006) and HC (-0.92 vs. -1.80; p = 0.0009), whereas no significant difference was detected between non-FC patients and HC (p = 0.61). Moreover, there was a significant effect of task (F(2,66) = 14.85, p = 0.000005), indicating that TD of food was steeper than TD of money (-1.16 vs. -1.80; p = 0.0001) and discount vouchers (-1.16 vs. -1.69; p = 0.0001), whereas no significant difference emerged between TD of money and discount vouchers (p = 0.30). There was no significant group × task interaction (p = 0.98). Group differences in TD were confirmed when the ANOVA was run on data from the money and discount voucher tasks only (see Appendix B), and using nonparametric tests (see Appendix B).

AUC. Similar results were obtained using AUC as the dependent variable. An

ANOVA on AUC scores with group and task as factors yielded a significant effect of group (F(2,33)= 5.90, $p = 0.006$).

Post hoc comparisons, performed with the Newman–Keuls test, showed that AUC was smaller (i.e., TD was steeper) in mOFC patients compared with non-FC patients (0.22 vs. 0.47; $p = 0.003$) and HC (0.22 vs. 0.42; $p = 0.01$), whereas no significant difference was detected between non-FC and HC ($p = 0.54$). There was a significant effect of task (F(2,66) = 16.86, $p = 0.000001$), indicating steeper TD of food than money (0.25 vs. 0.44; $p = 0.0001$) and discount vouchers (0.25 vs. 0.43; $p = 0.0001$), with no significant difference between TD of money and discount vouchers ($p = 0.86$). No significant group × task interaction emerged ($p = 0.91$). Group differences in TD were confirmed when the ANOVA was run on data from the money and discount voucher tasks only (see Appendix B), and using nonparametric tests (see Appendix B).

TD and mOFC. We investigated whether TD rate in mOFC patients correlated with lesion volume. As anticipated, brain lesions in mOFC patients overlapped maximally in BAs 11, 10, and 32. By using partial correlation analyses, we investigated the relation between AUC scores and lesion volume in each of the three BAs, partialing out the effect of lesion volume in the other two BAs. We found that lesion volume in BA 11 correlated significantly with AUC scores for money ($r = -0.91$; $p = 0.01$, two-tailed; Fig. 5), and, marginally, with AUC scores for food ($r = -0.83$; $p = 0.056$, two-tailed) and discount vouchers ($r = -0.78$; $p = 0.08$, two- tailed): the larger the lesion in BA 11, the steeper the TD. We also observed a marginal correlation between lesion volume in BA 32 and AUC scores for money ($r = -0.81$; $p = 0.07$, two-tailed). No other correlations were significant ($p > 0.15$ in all cases). Although these results should be taken with caution due to the small sample size, they suggest that BA 11 of mOFC may play a privileged role in governing TD across types of reward.

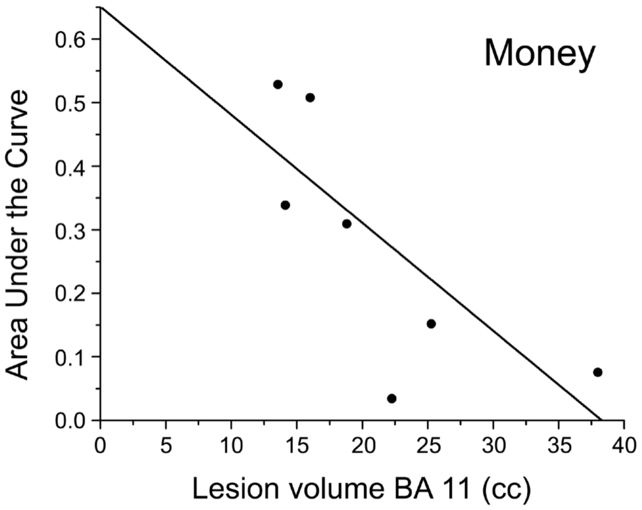

Figure 5. Scatter plot of the correlation between lesion volume in BA 11 and degree of TD for money (AUC scores).

Self-reports of impulsivity. mOFC patients' self-reports did not reflect significantly higher levels of impulsivity than those of non-FC patients and healthy controls [F(2,33) = 2.18, p = 0.13]. Separate analysis on scores from the three subscales of the BIS-11 also failed to yield statistically significant group differences [AI subscale: F(2,33) = 1.91, p = 0.16; INP subscale: F(2,33) = 2.85, p = 0.08; MI subscale: F(2,33) = 2.64, p = 0.09], although the results trended toward more impulsive nonplanning and motor impulsivity in mOFC patients than in controls. This finding was surprising in light of mOFC patients' poor valuation of the future in the TD tasks. It is important to note, however, that self-reports assess awareness of a behavior, which may dissociate from more objective measures of the same behavior (Schooler, 2002), especially in patients with damage to vmPFC regions (Ciaramelli and Ghetti, 2007; Modirrousta and Fellows, 2008), who may lack self-insight (Barrash et al., 2000; Beer et al., 2006). mOFC patients, therefore, may have had problems introspecting on their impulsive behaviors.

The results indicate that mOFC patients discounted delayed rewards more steeply than normal controls. Crucially, large TD rates were not a general consequence of brain damage. Patients with lesions outside the frontal lobe, indeed, did not exhibit TD rates different from normal controls. These findings argue for a necessary role of mOFC for valuation of future rewards. Before discussing these results further, it is important to rule out the possibility that differences in TD rates between mOFC patients and control groups depended on factors other than TD, such as poor comprehension of the task, or the presence of inconsistent preferences in mOFC patients. The fact that hyperbolic functions described TD behavior equally well in mOFC patients and control groups, and better than did exponential functions, argues against this possibility: mOFC patients' TD behavior obeyed the typical (hyperbolic) curves, though reflecting a reliable increase in the parameter k. As a more direct (and model-free) test for the ability to perform the task, we counted the number of inconsistent preferences participants had evinced. By definition, TD behavior should result in a monotonic decrease of the subjective value of the future outcome with delay (Johnson and Bickel, 2008). That is, if R1 is the subjective value of a reward R delivered at delay t1, R2 is the subjective value of R delivered at delay t2, and $t2 > t1$, then it is expected that $R2 < R1$. As a consequence, subjects exhibit inconsistent preference when the subjective value of the future outcome at a given delay is greater than that at the preceding delay, i.e., $R2 > R1$ (Johnson and Bickel, 2008). To allow variability in the data, we considered as indicative of inconsistent preferences only those data points in which the subjective value of a reward overcame that at the preceding delay by a value of >10% of the future outcome, i.e., $R2 > R1 + R/10$, as recommended by Johnson and Bickel (2008).

The mean number of inconsistent preferences was small, and comparable across participant groups [money task: HC, 0.40; mOFC, 0.57; non-FC, 0.44, F(2,33) = 0.15, p = 0.86; discount voucher task: HC, 0.75; mOFC, 0.42; non-FC, 0.55, F(2,33) = 0.57; p = 0.56; food task: HC: 0.55; mOFC: 0.57; non-FC: 0.33, F(2,33) = 0.33; p = 0.71]. This held even if all deviations from a monotonically decreasing function were counted as inconsistent preferences, regardless of their magnitude, i.e., R2 > R1 (see Appendix B). Moreover, no participant in any group followed a response heuristic, such as always selecting the larger-delayed amount or the smaller-immediate amount across delay and reward conditions, regardless of the options at stake. Together, the findings that lesion to mOFC did not result in changes to the shape of the discounting function aside from its steepness, inconsistent preferences, or response heuristics, strongly suggest that mOFC patients' behavior was indeed reflective of increased TD, and not poor task comprehension or idiosyncratic preferences.

One further aspect of the present study deserves attention. Participants did not receive the actual consequences of their choices, but instead made choices about hypothetical rewards. Hypothetical outcomes have the advantage of allowing the use of reward amounts and delays that are large enough to be meaningful to participants, which are generally infeasible in studies involving real outcomes (Frederick et al., 2002; Jimura et al., 2009). Hypothetical outcomes, on the other hand, have the disadvantage that people may not be motivated to, or capable of, accurately predicting what they would do if outcomes were real (Frederick et al., 2002; Jimura et al., 2009). For this reason, although there is, as of yet, no evidence that hypothetical rewards are discounted differently from real rewards, either in terms of the degree of TD (Johnson and Bickel, 2002), the shape of TD curves (Kirby and Herrnstein, 1995; Kirby and Marakovic, 1995; Johnson and Bickel, 2002), or the neural bases of TD (Bickel et al., 2009), we conducted a corollary investigation of TD for money in mOFC patients and healthy controls using real rewards. We confirmed our results: mOFC patients discounted real monetary rewards more steeply than controls (see Appendix B).

Discussion

The present study investigated the role of mOFC in intertemporal choice. Patients with lesions in the mOFC, control patients with lesions outside the frontal lobe, and healthy individuals made a series of hypothetical choices between small-immediate rewards and larger-delayed rewards. Since decisions about money are not necessarily representative of all decisions, and to examine the role of the mOFC across a wide range of contexts, we varied the type of outcome, which included both primary (food) and secondary (money and discount vouchers) rewards. The study yielded two main findings. Lesions to the mOFC increased significantly the preference for small-immediate over larger-delayed rewards, resulting in steeper TD of future rewards in mOFC patients compared with the control groups. This finding held for both primary and secondary rewards. Damage to the mOFC, however, did not alter the normal tendency to discount different types of rewards at different rates, such that food was discounted more steeply than money and discount vouchers across groups.

Our primary finding that damage to mOFC caused steep TD of future outcomes is consistent with a large body of literature. Single-neuron studies of OFC (Roesch et al., 2006) in rodents show that neural response to reward is affected by the delay preceding its delivery. Moreover, disruption of the OFC in animals affects discounting of future rewards (Mobini et al., 2002; Cardinal et al., 2004; Winstanley et al., 2004; Rudebeck et al., 2006).

In humans, fMRI studies have detected consistent activation of mOFC and adjacent mPFC during intertemporal choice (McClure et al., 2004, 2007; Kable and Glimcher, 2007). Our results confirm and extend previous evidence by providing, for the first time, evidence for a necessary role of mOFC in valuing delayed outcomes in humans.

Although fMRI studies have reported wide activation of vmPFC areas during TD tasks, there may be heterogeneity in the causal involvement of different regions within vmPFC in TD behavior. As extensively reported in Part I of this dissertation, a previous neuropsychological study in patients with lesions to vmPFC, overlapping maximally in mPFC with some patients having spared OFC, found no deficit in TD (Fellows and Farah, 2005). Together with our findings, this null effect raises the possibility that mOFC, but not mPFC, is necessary for normal discounting behavior. Consistent with this proposal, ablation studies in animals have found that lesions in the OFC, but not mPFC, affect reward-based decision-making (Noonan et al., 2010) and increase delay discounting (Rudebeck et al., 2006). Moreover, in our study, lesion volume in BA 11 of mOFC showed the strongest association with behavior. This proposal, of course, will need to be tested empirically in future studies.

The present results have important implications for current neurobiological models of intertemporal choice. According to the ß-∂ model (McClure et al., 2004, 2007), limbic areas, including the mOFC, VS, and PCC, form an impulsive (ß) system that places special weight on immediate rewards, whereas a more providential cognitive (∂) system, based in the lateral prefrontal cortex and posterior parietal cortex, is more engaged in patient choices. During intertemporal choice, activation of the ß system would favor the immediate option, whereas activation of the ∂ system would favor the delayed option (McClure et al., 2004). Our finding that damage to the mOFC increases impatient choices is not in line with the hypothesis that mOFC acts as a neuroanatomical correlate of the impulsive system (McClure et al., 2004). Were this the case, lesions to mOFC should lead to a weakening of the ß system relative to the ∂ system, and, consequently, more patient choices.

Our results can be understood in the context of an alternative model of intertemporal choice (Kable and Glimcher, 2007, 2010; Peters and Büchel, 2009; see also the general discussion of this dissertation), according to which a unitary system, encompassing mOFC and adjacent mPFC, VS, and PCC, represents the value of both immediate and delayed rewards, and is subject to top-down control by lateral prefrontal cortex (Hare et al., 2009; Figner et al., 2010). Within this network, the mOFC is thought to signal the subjective value of expected outcomes during choice (Rudebeck et al., 2006; Schoenbaum et al., 2006, 2009; Murray et al., 2007; Rushworth et al., 2007; Talmi et al., 2009), by integrating different kinds of information and concerns (e.g., magnitude, delays) into a common 'neural currency' (Montague and Berns, 2002).

Though generally more impulsive than controls, mOFC patients retained the same tendency of the controls to discount food more steeply than money and discount vouchers. This finding confirms previous evidence that TD depends strongly on reward type (McClure et al., 2007): Delayed monetary rewards are discounted less steeply than directly consumable rewards (Odum and Rainaud, 2003; Estle et al., 2007; Rosati et al., 2007; Charlton and Fantino, 2008). Why this difference occurs is not entirely clear. People may discount delayed money less steeply than consumable rewards because money can be stored, exchanged for other primary and secondary reinforcers (Catania, 1998), and retains its utility despite fluctuations of desire and changes in the internal state of the organism. In the present study, the interpretation of differences in TD for primary versus secondary rewards is complicated by the fact that delays and amounts used, though comparable to those used in previous research (Odum and Rainaud, 2003; Estle et al., 2007; Charlton and Fantino, 2008), may have been more suited for the assessment of TD for money than for food (Jimura et al., 2009). For example, 40 chocolate bars may reach saturation and may therefore be less appetitive than 40 units of money.

Our finding that mOFC patients discounted all types of reward more steeply than controls, and that differences in TD rates between mOFC patients and controls were not modulated by the type of reward, is important in many respects. First, it reinforces the suggestion that the role of the mOFC during valuation and choice is generalized across a wide range of stimuli and contexts, ranging from primary to secondary rewards (Chib et al., 2009; FitzGerald et al., 2009; Hare et al., 2010). Second, it is consistent with the hypothesis that the mOFC is necessary to encode the prospective value of available goods to choose between them (Padoa-Schioppa and Assad, 2006), but not to encode the incentive value of a stimulus per se, regardless of whether an economic choice is required (for review, see O'Doherty, 2004). Indeed, in experiments that compared conditions in which subjects did or did not make a choice, mOFC was significantly more active in the choice condition (Arana et al., 2003). By contrast, neural responses in the amygdala were related to incentive value, and independent of behavioral choice. Finally, the preserved effect of reward type on TD after mOFC lesion rules out the possibility that increased choosing of smaller-immediate rewards in mOFC patients simply resulted from poor motor impulse control (Bechara and Van Der Linden, 2005): mOFC patients in the money task faced a situation identical to that in the food task, yet showed increased willingness to wait for a larger reward.

In conclusion, we have shown, for the first time in humans, that damage to mOFC causes abnormally steep TD of delayed rewards, indicating that mOFC is necessary for optimal weighting of future outcomes during intertemporal choice. mOFC may be crucial to form vivid representations of future outcomes, capable of competing with immediate ones, or to incorporate top-down signals promoting resistance to immediate gratification in the valuation process, ultimately extending the reach of humans' choices into the future. We will further discuss these findings at the end of this dissertation taking into account lesional evidence on insular damaged patients (Study II-Part II, Sellitto et al., under submission), preliminary imaging results (Study III-Part III) and all behavioral findings reported in Part III of this thesis.

Study II – Insular damage increases willingness to wait in intertemporal choice

[This data are under submission in Sellitto et al.]

Introduction

As outlined before (see Part I and Study I-Part II; Sellitto et al., 2010, 2011), the extant cognitive neuroscience evidence show that limbic structures, including the mOFC and the VS, and the dorsolateral prefrontal cortex, are core areas of the valuation and the control network, respectively (Rangel et al., 2008; Hare et al., 2009; Figner et al., 2010; Sellitto et al., 2010, 2011), governing intertemporal choice.

Emotions and drive states (e.g., hunger, drug craving) influence choice markedly (Bechara and Damasio, 2005; see also Part I). By signaling the current needs of the body, such inputs influence the valuation of different goods. For example, bodily signals may convey the urge to obtain a reward soon, overwhelming attempts to implement far-sighted decisions (Loewenstein, 1996; Camerer et al., 2004). Consistently, TD is elevated when people are hungry or tired, so that emotional responses promoting impulsivity are maximal (van Boven and Loewenstein, 2003).

The insula plays a critical role in emotion (Bechara, 2005; Craig, 2009). It has been proposed that the insula mediates the conscious representation of bodily states, and the anticipation of the bodily effects of emotional events (Rolls, 1999; Craig, 2009; Damasio et al., 2000). As such, the insula may play a critical role in TD, influencing participants' valuation of rewards available at different times. Functional neuroimaging (fMRI) studies have shown that insula activity modulates according to the time availability of rewards.

Increased insula activity, however, has been reported in association with both delayed (Wittmann et al., 2007; Claus et al., 2011; Kayser et al., 2012) and immediate rewards (Tanaka et al., 2004; McClure et al., 2007; Wittmann et al., 2010), and therefore its role in TD is unclear. To overcome this limitation, we used a lesion approach.

Patients with lesion to the insula (Insular patients), control patients with lesions outside the insula, and healthy participants chose between smaller-sooner rewards and larger-later rewards. Participants were tested in two conditions: in one, the earlier quantity of money was delivered immediately, whereas in the other it was delayed by 60 days (Kable and Glimcher, 2010). If the insula is necessary to represent the emotional/bodily states associated with sooner and later rewards, Insular patients' choices should be relatively devoid of emotion, and governed by a heuristic of quantity, making patients more willing to wait to larger-later rewards than controls (reduced TD). This tendency could be even more pronounced when a reward is available immediately, maximizing the involvement of emotion on choice.

Materials and Methods

Participants

Participants included 25 patients with brain damage and 30 healthy individuals (see Table 1 for demographic and clinical information). Patients were recruited at the Centre for Studies and Research in Cognitive Neuroscience, Cesena, Italy, and at the Spedali Civili of Brescia, Italy. They were selected on the basis of the location of their lesion evident on magnetic resonance imaging (MRI) or computerized tomography (CT) scans, and divided into two groups based on their lesion location.

	Sex (M/F)	Age (years)	Education (years)	BDI-II	MMSE	DS	CRM	Lesion volume (cc.)
Insular (n=12)	5/7	60.6 (14)	10.5 (4.9)	10.6 (8.7)	25.1 (2)	5 (1.2)	28.8 (4.6)	33.3 (23.5)
Non-insular (n=13)	7/6	59 (12.7)	10.1 (3.8)	10 (7.1)	25.6 (1.6)	5.8 (1.3)	25.5 (3.1)	25.4 (11.7)
HC (n=30)	15/15	63 (10.9)	8.5 (3.2)	10.2 (7.3)	27 (1.4)	5.5 (0.8)	-	-

Table 1. Participant groups' demographic and clinical data. Insular = patients with lesions in the insular cortex; Non-insular = patients with lesions outside the insula; HC = healthy controls; F = female; M = male; MMSE = Mini Mental State Examination (corrected score); CRM = Coloured Raven Matrices (corrected score); DS = digit span forward (corrected score); BDI-II = Beck Depression Inventory scale. The values in parentheses are standard deviations.

Twelve patients (5 females) had lesions involving the insular cortex, hidden in the lateral sulcus, covered by frontal, temporal, and parietal opercula, as well as surrounding grey and white matter (Fig. 1). Since lesions predominantly involved the insular cortex (see Lesion analysis), we henceforth refer to this group as "Insular patients". Lesions were caused by an ischemic or hemorrhagic stroke of the middle cerebral artery (MCA) and were unilateral in all cases (left hemisphere: 8 cases, right hemisphere: 4 cases). Thirteen patients (7 females) had brain damage that spared the insular cortex in both hemispheres. We henceforth refer to this group as "Non-insular patients". Lesions were caused by ischemic or hemorrhagic stroke (9 cases) or tumor resection (4 cases), were unilateral in all cases (left hemisphere: 7 cases, right hemisphere: 6 cases), and mainly involved the occipital cortex, the temporal cortex, and the superior frontal cortex. In no case did patients' lesions involve the mOFC. There was no significant difference in lesion volume between Insular patients and Non-insular patients (33.33 vs. 25.36 cc.; p = 0.29).

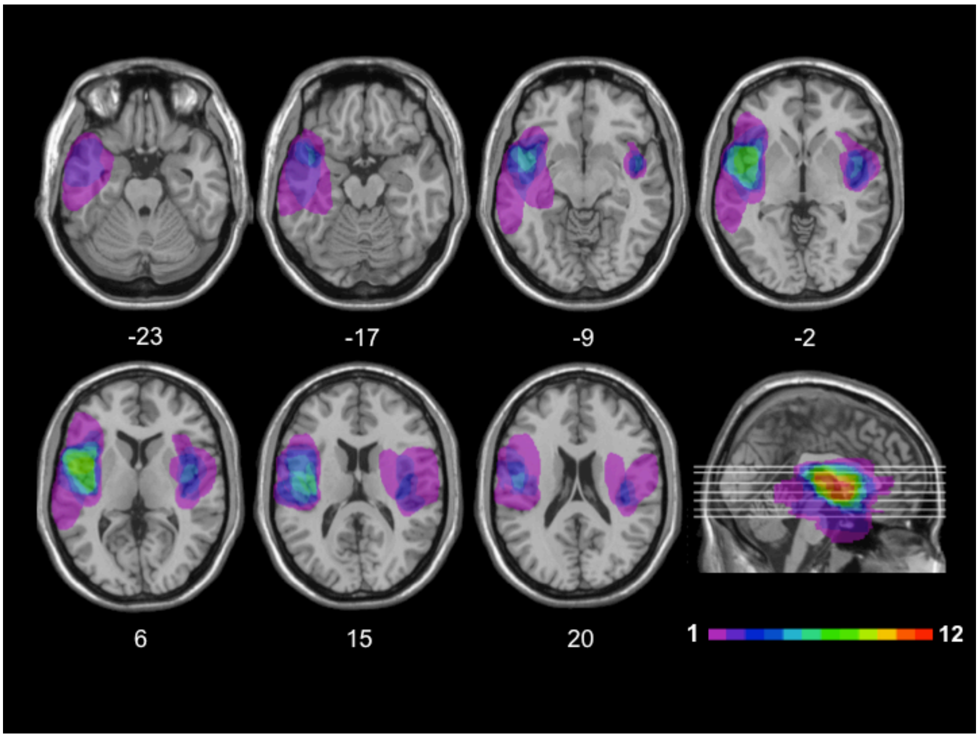

Figure 1. Location and overlap of brain lesions. The panel shows the lesions of the Insular patients projected on the same seven axial slices and on the mesial view of the standard Montreal Neurological Institute brain. The level of the axial slices has been marked by white horizontal lines on the mesial view of the brain. z-coordinates of each axial slice are given. The colour bar indicates the number of overlapping lesions. In each axial slice, the left hemisphere is on the left side.

All patients were in the chronic phase of recovery (at least 12 months post onset), were not receiving psychoactive drugs, and had no other diagnosis likely to affect cognition or interfere with the participation in the study (e.g., significant psychiatric disease, alcohol abuse, history of cerebrovascular disease). Patients' general cognitive functioning was generally preserved, as indicated by the scores they obtained in the Mini-Mental State Examination (MMSE, Folstein et al., 1975), the digit span forward test (DS), and the Colored Raven Matrices (CRM), which were within the normal range in all cases (Spinnler and Tognoni, 1987) (Table 1). In addition, left-damaged patients had no aphasia documented, and right-damaged patients had no hemispatial neglect documented.

The healthy control group comprised 30 individuals (15 females) matched to the patients on demographic ground, including mean age, gender, and level of education. Control participants were not taking psychoactive drugs, and were free of current or past psychiatric or neurological illness as determined by history.

All participants gave informed consent, according to the Declaration of Helsinki (International Committee of Medical Journal Editors, 1991) and the Ethical Committee of the Department of Psychology, University of Bologna.

Lesion analysis

Individual lesions extent and location were documented by using the most recent clinical CT or MRI. Lesions were traced by a neurologist expert in image analysis on the T1-weighted template MRI scan from the Montreal Neurological Institute provided with the MRIcron software (Rorden and Brett, 2000). This scan is normalized to Talairach space and is a widely used template for normalization in functional brain imaging (e.g., Moretti et al., 2009). Lesions' location was identified by loading the lesion drawings onto the Brodmann template provided with MRIcron, and the Automated Anatomical Labeling template (AAL, Tzourio-Mazoyer et al., 2002).

Figure 1 shows the extent and overlap of brain lesions in Insular patients. As is evident, although all patients had damage that included the insula, areas adjacent to the insula that are within the MCA blood supply territories were damaged to some degree as well. This included parts of the somatosensory cortex, the basal ganglia (e.g., caudate, putamen), the temporal lobe (especially the superior portions), the dorsolateral and/or ventrolateral prefrontal cortex, the inferior parietal lobule, the occipito-parietal junction, and the dorsomedial sectors of the occipital lobe. Lesions of Insular patients overlapped maximally in BA 20 (M = 7.0 cc., SD =11.0 cc.), BA 21 (M = 2.7 cc., SD =5.5 cc.), BA 38 (M = 2.1 cc., SD = 2.7 cc.), and BA 22 (M = 1.3 cc., SD = 2.2 cc.), as well as not numbered areas (M = 18.1 cc., SD = 6.4 cc.). Since the insular cortex is part of the areas with no Brodmann label (e.g., Kurth et al., 2010), we calculated maximal overlap location also using the AAL template. This included the left (M = 6.6 cc., SD = 2.7 cc.) and the right (M = 6.5 cc., SD = 1.3 cc.) insula, as well as the temporal lobe bilaterally [pole (M = 1.9 cc., SD = 2.4 cc.); superior portions (M = 5.2 cc., SD = 3.3 cc.)].

Temporal discounting tasks

In a computerized TD task, participants chose hypothetically between an amount of reward that could be received sooner and an amount of reward that could be received later (e.g., Kirby and Herrnstein, 1995; Myerson et al., 2003; Figner et al., 2010; Sellitto et al., 2010). Two temporal conditions were included. In the Now condition, participants made a series of choices between a smaller amount of money (in €) that could be received immediately (now), and 40 € that could be obtained after a variable delay. In the Not-now condition, choices involved a smaller amount of money that could be received in 60 days, and 40 € that could be delivered after a variable delay larger than 60 days, while maintaining the same temporal gaps between earlier and later rewards as in the Now condition. Thus, in the Now condition participants made five choices at each of six delays: 2, 14, 30, 90, 180, and 365 days, whereas in the Not-now condition the delays were 62, 74, 90, 150, 240, and 425 days.

Within each block of five choices, the amount of the sooner reward was adjusted based on the participant's previous choice, using a staircase procedure that converged on the amount of the sooner reward that was equal, in subjective value, to the later reward. The first choice was between a later amount of 40 € and a sooner amount of 20 €. If the sooner reward was chosen, then the amount of the sooner reward was decreased on the next trial; if the later reward was chosen, then the amount of the sooner reward was increased on the next trial. The size of the adjustment in the sooner reward decreased with successive choices: the first adjustment was half of the difference between the sooner and the later reward, whereas for subsequent choices it was half of the previous adjustment (Myerson et al., 2003). This procedure was repeated until the subject had made five choices at one specific delay, after which the subject began a new series of choices at another delay/temporal condition. For each trial in a block, the sooner amount represented the best guess as to the subjective value of the later reward. Therefore, the sooner amount that would have been presented on the sixth trial of a delay block was taken as the estimate of the subjective value of the later reward at that delay.

Moreover, two control conditions were included. In one, subjects made five choices between 40 € and a smaller amount of money, both available immediately. In the other, participants made five choices between 40 € and a smaller amount of money, both available in 365 days. The amount of the sooner option of the two control conditions was adjusted based on the staircase procedure described above. Both patients and healthy subjects always chose the larger reward in the two control conditions, suggesting adequate comprehension of the task as well as adequate sensitivity to reward.

The blocks of choices pertaining to the two temporal and control conditions were interspersed, and the order of blocks of choices relative to different delays of both temporal conditions was randomized for each participant.

Participants did not receive the actual consequences of their choices, but instead made choices about hypothetical rewards. While using hypothetical rewards has both advantages and disadvantages, there is no evidence that hypothetical rewards are discounted differently from real rewards, either in terms of the degree, shape, and neural bases of TD (Johnson and Bickel, 2002; Bickel et al., 2009). Moreover, in a previous work, we confirmed our results on hypothetical rewards using real rewards (Sellitto et al., 2010).

Self-report depression scale

Given that the insular cortex has been implicated in depression (e.g., Takahashi et al., 2010; Sprengelmeyer et al., 2011), participants in the present experiment were administered the Beck Depression Inventory-II (BDI-II, Beck et al., 1996; Ghisi et al., 2006), a 21-item self-report questionnaire evaluating the presence and the severity of several aspects of depression symptoms. The BDI-II assesses, on a 4-point Likert scale, two components of depression: the affective component (AC subscale, e.g., “I do not expect things to work out for me”), and the somatic component (SC subscale, e.g., “I have less energy than I used to have”) (e.g., Steer et al., 1999). A total score between 0 and 13 indicates minimal depression, 14-19 indicates mild depression, 20-28 indicates moderate depression, and 29-63 indicates severe depression.

Procedures

Before the beginning of the experimental session, participants were told that, on each trial, two hypothetical amounts of money would appear on the screen. One could be received sooner, and one could be received later. They were informed that there were no correct or incorrect choices, and were required to indicate the option they preferred by pressing one of two buttons (Sellitto et al., 2010).

The experimental paradigm is shown in Figure 2. Each trial began with a 1 sec fixation screen, followed by a screen depicting the two available options. The two options appeared on the left and right side of the screen, indicating the amount and the delay of delivery of the reward. After the participants made their decisions, the non-chosen option disappeared, whereas the preferred option remained on the screen for 1 sec, with a triangle underneath it. The inter-trial interval was 1.5 sec.

Once the TD task was over, participants were administered the BDI-II.

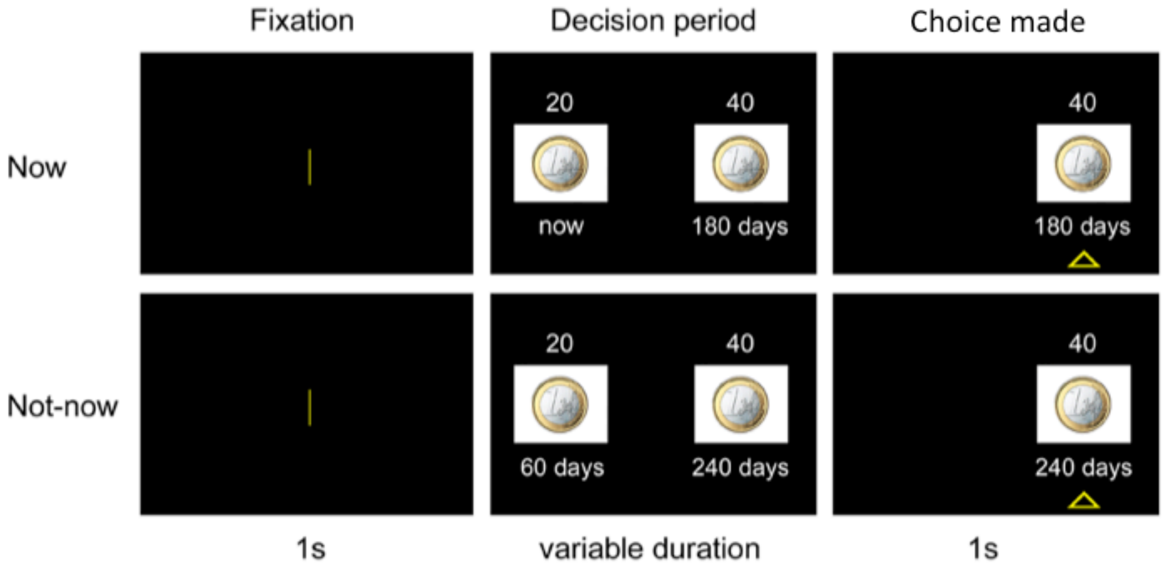

Figure 2. Experimental paradigm. In each trial, after a 1 s fixation period, subjects chose between a small amount of money delivered sooner and a larger amount of reward delivered after a delay. The preferred option remained highlighted for 1 s. Upper panel, a trial for the Now temporal condition is shown, in which the sooner option is available immediately (‘now’). On the bottom, a trial for the Not-now temporal condition is shown, in which a fixed delay of 60 days was added to both options in the Now condition. See Materials and Methods for a more detailed explanation of procedures.

Data analysis

For each task, the rate at which the subjective value of a reward decays with delay (TD rate) was assessed through the same two indices used in Sellitto and colleagues (2010;

Study I-Part II): the temporal discounting parameter (*k*) (Mazur, 1987; Rachlin et al., 1991; Green and Myerson, 2004), and the area under the empirical discounting curve (AUC) (Myerson et al., 2001).

Estimation of k. For the estimation of *k* see Study I-Part II. Subjective preferences were well characterized by hyperbolic functions, as indexed by high R^2 across participant groups and temporal conditions ($R^2 > 0.61$ in all cases). For comparison purposes, we also assessed the fits to the data of an exponential discounting model. For each TD task, the exponential function $SV = e^{-kD}$ was fit to the data to determine the *k* constant of the best fitting function. The hyperbolic function proved to fit the data better than the exponential functions across participant groups and temporal conditions. We entered R^2 scores as the dependent variable in an analysis of variance (ANOVA) with Group (Insular patients, Non-insular patients, healthy controls) as a between-subject factor, and Model (hyperbolic, exponential) and Temporal condition (Now, Not-now) as within-subject factors. There was a significant effect of Model [$F(1, 52) = 22.95$, $p = 0.00001$]. Post hoc comparisons, performed with the Fisher test, showed that R^2 values were significantly higher for the hyperbolic than the exponential model (0.73 vs. 0.70, $p = 0.000003$). No other effects were significant ($p > 0.12$ in all cases). Given the superiority of the hyperbolic over the exponential model in describing TD behavior, hyperbolic *k* values were adopted as measures of TD. The hyperbolic *k* constants were normally distributed after log-transformation (Kolmogorov-Smirnov $d < 0.09$, $p > 0.20$ in all cases), and therefore comparisons were performed using parametric statistical tests.

Estimation of AUC. For estimation of AUC see Study I-Part II. The AUC scores were normally distributed (Kolmogorov-Smirnov $d < 0.10$, $p > 0.20$ in all cases), and therefore comparisons were performed using parametric statistical tests.

Voxel-based Lesion-Symptom Mapping

Standard groupwise comparisons were supplemented with a VLSM analysis oriented at investigating the relation between brain damage and behavior on a voxel-by-voxel basis. VLSM allows lesion-behavior associations to be tested without assigning patients to arbitrary groups. In this method, a behavioral measure is entered as the dependent variable, and the lesion status of each voxel (lesioned or not) is the independent variable. Then, for each voxel, statistical comparisons are made between the performance of subjects with vs. without lesions affecting that voxel. The output is a statistical map indicating voxels associated with poor performance when lesioned (Bates et al. 2003).

We entered patients' TD scores (*k* and AUC) in the Non-Parametric Mapping software (NPM, Rorden et al., 2007), separately for the Now and Not-now condition. The software compares performance of patients with vs. without damage at each voxel using the nonparametric Brunner-Munzel (BM) rank-order test (Brunner and Munzel, 2000). Only voxels affected in at least 20% of cases were included for the analysis. The alpha level of significance was set at $p < 0.05$, corrected for False Discovery Rate (FTD; Nichols and Hayasaka, 2003), and an extent threshold of 50 voxels per cluster was adopted (see also Gläscher et al., 2010).

Results

Figure 3 shows TD curves by participant group and temporal condition. The *k* value for each curve reflects the geometric mean of the group − which corresponds to the mean of the log-transformed values − and thus provides a better measure of central tendency for positively skewed metrics, such as TD rates, than do the arithmetic mean. Figure 4 shows the AUC for each participant group and temporal condition. As is evident from the figures, Insular patients discounted future rewards less steeply than the control groups. For example, the delay at which 40 € decreased to 50% of their original value (so that they were worth 20 € now) was about 33 days for normal controls, but 100 days for patients. These impressions were confirmed by ANOVA analyses.

k. An ANOVA on log-transformed *k* values with Group (Insular patients, Non-insular patients, healthy controls) as a between-subject factor, and Temporal condition (Now, Not-now) as a within-subject factor yielded a significant effect of Group [F(2, 52) = 6.96, p = 0.002]. Post hoc comparisons, performed with the Fisher test, showed that TD was less steep in Insular patients compared to Non-insular patients (-2.12 vs. -1.46; p = 0.0009) and healthy controls (-2.12 vs. -1.62; p = 0.003), whereas no significant difference was detected between Non-insular patients and healthy controls (p = 0.30). Moreover, there was a significant effect of Temporal condition [F(1, 52) = 31.48, p = 0.000001], indicating that TD was generally steeper in the Now compared to the Not-now condition (-1.52 vs. -1.86; p = 0.000001). There was no significant Group X Temporal condition interaction [F(2, 52) = 1.89, p = 0.16].

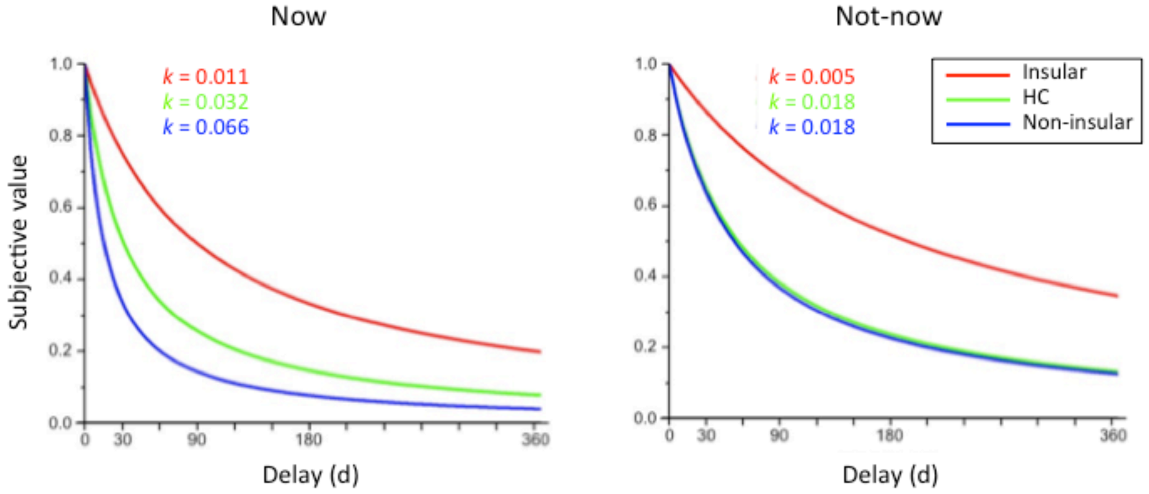

Figure 3. Temporal discounting functions by participant group (Insular = patients with lesions in the insular cortex; Non-insular = patients with lesions outside the insular cortex; HC = healthy controls) and type of temporal condition. The hyperbolic curves describe the discounting of subjective value (expressed as a proportion of the delayed amount) as a function of time (days). The discounting parameter *k* reflects the geometric mean of the group.

AUC. Similar results were obtained using AUC as the dependent variable. An ANOVA on AUC scores with Group and Temporal condition as factors yielded a significant effect of Group [F(2, 52) = 5.95, p = 0.005]. Fisher post hoc comparisons showed that AUC was larger (i.e., TD was slower) in Insular patients compared to Non-insular patients (0.49 vs. 0.28; p = 0.003) and healthy controls (0.49 vs. 0.32; p = 0.003), with no difference between the latter two groups (p = 0.56). Again, there was a significant effect of Temporal condition [F(1, 52) = 14.86, p = 0.0003], indicating smaller AUCs in the Now condition than in the Not-now condition (0.31 vs. 0.38; p = 0.0009), but no significant Group X Temporal condition interaction [F(2, 52) = 1.41, p = 0.25].

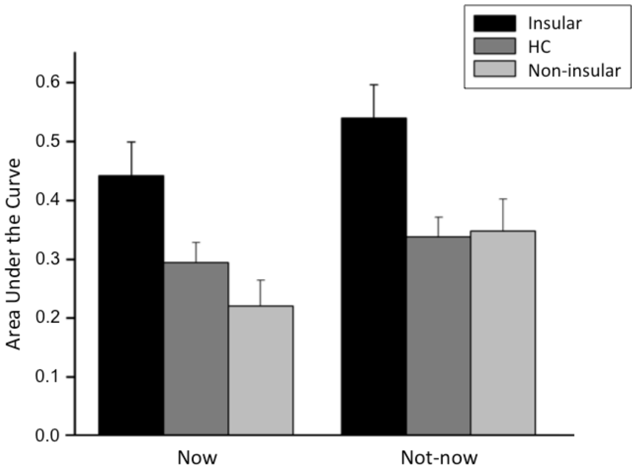

Figure 4. Area under the empirical discounting curve by participant group (Insular = patients with lesions in the insular cortex; Non-insular = patients with lesions outside the insular cortex; HC = healthy controls) and type of temporal condition. The error bars indicate the standard error of the mean.

VLSM. To investigate the relation between TD deficits and specific brain lesions, we performed a VLSM analysis. The VLSM analysis related patients' *k* rates and AUC values for the Now and Not-now conditions (in separate analyses) to their brain lesions. Figure 5 shows the statistical power map, indicating the voxels where we had adequate power to detect effects with a 5% FDR threshold (Rorden et al., 2007; Gläscher et al., 2010). The brain regions associated with reduced TD, along with the coordinates of their center of mass, based on the Montreal Neurological Institute (MNI) brain atlas, are listed in Table 2 and shown in Figure 6.

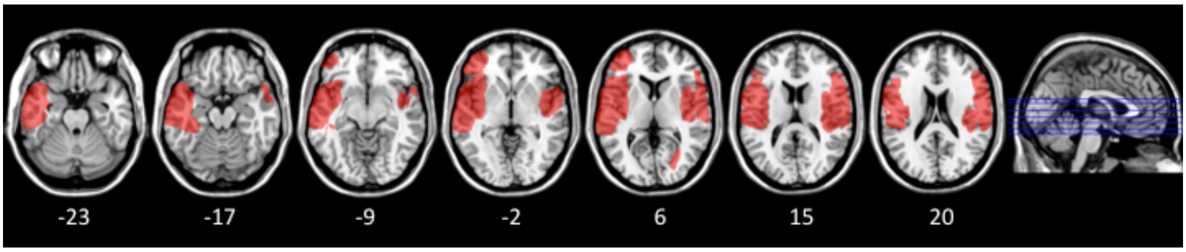

Figure 5. Statistical power map. Map showing the voxels (in red) where there is sufficient statistical power to detect an effect in this group of patients, overlaid on the MNI brain. In each axial slice, the left hemisphere is on the left side.

	Hemisphere	*x*	*y*	*z*	Cluster size (voxel)	BA	Max
K							
Now condition							
Insula	Right	44	8	-10	4596	-	2.67
Insula	Left	-37	6	9	295	-	2.30
Temporal Superior	Left	-63	3	-3	128	48	2.09
Temporal Medial	Left	-51	-34	-15	97	20	2.05
Temporal Inferior	Left	-50	-35	-24	276	20	2.04
Insula	Left	-34	21	6	333	48	1.96
Rolandic Operculum	Left	-40	-19	14	61	48	1.93
Insula	Left	-36	18	-9	133	47	1.80
K							
Not-now condition							
Insula	Right	41	8	-10	122	48	2.67
Fusiform Gyrus	Left	-38	-15	-22	28021	20	2.45
Temporal Superior	Left	-55	-14	13	76	48	1.69
AUC							
Now condition							
Insula	Right	43	8	-10	9733	48	-2.67
Temporal Inferior	Left	-50	-35	-24	276	20	-2.10
Temporal Medial	Left	-51	-34	-15	97	20	-2.10
Insula	Left	-36	18	-9	133	47	-1.79
AUC							
Not-now condition							
Insula	Right	44	8	-10	247	-	-2.48
Temporal Superior	Left	-57	2	1	11869	48	-2.37
Fusiform Gyrus	Left	-38	-23	-25	838	20	-2.14

Table 2. Note. Coordinates of the regions associated with reduced TD in the VLSM analysis on both *k* and AUC values, in MNI space. Region labels are taken from the automated anatomical labeling template (AAL). BA = Brodmann Area. Z = Maximum Brunner-Munzel *Z* statistics obtained for each cluster. *Z* scores are significant at a threshold of $p < 0.05$, FDR-corrected.

As indicated in Table 2, the largest clusters and the highest Z-values, for both the analysis on *k* and AUC values, were located in the insula. In both cases, in the Now condition, the highest concentration of significant voxels was in the right insula. A second distinct cluster of significant voxels was located in the left insula. There were other, smaller and less reliable clusters of voxels associated with reduced TD, including more anterior portions of the left insula and regions in the lateral temporal lobe, as listed in Table 2.

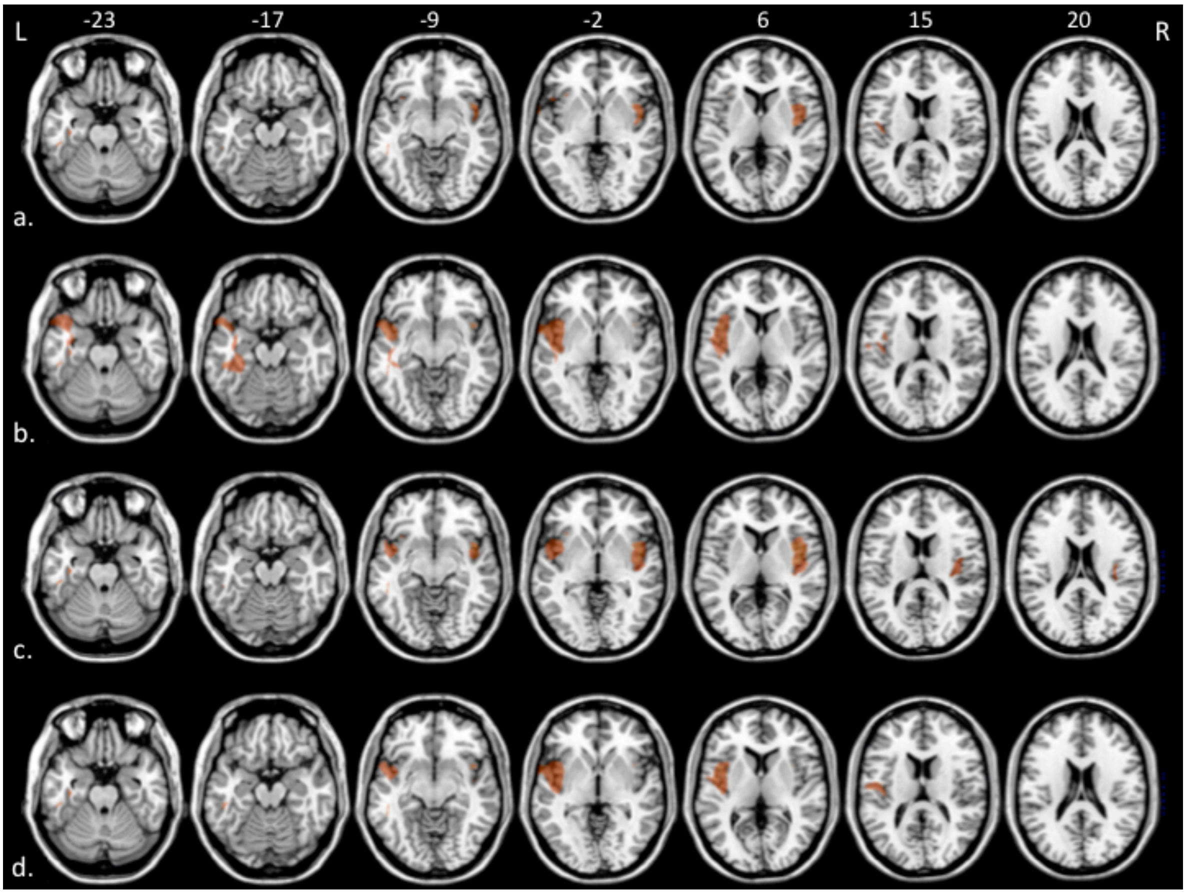

Figure 6. VLSM statistical map computed for *k* in the Now condition (a), *k* in the Not-now condition (b), AUC in the Now condition (c), and AUC in the Not-now condition (d), thresholded at $p < 0.05$, FDR-corrected, and shown on representative axial slices of the MNI brain. z-coordinates of each axial slice are given.

In the Not-now conditions, for both the analysis on *k* and AUC values, the voxels with the highest Z-values were again located in the right insula, and in an extended cluster in the left hemisphere – with peak in the left fusiform gyrus for the analysis on *k,* and in the superior temporal lobe for the analysis on AUC - that also included the insula. Again, smaller and less significant clusters were detected in the left temporal lobe.

Thus, the VLSM results confirm that the abnormal TD behaviour of Insular patients was mainly driven by damage to the insula. As anticipated, the VLSM analysis also revealed other regions, mainly in the temporal lobe, that were also related to TD behavior, although less reliably. The emergence of these additional regions in the VLSM analysis is difficult to interpret, primarily because we have no hypotheses on their putative role on TD. Additionally, damage in some of those regions (operculum, superior temporal pole) correlates with insula damage in this data set.

Self reports of depression. Insular patients' self-reports did not evince significantly higher levels of depression at the BDI-II than did those of Non-insular patients and healthy controls [$F(2,52) = 0.18$; $p = 0.84$; Table 1]. Separate analysis on the scores from the affective and somatic subscales of the BDI-II also failed to yield statistically significant results ($p > 0.83$ in both cases).

Discussion

The present study investigated the role of the insular cortex in intertemporal choice. Patients with lesions involving the insular cortex and control participants made a series of choices between smaller-sooner and larger-later amounts of money. Two temporal conditions were tested: in one, the earlier quantity of money was delivered immediately, whereas in the other it was delayed by 60 days. Lesion to the insular cortex significantly reduced TD of future rewards: Insular patients behaved more prudently than control participants, being more willing to wait for the larger-later reward. This finding held in both the Now and Not-now condition. Notably, all participants, including Insular patients, showed a significant decrease in TD in the Not-now compared to the Now condition: They behaved more impatiently when the sooner option was available immediately than when both options were delayed in time, replicating previous findings in healthy individuals (Ainslie, 1975; Frederick et al., 2002; McClure et al., 2004; Green et al., 2005; Figner et al., 2010; but see Kable and Glimcher 2010).

Reduced TD in Insular patients is not attributable to a general effect of brain damage, because Non-insular patients showed normal TD. Moreover, in our previous report (Study I-Part II, Sellitto et al., 2010), we showed that patients with lesion to the mOFC consistently prefer smaller-sooner over larger-later reward, a behavior that is opposite to the one exhibited by Insular patients. It is also unlikely that our findings were due to a general insensitivity to reward, or blatant problems at estimating the passage of time in Insular patients. Indeed, all patients consistently chose the larger of two rewards in the control conditions of the TD task. Moreover, Insular patients behaved more impulsively in the Now compared to the Not-now condition, and this tendency was as pronounced in Insular patients as it was in the control groups, indicating that Insular patients were generally able to represent the passage of time, and sensitive to the saliency of an immediate reward. Furthermore, it is worth noting that in our preliminary fMRI results (Study III-Part II), when using a multivariate analysis to investigate neuronal patterns able to discriminate between offers with and without an immediate option available, no insular recruitment has been found. This gives further support to the idea that insula is not responsible for differentiating between those two types of offer. Were this the case, a damage to insula should have resulted in no difference in TD rates in our insular patients when faced with Now and Not-now trials.

Thus, our findings indicate that the insula plays a crucial role during intertemporal choice, contributing to shape TD behavior. Several fMRI studies have implicated the insula in choice about money, drug, and other goods (e.g., Knutson et al., 2000; Guillem et al., 2010; Tusche et al., 2010). Moreover, activity in the insula modulates according to the time of availability of edible and monetary outcomes (Tanaka et al., 2004; McClure et al., 2007; Wittmann et al., 2007, 2010; Claus et al., 2011; Liu and Feng, 2012; Luo et al., 2012). fMRI evidence, however, have not univocally associated insula activity with choice of either delayed (Wittmann et al., 2007; Claus et al., 2011; Liu and Feng, 2012; Luo et al., 2012; Kayser et al., 2012) or immediate options (Tanaka et al., 2004; McClure et al., 2007; Wittmann et al., 2010), and therefore cannot clarify whether it is imperative for, or instead merely associated with, intertemporal choice. The fact that Insular patients behaved more patiently than controls, forgoing sooner rewards to receive larger-later ones, confirms that the insula is necessary during intertemporal choice, and suggests that it is normally implicated in upregulating the incentive value of relatively sooner reward options. How does the insula accomplish such a role?

The insula has been implicated in the conscious representation of bodily states (Rolls, 1999; Bechara, 2001; Kringelbach, 2004; Craig, 2009; Jones et al., 2011). During decision-making, the insula may anticipate the emotional/bodily effects of different choice options, contributing to their incentive value (Barrett et al., 2007), and translate such signals into conscious urges capable of driving behavior (e.g., Craig, 2009; Naqvi and Bechara, 2009). In a TD task involving receiving rewards at different delays, the insula may signal the urge to obtain a reward as soon as possible. Damage to the insula, therefore, would diminish the motivation to obtain a reward soon, allowing patients to wait for larger-later outcomes, resulting in reduced TD. This interpretation makes contact with extensive evidence implicating the insula in craving associated with cigarette and alcohol addiction, a paradigmatic condition of capitulation to immediate rewards despite bad long-term consequences (e.g., Wang et al., 2007; Hoffman et al., 2008; Naqvi and Bechara, 2009; Paulus et al., 2009; Kenny, 2010; Claus et al., 2011; Kang et al., 2012; Sutherland et al., 2012; Vaidya et al., 2012). Crucially, lesion to the insula disrupts addiction to smoking (Naqvi et al., 2007), as if the patients' "body forgot the urge to smoke" (p. 534), confirming that insula activity promotes courses of action directed at satisfying current needs. Another clinical population exhibiting an apparent ability to resist current temptations is that of individuals with anorexia nervosa, who sustain self-denial of food (Kaye et al., 2009). Patients with anorexia nervosa, too, show reduced TD (Steinglass et al., 2012), and functional abnormalities in the insula (Frank et al., 2012; Gaudio and Quattrocchi, 2012).

Another possibility is that, instead of reducing the urge for reward, damage to the insula reduced the feeling of uncertainty related to waiting for delayed rewards (Tom et al., 2007; Clark et al., 2008; Christopoulos et al., 2009; Weller et al., 2009). Even though intertemporal choices are not typically designed as risky choices, delay may influence choice via the perceived risk of loss inherently associated with waiting (Paulus et al., 2003; Kuhnen and Knutson, 2005; Knutson et al, 2007). Consistent with this hypothesis, the insula is preferentially activated during decisions involving uncertainty (Huettel et al., 2006), and its activity is negatively correlated with expected value, the product of probability of an uncertain option and outcome magnitude, but not with outcome magnitude (Rolls et al., 2008). Moreover, whereas healthy individuals make choices based on both probability and outcome magnitude in a task involving decision under uncertainty, patients with damage to the insula may be insensitive to outcome probability levels (Weller et al., 2009; see also Clark et al., 2008).

Although our design does not allow distinguishing whether damage to the insula reduced the urge to obtain something positive (a reward soon), or to avoid something negative (the fear of loss related to waiting for a later reward), we emphasize that both possibilities point to the insula as crucial to provide emotional inputs to intertemporal choice. On this view, reduced TD in Insular patients arises as a consequence of a failure in anticipating the bodily signals associated with receiving rewards at different delays, resulting in choices governed by a heuristic of quantity (i.e., based on the larger disposable amount). We note that Insular patients showed steeper TD in the Now compared to the Not-now condition, as did the control groups. This unexpected finding suggests that unilateral damage to the insula does not result in a blatant inability to appreciate the saliency of an immediate reward, but in a more subtle problem at contributing interoceptive signals for the valuation of, and choice between, competing options (see also Weller et al., 2009).

As we discussed earlier, the results on Insular patients in the present study are at odds with those obtained on patients with lesion in the mOFC (Study I-Part II, Sellitto et al., 2010), who showed steeper TD compared to controls. The present findings allow us refining the architecture of the neural network underlying intertemporal choice (see the general discussion of this dissertation), with the mOFC and adjacent medial prefrontal regions weighting the long-term prospects of a given choice (Schoenbaum et al., 2009; Sellitto et al., 2010), and the insula, which possesses connections with both the vmPFC and the VS (Reynolds and Zahm, 2005), relaying interoceptive inputs about need states to both systems, determining the strength with which the individual will pursue a reward option or the other (Weller et al., 2009). According to this model, damage to the mOFC would cause a problem envisioning future outcomes, leading to steep TD, whereas damage to the insula would lead to emotionally blunt intertemporal choices based on a heuristic of quantity, and therefore reduced TD, which is what we have observed in brain damaged patients.

In conclusion, we have shown that damage to the insula causes increased willingness to wait in intertemporal choice. While far-sighted decision-making has obvious advantages, in many situations in life it is important, and preferred, to pursue current opportunities instead of waiting for potential future ones, as captured in the popular saying “every missed chance is lost forever”. The present results point to the insula as crucial to pursue current rewards, and take chances as soon as possible, favoring action over prospection.

Study III – Neural basis of carry-over effect during intertemporal choice: Preliminary results of an fMRI experiment

Introduction

As highlighted in Part I, over the last few years, an increasing number of imaging studies on TD in humans has been carried out (see Appendix A). Whatever be the manipulation, the target population, the focus (e.g., behavioral, genetic, personality traits) and so on, fMRI studies evidenced, sometimes with a high consistency, the engagement of several recurrent brain areas activated during intertemporal decision-making. However, nearly all previous imaging studies in this domain (except Clithero et al., 2009, and Murawski et al., 2012) have used a version of the basic univariate contrast.

The present study investigated for the first time the carry-over effect during intertemporal choice in healthy young individuals using fMRI with also both univariate and multivariate approaches. With carry-over effect here we do not mean the phenomenon that previous studies investigated at a behavioral level. Indeed, carry-over effect during intertemporal choice in literature refers to how tasks people engage in prior to making intertemporal decisions affect their discounting levels. Some situations can evoke concrete mindset (enhancing focus on the context and the details, biasing choices toward the sooner smaller option) or facilitate abstract mindset (enhancing focus on the big picture, thereby decreasing the discount rate) (e.g., Malkoc et al., 2010), by influencing the construals (i.e., mental representations) of those specific rewards ('construal level theory', Liberman and Trope, 1998, 2008; Trope and Liberman, 2003; see Study III-Part III). Some emotions, moreover, like fear, can prime in different ways subsequent intertemporal decisions (Lerner et al., 2004; Luo et al., 2012). We investigated this kind of carry-over effect in Part III, associating mental time travel with intertemporal choice, manipulating outcome construals, and conditioning participants through the association between rewards and aversive events.

Instead, the carry-over effect we were interested in here refers to the influence that a previous monetary intertemporal choice can have on the subsequent one at neural level. Specifically, we address to investigate the modulation of the neural response (by the means of detecting the BOLD signal) to the current stimulus (a binary offer) by the preceding stimulus, manipulating the presentation ordering (e.g., Aguirre, 2007; 2011). Several neural measures of carry-over effects have been used, like anticipation, priming, and bias (Kahn et al., 2010). Here we used the measure defined as ‘repetition suppression’ (Henson and Rugg, 2003). Namely, the reduction in the magnitude of neurons response that can be seen toward stimuli sharing a particular property is considered the proof that the identified voxel contains a population of neurons that code that specific dimension (Fig. 1; Aguirre, 2007; Grill-Spector and Malach, 2001). In other words, stimuli perceived to be similar are represented by similar neural states, so that, during stimulus repetition a reduced firing rate of cells can be observed (Henson and Rugg, 2003; Aguirre, 2007). To study the impact of stimulus history and context upon neural response, a counterbalanced stimulus sequence, where each stimulus is included an equal number of times, is required (Aguirre, 2007). While traditional fMRI analysis provides evidence about how an event is represented on average across a population of neurons within a voxel (e.g., Friston et al., 1995a,b), ‘repetition suppression’ fMRI makes inferences about neural populations within a voxel (Grill-Spector and Malach, 2001; Henson and Rugg, 2003, Aguirre, 2007).

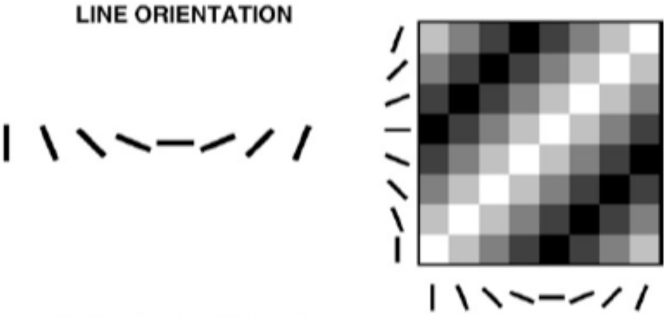

Figure 1. Example of similarity matrix for a set of 8 stimuli consisting of a bar of light rotated in 22.5º increments (Adapted from Aguirre, 2007). The lighter the square, the more stimuli will be represented by the same neural population in a given voxel.

How do neurons react, or adapt, to a continuous sequence of intertemporal choices based on specific features? The aim of this study was to identify if different features of binary monetary intertemporal choices were differently represented within and across voxels, in a small sample of young participants. We mostly focused on choices where an immediate option was provided against choices were both options were offered delayed in time, and on the size of the temporal gap between the earlier and the later option. We examined both the average response to each stimulus type (i.e., univariate analysis) and the effect of stimulus history (i.e., the carry-over effect, within voxels).

Moreover, a further advantage of the present approach is that, since we can get a measure for each voxel of the response to each condition, we also performed a distributed pattern analysis to ask about how the representations of stimuli are distributed across local regions (Haxby et al., 2001; Haynes and Rees 2006; Norman et al. 2006; Aguirre, 2007; Oosterhof et al. 2010). This approach, called multi-voxel pattern analysis (MVPA), examines the mean difference in the neural response between stimuli across voxels.

We expected to find (1) activity in brain areas commonly engaged in coding the subjective value of intertemporal choice (see Part I), e.g., mOFC, vmPFC, including ACC, PCC, dlPFC, and insular cortex, with a specific engagement of areas included in the 'default network' (Schacter et al., 2007) when distinguishing between offers with and without an immediate option; (2) (a reduction in the) activity in brain areas when options are preceded by similar options as an index that they code specific properties; (3) neuronal patterns able to discriminate, within-modality, among options features. The results we will present are meant to be considered preliminary.

Materials and Methods

Participants

Four healthy volunteers (2 females, all right-handed, mean age 24 years) were recruited from the Bangor University community. All participants had normal or corrected-to-normal vision. Participants satisfied all requirements in volunteer screening and gave informed consent. Procedures were approved by the Ethics Committee of the School of Psychology at Bangor University. Participation was compensated at £15 at the end of the scanning session.

Design

Our subjects were presented stimuli in a rapid counter-balanced sequence of continuous binary monetary offers. Specifically, each stimulus preceded each other for an equal number of times (Aguirre, 2007). We restricted the sequential dependence of the response to influences from the previous (*n-1*) stimulus. To this purpose, we generated for each participant a unique sequence of stimuli, where each stimulus consisted of a pair of monetary options, where the larger one was always set at £ 50. However, since the aim of the present study was to investigate the effect of the preceding offer on the subsequent one, we had to make sure that our participants were (approximately) ‘indifferent’ between the two options presented each time in each trial (e.g., Frederick et al 2002, see also Part I). For this reason, one week before the fMRI session, participants underwent to a TD task that allowed us to estimate their individual k rates.

Behavioral prescanning task. The TD task was displayed using Matlab (MathWorks, Inc®) and Psychophysics Toolbox (Brainard, 1997; Pelli, 1997), and the delays and the titration procedure were the same as in Study II-Part II, as well as the timing and the no time limit to respond. This time, however, we presented amounts and delays only, on a black screen (Sellitto et al., 2010, see also Study I-Part II). The larger amount, £ 50, was paired with a smaller amount of money along two different temporal conditions. During the Now condition, the earlier option was always immediately available (‘this minute’), whereas the larger amount was offered with a delay of 2 days, 2 weeks, 1 month, 3 months, 6 months, and 1 year. During the Not-now condition, the sooner option was always available in 2 months, whereas the larger amount was offered with a delay of 2 months and 2 days, 2 months and 2 weeks, 3 months, 5 months, 8 months, and 1 year and 2 months. Along 5 trials, using the staircase procedure of Du and colleagues (2002; Sellitto et al., 2010), the indifference points for all delays were derived. Once applied the hyperbolic function $SV = 1/(1+kD)$ to the subject’s data [where SV = subjective value (expressed as a fraction of the delayed amount), D = delay (in days), and k = discounting coefficient] using a nonlinear, least-squares algorithm, as implemented in Statistica, (Statsoft®), the temporal discounting k parameter was calculated, for both Now and Not-now conditions (Mazur, 1987; Rachlin et al., 1991; Green and Myerson, 2004; Sellitto et al., 2010).

Behavioral scanning task. Using the two derived k parameters for each participant, we applied the same hyperbolic function to calculate the indifference points at each delay we included in the task for the fMRI session. These indifference points were used as smaller sooner options for this task. Moreover, to make the task less repetitive, and to avoid participants remembering amounts paired with delays, and then their choices, we slightly changed quantities by randomly adding or subtracting some pence from the calculated indifference point (10 pence < x < 90 pence). In the scanning task, during the Now condition, £ 50 were available at each of 9 delays: in 6 days, 3 weeks, 2 months, 5 months and 6 days, 5 months and 3 weeks, 7 months, 9 months and 6 days, 9 months and 3 weeks, and 11 months. During the Not-now condition, £ 50 were available at each of nine delays: in 2 months and 6 days, 2 months and 3 weeks, 4 months, 7 months and 6 days, 7 months and 3 weeks, 9 months, 11 months and 6 days, 11 months and 3 weeks, and 1 year and 1 month. As is evident, we maintained the same temporal gaps between earlier and later rewards in both temporal conditions, as in the behavioral prescanning task. This allowed us to group the first three delays as Short gap, the second three delays as Medium gap, and the third three delays as Long gap.

The fMRI task had then a 2 × 3 event-related design (Fig. 2): 2 temporal conditions (Now, Not-now), and 3 temporal gaps (Short, Medium, Long). Moreover, null trials (a black blank screen) were included in the sequence in an equal number as the other conditions (the seventh condition). Having these variables in mind, we generated a 1-back order sequence using a custom written script in Matlab (MathWorks, Inc®). This means that for each of the seven conditions, 49 trials were generated in a unique sequence, where each type of condition preceded each type of condition. However, the number of trials was too high for subjects to be presented at once. We then divided the sequence in 7 chunks, making sure that each chunk started with the last type of trial of the previous chunk, to do not lose the 1-back order. This resulted in 7 blocks of 50 trials each. Moreover, to make sure that the attention of our participants remained constant along the experiment, we included in each block 3 catch trials, for a total of 371 trials presented in 7 blocks of 53 trials each. Catch trials were randomly included in each block, making sure that at least one of the three was in the first half of the trials, and at least one was in the other half of the trials. Nine types of catch trials were provided. In one, both the smaller and the larger option were available 'this minute', in one, both options were available 'in 2 months', and in the others we used some of the delays included in the real conditions, but having the earlier option a larger amount than the later option.

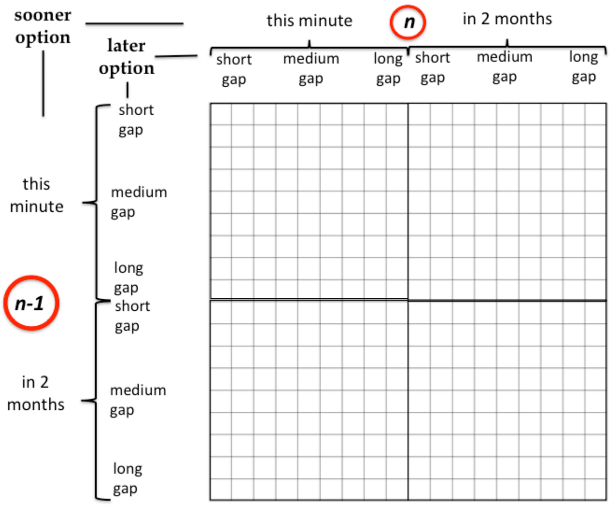

Figure 2. fMRI task 2 × 3 design where the *n* trial is preceded by the *n-1* trial. The sooner option could be available immediately ('this minute') or 'in 2 months'. Delay gaps between the availability of the sooner and the later option could be 'short', 'medium', 'long'.

Figure 3 shows the timing of a trial displayed using Matlab (MathWorks, Inc®) and Psychophysics Toolbox (Brainard, 1997; Pelli, 1997). The position of stimuli was randomly determined (between the left and the right side of the screen), and participants had 4000 ms to choose their preferred option on each trial. All options pairs remained on the screen for 4000 ms independently of subjects' response, and no feedback was given about their choice. Each chunk of trials lasted 4.5 minutes.

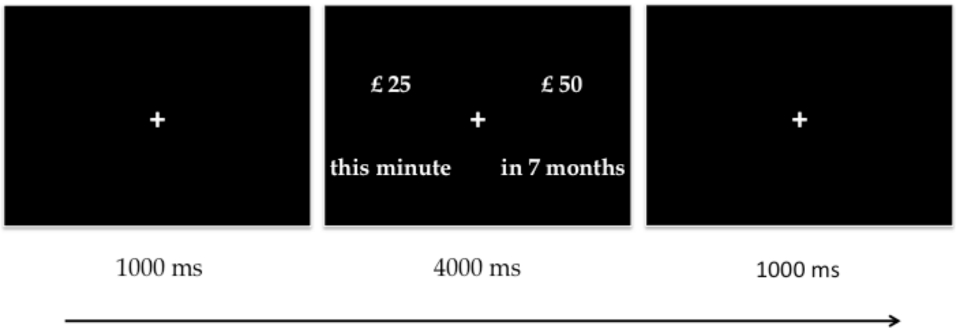

Figure 3. Timing of a trial. After 1000 ms of fixation cross, the two monetary options appeared for 4000 ms, and then a new trial began.

Data acquisition

Imaging data were recorded using a 3T Philips Achieva MRI scanner, equipped with a SENSE parallel head coil (Philips, Best, Netherlands). Stimuli were presented using a Sanyo LCD projector (Sanyo, Osaka, Japan) directed at a rear-projection screen and was administered using Matlab (MathWorks, Inc®) and Psychophysics Toolbox (Brainard, 1997; Pelli, 1997), running on an Apple Mac Pro computer. Participants' responses were recorded using a nonferrous, fiber-optic response keypad by the means of two buttons positioned according to the spatial positions of stimuli on the screen (one on the left, and one on the right) (Current Designs, Philadelphia, PA). Functional data acquisition was achieved with T2*-weighted scans using a single-shot echo planar (EPI) sequence. Acquisition parameters for all participants were: 28 slices acquired in a square root interleaved order, no slice gap, 80×80 matrix, slice thickness = 3mm, voxel dimensions = 3×3 mm in-plane; echo time (TE) = 35 ms; repetition time (TR) = 2000ms; flip angle = 90◦. Coverage included the entire cortex, principally the orbitofrontal lobe. Parameters for T1-weighted scans, which served as an anatomical reference for each participant, were: 256×256 matrix; slice thickness = 1.3mm; voxel dimensions = 1mm×1mm in-plane; TR = 16ms, TE = 3ms; flip angle = 8◦. Nine dummy volumes were obtained prior to each scan in order to minimize T1 saturation effects.

Data preprocessing

Preprocessing and statistical analyses of the MRI data were performed using BrainVoyager QX 2.2.0 (Brain Innovation, Maastricht, The Netherlands), and custom written scripts in Matlab (MathWorks, Inc®). Functional data were motion corrected, and low-frequency drifts removed with a temporal high-pass filter (0.004 Hz), and spatial smoothing was applied. Functional data were automatically co-registered with the three-dimensional anatomical T1 scans. The three-dimensional anatomical scans were transformed into Talairach space (Talairach & Tournoux, 1988), and the parameters from this transformation were subsequently applied to the co-registered functional data that were re-sampled to 1mm×1mm×1mm voxels.

Data analysis

Data were modeled and analyzed using BrainVoyager QX. Given the low number of participants, we decided to perform a whole-brain fixed effect analysis at the group level, for each contrast of interest, as exploratory analysis. For each participant, general linear models (GLMs) were created to investigate the average response to each stimulus type (i.e., univariate analysis), the effect of stimulus history and context (i.e., the carry-over effect and the repetition suppression, within voxels), and the local pattern analysis.

Whole-brain univariate analysis. We constructed parametric regressors to investigate activation differences between trials in which an immediate option was presented (Immediate) and trials in which no immediate option was presented (Not-immediate), and trials with different time gaps between the sooner and the later option (Short, Long). At this stage of analysis (preliminary data), we did not include a regressor for the Medium gap. On the one hand we contrasted 2 conditions: Immediate and Not-immediate; on the other hand, we contrasted 2 conditions: Short delay gap and Long delay gap. The model also included a constant as regressor of noninterest. Uncorrected voxelwise threshold was set at $p < 0.005$, FDR, and *t* maps will be displayed.

Carry-over effect analysis. We constructed parametric regressors in order to investigate, on the one hand, trials with/without an immediate option preceded by trials with/without an immediate option, and on the other hand, trials with a short/long delay gap preceded by trials with a short/long delay gap. To this purpose, we contrasted in one case 2 conditions: Same preceding trial and Different preceding trial. This means that a trial with an immediate option preceded by a trial with an immediate option is considered the same as a trial with no immediate option preceded by a trial with no immediate option. Figure 4 shows the similarity matrix for these two conditions.

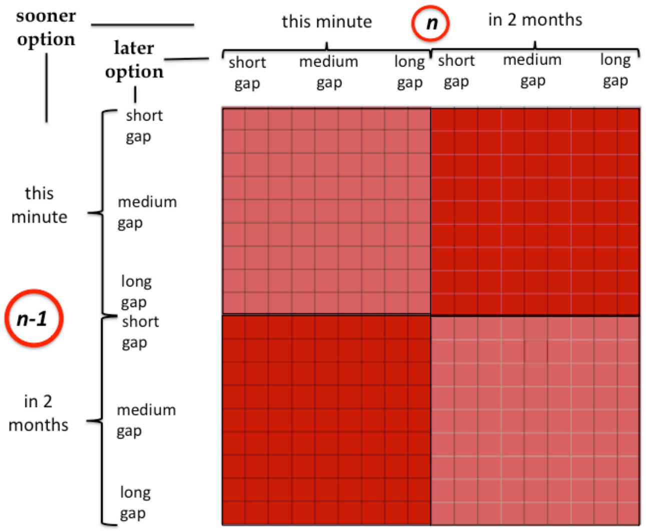

Figure 4. Similarity matrix for trials preceded by the same or a different type of trial, based on the availability or not of an immediate option. Trials preceded by the same type of trial will be represented in the same way by a given neural population (lighter color), so that their firing rate will be reduced as compared to trials preceded by a different type of trial (darker color).

Based on the delay gaps, with these preliminary data we focused only on trials with a short and a long delay gap between the two options, so that we contrasted 2 conditions: Same preceding delay gap and Different preceding delay gap. Figure 5 displays the similarity matrix for these two conditions. This means that a trial with a short delay gap between earlier and later reward preceded by a trial with a short delay gap between options is considered the same as a trial with a long delay gap between the options preceded by a trial with a long delay gap between the options. The model also included a constant as regressor of noninterest. Uncorrected voxelwise threshold was set at $p < 0.005$, FDR, and *t* maps will be displayed.

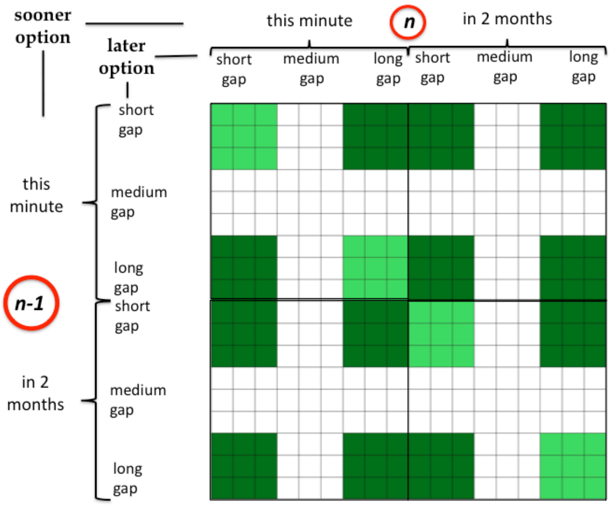

Figure 5. Similarity matrix for trials preceded by the same or a different type of trial, based on the delay gap (short or long) between the two options. Neural response is hypothesized to be reduced if a trial is preceded by the same type of trial (light green), as compared to when it is preceded by a different type of trial (dark green). Medium delay gaps are not considered in this preliminary data analysis.

MVPA. This analysis makes inference about distributed responses without requiring focal activations or certain topological response features (Haxby et al., 2001). Basically, it investigates how similar are the patterns of activity produced by the same conditions across scans, relative to the similarity of patterns of activity produced by different conditions. We determined whether the distributed pattern of responses evoked by the availability of an immediate option in the binary choice could be distinguished from the pattern of responses to choices in which no immediate option was offered in the pair. Figure 6 illustrates the similarity matrix for our design. With these preliminary data we did not investigate patterns of neural activity related to different delay gaps between outcomes.

Each participant’s data were analyzed with a whole-brain information mapping approach (‘decoding searchlight analysis’), without restricting our analysis to predefined regions of interest (Kriegeskorte et al. 2006; Haynes et al., 2007; Kriegeskorte and Bandettini, 2007; Oosterhof et al. 2010), implemented in Matlab (The MathWorks, Cambridge, UK). For every voxel we constructed a searchlight corresponding to a spherical cluster of 7 voxels. The searchlight classifier is defined as the mean signal of all voxels in the searchlight, calculated extracting at each voxel the patterns from the surrounding voxels. Inputs for the classifier consisted of the number of conditions of interest (2: availability of an immediate option in the binary choice vs. no immediate option offered in the pair) by seven runs β-estimates in order to construct a correlation matrix to contrast patterns of response. Both conditions in each run are correlated resulting in a 2 × 2 correlation matrix and a single performance metric is calculated, by checking how often the diagonal elements of the correlation matrix are greater than the off-diagonals (Haxby et al., 2001). We tested the classifier against performance of a chance (50%), $p < 0.05$, FDR. The quality of the classifier was calculated by averaging across runs and participants (see also Aguirre, 2007; Clithero et al., 2009; Murawski et al., 2012).

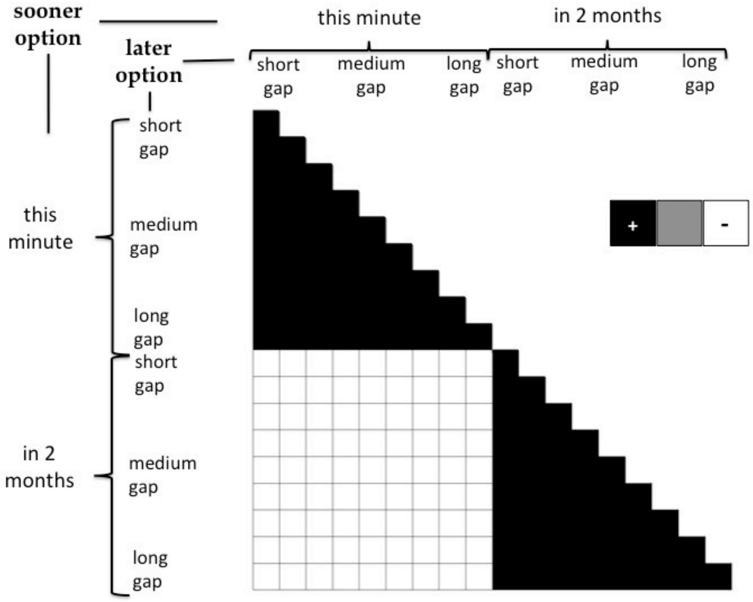

Figure 6. Similarity matrix for neural patterns. The more neural patterns are hypothesized to be similar, the darker the square. Here we are considering only neural patterns coding for offers where an immediate option was available vs. offers where no immediate option was included (only half matrix has been displayed).

Results

Behavioral scanning task. An ANOVA on log-transformed *k* values with Chosen option (sooner, later) and Position of the option (left, right) as a within-subject factors showed that participants chose indifferently between both the sooner and the later option [F(1, 3) = 0.35, p = 0.60] and left- and right-positioned options [F(1, 3) = 4.80, p = 0.12], with no significant interaction between Chosen option and Position of the option [F(1, 3) = 0.50, p = 0.53].

Whole-brain univariate analysis. In order to display results, we averaged the anatomical images of all four participants previously transformed in Talairach space. We set the threshold at p = 0.002 to avoid excessive false positives. In this analysis, the contrast Immediate > Not-immediate produced significant activations in several brain areas (Fig. 7a). These were mainly clustered bilaterally around the medial frontal gyrus (including ACC), the superior frontal gyrus (BA 9), the PCC (BA 23), and the left lateral PPC, including the precuneus and the angular gyrus.

The contrast Not-immediate > Immediate produced significant activations (Fig. 7b) in areas principally clustered bilaterally on the insula (including BA 13), the medial frontal gyrus and the superior frontal gyrus (BA 9), the left precuneus, and the left occipital lobe.

As is evident from the first contrast, the average neural response during trials where an immediate option was available was preferentially located in the medial frontal cortex, including ACC, and the PCC, the precuneus and the angular gyrus, suggesting that the computation of the subjective value for those choices was probably given a special weight to the immediately available smaller option, matching the areas found by McClure and colleagues (2004, 2007) associated with their hypothesized *ß*-system.

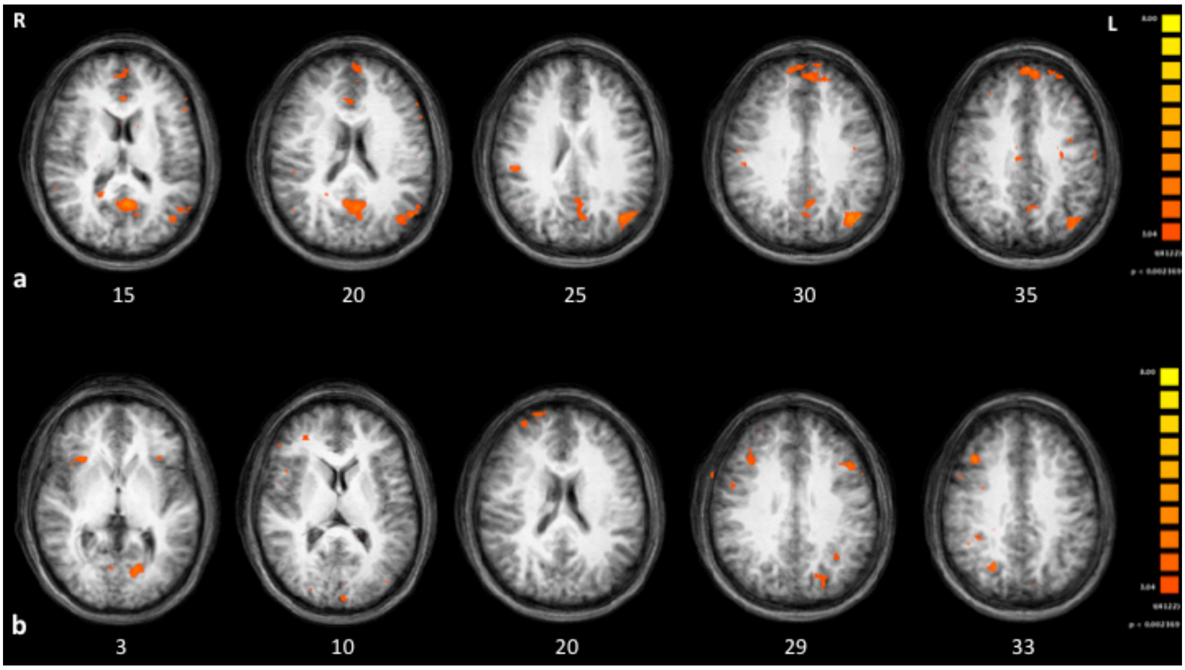

Figure 7. Activations from the whole-brain analysis (overlaid on the average anatomical scan from all 4 participants). a. Immediate > Not-immediate contrast; b. Not-immediate > Immediate contrast. z-coordinates of each axial slice are given.

In the opposite contrast, when no immediate option was offered in the pair, bilateral activations principally located in the lateral prefrontal cortex and on the anterior insula were found, matching this time areas identified by McClure and colleagues (2004, 2007) as part of the ∂-system, including part of the occipital cortex. However, while these functional activations are reminiscent of the dual-system model of McClure and colleagues (2004, 2007) the finding that medial frontal gyrus and the precuneus responded to both immediate and delayed rewards (as in Ballard and Knutson, 2009) better fits with the unitary model proposed by Kable and Glimcher (2007, 2010; Peters and Büchel, 2010; see Part I and the general discussion of this dissertation).

The contrast Short delay gap > Long delay gap (Fig. 8a) yielded activity in areas mostly clustered on the bilateral insula (including BA 13), the BA 10 of OFC, and in several bilateral portions of the frontal (superior and inferior gyri, including BA 9 and 6) and the parietal (including the BA 7 and 19) lobes. On the contrary, the contrast Long delay gap > Short delay gap produced several significant activations (Fig. 8b) mainly located in the right temporal lobe (both inferior and superior gyri), the right inferior parietal lobe, and the left occipital lobe.

Contrasting short and long gaps activations located mainly in the anterior insula and the frontal cortex, including the OFC, emerged when the temporal distance between the two options was short, suggesting that the recruitment of those areas commonly responsible for the computation of the subjective value is necessary when both options are enough salient, because both close in time at the same way. Conversely, more dorsal activations located in the temporal and parietal lobe were found according to a longer delay gap between the two offers. These results suggest that mechanisms like mental simulation and future envisioning are required when thinking about very far options, recruiting regions like the temporal and the parietal lobe, both part of the 'core brain network' (Schacter et al., 2007).

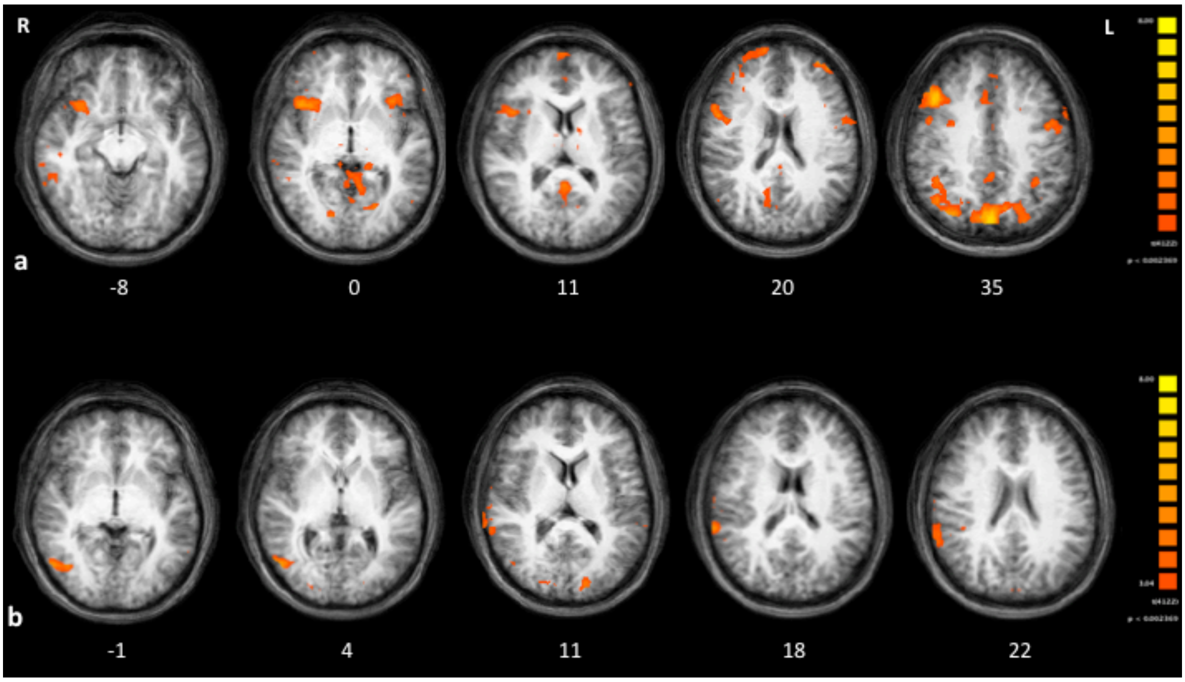

Figure 8. Activations from the whole-brain analysis (overlaid on the average anatomical scan from all 4 participants). a. Short delay gap > Long delay gap contrast; b. Long delay gap > Short delay gap contrast. z-coordinates of each axial slice are given.

Carry-over effect analysis. In this analysis, the contrast Same preceding trial > Different preceding trial, based on whether an immediate option is present or not, produced significant activations in several brain areas (Fig. 9a). These were mainly clustered bilaterally around the insular cortex (including BA 47 and 13), the frontal lobe, including the middle frontal gyrus, the superior temporal gyrus, and the lentiform nucleus of the putamen.

The contrast Different preceding trial > Same preceding trial revealed significant activations (Fig. 9b) principally located bilaterally in the frontal lobe, including the vmPFC (middle frontal gyrus, BA 9), the BA 4, and the superior frontal gyrus, and the ACC (BA 24). Moreover, significant clusters emerged bilaterally from the temporal lobe, including the middle temporal gyrus, the superior temporal gyrus, and the BA 39.

From both contrasts, significantly activated clusters emerged from the frontal (including the middle gyrus) and the temporal lobe (including the superior temporal gyrus), commonly engaged during intertemporal choice as also evidenced with the univariate analysis above. In a repetition suppression paradigm these activations are indicative of areas coding a certain property, so that a reduced firing is expected when the same offer is repeated (based on the time availability of the sooner option).

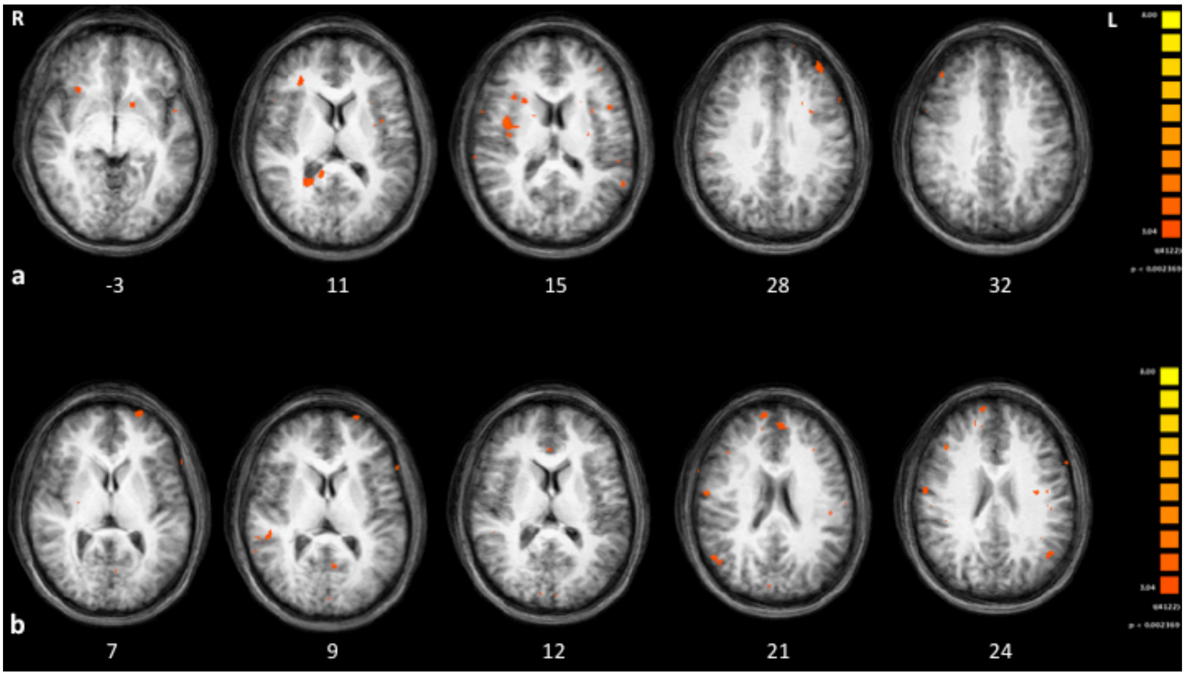

Figure 9. Activations from the whole-brain analysis (overlaid on the average anatomical scan from all 4 participants). a. Same preceding trial > Different preceding trial contrast; b. Different preceding trial > Same preceding trial contrast. z-coordinates of each axial slice are given.

Significant activations for the contrast Same preceding delay gap > Different preceding delay gap (Fig. 10a) mainly clustered bilaterally on PCC and the frontal lobe (including BA 10, superior, middle, and inferior frontal gyri), and on the right insular cortex and the right putamen.

The opposite contrast, Different preceding delay gap > Same preceding delay gap (Fig. 10b) produced significant activations principally clustered bilaterally on the insular cortex (including the BA 13), the temporal lobe (superior and medial gyri, including BA 38), the superior and inferior frontal gyri (including the BA 47), the parietal lobe, the right PCC, and the left lentiform nucleus of the globus pallidus.

When contrasting trials proceeded by the same or a different type of trial based on the delay gap criterion, activity in areas like insular cortex, PCC, and the frontal lobe emerged. Again, in a repetition suppression paradigm like this, these activations are indicative of areas coding a certain property, so that a reduced firing is expected when considering offers preceded by the same type of offer based on the temporal gap between the two options. All these impressions will be tested in a second phase of this study, when more participants will be scanned.

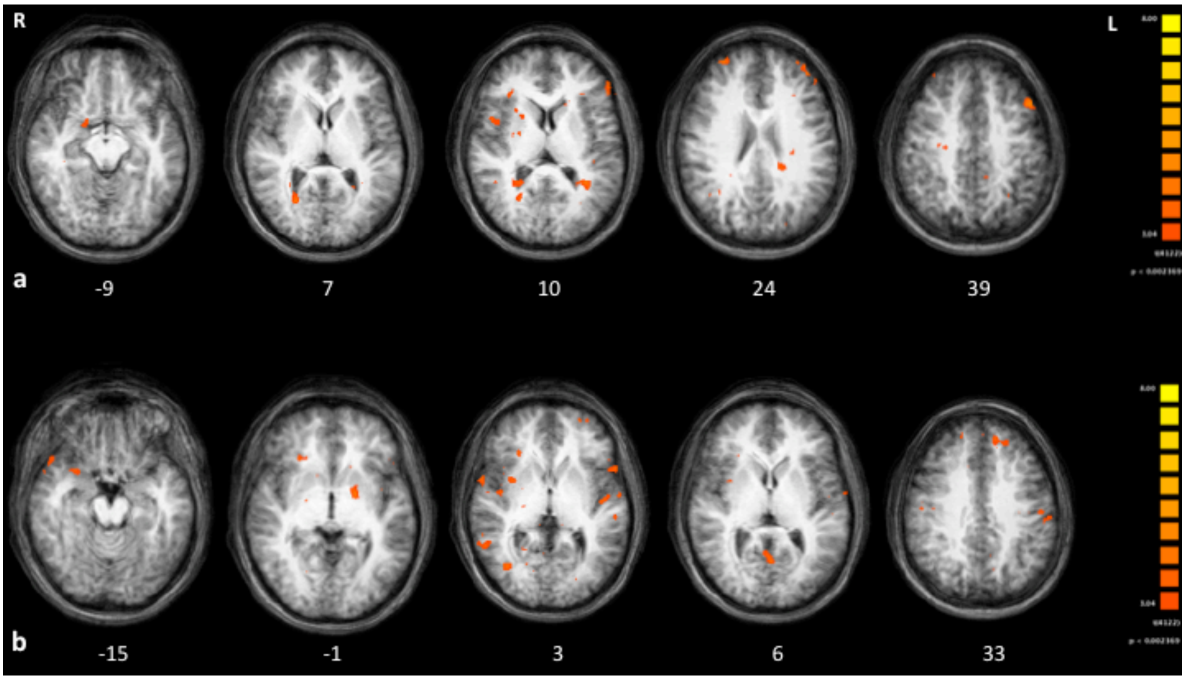

Figure 10. Activations from the whole-brain analysis (overlaid on the average anatomical scan from all 4 participants). a. Same preceding delay gap > Different preceding delay gap contrast; b. Different preceding delay gap > Same preceding delay gap contrast. z-coordinates of each axial slice are given.

MVPA. The searchlight analysis revealed several brain areas able to distinguish distributed patterns of response evoked by the availability of an immediate option in the binary choice from patterns of response to choices in which no immediate option was offered in the pair, with predictive accuracy greater than 90%. Due to a small sample, we set a very strict threshold ($p < 8.4707^{-25}$) and cluster size = 50 voxels to trim the number of activations down. Patterns of response predominantly clustered bilaterally on the occipital lobe (e.g., BA 19) and the parietal lobe (e.g., precuneus, BA7, BA 39), on the parahippocampal gyrus (e.g., B 35), and the inferior and middle frontal giri (e.g., BA 6, BA 9) (Fig. 11). We will discuss these results later.

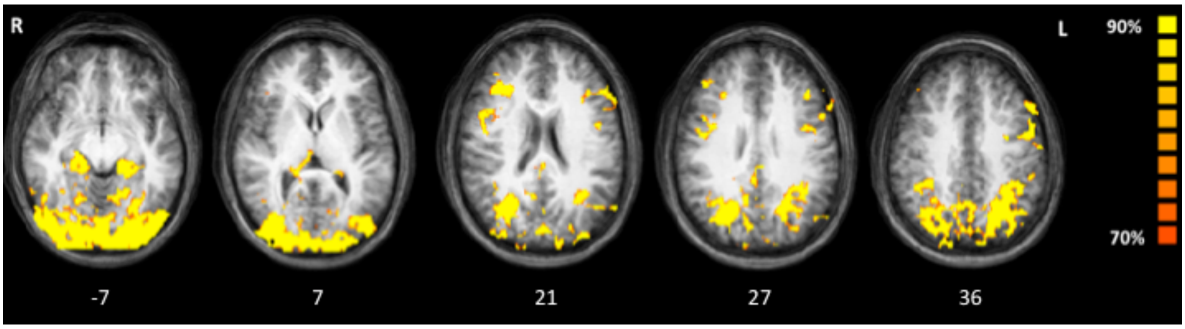

Figure 11. Brain areas able to distinguish distributed patterns of response evoked by the availability of an immediate option in the binary choice from patterns of response to choices in which no immediate option was offered in the pair. z-coordinates of each axial slice are given.

Discussion

In this study we provided for the first time preliminary evidence about neural regions involved in intertemporal choice, by way of a carry-over (repetition suppression) measure and both univariate and multivariate approachs. We presented participants a rapid series of monetary binary offers. Offers differed on the availability of an immediate option in the pair, and on the temporal gap between the earlier and the later option in each trial. We tuned amounts on subjects' individual discount rates to make sure that they were indifferent between options along trials. This procedure aimed to identify areas coding properties of intertemporal choices based on the suppression of the neural response during trials preceded by similar trials.

We firstly localized with a traditional univariate analysis areas preferentially responding to offers when a money amount was immediately available, and those preferentially responding to offers where both amounts were offered delayed in time. When an immediate option was available, the signal was preferentially located in areas also identified by McClure and colleagues (2004, 2007) and called as *ß*-system. This network comprised the medial frontal cortex, including ACC, PCC, the precuneus and the angular gyrus, suggesting that the computation of the subjective value for those choices was probably given a special weight to the immediately available option, which is the more tempting one. When no immediate amount was offered, neural activity was located in areas identified by McClure and colleagues (2004, 2007) as part of the ∂-system, as the lateral prefrontal cortex, the anterior insula, and the occipital cortex. This result suggests that when choices were more difficult, because no immediate tempting option was offered but both were projected in time, more dorsolateral areas activity, involved in planning and implementation of self-control, was required. Moreover, the recruitment of the anterior insula could have been necessary to anticipate and simulate feelings associated with outcomes in order for choices to be guided by the estimated desirability. Anterior insula is also involved in the reproduction of temporal intervals (Wittmann et al., 2010) and awareness across time (Craig, 2009), suggesting a role in time computation (Harrington et al., 2004). However, even if these functional activations are reminiscent of the dual-system model of McClure and colleagues (2004, 2007), the finding that further clusters located in the medial frontal gyrus and the precuneus responded to both immediate and delayed rewards (as in Ballard and Knutson, 2009) better fits with the proposed unitary model we will outline at the end, in the general discussion of this dissertation (Kable and Glimcher, 2007, 2010; Peters and Büchel, 2010; Part I).

Contrasting short and long gaps, activations emerged mainly in the anterior insula and the frontal cortex, including the OFC, when the temporal distance between the two options was short, suggesting that the recruitment of those areas commonly responsible for the computation of the subjective value is necessary to give a special weight to both options, highly salient, because both simultaneously close in time. Conversely, more dorsal activations located in the temporal and parietal lobe were found according to a longer delay gap between the two offers. These results suggest that mechanisms like mental time travel (see Study I-Part III) and future envisioning are required when thinking about very far options, recruiting regions like the temporal and the parietal lobe, both part of the 'core brain network' (Schacter et al., 2007).

Through the carry-over effect analysis, we confirmed the previous response profile. Indeed, in a repetition suppression paradigm, where subjects are presented a fast series of stimuli, emerging (attenuated) activations indicate that neurons are coding for the property shared by repeated stimuli. Activity in the insular cortex, the middle frontal gyrus, the superior temporal gyrus, and the lentiform nucleus of the putamen emerged when contrasting trials based on the same preceding type of trial (independently of if an immediate option was available or not). Activity in vmPFC, the superior frontal gyrus, the ACC and the temporal lobe emerged when contrasting trials based on the different preceding type of trial (independently of if an immediate option was available or not). These results suggest that these regions participate in coding offers at all times of availability (both with and without an immediate outcome available), not in line with the dual model hypothesis of McClure and colleagues (2004, 2007; see Part I). As extensively outlined before, areas located in the medial wall of the prefrontal cortex as well as subcortical structures have been long demonstrated to be necessary for the subjective value computation during economic choices (e.g., Kable and Glimcher, 2007, 2010). At the same time, activations in mPFC, the temporal lobe, and the parietal cortex (precuneus) relate to the 'default network' and the mechanism of future simulation during decision-making. Mentally travelling in time seems to be indeed necessary to project our-self far in time and to imagine future events, as future outcomes in our task, before making a decision, requiring the engagement of medial frontal regions, precuneus, and mesial and lateral portions of temporal regions (Buckner et al., 2008). Moreover, our findings are also in line with Wencil and colleagues (2010) results. They found that the activity in the superior temporal cortex and in the inferior frontal cortex increased with the difficulty of making a temporal comparison. These areas, together with parietal cortex, middle frontal areas, and thalamus are indeed recognized as having a role during the comparison and decision-making period of temporal discrimination tasks (Rao et al., 2001; Harrington et al., 2004; Livesey et al., 2007; Wencil et al., 2010). These preliminary results suggest that a repetition suppression approach not only can help to elucidate neural responses to specific features of stimuli, but also is a worth doing paradigm that allows to make stronger predictions when considering complex stimuli as our hypothetical monetary binary choices. This paradigm, focusing here on choices being under the influence of previous choices, demonstrated that several brain regions are activated both when an immediate option was offered and when it was not, allowing us to further support the unitary model we will outline in the general discussion of this dissertation, in line with Kable and Glimcher (2007, 2010)'s suggestion. The carry-over effect thus opens new scenarios for understanding how different brain regions code specific features of decisions, and if they work independently or conjointly (see Harris and Aguirre, 2010).

MVPA further supported previous findings. Distributed patterns of activity appeared to discriminate between offers with and without an immediate outcome. Activations were mostly located posteriorly (occipital and parietal lobe), on the parahippocampal gyrus, and along the inferior and middle frontal giri. In the specific, hippocampal activations are reminiscent of Peters and Büchel (2010a) findings about an involvement of this region in the valuation stage of intertemporal choices, predicting the degree to which future thinking modulated individual TD rates. Hippocampal regions have been found to affect decision-making in both humans (Hassabis et al., 2007; Gupta et al., 2009), and animals (e.g., Cheung and Cardinal, 2005; Mariano et al., 2009), suggesting a role in imagining novel experiences and mental time travel (e.g., Schacter and Addis, 2009). While occipital activations can account for visual features of offers (e.g., immediate options were shorter so faster to be read), as suggested by McClure and colleagues (2004), fronto-parietal activations can account for numerical processing (Dehaene et al, 1998), inhibition of impulsive choices, or in projection of future benefits providing top-down control to compete effectively with limbically mediated responses when present. The absence of insular cortex activity in this analysis is not surprising since in Study II-Part II we demonstrated that our insular patients were still able to distinguish between offers with an immediate available option and offers were both options were delayed in time, showing a reduced TD rate in the latter case. What this decoding analysis highlights here is that several regions are recruited to distinguish between offers with/without an immediate offer available. While with the univariate analysis reported above we could affirm that a special weight was placed on the immediate option, because salient and tempting, and that other areas are mostly activated when decision are more difficult, MVPA clearly evidenced that the recruitment of areas involved in both memory and future envisioning (Schacter et al., 2007) seem necessary when processing intertemporal choices. This could be because, as suggested by Bechara (2005), affective reactions to stimuli can emerge from recall of personal emotional experiences, or from the imagination of hypothetical affective events (somatic-marker hypothesis, Damasio, 1994; Bechara and Damasio, 2005; Verdejo-García and Bechara, 2009; see also anticipatory-utility perspective, Rae, 1834; Frederick et al., 2002). Results of MVPA also support our proposed unitary neural model generating the subjective value for outcomes to choose through both mechanisms of valuation and prospection. The conceptual appeal of pattern-information fMRI is that it allows to ‘look into’ the regions and investigate their representational content, suggesting that neuroeconomics might benefit from this approach (Mur et al., 2009).

All the activations reported here support the idea that intertemporal decision-making relies on a brain network in which regions work in producing multiple signals integrated at the end as they were in a unitary system. We will further discuss these observations at the end of this dissertation.

PART III – Behavioral modulations of intertemporal choice and temporal discounting: Transcending the ‘hic et nunc’

Précis

When faced with intertemporal choice, what makes people lean towards one option rather than another? Consider you are on a diet and have to decide if eating a slice of chocolate cake or a fruit salad for dessert. Whilst the tempting option would lead to immediate gratification, only the less pleasurable option would lead to avoid put on weight in the future. On the one hand, choosing the first is considered an impulsive decision: you are giving in to temptation of a tasty dessert now, forgetting long-term gains of your diet. On the other hand, choosing the second option is considered a prudent decision: you are giving up the immediate pleasure of the cake, arguably with a little bit of wrench, of course, but avoiding future weight gain instead, going for the healthier option. What guides people to behave impulsively or prudently when choosing between earlier good and long-term gain? And, why do attempts to resist immediate gratification often fail?

We found different effective ways to address this question by indirectly modulate behavior on several domains to actively change it with reliable effects at least in the short-term. The purpose of the present study, of course, was to reduce people's propensity towards the *'hic et nunc'* (from Latin, 'here and now') and consequently the discount rate of future rewards. Here I report three studies in which we manipulated in different ways people's behavior towards monetary and/or edible outcomes during intertemporal choice, basing our ideas on both recent neural and behavioral evidence. Moreover, a link with moral judgment and aging will be provided along two corollary studies, to provide further support to the proposed unitary model we will outline at the end in the general discussion of this dissertation.

Study I – Mental time travel toward past and future reduces temporal discounting of monetary but not edible rewards

Introduction

Shortsighted decision-making occurs in part because people fail to take into account their future interests (Gilbert et al., 2002). Faced with a tempting option (the slice of chocolate cake of my introductive example), people neglect the beneficial effects of the long-term outcome (losing weight).

In daily life, individuals frequently engage in envisaging possible future events (Suddendorf and Corballis, 2007), simulating and anticipating 'here and now' the affective impact they might have on themselves in the long run. This process is defined as episodic prospection or self-projection (Hassabis and Maguire, 2007; Schacter et al., 2007; Spreng et al., 2009), and recent neural evidence extensively showed that areas like mOFC and vmPFC, the same recurrent areas subserving intertemporal decisions, underpin it. These areas are also commonly identified as part of the so-called 'default network' (Gusnard et al., 2001), indicating a set of brain regions more active during rest or passive thought than directed cognitive processing (Buckner et al., 2008). This network extends to the neighbouring medial frontal and precuneas regions, as well as mesial and lateral aspects of the temporal lobes. Raichle and colleagues (2001) labelled it the 'default mode' because of the consistency of this activity pattern in undirected tasks.

It comes quite intuitively to imagine that when people are at rest, but awake, they think about something related to themselves, such as personal events occurred in the past (e.g., what happened yesterday when I came to visit my grand-mother), or to occur in a possible future (e.g., how should I dress tonight for my friends' party?). This might explain why activations in the ‘default network’ regions are remarkably similar to those during the act of self-projection, including imagining the future (prospection), and remembering the past (Buckner and Carroll, 2006): as is evident, in both processes mental time travel (MTT; Schacter et al., 2007) is required. The notion of MTT has been largely developed by Suddendorf and Corballis (1997), and refers to human beings’ capacity to both re-experience episodes from one’s personal past, and pre-experience possible events that may occur in the future (see Wheeler et al., 1997; Atance and O’Neill, 2001; Tulving, 2001; Suddendorf and Busby, 2003; Suddendorf, 2006; Botzung et al 2008). Interestingly, as Schacter and colleagues (2007) suggested, the brain areas included in the ‘default mode’ could be necessary to adaptively integrate information about relations and associations deriving from past experiences (memory) to construct mental simulations about possible future episodes (prospection and forecasting) (see Part I).

MTT and temporal discounting have been linked in several ways. For instance, Peters and Büchel (2010a) found that cued episodic future thinking during an intertemporal choice task reduced TD significantly. More specifically, participants performed a standard TD task, and a modified TD task with embedded cues to pre-experience future events. Future rewards were discounted significantly less in the latter compared to the former condition. This correlated with self-report imagery for the future episode and brain activity in ACC (coupled with hippocampus and amygdala activity) during cue processing, predicting how much individuals changed their preferences toward more future-minded choice behavior (Peters and Büchel, 2010a). Also, Ersner-Hershfield and colleagues (2009) tested the association between the ‘future self-continuity’, namely individual differences in the perception of one’s present self as continuous with a future self, with a discounting measure. They found that that current self- vs. future self-relevant information activated a rostral portion of the ACC, and that individual differences in the magnitude of this effect predicted the tendency to discount future outcomes. More recently, Benoit and colleagues (2011) provided further evidence in favour of the hypothesis that imagining the future biases subsequent monetary decisions toward options associated with a higher long-term pay-off. Specifically, in an fMRI study, they found that participants were more likely to choose a delayed but larger reward instead of a current but smaller reward if they had previously imagined the consumption of the delayed reward. Thus, episodic prospection effectively attenuated TD. Importantly, they found that the activation of the medial rostral prefrontal cortex (mrPFC) was associated with the simulation of future episodes as well as with the considered reward magnitude (Benoit et al., 2011).

In light of imaging (e.g., Kable and Glimcher, 2010; Peters and Büchel, 2010a; Benoit et al., 2011) and lesion (Sellitto et al., 2010) evidence about an involvement of vmPFC and mOFC in both TD and in MTT, we decided to test more downrightly the relationship between these two phenomena. Differently from the previous mentioned studies (Ersner-Hershfield et al., 2009; Peters and Büchel, 2010a; Benoit et al., 2011), we used the TD task we proposed in previous works (Sellitto et al., 2010; Sellitto et al., under submission; see also Study I, II-Part II) and a manipulation of MTT preceding, and unrelated to, the TD task. We also investigated if this manipulation had the same effect result in different types of rewards, namely, monetary and edible ones. We hypothesized that individuals trained to think to a distant time (past or future) would have reduced TD compared to individuals who thought about the present time, especially regarding monetary rewards.

Materials and methods

Participants

Two hundred and thirty participants were recruited both in Bologna and Cesena (Italy). Participants gave informed consent, according to the Declaration of Helsinki (International Committee of Medical Journal Editors, 1991) and the Ethical Committee of the Department of Psychology, University of Bologna, and they were randomly assigned to four different groups (see Table 1 for demographic information). Groups did not differ regarding sex, age, level of education, Body Mass Index (BMI, Borghans and Golsteyn, 2006), and hours of fasting (all ps > 0.10).

Groups	Number	Mean age (years)	Education	BMI	Fasting (hours)
Past	30 f / 23 m	37.4 (12.2)	15.4 (3)	23 (2.5)	3 (2)
Future	39 f / 23 m	36 (12)	16 (3)	24 (5)	3.4 (3)
Present Described	25 f / 20 m	42 (12.5)	14.4 (3.5)	24 (3.5)	3.2 (2.2)
Present Imagined	45 f / 25 m	37 (14)	15.1 (3.4)	23.6 (4)	3.1 (3)

Table 1. Participants' demographic data. f = female, m = male, BMI = Body Mass Index. Numbers in parenthesis are standard deviations.

Time manipulation task and ratings

Participants underwent to different time manipulations based on the group they were randomly assigned to by the experimenter. Subjects assigned to the Past group were trained to think to the past before performing two TD tasks. Specifically, they had to recall an event occurred in the last year that they had experienced personally, trying to re-experience it in the present, and write it down on a paper sheet. After that, they rated on three separate

5 points scale (from ‘a lot’, to ‘not at all’) how easy they found the act of remembering that event (difficulty scale), the level of emotion felt upon recalling the event (e.g., moved or excited, emotionality scale), and the degree to which how they felt to re-live the event (reliving scale). Ratings were the same for all groups in this experiment. Afterward, they had to think about a second event occurred in the last 3 years, write it down, and rate it in the same way they did for the previous event.

Participants in the Future group followed the same procedure, with the difference that they had to envisage possible future events and write a first time about a plausible scenario that may occur them 1 year later in the future. After the rating, they had again to imagine and write as more detailed as possible about another plausible scenario that might have occurred to them 3 years later, and then rate it.

Subjects included in the Present Described group the first time had to describe the more precise and detailed they could what they were seeing on the desk in front of them, and the second time what was happening around them. As for the other groups, they had to rate both times the difficulty, the emotionality, and the subjective experience of ‘living’ the current reality during the task. However, since we thought that this task might have been quite easy in terms of cognitive effort, and for someone maybe quite fast to be executed, we included a condition (group), the Present Imagined, in which participants had to think about two plausible experiences that may happened in the present moment and in the present spatial context different from what was actually happening. Again, participants underwent the three different ratings after both writings.

Procedure

After collecting demographic data, all groups performed the time manipulation task together with ratings (about 10-15 minutes; see next section), and then they underwent two TD tasks, based on two different reward types: in one we offered them money amounts (Euro), and in the other we offered them chocolate bars as reward (making sure at the beginning that participants liked it). The two TD tasks were administered in a randomized order and were the same (both amounts and delays) we used in Study I-Part II, as well as the titration procedure to adjust quantities of reward (Sellitto et al., 2010).

Results

Temporal discounting tasks. The *k* value for each curve reflects the geometric mean of the group. To analyse data, we used the same procedure as in Study I-Part II (Sellitto et al., 2010). Since we found in all our previous studies that hyperbolic model was always superior to the exponential model, here we will analyse only hyperbolic *k* parameters, and no AUCs were calculated.

An ANOVA on log-transformed *k* values with Group (Past, Future, Present Described, Present Imagined) as a between-subject factor, and Reward type (money, chocolate) as a within-subject factor, yielded no significant effect of Group [F(3, 226) = 2.35, p = 0.07], a significant effect of reward type [F(1, 226) = 42, p = 0.000001], and no significant Group × Reward type interaction [F(3, 226) = 1.51, p = 0.21]. Post hoc comparisons, performed with the Newman-Keuls test, showed that TD was less steep when participants chose between monetary amounts rather than chocolate bars (-2.1 vs. -1.4; p = 0.00001). The result that subjects behaved less impulsively toward money than food is completely in line with our previous results and literature as well (Charlton and Fantino, 2008, Estle et al., 2007; Odum and Rainaud, 2003; Sellitto et al., 2010). Moreover, when we performed an ANCOVA including, separately, participants' BMI scores and fasting hours as covariates, a similar pattern of results was found.

Although no significant interactions have been found, taking into account the significant tendency of the group effect, for completeness purpose, we decided to repeat the analysis separately for reward, to be sure we were not underestimating any significant result.

An ANOVA on log-transformed *k* values for the monetary TD task with Group (Past, Future, Present Described, Present Imagined) as a between-subject factor, revealed a significant effect of Group [F(3, 226) = 4.35, p = 0.005]. Post hoc comparisons, performed with the Newman-Keuls test, showed that TD was significantly reduced in participants previously trained with the Past and the Future tasks as compared to participants in the Present Described and in the Present Imagined groups. Participants in the Past group had the same mean discount rate as participants in the Future group (-2.35 vs. -2.30; p = 0.63), significantly smaller than that of participants in the Present Described group (-2.35 vs. -1.9; p = 0.03) and of those in the Present Imagined group (-2.35 vs. -1.8; p = 0.02). Similarly, subjects in the Future group had a smaller discount rate than those in the Present Described group (-2.3 vs. -1.9; p = 0.04) and of those in the Present Imagined group (-2.3 vs. -1.8; p = 0.04). Conversely, no difference in the TD between the Present Described group and the Present Imagined group was detected (-1.9 vs. -1.8; p = 0.70) (Fig. 1).

When we performed the same analysis on log-transformed *k* values for the TD task with food, no significant difference among groups emerged [F(3, 226) = 0.80, p = 0.50], suggesting that, while our manipulation differently influenced discount rates for monetary amounts based on which kind of MTT we induced (or the lack thereof), this did not affect the discounting behavior for the primary reward (Fig. 1). We will further discuss these results later.

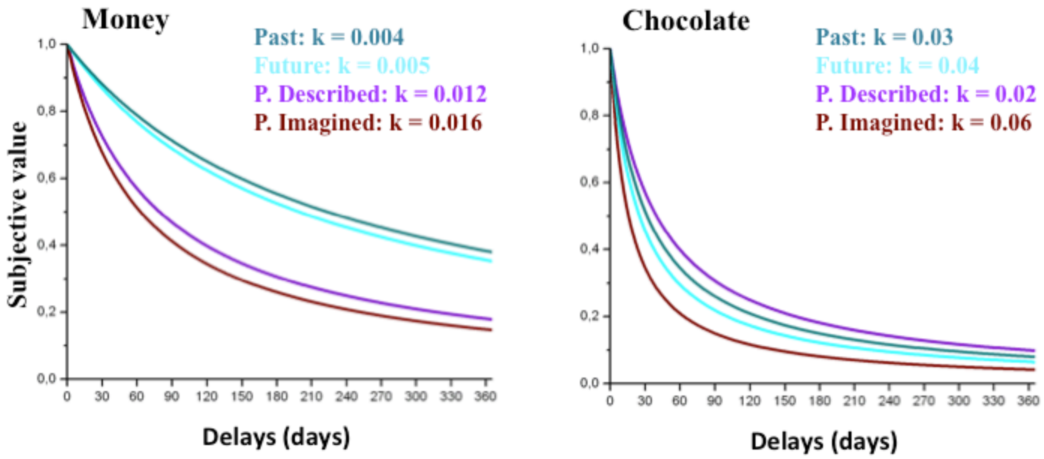

Figure 1. On the left, TD functions for money by group. On the right, TD functions for chocolate by group.

Time manipulation ratings. We compared the four groups on all ratings they performed twice during the time manipulation phase. It is important to note that smaller numbers correspond to higher ratings, due to the way in which we asked the three questions (see the Time manipulation section). An ANOVA on scores about the difficulty of the task with Group (Past, Future, Present Described, Present Imagined) as a between-subject factor, and Time of rating (first, second) as a within-subject factor, yielded no significant effect of Group [F(3, 226) = 2.1, p = 0.10], a significant effect of Time of rating [F(1, 226) = 12, p = 0.0006], and a significant Group × Time of rating interaction [F(3, 226) = 5, p = 0.002]. Post hoc comparisons, performed with the Newman-Keuls test, showed that the second time subjects had to perform the task the difficulty incremented as compared to the first time (2.1 vs. 1.8; $p = 0.002$). This result might be explained by the ego depletion due to the cognitive effort required the first time they performed the task, but also because travelling farther in time, be this towards the past or the future, as well as describing a more complex situation (for the Present Described group), and imagining again something different from the actual present (for the Present Imagined group), was sensibly more difficult. In accordance with our intuitions, the first attempt to describe the present (Present Described group) was rated as significantly easier than the second attempt (1.33 vs. 2.04; $p = 0.0007$), and than all other (MTT) conditions. (all $ps < 0.05$). All other comparisons did not reach statistical significance (all $ps > 0.10$).

An ANOVA on scores about the emotionality of the task with Group (Past, Future, Present Described, Present Imagined) as a between-subject factor, and Time of rating (first, second) as a within-subject factor, yielded a significant effect of Group [$F(3, 226) = 45$, $p = 0.000001$], but no significant effect of Time of rating [$F(1, 226) = 0.04$, $p = 0.83$], and no significant Group × Time of rating interaction [$F(3, 226) = 1.23$, $p = 0.30$]. Post hoc comparisons, performed with the Newman-Keuls test, showed that while participants in the Present Described group were those who experienced less emotion during the task (4.05; all $ps < 0.00006$), those in the Future group experienced the highest emotionality (2.10; al $ps < 0.004$). Finally, the Past and the Present Imagined groups experienced the same level of emotion (2.6 vs. 2.8; $p = 0.14$).

Finally, an ANOVA on scores about the reliving during the task with Group (Past, Future, Present Described, Present Imagined) as a between-subject factor, and Time of rating (first, second) as a within-subject factor, revealed no significant effect of Group [$F(3, 226) = 2.2$, $p = 0.09$], no significant effect of Time of rating [$F(1, 226) = 3$, $p = 0.10$], and no significant Group × Time of rating interaction [F(3, 226) = 2, p = 0.15]. We will discuss these findings in the next session.

Discussion

In this study we trained participants to either think about past events (Past group) or future possible scenarios (Future group) before making intertemporal decisions, while two control groups were trained to either describe the present situation (Present Described) or imagine an alternative present situation (Present Imagined). Following null results in the principal analysis, we repeated it separately for commodities (money and food) to be sure we were not missing any significant effect. As compared to control groups, the Past and the Future groups made significantly less shortsighted decisions. However, this result yielded only for amounts of money, whereas no difference has been detected between groups when choosing among amounts of edible reward. When analysing participants' ratings about the MTT task, we found that, among the others, participants in the Present Described group judged the task, the first time they did it, as significantly easier then the other participants did other times, suggesting that their task was different in the cognitive effort we required them. However, both Past and Future groups differed from the Present Imagined group in the discount rates for money but not in the difficulty rating, indicating that our MTT manipulation succeed. Moreover, while we observed that the four groups did not differ from each others regarding the re/pre-living experience, we found a difference in the way they rated the emotion experienced during the time manipulation task. Indeed, while participants in the Present Described group revealed lower levels of emotionality during the MTT task, those in the Future group had significantly higher levels of emotionality as compared to all other groups, whereas no difference was detectable between the Past and the Present Imagined. This result might suggest that the experienced emotion is associated more than anything else to the act of imagining something not yet real, because it is yet to come, but also, to a lesser extent, to the imagery about something that is not happening now, and to recollect events happened in the past, rather then to the movement of our self in the future time only.

Taking together the findings of the present study, it seems that it is not to travel in a particular time direction, but, rather, transcending the ‘here and now’, moving one’s self in time, that has the effect to unbind people from their sensorial self. Thinking about events not linked to the current surrounding environment is sufficient to become less discounter and to make less shortsighted decisions toward monetary outcomes. However, these considerations are not true for edible rewards. It is important to note, indeed, that edible rewards are characterised by perishability, they lead to satiety and saturation very quickly (this is difficult to happen with money, indeed!), and they are not exchangeable for other outcomes like secondary rewards. Moreover, here we tested only one food. All these factors might have influenced the present results. We will further analyse this issue in Study III-Part III.

In light of our previous finding about the causal involvement of mOFC in intertemporal decision-making (Sellitto et al., 2010; Ciaramelli and di Pellegrino, 2011; Study I-Part II), present results support the idea that one of the possible mechanisms through which mOFC may influence valuation and judgment of future rewards relies in its role in enabling us to shift perspective to alternatives in time other than the present (Buckner and Carroll, 2006; Andrews-Hanna et al., 2010), that is self-projection. When faced with an intertemporal choice, mOFC may serve to recall past experiences associated with rewards, anticipate future feelings, and modulate the subjective value of future outcomes based on the resulting affective states (Bechara, 2005). For instance, mOFC may be responsible to the ability to remember, and then imagine and reproduce how we will feel in two weeks after collecting € 40. Moreover, vmPFC activity predicted both how much people would enjoy something in the future and the extent to which they made impulsive monetary decisions (Mitchell et al., 2010), and also future forecasting reduced discount rates (Benoit et al., 2011; Peters and Büchel, 2011), suggesting that damage to mOFC would result in a poor representation of future outcomes and, consequently, in imprudent behavior (Ciaramelli and di Pellegrino, 2011). As a consequence, mOFC patients of our first study (Study I-Part II, Sellitto et al., 2010) might have been unable in the imagery of future rewards, being thereby overwhelmed by salient, current rewards. This idea is also supported by a study of Moretti and colleagues (2009) who found that vmPFC patients accepted unfair offers during an ultimatum game, in the same way control participants did, only when monetary outcomes were visible and readily available. That is, the concreteness with which gains were presented, and how soon they will have been experienced, influenced their choices, whereas they substantially reduced their acceptance rate of unfair offers when financial gains were presented as abstract amounts to be received later (Moretti et al., 2009). Moreover, our result supports imaging findings (Peters and Büchel, 2010a) about TD being predicted by the degree of spontaneous episodic imagery during decision-making.

Recently, Smallwood and colleagues (2013) demonstrated that the ability to delay gratification was related to mind-wandering (Antrobus et al., 1966; Klinger, 1978a,b; Killingsworth and Gilbert, 2010; Baumeister et al., 2011; Smallwood et al., 2011). That is, when the environment is poorly interesting, people engage in task-unrelated thoughts, they start off-thinking. The degreeto which their participants engaged in task-unrelated thoughts during a simple RT task positively correlated with the degree to which they discounted delayed monetary rewards (in a separate TD task session that could have occurred before or after the RT task) (Smallwood et al., 2011). Smallwood and colleagues (2013) suggested that this capacity to let go of the present and concentrate on more personally relevant issues helped individuals to make decisions about their personal futures, probably because both protecting the internal goals from distraction and interference, and promoting the episodic projection into future and past situations, instead of resulting in a cognitive interference (but see McVay and Kane, 2011).

The fact that in the present study also individuals trained to think about past events reduced their discount rates, together with the evidence that future forecast lessened discounting behavior, and that individual differences in the differential activation of medial prefrontal regions for current vs. future self-relevant information predicted the degree to which subjects were capable to save money for the future (i.e., greater the activation in medial prefrontal regions, larger the impatience in discounting future rewards; Ersner-Hershfield et al., 2009; Pronin et al., 2008), supports Schacter and colleagues (2007)' idea that the brain areas included in the 'default mode' are necessary to adaptively integrate information about relations and associations deriving from past experiences (memory), to construct mental simulations about possible future episodes. Clinical data also endorse this idea, since patients with lesions to those areas were found to be dysfunctional not only during episodic memory tasks, but also in episodic future thinking (Atance and O'Neill, 2001; Ciaramelli and Ghetti, 2007).

From an evolutionary perspective, Boyer (2008) proposed that the engagement with past and future events enrich them with motivational force: both memory and imagination may break impulsiveness or boost on patience by associating plans with non-opportunistic rewards. MTT would lead to activate stored knowledge against which to compare imagined future events, bypassing current goals. This could be the best way to get adapted to new contingencies, escaping form errors made in the past, and consequently reducing TD.

Another possible explanation of why our MTT training had the effect of lessening impulsivity during monetary intertemporal choices, without excluding our previous suggestion though, could be that forecasting about oneselves or remembering oneselves can highlight differences between far selves and present selves (Ersner-Hershfield et al., 2009), helping in making the optimal decision. This can be considered an alternative way to think about future rewards using more abstract construals (i.e., mental representation; Liberman and Trope, 1998, 2008; Trope and Liberman, 2003). Indeed, looking at something from a distant view, in a decontextualized manner, not linked to the surrounding actual situation, lead people to think in a 'colder' way about future outcomes, highlighting the fact that they are larger, and so more convenient, than sooner outcomes. I will examine more in depth this issue in Study III-Part III.

Study II – Intertemporal choice and moral judgement: When pre-experiencing future outcomes is necessary

Introduction

Can a moral judgement be considered an intertemporal choice? While during time-based decisions people have to choose whether to prefer a smaller but earlier reward or waiting for a larger but later reward, when faced with moral dilemmas, they have to decide if acting in some way can be considered moral or immoral. On the one hand, when you have to choose, for instance, if staying at home writing your PhD thesis or spending the day out enjoying sun with friends, you are considering if enjoying something pleasurable in the short run or wait for the future but greater gratification (i.e., succeed in your viva voce). On the other hand, consider you are on a footbridge above railway tracks and an oncoming train is going to kill five persons if you will do anything ('footbridge dilemma'; Thomson, 1985). If you decide to throw out a large person standing near you, you will stop the train saving the five people but killing him. When you choose what to do in this case, you are comparing a short-term gain, saving five lives at the cost of killing one person, with a long-term gain, having no future remorse for having been respectful of social rules. Moral dilemmas require people to judge weather it is appropriate or not to incur a moral violation to follow utilitarian, more reasoned, considerations (i.e., maximize overall consequences saving five persons; Greene et al., 2001). However there is a distinction to be made. The example above is considered a personal dilemma, in which the moral violation consists in causing serious bodily harm to someone through one's own agency. On the contrary, if you are required, for instance, to choose whether or not to hit a switch that will turn the trolley to an alternate set of tracks, where it will kill one person instead of five (‘trolley dilemma’; Foot, 1967), is considered an impersonal moral judgment, because the violation do not involve one’s own agency and, therefore, may induce a less intense emotional experience in individuals (Greene et al., 2001). Accordingly, Greene and colleagues (2001, 2004) found that, emotional processes were mostly active when individuals in the scanner were making judgments about personal moral scenarios, whereas cognitive mechanisms were predominant when they were making judgments about impersonal moral dilemmas (Greene et al., 2001, 2004, 2008). Ugazio and colleagues (2012) proposed that these results show that cognitive mechanisms inform moral judgments based predominantly on action’s consequences (utilitarian judgments), while emotional mechanisms primarily inform moral judgments focusing on the means used to obtain a given outcome (deontological judgments). Sometimes, moral reasoning is more concerned with adherence to duties and proscriptions than with consequences (Bennis et al., 2010). Moreover, as suggested by Frank (1988), moral problems require people to make commitments to behave in ways that may later prove contrary to their interests (Loewenstein, 1992). Indeed, anticipating non-egoistic emotions, like feelings of guilt or embarrassment, can prevent someone, in his examples, from cheating on someone or stealing something in a shop (Loewenstein, 1992). This demonstrates that, as intertemporal choices do, also moral dilemmas require people to exercise self-control, referred to by Baumeister’s research group (e.g., 1998, 2003, 2007) as the ‘moral muscle’ because it provides the power to do what is right.

Neurally, both the process of intertemporal decision-making and the process of moral judgment share a common brain network, engaging vmPFC. In spite of preserved general intellectual abilities, patients with vmPFC lesions show several deficits regarding judgment, decision-making, social conduct, and personality (e.g., Bechara and Damasio, 2005; see also Part I). This cortex is generally deemed as responsible for mediating aversive emotional responses toward moral violations to prevent people from approving immoral acts, even if at costs (Greene et al., 2001). Moreover, as we demonstrated before (Study I-Part II), mOFC patients were less willing to wait for future rewards, increasing their preferences for immediate outcomes (impulsivity), regardless of the good type (Sellitto et al., 2010), and they were more willing to accept moral violations, especially when there was high conflict between the emotional and the utilitarian component (Ciaramelli et al., 2007).

Here we investigated the relationship between intertemporal choice and moral judgment in healthy participants through a TD task (Sellitto et al., 2010) and several personal and impersonal moral dilemmas (Ciaramelli et al., 2007). We expected to determine how mind decisions relate to the balance of short- versus long-term choices that people make. Specifically, we expected a linear relationship between TD and moral violations, namely, the larger the impulsivity in intertemporal choice, the larger the willingness to accept moral violations, thereby suggesting that a common MTT mechanism can drive both processes with the anticipation of future outcomes.

Materials and methods

Participants

We tested 32 healthy individuals [24 females; mean age: 34 years (standard deviation: 8.4), mean education: 14 years (standard deviation: 3.0)] who were not taking psychoactive drugs, and were free of current or past psychiatric or neurological illness as determined by history. All participants gave informed consent, according to the Declaration of Helsinki (International Committee of Medical Journal Editors, 1991) and the Ethical Committee of the Department of Psychology, University of Bologna.

Neuropsychological assessment

We assessed the general cognitive functioning of participants through several neuropsychological tests widely used in clinical practice to exclude that results could have been explained by poor reasoning abilities or other cognitive defects. Analytic abilities were evaluated with the Coloured Progressive Matrices of Raven (CPM, Raven, 1981; Basso et al., 1987). Cognitive flexibility was assessed through the Wisconsin Card Sorting Test (WCST, Berg, 1948; Spinnler and Tognoni, 1987). Attention and speed of information processing were assessed using the Paced Auditory Serial Addition Test (PASAT, Gronwall, 1983) (3-s and 2-s versions). Language was assessed through phonetic and semantic fluencies (Novelli et al., 1986b). Memory was assessed with a series of tests: digit span test (Orsini et al., 1987) and short story test for the short-term memory (Novelli et al., 1986a), Corsi's test for the visuo-spatial span (De Renzi and Nichelli, 1975; Splinner et al., 1987), Rey-Osterrieth Complex Figure Test (ROCF, copy and recall, Carlesimo et al., 1996; Osterrieth, 1944; Rey, 1941) for visuo-spatial abilities and long-term memory. All participants obtained scores in the normal range for their gender, age and education.

Temporal discounting task

The TD task was the same used in the Study II-Part II (see also Sellitto et al., 2010). Hypothetical monetary amounts (€) were offered participants in two different temporal condition: the Now condition, where a smaller current option was paired with a larger but delayed option, and the Not-now condition, where the sooner option was always available in 60 days. Task procedure, delays and titration procedure were exactly the same we used in that previous study.

Before the beginning of the experimental session, participants were told that, on each trial, two amounts of hypothetical money would appear on the screen. One could be received sooner, and one could be received later. They were informed that there were no correct or incorrect choices, and were required to indicate the option they preferred by pressing one of two buttons on a keyboard with no temporal constrictions (see Study I-Part II, Sellitto et al., 2010).

Moral dilemmas task

Participants were submitted to 12 personal moral dilemmas, and 12 impersonal moral dilemmas, translated into Italian after being randomly selected from a battery of 60 dilemmas developed by Greene and colleagues (2001; the complete battery is available at: www.sciencemag.org/cgi/content/full/293/5537/ 2105/DC1). Contrary to non-moral decisions, all moral dilemmas are supposed to elicit moral emotions (Greene et al., 2001; Ciaramelli et al., 2007). Personal moral dilemmas in the present study included scenarios in which the action was driven by the agent willingness, for instance when deciding if practicing a lethal injection to discover a new vaccine, or pushing down people from a lifeboat to avoid sinking. Conversely, impersonal dilemmas induce people to decide if being involved in a risky but predetermined situation, as for instance when deciding if pushing or not a level to move railway tracks to change the oncoming train direction to kill one person instead of five. Participants' judgement was based on their on-line appraisal of the specific situation they were contemplating (Ciaramelli et al., 2007).

Each dilemma was presented as text through a series of three screens. The first screen described the scenario. The second screen posed a question about the appropriateness of an action one might perform in that scenario (i.e. the 'dilemmatic question') (e.g. 'Is it appropriate to save the five persons by pushing the stranger to death?'). After reading the scenario (with no time limits), subjects pressed a button to advance from one screen to the next, where the dilemmatic question appeared, and they responded 'appropriate' ('yes, it is appropriate to do that') or 'inappropriate' ('no, it is not appropriate to do that') by pressing one of two buttons. Participants were told to respond as soon as they had reached a decision, within no more than 60 seconds. For all dilemmas being tested, 'appropriate' responses implied the maximization of overall consequences (Greene, 2003; Ciaramelli et al., 2007), e.g. killing one instead of five persons. Both the number of 'appropriate' responses and response times (RTs; i.e. the time from the onset of the dilemmatic question to the moment a response was given) were collected. Once a response was given, a 5 sec-fixation cross appeared, signalling the beginning of the new moral scenario.

Procedure

TD task and moral dilemmas were administered in a random and counterbalanced order across subjects. Both tasks were completed seating in front of the same laptop in a quiet room after receiving adequate instructions. The whole experiment required about 45 minutes.

Results

Temporal discounting task. To analyse data, we used the same procedure as in Study II-Part II (see also Sellitto et al., 2010). Since we found in all our previous studies that the hyperbolic model was always superior to the exponential model, here we will analyse only hyperbolic *k* parameters, and no AUCs were calculated.

An ANOVA on log-transformed *k* values with Temporal condition (Now, Not-now) as a within-subject factor yielded a significant effect of Temporal condition [F(1, 30) = 26.2, p = 0.00001]. Post hoc comparisons, performed with the Newman-Keuls test, showed that TD was significantly steeper in the Now condition than in the Not-now condition (-1.27 vs. -1.80; p = 0.0001) (Fig. 1). This result is completely in line with our previous findings, suggesting that subjects differently as well as correctly performed intertemporal decisions when an immediate option was offered and when it was not.

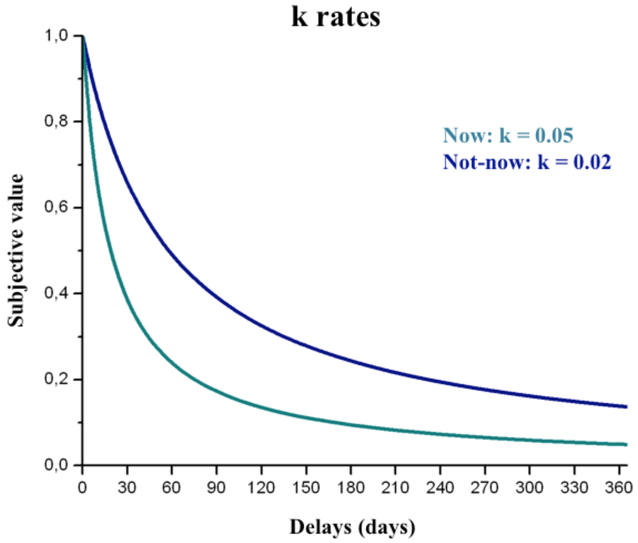

Figure 1.TD functions for money by temporal condition.

Moral dilemmas task. An ANOVA on the number of times participants made moral violations (namely, they accepted that the action described in the moral scenarios was appropriate) with Dilemma (Personal, Impersonal) as a within-subject factor yielded a significant effect of Dilemma [F(1, 30) = 5.63, p = 0.01]. Post hoc comparisons, performed with the Newman-Keuls test, showed that participants made a larger number of violations during impersonal than personal dilemmas (6.4 vs. 5.4; p = 0.03). This result is in line with the literature, suggesting that our participants were more willing to make violations during impersonal moral decisions, rather than during personal dilemmas (Fig 2.).

Figure 2. Number of violations for personal and impersonal moral dilemmas.

An ANOVA on mean RTs (in milliseconds) with Response ('appropriate', 'inappropriate') and Dilemma (Personal, Impersonal) as within-subject factors, yielded no significant effect of Dilemma [F(1, 30) = 0.16, p = 0.70], and no significant effect of Response [F(1, 30) = 0.04, p = 0.84], but a significant Response × Dilemma interaction [F(1, 30) = 9, p = 0.006]. Post hoc comparisons, performed with the Newman-Keuls test, indicated that during personal dilemmas participants were marginally significantly slower when judging 'appropriate' rather than 'inappropriate' the described scenario (9616.4 vs. 7776; comparison tending to be significant, p = 0.07), while no difference was detectable during impersonal dilemmas between 'appropriate' and 'inappropriate' responses (8222 vs.

9734; p = 0.15), replicating previous findings (Greene et al. 2001, 2004; Ciaramelli et al., 2007) (Fig. 3).

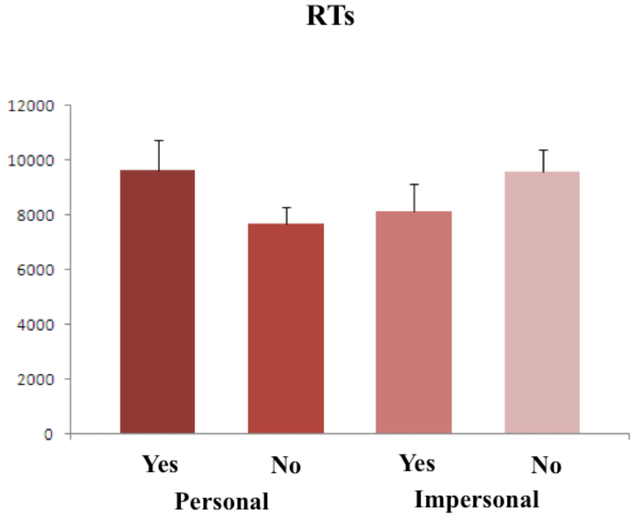

Figure 3.RTs for accepting and refusing moral violations for personal and impersonal moral dilemmas.

Temporal discounting task and moral dilemmas task. By using partial correlation analyses, we investigated the relation between *k* rates for both temporal conditions (Now, Not-now) and the number of moral violations for both types of dilemmas (Personal, Impersonal). We found that the discount rate for the Now temporal condition correlated significantly with both the number of personal (r = 0.38; p = 0.03, two-tailed) and impersonal (r = 0.52; p = 0.002, two-tailed) violations during the moral dilemmas task (Fig. 4a,b). Conversely, the discount rate for the Not-now temporal condition did not correlate significantly with either the number of personal (r = 0.20; p = 0.30, two-tailed) or impersonal violations (r = 0.04; p = 0.83, two-tailed). These positive correlations indicated that the larger the impulsivity during intertemporal choices when an immediate reward was available, the more individuals tended to accept violations during both personal and impersonal moral dilemmas.

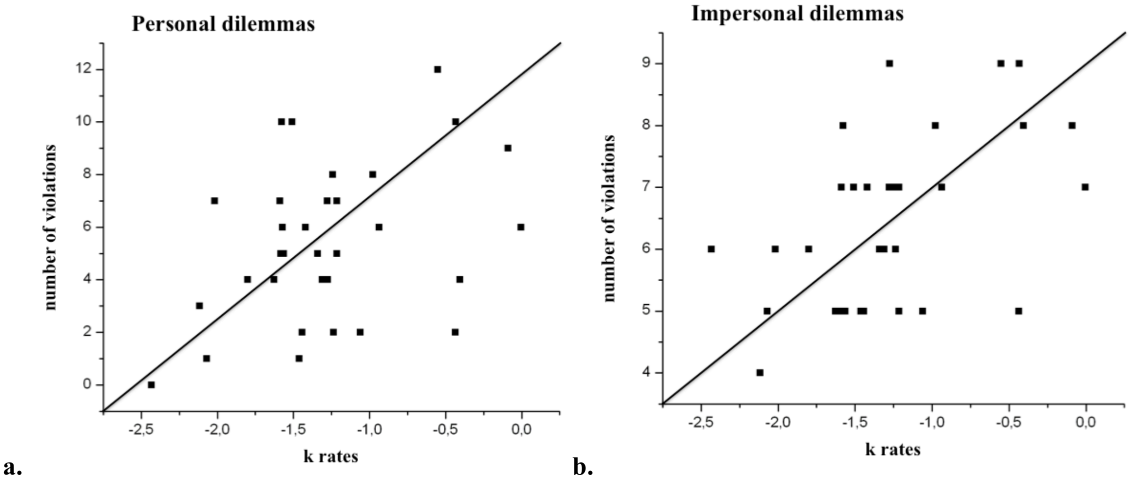

Figure 4. a. Correlation between TD rates and number of violations for personal dilemmas. b. Correlation between TD rates and number of violations during impersonal dilemmas.

However, when we performed partial correlations to investigate the relationship between *k* rates for both temporal conditions (Now, Not-now) and RTs (‘appropriate’, ‘inappropriate’) for both types of dilemmas (Personal, Impersonal), we found that *k* rates for the Now temporal condition significantly correlated only with the RTs during ‘appropriate’ responses for personal dilemmas (r = -0.41; p = 0.02, two-tailed) (Fig. 5). No other significant correlation, indeed, was found between TD rates and RTs (all ps > 0.36). This negative correlation indicated that people more impulsive in choosing between smaller but immediate and larger later rewards (larger *k* values) were also faster in accepting as appropriate a personal moral dilemma (smaller RTs).

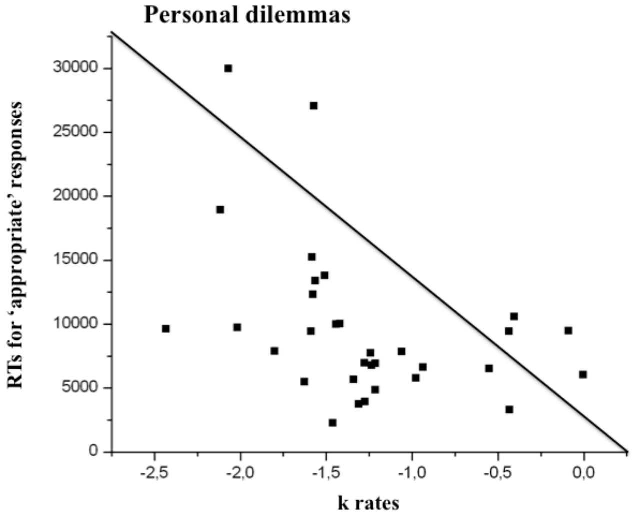

Figure 5. a. Correlation between TD rates and RTs for violations during personal dilemmas.

Discussion

In the present study we related the monetary discounting behavior to the moral judgement. On the one hand, during TD tasks, subjects were more impulsive when we offered them a larger delayed reward against a smaller but current one, rather than when both options were delayed in time, replicating previous findings (e.g., Frederick et al., 2002; McClure et al., 2004, 2007; Sellitto et al., under submission). On the other hand, during moral judgements, the same subjects made fewer violations during personal rather than during impersonal dilemmas. Moreover, while it took them the same time to both accept and condemn actions described in impersonal dilemmas, the decision took longer when defining as 'appropriate' rather than 'inappropriate' the scenario of personal dilemmas, replicating again literature findings (Greene et al. 2001, 2004; Ciaramelli et al., 2007). When we put in relation both discounting and moral behaviors, we found that the more our participants were imprudent during intertemporal choices when an immediate option was available, the more they were willing to define as 'appropriate' both personal and impersonal dilemmas. However, when we repeated this analysis on RTs instead of the number of violations, we found that the more subjects were impulsive during intertemporal choices when an immediate option was available, the faster they were in accepting violations during personal dilemmas only. On the one hand, intertemporal choices between a current reward and a delayed one put people through a conflict generated by the presence of the tempting gratification available very close in time, even when outcomes are just hypothetical. The conflict between the two options is attenuated when replacing the immediate reward with a sooner yet not immediate one. On the other hand, people experience higher conflict when judging a personal moral dilemma rather than an impersonal one, also taking longer to authorize a personal violation. Both processes (TD and moral judgement) share a common brain network, engaging vmPFC and mOFC. Indeed, in spite of preserved general intellectual ability, patients with vmPFC and mOFC lesions show several deficits regarding judgment, decision-making, social conduct, and personality (e.g., Bechara and Damasio, 2005; Moretti et al., 2009). The present results parallel both findings of Sellitto and colleagues (2010; see Study I-Part II) about the increased impulsivity in mOFC patients (‘myopic discounting’), and findings of Ciaramelli and colleagues (2007) about the increased inclination to approve, more quickly as well, personal moral violations, in vmPFC patients. Having damage in those cortices, indeed, decreased both the willingness to wait for future rewards and the reluctance in accepting moral violation, especially when there was high conflict between the emotional and the utilitarian component (Ciaramelli et al., 2007). It is also worth to note that, as mOFC patients were more willing to wait for delayed money and discount vouchers than for delayed food, like control participants did (Sellitto et al., 2010), vmPFC patients (Ciaramelli et al., 2007) had normal behavior in impersonal and non-moral dilemmas, suggesting that those behaviors cannot be explained with a mere poor motor impulse control or impulsiveness to approve the behaviors at stake without evaluating their merit properly.

To make these two types of judgement, we call into play visceral sensations. Anticipating emotions (e.g., ‘how will I feel after doing that?’) drives our choices based on previous experiences of the probability of feeling pleasure or pain as a consequence of an act (Bechara, 1994, 2005; Mellers et al., 1999; Mellers and McGraw, 2001; Ciaramelli and di Pellegrino, 2011). As suggested by Bechara (2005), affective reactions to stimuli can emerge from recall of personal emotional experiences, or from the imagination of hypothetical affective events (somatic-marker hypothesis, Damasio, 1994; Bechara and Damasio, 2005; Verdejo-García and Bechara, 2009).

In the model we are proposing here (Sellitto et al., 2010, 2011), mOFC, vmPFC, VS, and PCC signal the subjective value of both immediate and delayed reward, with a specific role for mOFC in considering and mediating low-level signals coming from insula (see Study II-Part II, Sellitto et al., under submission) with top-down signals deriving from cognitive control structures (e.g., dlPFC; Christakou et al., 2009, 2011; Hare et al., 2009; Figner et al., 2010; Sellitto et al., 2010, 2011; see the general discussion of this dissertation). Abnormalities in this mechanism can compromise the ability to make advantageous long-term choices (Bechara, 2001; Clark et al., 2008), failing in mediating intentions’ understanding, and in overriding prepotent responses to salient outcomes (Ciaramelli et al., 2012). However, what the present data also support, is that the process of considering the future consequences of an action is required both when people are asked to accept a future reward instead of an immediate gratification, and when they are asked to take into account the future outcome of having broken a social rule. When this process is dysfunctional, they do not envision optimally future outcomes (both monetary and moral) of their actions, thereby neglecting future consequences (e.g., gain a larger monetary amount, and have remorse) (Ciaramelli and di Pellegrino, 2011; but see also the ‘intervention myopia hypothesis’, Waldmann and Dieterich, 2007). As Ciaramelli and di Pellegrino (2011) suggested, this might happen not only because one can be unable to prefeel and recall visceral emotions associated with a future outcome (‘gut feelings’; Hume, 1777/1960; Haidt, 2001; Wheatley and Haidt, 2005; Prinz, 2007; Schnall et al., 2008; Ugazio et al., 2012), as in our insular patients (see Study II-Part II, Sellitto et al., under submission), but also because actually unable to envision future events in the first place, through an adequate MTT, and how they will feel after a specific decision.

Study III – Visual spatial travel and monetary intertemporal choice

Introduction

As said before, when faced with tempting sooner outcomes, people frequently tend to prefer sooner smaller outcomes during intertemporal choice, being attached to the '*hic et nunc'* of the moment, deciding to go for the less advantageus option. One way to exercise the required self-control to achieve the larger later reward is to emphasize its abstract and core features in presence of the more salient sooner, even if smaller, reward.

We based the idea of the present study upon the Construal Level Theory (CLT, e.g., Liberman and Trope, 1998, 2008; Trope and Liberman, 2003; Fujita et al., 2006; Fujita and Carnevale, 2012), that links psychological distance from objects to their mental construal. Namely, different dimensions of psychological distance correspond to different ways in which objects or events can be represented: An object can be psychologically distant in time (past or future), in space, in the social dimension (e.g., because linked to others' experience; ingroup vs. outgroup), or in the probability domain (e.g., if it is a matter of hypothetical rewards, it is likely to do not occur) (Liberman and Trope, 2008).

The CLT assumes that the more one is able to remove objects from the self, the more she construes them at a higher abstract level. Accordingly, any event or object can be represented at lower-level construals, that are concrete and contextualized representations that include subordinate and incidental features of events, or at higher-level construals, that are abstract, schematic, and decontextualized representations (Liberman and Trope, 2008). A demonstration of how construals affect one's way of thinking comes from a study of Bar-Anan and colleagues (2007): A modified version of a

Stroop Task (Fig. 1) required participants to indicate the location of an arrow and to identify the word on it. In congruent trials, a word denoting social proximity (e.g., ‘us’) was located near the observer, and a word denoting social remoteness (e.g., ‘them’) was located far from the observer. The opposite condition was denoted as incongruent. Because spatial distance is associated with social distance, participants were slower when social proximity words were located in the distant space and vice versa. There are many others ways to change the level of construal of a good at stake, and so the mindset to think about it. These range from changing the spatial position of visual objects, to the substitution of adjectives reminding low-level meanings, with abstract features reminding high level goals that can be reached through that good. For instance, in the example at the beginning of Part III, one could have said ‘delicious and creamy slice of chocolate cake’, or ‘fresh and healthy fruit salad’.

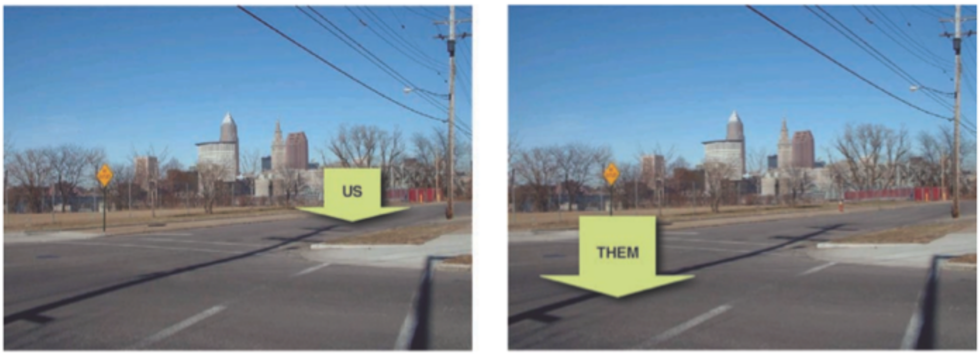

Figure 1. In the context of CLT and psychological distance, two examples of incongruent visual stimuli: a word denoting social proximity, ‘us’, located far from the observer, and a word denoting social remoteness, ‘them’, located near the observer. Because spatial distance is associated with temporal distance, social distance, and hypotheticality, participants are slower to indicate the location of the arrow and to identify the word on it with incongruent stimuli than with con- gruent stimuli (‘us’ located near the observer and ‘them’ located far from the observer) (Adapted from Bar-Anan et al., 2007; Liberman and Trope, 2008).

The prediction of CLT is that increased psychological distance should shift the overall attractiveness of an outcome closer to its high-level construal value and away from its low-level construal value. In terms of CLT accounting for intertemporal choice, the value of the outcome (i.e., the magnitude of the reward) is considered a high-level construal, while the length of time one needs to wait to obtain that outcome (i.e., its delay) is considered a secondary low-level feature of the outcome. When the attention is focused on the low-level value of an outcome, being more concerned with the outcome delay, TD would result, so that the future outcome would be less attractive. When the attention is focused on the high-level value of an outcome, the future outcome should be more attractive (Leiser et al., 2008). The trick is to shift attention toward higher construals. Fujita and colleagues (2006) provided preliminary evidence by manipulating the participants' willingness to pay towards both immediate and delayed outcomes. In a between-subjects design, participants primed with high-level construal questions (e.g., 'why do you do this?'), as compared to those primed with low-level construal questions (e.g., 'how do you do this?'), displayed then a reduced tendency to prefer immediate over delayed outcomes. Switching objects' high-level representations on enabled people to be more willing to wait for larger later outcomes, as we did in Study I-Part III, training people to think about far time, consequently reducing their discount rates of future monetary rewards.

The present study aimed to explore if influencing outcomes representations can reduce TD. In a previous study (Study I-Part III), by way of MTT procedure, we trained participants to project their self in the distant time to detach them from their sensorial self, therefore reducing TD. Here we increased the psychological distance from the outcome by moving the outcome itself, in the spatial dimension, thereby allowing participants being attracted by high-level construal of future options (i.e., the magnitude) and less attracted by its low-level property (i.e., longer time to be waited), thus reducing TD. To address this question we manipulated the physical position of monetary rewards in order to change their perceived spatial distance from decision-makers during binary intertemporal choices. Along two experiments, in one case both options were positioned in the near or in the far space at the same time. In another case, while one option was positioned in the far space, the other was positioned in the near space. We predicted that, when both options are perceived as more spatially distant, or when the larger later option is perceived as more spatially distant, abstract features are highlighted (i.e., enriched with high level attributes), leading people to shift their preference toward the larger delayed outcome, thus reducing TD.

Experiment 1

Materials and methods

Participants

Fifty-nine undergraduate students were recruited through the research website Sona Systems Ltd. at the Bangor University, earning school and printer credits for their participation. This study has been approved by the ethics committee of the School of Psychology of Bangor University (Ethics Review Board Approval Code 2012-6142). Participants were randomly assigned to two different groups matched for sex and age (see Table 1 for demographic information), and performed a series of hypothetical monetary intertemporal choices along two different tasks.

Groups	Number	Mean age (years)
Space	29 (19 f)	20 (2)
No-space	30 (18 f)	20 (3)

Table 1. Note: f = females; numbers in parenthesis for age are standard errors.

Tasks

Experimental tasks were displayed using E-Prime 2.0 software (Psychology Software Tools ©). All participants were administered, in a counterbalanced order, two different intertemporal choice tasks, differing in the spatial positions of monetary options (Near-Far manipulation and Congruent-Incongruent manipulation). Two groups (Space condition and No-space condition) saw both tasks on a different spatial background.

The group assigned to the Space condition (Space group) saw all intertemporal choices on a spatial background depicted on the screen: Options appeared in each trial superimposed to the drawing of a spatial perspective (Fig. 2a). Conversely, the group assigned to the No-space condition (No-space group) saw all intertemporal choices on a grey background on the screen with no evident spatial clues (Fig. 2b).

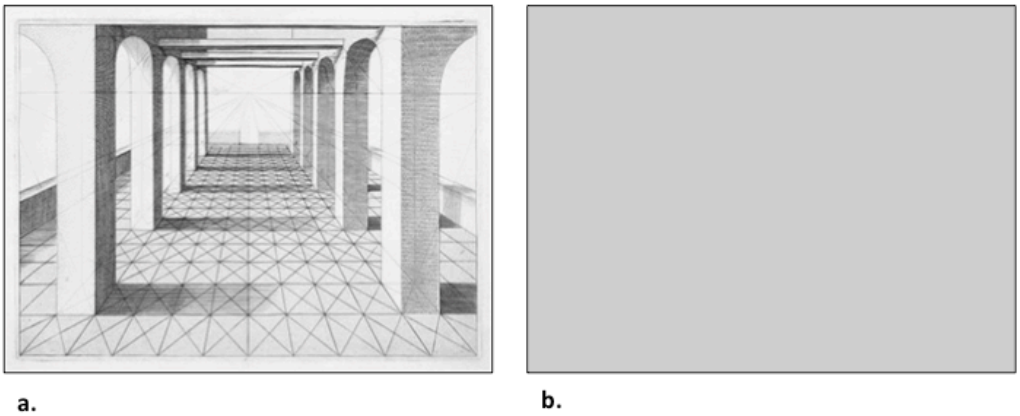

Figure 2. a. Spatial background for the Space group. b. Grey background for the No-space group.

Near-Far manipulation. Along all intertemporal choices in the Near-Far manipulation, two different options could appear on the bottom part of the screen (Near), or on the top part of the screen (Far), randomly positioned one on the left and one on the right side of the screen. We refer to this manipulation as Near-Far because options on the lower part of the screen should have been perceived, at the least by participants in the Space group, due to the presence of the spatial background, as close to subjects, and those on the higher part of the screen as far from subjects. All options were depicted with a £1 coin picture, and the amount and the delay of availability as text (Fig. 3). In order to maintain coherence in our manipulation, and to avoid retinal mismatch (we know in our daily life that far objects are smaller than when they are near in space), options were smaller than those in the Near space.

Figure 3. On the left, an example of a Near trial for the No-space group. On the right, an example of a Far trial for the No-space group.

Congruent-Incongruent manipulation. In each trial of the Congruent-Incongruent manipulation, one option was displayed on the top part of the screen, and the other was displayed on the down part of the screen. When the later option was displayed on the top, and the sooner option was displayed on the bottom, the trial was defined as Congruent, because what was sooner in time should have also been perceived as close in space, and what was later in time should have also been perceived as distant in space, at least for participants in the Space group. The opposite case was defined as Incongruent (Fig. 4).

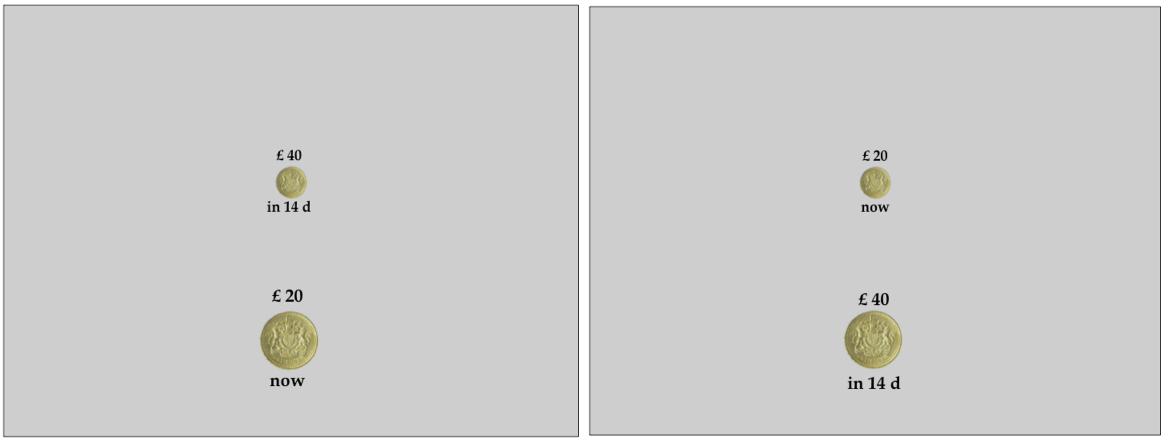

Figure 4. On the left, an example of a Congruent trial for the No-space group. On the right, an example of an Incongruent trial for the No-space group.

In both tasks, each trial began with a 1 sec fixation cross, followed by the two options (there was no time limit to respond). After choosing, the preferred option remained highlighted for 1 sec, and then a new trial started. To express their preference, participants pressed two buttons on a keyboard according to the spatial position of their chosen options.

Along both tasks, participants chose hypothetically between an amount of reward that could be received sooner and an amount of reward that could be received later (e.g., Kirby and Herrnstein, 1995; Myerson et al., 2003; Figner et al., 2010; Sellitto et al., 2010). Two temporal conditions were included. In the Now condition, participants made a series of choices between a smaller amount of money (£) that could be received immediately (now), and £ 40 that could be obtained after a variable delay. In the Not-now condition, choices involved a smaller amount of money that could be received after 60 days, and £ 40 that could be delivered after a variable delay larger than 60 days, while maintaining the same temporal gaps between earlier and later rewards as in the Now Condition. Thus, in the Now condition, participants made five choices at each of six delays: 2, 14, 30, 90, and 180 days, whereas in the Not-now condition the delays were 62, 74, 90, 150, and 240 days. The blocks of choices pertaining to the two temporal conditions were interspersed, and the order of blocks of choices relative to different delays of both temporal conditions was randomized for each participant. The titration procedure used to adjust sooner amounts based upon participants' previous choice is the same we used in the Study 1-Part II (Du et al., 2002; Sellitto et al., 2010).

Moreover, four control conditions were included. Subjects made five choices between a smaller amount of money and £ 40, both available immediately, in both Near and Far conditions for the Near-Far manipulation, and in both Congruent and Incongruent conditions for the Congruent-Incongruent manipulation. Moreover, subjects made five choices between a smaller amount of money and £ 40, both available in 180 days, in both Near and Far conditions for the Near-Far manipulation, and in both Congruent and Incongruent conditions for the Congruent-Incongruent manipulation. The smaller amount of these control conditions was adjusted, along the block of choices, based on the same staircase procedure of the other blocks of choices (Du et al., 2002). Control conditions were randomly interspersed during the experimental session. All subjects included in the study always chose the larger reward in all control conditions along both tasks, suggesting adequate comprehension of the task as well as sensitivity to reward.

Procedure

In a quiet room, after collecting demographic data, all participants (both Space and No-space groups) underwent the two different TD tasks (the one with the Near-Far manipulation, and the one with the Congruent-Incongruent manipulation) in a counterbalanced order on a laptop with a 13” screen. They were asked to choose their preferred option between the two displayed each time on the screen, with no time limit to respond, and they were reassured that there were no right or wrong answers. However, to avoid participants to remember their choices for the first TD task when submitted to the second TD task, they all performed a brief task between the two that was completely unrelated to TD. In this task, displayed using E-Prime 2.0 software (Psychology Software Tools ©) on the same laptop, real and scrambled images of neutral human faces of different gender (both males and females) were presented, one on the right and one on the left side of the screen. The faces we used were static black and white pictures selected from the Pictures of Facial Affect series (Ekman and Friesen, 1975). Along 144 trials, all combinations of both real and/or scrambled faces were shown, also counterbalanced for gender. Participants were asked to maintain their eyes on a fixation cross in the middle of the screen, and push the space bar (within a time window of 1000 ms) only when they perceived two real faces on both sides of the fixation cross, trying to be as accurate as possible. Neither rewards or punishments, nor memory or emotion were involved in this task. All participants performed this task with accuracy greater than chance level (50%).

Once the second TD task was over, subjects were debriefed. The whole experiment took about 45 minutes.

Results

To analyse data we used the same procedure as in Study II-Part II (see also Sellitto et al., 2010). Since we found in our previous studies that the hyperbolic model was superior to the exponential model, we will henceforth fit only hyperbolic curve, and no AUCs were calculated.

Near-Far manipulation. An ANOVA on log-transformed *k* values with Group (Space and No-space) as a between-subject factor, and Spatial position (Near, Far) and Temporal condition (Now, Not-now) as within-subject factors, yielded no significant effect of Group [F(1, 57) = 2.25, p = 0.14], no significant effect of Spatial position [F(1, 57) = 3.10, p = 0.08], and no significant effect of Temporal condition [F(1, 57) = 0.01, p = 0.91]. Moreover, there was no significant Group × Spatial position interaction [F(1, 57) = 0.27, p = 0.61], no significant Group × Temporal condition interaction [F(1, 57) = 0.58, p = 0.45], no significant Spatial position × Temporal condition interaction [F(1, 57) = 2.53, p = 0.13], and no significant Group × Spatial position × Temporal condition interaction [F(1, 57) = 1.25, p = 0.27].

However, taking together the significant tendency of both the manipulation of interest, that is, the Spatial position factor, and the Spatial position × Temporal condition interaction, we repeated the analysis separately for temporal conditions (Now and Not-now) to be sure we were not underestimating a significant result.

Now temporal condition. An ANOVA on log-transformed *k* values with Group (Space and No-space) as a between-subject factor, and Spatial position (Near, Far) as a within-subject factor yielded a significant effect of Spatial position [F(1, 57) = 4.25, p = 0.04], with no significant effect of Group [F(1, 57) = 2.40, p = 0.13], and no significant Group × Spatial position interaction [F(1, 57) = 1.01, p = 0.32]. A post-hoc analysis

(Newman-Keuls test) revealed that our manipulation was effective when an immediate option was offered in the pair (Near: $k = -2.20$, Far: $k = -2.30$; $p = 0.04$), with no differences between the two groups (Fig. 5a). Both groups tended to have smaller discount rates when options were offered far in space as compared to when options were offered close to them. This result suggests that future goods presented far from individuals were represented in a more abstract way, highlighting higher construals (representations), thus lessening impatience during choice. However, this finding cannot be explained with our principal manipulation, namely, a spatial background behind monetary options for one group but not for the other, but with the presence of other spatial cues. We will further discuss this result later.

Not-now temporal condition. An ANOVA on log-transformed k values with Group (Space and No-space) as a between-subject factor, and Spatial position (Near, Far) as a within-subject factor yielded no significant effect of Spatial position [$F(1, 57) = 0.10$, $p = 0.76$], with no significant effect of Group [$F(1, 57) = 1.70$, $p = 0.20$], and no significant Group × Spatial position interaction [$F(1, 57) = 0.20$, $p = 0.66$]. This analysis on Not-now trials suggested that our manipulation had no effect when no immediate option was offered in the pair, with no differences between the two groups (Fig. 5b).

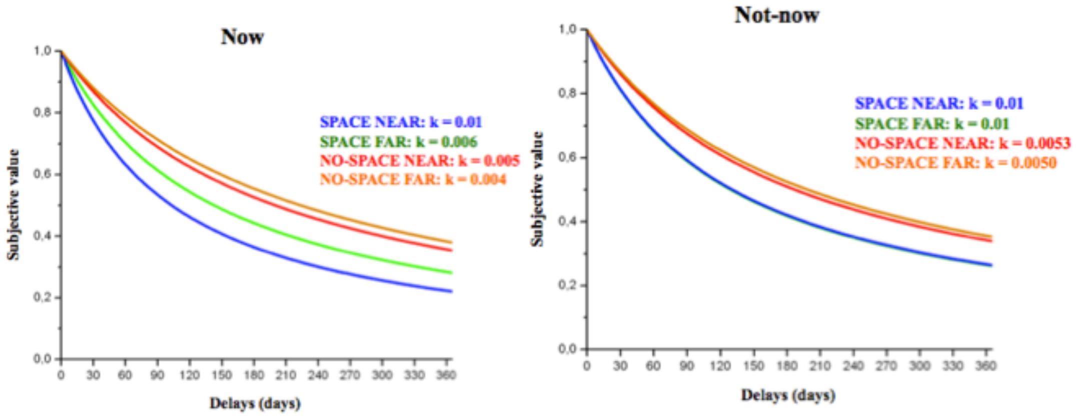

Figure 5. On the left, TD functions by group (Space, No-space) and type of trial (Near, Far) for the Now temporal condition. On the right, TD functions by group (Space, No-space) and type of trial (Near, Far) for the Not-now temporal condition. The discounting parameter *k* reflects the geometric mean of the group (mean of the log-transformed values).

Congruent-Incongruent manipulation. An ANOVA on log-transformed *k* values with Group (Space and No-space) as a between-subject factor, and Spatial position (Congruent, Incongruent) and Temporal condition (Now, Not-now) as within-subject factors, yielded no significant effect of Group [F(1, 57) = 2.43, p = 0.12], no significant effect of Spatial position [F(1, 57) = 0.40, p = 0.55], and a significant effect of Temporal condition [F(1, 57) = 4.40, p = 0.04]. A post-hoc analysis (Newman-Keuls test) revealed that both groups tended to behave more prudently when both option were delayed in time as compared to trials in which an immediate option was provided in the pair (Now: -2.13; Not-now: -2.21), in line with literature and results of our previous studies. Moreover, there was no significant Group × Spatial position interaction [F(1, 57) = 2.10, p = 0.15], no significant Group × Temporal condition interaction [F(1, 57) = 0.30, p = 0.60], no significant Spatial position × Temporal condition interaction [F(1, 57) = 0.71, p = 0.40], and no significant Group × Spatial position × Temporal condition interaction [F(1, 57) = 2.40, p = 0.13].

Although no significant interactions between factors have been found, for completeness purpose and to be sure we were not underestimating a significant result, we decided to repeat the analysis separately for temporal conditions (Now and Not-now), as we did for the Near-Far task.

Now temporal condition. An ANOVA on log-transformed *k* values with Group (Space and No-space) as a between-subject factor, and Spatial position (Congruent, Incongruent) as a within-subject factor, yielded no significant effect of Spatial position [F(1, 57) = 1.02, p = 0.32], with no significant effect of Group [F(1, 57) = 1.70, p = 0.20], and a significant Group × Spatial position interaction [F(1, 57) = 4.30, p = 0.04]. A post-hoc analysis performed with the Newman-Keuls test revealed that, while the No-space group (i.e., the one where no perspective drawing was provided under options on the screen) behaved in a significantly different way between Congruent and Incongruent conditions, showing higher discount rates for Congruent trials as compared to Incongruent trials (-2.20 vs. -2.29; p = 0.03), the Space group did not make any difference between the two (-2.10 vs. -2.01; p = 0.46) (Fig. 6a). All other contrasts did not reach statistical significance (all ps > 0.30). This result indicates that only participants in the No-space group differently decided between conditions, behaving more prudently when the larger option was perceived as close to participants. We will further discuss this result later.

Not-now temporal condition. An ANOVA on log-transformed *k* values with Group (Space and No-space) as a between-subject factor, and Spatial position (Congruent, Incongruent) as a within-subject factor, yielded no significant effect of Spatial position [F(1, 57) = 0.06, p = 0.80], with no significant effect of Group [F(1, 57) = 3.03, p = 0.09], and no significant Group × Spatial position interaction [F(1, 57) = 0.05, p = 0.82] (Fig. 6b), thus suggesting that our manipulation had no effect when no immediate option was offered.

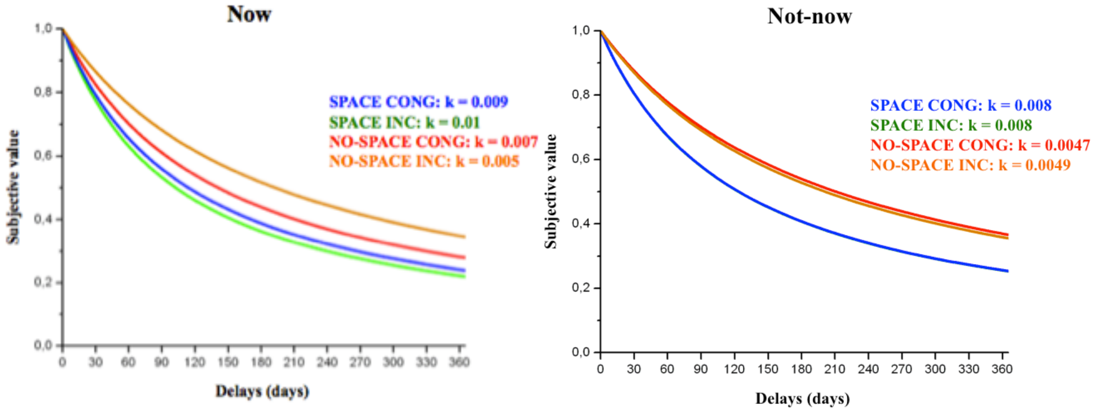

Figure 6. On the left, TD functions by group and type of trial (Congruent, Incongruent) for the Now temporal condition. On the right, TD functions for the Not-now temporal condition. please, note that the blue and the green curves in the right panel are overlapping.

Discussion

Based on the results of the Near-Far manipulation of Experiment 1, we concluded that, according to our hypothesis and to CLT, all participants behaved more prudently when choosing between options perceived as far in the space rather than near in the space, but only when an immediate option was offered. Indeed, since the principal analysis yielded a significant tendency for the interaction between groups and Temporal conditions, to be sure we were not underestimating a significant result, we decided to repeat the analysis separately for Now and Not-now trials. This analysis, as anticipated, however, did not reveal any difference between groups. Our post-hoc interpretation is that, since the coin picture size was arranged along trials in the same way for both groups, it did not matter if a spatial background was provided or not. Indeed, coin picture size is still an important index of deepness that could have affected responses of subjects in the No-space group in the same way it did for the Space group: the small/large coin picture size was a sufficient clue to perceive options in the Near condition as close in space, and the options in the Far condition as far in space, no matter if a spatial background was attended or not.

Considering the Congruent-Incongruent manipulation, the principal analysis revealed only that both groups tended to behave more prudently when both options were delayed in time as compared to trials in which an immediate option was provided in the pair, in line with literature and our previous studies. However, although no significant interaction between groups and Temporal condition has been found, for completeness purpose, we decided to repeat the analysis separately for Now and Not-now trials to be sure we were not underestimating a significant result, as we did for the Near-Far task. From this analysis we found that when a spatial background was displayed, subjects did not make any difference between Congruent and Incongruent conditions, for both Now and Not-now conditions. Conversely, when there was no spatial background, and when an immediate option was offered, individuals decided more prudently when the larger later option was perceived as close to them (Incongruent condition) as compared to the opposite condition. In this task, according to the CLT, subjects' attention should have been grabbed on the higher-level construals of the option perceived far away. However, the option perceived as close to participants at the same time could have strengthened the low-level representations of options, making difficult to disentangle which process was driving the obtained effect. Our manipulation could have affected the salience of the option perceived closer. In the Congruent condition, the focus is on the immediacy of the sooner option. In the Incongruent condition the focus is on the larger quantity. It might be that we made the larger later option more salient than the smaller immediate one, conveying participants' decisions toward the bigger amount, probably because of the way we used to depict that option (bigger coin). However, this consideration did not apply to the Space group who, as said before, did not show any significant effect of this manipulation. We speculated that, in the context of the Congruent-Incongruent manipulation, the spatial background attended by the Space group made the scene more crowded, so that no effect could emerge: in light of the different spatial position of the two options at the same time, indeed, the presence of the drawing could have made the task more difficult, having participants to process both near and far space at the same time, with the presence of all other elements in the scene. This did not happen in the Near-Far manipulation, where, on the spatial background, only the representation of either the near space or the far space needed to be activated.

Finally, the fact that significant results of our manipulations yielded only for Now trials in both the Near-Far and the Congruent-Incongruent tasks (with the difference that in the latter participants behaved overall significantly more prudently during Not-now trials than during Now trials, as compared to the former) might be explained by the lower saliency of options when both projected in the future, thus inducing to a ceiling effect.

For all the reasons explained above, we decided to carry out another experiment with a different manipulation, avoiding all previous confounding elements. To this aim, we decided to manipulate the distance between options and participants using different distances from screens (close or far), so that no font size adjustment was required. No spatial background underneath the options was provided, and we did not use any coin picture. Moreover, we submitted participants only to intertemporal choices in which an immediate option was offered (Now trials).

Experiment 2

In a within-subjects study all participants underwent both the Near-Far condition and the Congruent-Incongruent condition in a randomized order. No spatial or grey background was provided under the options at stake. Participants performed the experiment on two different screens at the same time. One screen was positioned far away from them, and one screen was positioned close to them. The near screen was used to depict both options during the Near condition in the Near-Far task and to depict close options (both congruent and incongruent trials) in the Congruent-Incongruent task. The far screen was used to depict both options for Far trials in the Near-Far task and for far options (both congruent and incongruent trials) in the Congruent-Incongruent task. This time subjects performed only Now trials, pairing the larger later option (£ 40) always with a smaller option immediately available ('now').

Materials and methods

Participants

Twenty-eight undergraduate students (14 females, mean age = 20 years old, standard deviation = 2.03) were recruited through the research website Sona Systems Ltd. at the Bangor University, earning school and printer credits for their participation. This study has been approved by the ethics committee of the School of Psychology of Bangor University (Ethics Review Board Approval Code 2012-6142).

Tasks

Experimental tasks were displayed using Psychophysics Toolbox (Psychtoolbox-3, GNU General Public License, http://www.psychtoolbox.org) for Matlab 2010b (MathWorks, Inc ®). All participants were administered two different intertemporal choice tasks, in a counterbalanced order. The two tasks, similarly to the first experiment, differed in the spatial positions of options (Near-Far manipulation and Congruent-Incongruent manipulation), with the manipulation achieved through the use of two different screens (22”) at the same time. On a long desk, one screen was positioned far from the subject (about 110 centimeters distant), and the other was positioned close to the subject (about 40 centimetres distant) (Fig. 7). To make both screens visible at the same time by participant, one was positioned on the right of the midline and the other on the left of the midline. To avoid any confounding due to this difference in screens position, we counterbalanced the left-right position between the close-far screens. This means that for half of our participants, the near screen was on the left and the far screen was on the right, whereas for the other half, the near screen was on the right and the far screen was on the left (Fig. 7). We found no difference in TD between participants who had the close screen on the left and the far screen on the right, and those in the opposite condition.

Figure 7. Setting of Experiment 2.

Along all intertemporal choices in the Near-Far manipulation, two different options could appear on the screen positioned close to the subject (Near), or on the screen positioned far from the subject (Far), randomly positioned one on the left and one on the right side of the screen. All options were indicated with the written amount and the delay of availability with a white font on a black background (Fig. 8). Font size was the same for both screens. For the Congruent-Incongruent manipulation, in each trial, one option was displayed in the middle of the far screen, and the other was displayed in the middle of the close screen. When the later option was displayed on the far screen, and the sooner option was displayed on the close screen, the trial was defined as Congruent. The opposite case was defined as Incongruent. Each trial began with a 1 sec fixation cross, followed by the two options (there were no time limit to respond). After choosing, the preferred option remained highlighted for 1 sec, and then a new trial started. To express their preference, participants, sitting in front of the desk, pressed two buttons on a keyboard according to the spatial position of their chosen options.

Figure 8. Example of options presentation during the Near-Far task. See the main text for procedure details for both Near-Far and Congruent-Incongruent tasks.

In both tasks, participants made a series of hypothetical choices (e.g., Kirby and Herrnstein, 1995; Myerson et al., 2003; Figner et al., 2010; Sellitto et al., 2010) between a smaller amount of money (in £) that could be received immediately (now), and £ 40 that could be obtained after a variable delay. Specifically, participants made five choices at each of seven delays: 2 days, 2 weeks, 1 month, 3 months, 6 months, and 1 year. The order of blocks of choices relative to different delays was randomized for each participant. The titration procedure used to adjust sooner amounts based on participants' previous choice is the same we used in the Study 1 (Part II; Du et al., 2002; Sellitto et al., 2010).

Moreover, four control conditions were provided. Subjects made five choices between a smaller amount of money and £ 40, both available immediately, both in the Near and in the Far condition for the Near-Far manipulation, and in the Congruent and Incongruent condition for the Congruent-Incongruent manipulation. Moreover, subjects made five choices between a smaller amount of money and £ 40, both available in 1 year, both in the Near and in the Far condition for the Near-Far manipulation, and in the Congruent and Incongruent condition for the Congruent-Incongruent manipulation. The sooner amount of these two control conditions was adjusted, along the block of choices, based on the same staircase procedure of the other blocks of choices (Du et al., 2002). The control conditions were randomly presented during the experimental session. All subjects included in the study always chose the larger reward in the control conditions along both tasks, suggesting adequate comprehension of the task as well as sensitivity to reward.

Procedure

In a quiet room, after collecting demographic data, all participants underwent the two different TD tasks (Near-Far manipulation, and Congruent-Incongruent manipulation) in a counterbalanced order. To avoid participants remembering their choices in the first TD task when submitted to the second TD task, they all performed a brief task between the two that was completely unrelated to TD. In this task, they were asked to copy on a white A4 sheet the Rey-Osterrieth Complex Figure (Osterrieth, 1944). Neither rewards or punishments, nor memory or emotion were involved in this task. All participants performed the task accurately. After the second TD task was over, subjects were debriefed. The whole experiment took about 25 minutes.

Results

To analyse data, we used the same procedure as in Study I-Part II (Sellitto et al., 2010). Since we found in previous studies that hyperbolic model was always superior to the exponential model, we will only fit the hyperbolic curve, and no AUCs were calculated.

Near-Far manipulation. An ANOVA on log-transformed *k* values with Spatial position (Near, Far) as within-subject factor yielded no significant effect [F(1, 27) = 0.50, p = 0.50], indicating that our manipulation of space did not affect in any direction our participants' intertemporal choice behavior (Fig. 9). When we used as a covariate the participants' gender and age, we found a similar pattern of results.

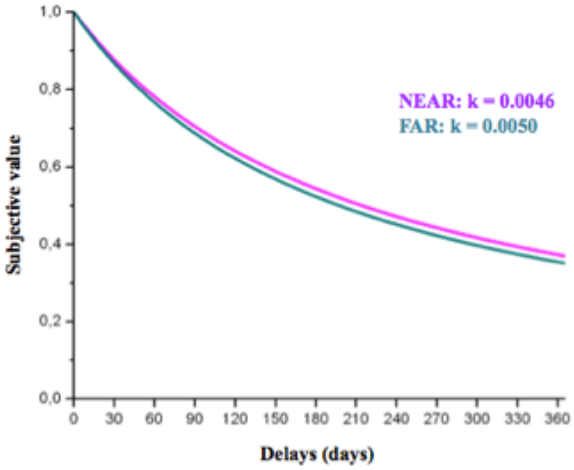

Figure 9. Results on log-transformed k scores for the Near-Far manipulation.

Congruent-Incongruent manipulation. An ANOVA on log-transformed *k* values with Spatial position (Congruent, Incongruent) as within-subject factor yielded a significant effect of Spatial position [F(1, 27) = 4.50, p = 0.04], indicating that our participants tended to behave more prudently when the larger later option was presented on the screen close to them (incongruent condition) as compared to the congruent condition (-2.36 vs. -2.27) (Fig. 10). This result replicates that of the Congruent-Incongruent manipulation we used in Experiment 1. Subjects chose more impulsively when the larger later option was perceived far away from them. We will further discuss this result later. Finally, when correcting for participants' gender and age, a similar pattern of results has been found.

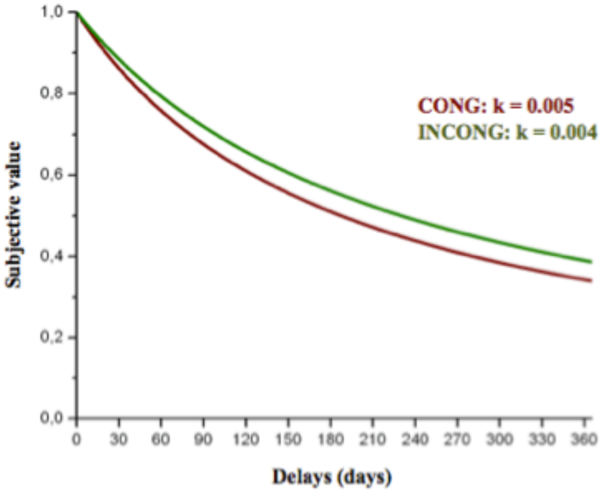

Figure 10. Results on log-transformed k scores for the Congruent-Incongruent manipulation. The larger the bar, the higher the impulsivity.

Discussion

In Experiment 2 we manipulated the actual position of two screens on which we presented the smaller immediate option and the larger later option. This held for both the Near-Far condition, when options were both depicted either in the near or in the far space, and the Congruent-Incongruent condition, when one option was always displayed in the near space and one was always displayed in the far space.

The Near-Far manipulation was not effective: participants had the same discount rate for the future monetary reward, no matter the spatial position of the options. Two considerations can be made about why we did not replicate results of Experiment 1. First, we have to take into account the absence of Not-now trials. Indeed, the presence of offers without an immediate option helps in polarize evaluation (e.g., Tesser and Conlee, 1975; Dai and Fishbach, 2013), inducing people to simulate more extensively offers with an immediate outcome (i.e., enabling an increase in the perceived difference between options): this allows the Near-Far effect to emerge during Now trials, where options are considered more extreme. Second, we have to consider the different context of Experiment 2. Indeed, in Experiment 1 the screen was always the same, allowing the Near-Far effect to emerge, since participants always considered the same scene independently of Near and Far trials. Conversely, here, participants made decisions considering either a screen or the other, so that a comparison between a close and a far space (screen) was basically not required. This consideration can be better understood in light of the Congruent-Incongruent manipulation, where the effect of space emerged (see below). Indeed, in that case, a comparison between the two screens, and so between the two different spaces, was always required (being the options always showed one on a screen and one on the other), so that the spatial manipulation could have effect.

As anticipated, the Congruent-Incongruent manipulation yielded significant results. Specifically, we replicated findings of Experiment 1: subjects performed intertemporal choices less impulsively when the larger later option was presented in the close space (Incongruent condition). Both experiments shared the presence of an immediate option in the pair, and no spatial background was provided under the options. Indeed, in Experiment 2, no perspective drawing was used to clue participants with closeness and farness, but options were physically close or far from them.

General discussion

According to the CLT (Liberman and Trope, 1998, 2008; Trope and Liberman, 2003; Fujita et al., 2006; Fujita and Carnevale, 2012), different dimensions of psychological distance correspond to different ways in which objects or events can be represented. CLT posits that the more we are able to remove objects from the self, the more we construe (represent) them at a higher abstract level (Liberman and Trope, 2008). During intertemporal choice, people tend to prefer the sooner smaller option to a larger later one. How can we meke them able to transcend the 'here and now' and decide to go for the larger later option? Being engaged in high level (abstract) construals should lead people to have greater self-control when deciding between short-term and long-term goals (Trope and Liberman, 2010; Fujita and Carnevale, 2012). We investigated if highlighting abstract features of money amounts offered along a series intertemporal choices could lead individuals to reduce TD. We attempted this through a visual spatial manipulation of relative positions of options at stake.

In a first manipulation (Near-Far), participants performed a task in which both offers were presented either in the far space or in the near space. In Experiment 1 we induced more willingness to wait for the larger later reward when paired with a sooner immediate reward, when both options were depicted far in space. This finding, in line with our hypothesis and CLT, however is not the result of our principal manipulation. Indeed, participants of both groups showed the same effect. We explain this result with the presence of other spatial cues present along trials, i.e., coins and the text size to depict options. This means that a sort of spatial manipulation was still present, but equally in both groups, allowing us to demonstrate that subjects tended to look at, and think of, options in a more abstract and schematic way when they were perceived as far away from them (because represented with smaller pictures and text), whereas subjects represented them in a more concrete and contextualized way when they were perceived as close and more physically reachable (because represented with bigger pictures and text). However, in Experiment 2, where we released options on different screens to make closeness and farness more physically real, we failed to replicate the above finding. We explained this result in light of both the absence of Not-now trials, which helps in polarize decisions when faced with Now trials, and the use of two screens that made difficult to cosider the whole scene with a near and a far space (see above).

In a second manipulation (Congruent-Incongruent), we offered participants the smaller sooner option and the larger later option in different spatial positions. When a spatial background was displayed (Experiment 1), subjects decided in the same way in both Congruent (smaller sooner option close, larger later option far) and Incongruent condition. We suggested that the spatial background contributed in making the scene more crowded, having participants to process both near and far space at the same time in light of all other elements in the scene, so that no effect could emerge. Conversely, when there was no spatial background, when an immediate option was offered, individuals decided more prudently when the larger later option was perceived as close to them (Incongruent condition) as compared to the opposite condition. This result yelded also in Experiment 2. In this task, according to the CLT, subjects' attention should have been grabbed on the higher-level construals of the option perceived far away. However, the spatial closeness of the larger later option in the Incongruent condition could have strengthened its low-level representations, making difficult to disentangle which process was driving the obtained effect. In other words, paradoxically, our manipulation could have actually affected the salience of the option perceived closer. While in the Congruent condition, the focus is on the immediacy of the sooner option, in the Incongruent condition the focus is on the larger quantity. It might be that, in the Incongruent condition, we made the larger later option as more salient than the smaller immediate one, conveying participants' decisions toward the bigger amount, probably because of the way we used to depict that option (bigger coin). This result could also be explained with the difficulty in activating at the same time a more abstract representation for the larger later option when far in space, in place of a more concrete representation for the smaller immediate option. This could have resulted in choosing significantly more times the larger later option when it was represented close in space because, paradoxically, more salient, voiding our manipulation.

Overall, allowing people to think about rewards in a more abstract way seems to have reduced TD only during easier tasks, that is: (1) when an immediate option was offered against a delayed one; (2) when sterling coins (and text) size represented the actual spatial cue; (3) when instead of directly manipulating the coins (and text) size we used two screens in different positions to depict options; (4) when both options were in the same spatial position (both far or near). This suggests that to engage in an effective spatial manipulation, only one variable at time should be manipulated. This allows subjects to truly focus on the most evident feature of the offer, that is, options are on a certain space, near or far. Only when both offers are in the same space, individuals focus on higher-level features of the two options (the larger amount) highlighting high-level construals, being less concerned with the effort related to wait a longer time for the larger option (e.g., Leiser et al., 2008). Conversely, when spatial position of options is manipulated differently, the larger later option become more salient and concrete to choose when it is perceived close to the decision-maker.

Based on the guidelines evidenced by this study, we can think about other and more effective spatial manipulations for the future to further investigate this issue.

Study IV – Errors modulate preference for food in intertemporal choice

Introduction

As we can see from previous studies, both training people to mentally travel in time before making an intertemporal choice, and influencing mental representations of both outcomes at stake (manipulating their spatial position), had the effect of lessening the discount rate of future rewards. However, when we tried to obtain the same result through the MTT on edible rewards, our efforts failed.

Are we so hopeless when faced with food? Are those impulsive behaviours (not related to pre-existent medical conditions) like obesity and other binge eating disorders[1] really unmanageable and impossible to overcome? People frequently experience conflict when intertemporal choice is difficult, particularly when visceral sensations are called into play, for instance, when craving for a tasty treat, consequently experiencing loss of self-control. Even the simple visual exposure to tempting foods, is a powerful trigger for immediate consumption (Hawk et al., 2004; di Pellegrino et al., 2011).

One way to successfully resist to immediate gratification is to reduce the appetitive value of reward. With food, this is usually obtained by satiating the subject selectively on the outcome (e.g., Haddad et al, 1976; Rolls et al., 1981; Placanica et al., 2002; di Pellegrino et al., 2011), or by pairing it with an aversive event (e.g., Baxter and Murray, 2002; Schultz, 2010).

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[1] i.e., recurrent episodes of eating an unambiguously large amount of food accompanied by a sense of loss of control in the absence of regular use of inappropriate compensatory behaviours (see Fortuna, 2012, for a review).

Errors are typically highly arousing, negative signals motivating avoidance responses. Indeed, they are considered aversive events, producing a negative neural wave (error-related negativity, ERN; Falkenstein et al., 1991; Gehring et al., 1995), generated in ACC (e.g., Miltner et al., 2003), when subjects become aware of having committed a mistake, thus priming defensive motivation (Hajcak and Foti, 2008).

Here, we investigated whether pairing desirable foods with errors decreased impatient behaviour towards those foods. In the main experiment, participants performed a Stop-signal task (Brown and Braver, 2005) in which food cues predicted errors in performance, and then they made intertemporal choices about the same foods. Since recent findings highlighted that women and men have different behavioral (e.g., Bates et al, 2009; Beer-Borst et al., 2000) and neural responses (e.g., DelParigi et al., 2002; Smeets et al., 2006) to food cues, hunger, and satiation, we decided to test women only. In a control experiment, we investigated if the Stop-signal task influenced judgements and emotions toward those foods used as cues in the task itself.

Materials and Methods

Participants

Forty young adult females participated in the experiment. All participants were normal weight and fasted for at least two hours at the moment of the experiment. Before the beginning of the experimental procedure, participants' personal data were collected (see Table 1 for all demographic information). Participants were not taking psychoactive drugs, and were free of current or past psychiatric or neurological illness as determined by history. Participants gave informed consent, according to the Declaration of Helsinki (International

Committee of Medical Journal Editors, 1991) and the Ethical Committee of the Department of Psychology, University of Bologna.

Subjects	Hunger rating	Fasting (hours)	Age (years)	Education (years)	BMI	DEBQ (external eating behavior)	BAS (tot)
40 f	2 (0.4)	4 (0.5)	25 (0.6)	15 (0.4)	21 (0.4)	3 (0.1)	39 (0.6)

Table 1. Participants' demographic data. BMI = Body Mass Index; Bas (tot) = total score obtained at the Behavioral Activation Scale. Numbers in parenthesis are standard errors.

Stop-signal task

Based on the paradigm of Brown and Braver (2005), a Stop-signal task was adjusted using foods as cues. Two types of conditions were included. Half of the trials had a Low-Error likelihood, and the other half had a High-Error likelihood. One food (Low-Error Food, LEF) was used as cue for the Low-Error trials. The other food (High-Error Food, HEF) was used as cue for the High-Error trials. Hence, for a given trial, food type predicted Low versus High-Error likelihood, respectively.

Figure 1 illustrates the experimental paradigm. Each trial began with a black and white picture of one of the two foods appearing for 1000 ms. Then, the black and white picture became coloured: this represented the Go signal. The Go signal required participants a button-press response as quickly as possible. However, on 33% of the trials, a Stop signal was postponed to the Go signal after a variable Stop-Signal Delay (SSD) relative to the Go signal onset. This Stop signal, a red circle appearing around the coloured picture, indicated that response to the Go signal was no longer required. Both Stop and Go signals remained visible until a response deadline of 1000 ms after Go signal onset, which indicated a time limit of 1000 ms to produce or not a response. After each trial, a black screen appeared as for a variable intertrial interval (500, 1000, 1500, 2000 ms). Error rates (low vs. high) were explicitly set and controlled by dynamically adjusting the SSDs for each error-likelihood condition independently with the use of a staircase algorithm. The Low-Error condition had shorter SSDs, whereas the High-Error condition had longer SSDs (Brown and Braver, 2005). The SSD started at 200 ms (after Go signal onset) for both Low- and High-Error conditions. During Low-Error trials, if the participant succeeded in withholding the response, the SSD increased by only 5 ms; conversely, if the subject failed, the SSD decreased by 50 ms on the next trial. During High-Error trials, if the participant succeeded in withholding the response, the SSD increased by 50 ms; conversely, if the subject failed, the SSD was decreased by 50 ms on the next trial (Logan et al., 1984).

After a correct response to the Go signal or a non-response to the Stop signal, a message ‘correct!’ (in Italian) appeared on the screen. If participant did not respond in time to the Go signal, or if he responded to the Stop signal, a message ‘error!’ appeared on the screen. If participant responded to the black and white picture, a message ‘too early!’ appeared on the screen. Low-Error trials and High-Error trials were presented in a random order. All cues and stimuli were presented centrally on a black screen.

Participants performed 240 trials in total, that is 80 Stop trials (40 for the Low-Error condition and 40 for the High-Error condition) and 160 Go trials (80 for the Low-Error condition and 80 for the High-Error condition) Data were analysed with regard to accuracy and RT effects of correct vs. error (no-response trials ignored), Low- vs. High-Error condition, and Stop vs. Go trials. The task lasted about 16 minutes.

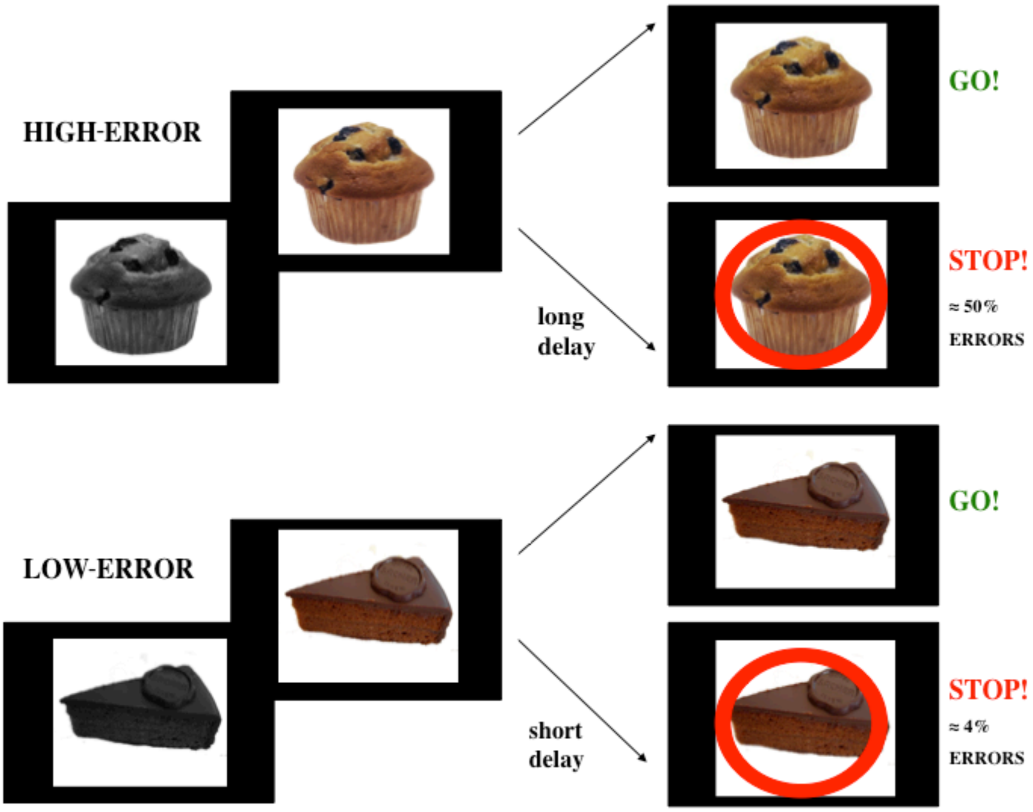

Figure 1. Stop-signal experimental paradigm. Muffin here is assigned to the High-Error condition. Conversely, the chocolate cake represent the cue for the Low-Error condition

Temporal discounting tasks

In each of two computerized TD tasks, participants chose between an amount of tastes (units) of a hypothetical food that could be received immediately and an amount of units of that food that could be received after some specific delay (e.g., Kirby and Herrnstein, 1995; Myerson et al., 2003). One task assessed subjective preferences in time for one food (LEF), and one task assessed subjective preferences in time for the other food (HEF). The two TD tasks were submitted in a random order across participants, and foods used were exactly the same used for the Stop-signal task.

In each task, participants made five choices at each of six delays: 2 days, 2 weeks, 1 month, 3 months, 6 months, and 1 year. The order of blocks of choices pertaining to different delays was randomly determined across participants. Within each block of five choices, the delayed amount was always 40 units (e.g., 40 tastes of muffin) (Sellitto et al., 2010). The task and the titration procedure used to adjust sooner amounts based on participants' previous choice is the same we used in the Study I-Part II (Du et al., 2002; Sellitto et al., 2010).

Self-report scales

External Eating Scale

The Dutch Eating Behavior Questionnaire (DEBQ, Van Strien et al., 1986; Italian version, Caccialanza et al., 2004) assesses individual's structure of eating behaviour. DEBQ has separate scales for emotional, external, and restrained eating. The restrained eating scale assesses if subjects are on a diet chronically. The emotional eating scale assesses how much emotional states trigger the overeating response, namely eating in response to emotional arousal states such as fear, anger, or anxiety. The emotional eating scale has two subscales: the first specifically assesses eating in response to diffuse emotions, and the second specifically assesses eating in response to clearly labelled emotions. The external eating scale assesses the sensitivity to external cues such as during food exposure (Van Strien et al., 1986). Participants have to report for each item the frequency of engagement to those behaviors on a 5-points Likert scale. For our purposes, subjects were administered only the external eating subscale of the DEBQ. A higher score at the external subscale corresponds to a higher sensitivity to external cues such as sight and smell of food (Van Strien et al., 1986).

Behavioral Activation System scale

The Behavioral Activation System (BAS) scale (Carver and White, 1994) is a self-report questionnaire providing a measure of the tendency to behave in response to reward. A behavioral approach system, indeed, is thought to regulate appetitive motivation, in which the goal is to move toward something desired. BAS scale is comprised of three subscales: BAS reward responsiveness, BAS drive, and BAS fun seeking. The reward responsiveness subscale assesses the tendency to positively respond to rewards; the drive subscale assesses the motivation and the ability in focusing to reach a goal; the fun seeking subscale assesses the impulsive tendency to pursue new pleasant rewards (Meyer et al. 2005). For each item, subjects has to indicate on a 4-points Likert scale (from 'completely disagree' to 'completely agree') how much they agree or disagree with what the item says. People with high BAS sensitivity respond more to cues of reward and experience more positive affect in the presence of such cues (Carver and White, 1994).

Procedure

The whole experiment took place in a quiet room. After collecting participants' personal data (including height and weight to calculate their BMI; Smalley et al., 1990; Borghans and Golsteyn, 2006), they rated on a paper and pencil 11-points Likert scale (-5, 5, 0 in the middle) their hunger level at the time (anchoring labels 'not hungry at all' and 'very hungry'), and, one at a time, how appetizing (appealing to eat) they find each of six foods depicted in picture (anchoring labels 'not at all' and 'very much') (Fig. 2). Pictures were matched for dimension, luminance, and contrast, and were presented in a random order across participants on a computer screen. Then, the experimenter chose, individually for each participant, the two favourite foods (that obtained the higher rating value) as stimuli for subsequent Stop-signal task and TD tasks, carried out through E-Prime 1.0 software (Psychology Software Tools ©). Since the two most attractive (favourite) foods often obtained a different evaluation, they were assigned in a counterbalanced order to the two different trial conditions of the Stop-signal task, so that, along participants, no difference in the attractiveness of one food over the other was provided [mean rate for LEF and HEF: 3 vs. 3; F(1, 39) = 0, p = 1]. For the whole duration of the Stop-signal task, no changes of cues were provided. After completed the Stop-signal task, participants underwent to the two TD tasks. At the end of the second TD task, participants were administered the DEBQ and the BAS scales.

Figure 2. The six foods rated by participants. From left to right: ice cream, doughnut, muffin, pudding, profiterole, chocolate cake.

Results

Stop-signal task

Figure 3 shows the percentage of errors committed by our participants at the Stop-signal task along both Go and Stop trials, for both Low- and High-Error conditions. An ANOVA with error likelihood (Low, High) and trial type (Go, Stop) as within subject factors was performed on the percentage of errors. This analysis evidenced a significant effect of error likelihood [F(1, 39) = 1537.53, p = 0.000001], a significant effect of trial type [F(1, 39) = 844.54, p = 0.000001], and a significant interaction error likelihood × trial type [F(1, 39) = 1122.91, p = 0.000001]. Post hoc comparisons, performed with the Newman-Keuls test, first of all showed that the percentage of errors was significantly higher during the High-Error condition than the Low-Error condition (28% vs. 11%; p = 0.0001), and that the number of errors committed during Stop trials was significantly higher than the number of errors committed during Go trials (32% vs. 1%; p = 0.0001). Moreover, while the percentage of errors committed during Go trials was the same along High and Low conditions (0.07 vs. 0.07; p = 0.99), the percentage of errors during Stop trials was significantly higher for the High-Error condition than the Low-Error condition (50% vs. 15%; p = 0.0001).

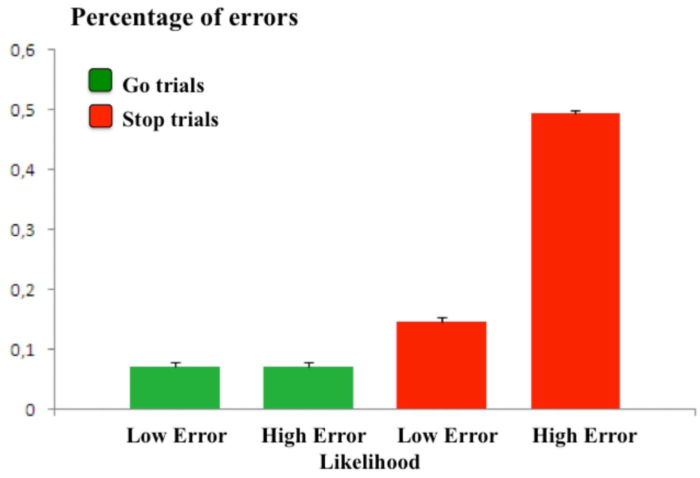

Figure 3. Percentage of errors committed by our participants at the Stop-signal task, separated by type of trial (Go, Stop) and error likelihood (Low, High).

We then entered RTs for correct trials in an ANOVA with error likelihood (Low, High) and trial type (Go, Stop) as within subject factors. This analysis evidenced a significant effect of error likelihood [F(1, 39) = 40, p = 0.000001], a significant effect of trial type [F(1, 39) = 420, p = 0.000001], and a significant interaction error likelihood × trial type [F(1, 39) = 45.50, p = 0.000001]. Post hoc comparisons, performed with the Newman-Keuls test, first of all showed that RTs were significantly higher (i.e., responses were slower) during the High-Error condition than the Low-Error condition (430 ms vs. 405.10 ms; p = 0.0001), and that RTs during Go trials were significantly higher than RTs during Stop trials (454 ms vs. 381 ms; p = 0.0001). Moreover, while RTs for correct responses during Go trials were the same along High and Low conditions (453 ms vs. 455 ms; p = 0.99), RTs for incorrect responses during Stop trials were significantly higher for the High-Error condition than the Low-Error condition (404 ms vs. 357 ms; p = 0.0001). These results, in line with previous findings (e.g., Brown and Braver, 2005), are indicative of the higher conflict (-driven ACC activity) during Low-Error likelihood condition.

Moreover, following the procedure of Logan (1994; see also Eagle et al, 2008), we calculated the Stop-Signal Reaction Time (SSRT) that measures the inhibition of a response that has already been initiated, namely, the ability to Stop. SSRT represents the time at which stopping finished relative to the Stop signal, and it is calculated subtracting the mean SSD from the mean RT during Go trials (for both Low-Error likelihood and High-Error likelihood). An ANOVA on SSRT values with error likelihood (Low, High) as within subject factor revealed a significant difference between High and Low-Error likelihood [F(1, 39) = 292.5, p = 0.0000001], evidencing how inhibition was higher during Low-Error trials (because easier) rather than during High-Error trials (353.88 vs. 242.0), that is, participants were worse, as expected, during High-Error likelihood trials. As suggested by Brown and Braver (2005), this result is indicative of the fact that the SSRT would be associated with increased ACC activity. These results support the validity of the paradigm of Stop-signal task in producing different patterns of errors for the Stop condition comparing to the Go condition, and for the High versus Low-Error likelihood. Indeed, participants clearly made a significantly higher number of errors during the High-Error condition only when performing Stop trials.

Temporal discounting tasks

Data analysis procedure is the same we used in Study I-Part II (Sellitto et al., 2010). Hyperbolic *k* values were entered in an ANOVA, with type of food (Low-Error Food LEF, High-Error Food HEF) as within subject factor. No significant effect of food type was found [F(1, 39) = 2.10, p = 0.16]. However, when performing an ANCOVA entering as covariate the hunger level, the BMI value, the SSRT, the DEBQ score, and the BAS score (both the total and the separate subscales), only the hunger level reached significant threshold [F(1, 38) = 6.62, p = 0.01], significantly interacting with our manipulation [F(1, 38) = 7.70, p = 0.01], yielding a significant effect of type food [F(1, 38) = 7.54, p = 0.01] (all others covariates, ps > 0.11). We then decided to divide our sample in three groups based on the median value of hunger rates (= 2.5) (Low-Hunger, Medium-Hunger, High-Hunger; see Table 2 for demographics), to further investigate the effect of our manipulation.

The three obtained groups did not differ among each other concerning both the percentage of errors and RTs for correct trials along Go and Stop trials for both Low and High-Error conditions (all ps > 0.44), while maintaining the same direction of results we previously found, that is, a significant higher number of errors for Stop trials than for Go trials, and a significant higher number of errors for Stop trials for the High-Error condition as compared to all other cases (all ps < 0.0000001).

Groups	Number of subjects	Fasting (hours	Age (years)	Education (years)	BMI	DEBQ (external eating behavior)	BAS (tot)
Low-Hunger	14	2.5 (0.3)	25 (1.2)	17 (0.5)	21 (1)	3.4 (0.1)	40 (1)
Medium-Hunger	13	4.6 (0.8)	25 (1)	16 (0.5)	22 (0.7)	3.2 (0.1)	37 (1)
High-Hunger	13	5.6 (1.0)	24 (1)	16 (0.5)	21 (0.7)	3.4 (0.1)	39 (1)

Table 2. Participants' demographic data after being divided in three groups. BMI = Body Mass Index; Bas (tot) = total score obtained at the Behavioral Activation Scale. Numbers in parenthesis are standard errors.

We also compared the three groups on SSRTs, finding no significant difference (all ps > 0.45). Moreover, as we expected, since they differed for the hunger level, the three groups differed in the overall rating of attractiveness for the two food chosen for the TD task [F(2, 37) = 6.43, p = 0.004], with the Low-Hunger group having significantly lower hunger as compared to the Medium- and High-Hunger groups (2.14 vs. 3.85 vs. 3.62; p = 0.007), whereas no difference was detectable between Medium- and High-Hunger groups (p = 0.66). However, no significant difference emerged between the overall rating between LEF and HEF [F(1, 37) = 0.0003, p = 0.98], and, more importantly, no significant interaction between food type and group has been revealed [F(2, 37) = 0.17, p = 0.85]. This allowed us to analyse *k* values for both LEF and HEF among the three different groups.

Hyperbolic *k* values were entered in an ANOVA, with group (Low-Hunger, Medium-Hunger, High-Hunger) as between subject factor, and with type of food (LEF, HEF) as within subject factor. No significant effect of group [F(2, 37) = 1.60, p = 0.22] and no significant effect of food type was found [F(1, 37) = 2.47, p = 0.12], in light of a significant group × food type interaction [F(2, 37) = 8.23, p = 0.001] (Fig. 4). Since geometric means of *k* values are very high, because discounting for food was very steep, to make the difference between groups and foods visible, this time we will represent mean non-log transformed *k* values as bars instead of curves as usual; the larger the bar, the higher the discount rate, the higher the impulsivity). Post hoc comparisons, performed with the Fisher test, showed that while in the Low-Hunger group TD was significantly steeper for the LEF as compared to the HEF (-0.72 vs. -1.45; p = 0.0007), in the High-Hunger group TD was steeper for the HEF as compared to the LEF (-0.20 vs. -0.62; p = 0.04). No difference in discount rate for the Medium-Hunger group between LHF and HEF was found (-0.50 vs. -0.75; p = 0.22). However, to better understand these findings, and to do not miss any important information, we decided to repeat this analysis between the three groups but separately for the two foods. While when entered *k* scores in an ANOVA for the three groups we found no significant difference between groups for the LEF (F(2, 37) = 0.15; p = 0.86), for the HEF the analysis yielded a significant difference between groups (F(2, 37) = 4.62; p = 0.02). Post hoc comparisons, performed with the Fisher test revealed that the Low-Hunger group significantly differed from the High-Hunger group (-1.45 vs. -0.18; p = 0.004) but not from the Medium-Hunger group (-1.45 vs. -0.75; p = 0.10), as well as no significant difference was detected between the High-Hunger group and the Medium-Hunger group (-0.18 vs. -0.75; p = 0.20). This demonstrates that the Stop-signal task had a differential effect on the two extreme groups, based on hunger level, only relatively to the food associated with a higher number of errors.

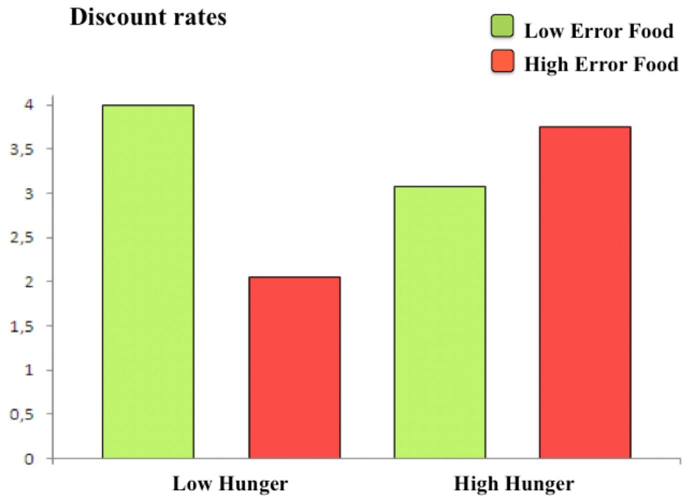

Figure 4. TD rates separated by group (Low-Hunger, High-Hunger) and error likelihood associated with food (Low, High). The larger the bar, the higher the discount rate, the higher the impulsivity.

Discussion

In this main experiment, we trained participants to associate two sweet foods with a different number of errors in performance during a Stop-signal task. Our purpose was to reduce impulsivity toward the one of those two foods that was associated with a higher number of errors as compared to the other. We measured this effect with two TD tasks. In one, subjects made intertemporal choices toward the food associated with a lower number of errors during the Stop-signal task, and, in the other, subjects made intertemporal choices toward the food associated with a higher number of errors during the Stop-signal task. The principal analysis did not yield a significant result. However, we found that this result covaried with the hunger level of participants at the beginning of the experiment. This allowed us to divide participants in three different groups: Low-Hunger group, Medium-Hunger group, and High-Hunger group. We then investigated again the difference in intertemporal choices about the two foods (one associated with a high number of errors and one associated with a low number of errors). We found an interesting interaction between groups and the two types of food. Our Stop-signal task, indeed, had the effect we hypothesised of reducing impulsivity toward the food previously associated with a larger number of errors. However, this yielded only for participants with a lower level of hunger. Conversely, our Stop-signal task had the opposite effect on participants with a higher level of hunger at the moment of the experiment. Indeed, these subjects behaved even more impatiently toward the food associated with the higher number of errors, as compared to the other. Our suggestion is that, while the association between one food and an aversive event (errors) negatively conditioned participants with no specific motivational states toward food thus avoiding that specific object, the arousing quality of the same aversive event could have been misinterpreted by hungry participants as hunger itself. We will further discuss this interpretation in the general discussion of this study.

However, we did not include a rating of desirability of the two foods at the end of the TD task, since we were concerned that this would have reduced or changed the effects of our emotion induction through the Stop-signal task (see Keltner et al., 1993; Dunn and Schweitzer, 2005) and led suspicion in participants about the experiment's aim. Instead, we ran an emotion manipulation check on a separate sample of participants in a control experiment to measure if their attitudes toward the two foods could have changed after the error task.

Control experiment

In this control experiment, before and after the Stop-signal task, we asked participants several judgements about both foods used as cues in that task. Judgements included desirability, pleasantness, healthiness, disgust, surprise, anger, anxiety, calmness, happiness, and sadness. We chose positive- and negative-valenced emotions to see if subjects' attitudes toward foods changed due to having committed more or less errors during the task.

Materials and Methods

Participants

Thirty-seven young adult females participated in this control experiment. All demographic characteristics of subjects (see Table 3) were matched with those of participants in the main experiment. This yielded when both we considered the two general samples, and we divided participants in subgroups. There were no differences in age, years of education, hours of fasting, hunger level, and BMI, DEBQ, and BAS between the two groups [all Fs(1, 75), ps > 0,12].

Subjects	Fasting (hours)	Age (years)	Education (years)	BMI	DEBQ (external eating behavior)	BAS (tot)
37 f	3.5 (0.5)	25 (0.6)	17 (0.2)	21 (0.7)	3 (0.1)	39 (0.6)

Table 3. Participants' demographic data. BMI = Body Mass Index; Bas (tot) = total score obtained at the Behavioral Activation Scale. Numbers in parenthesis are standard errors.

Participants were not taking psychoactive drugs, and were free of current or past psychiatric or neurological illness as determined by history. Participants gave informed consent, according to the Declaration of Helsinki (International Committee of Medical

Journal Editors, 1991) and the Ethical Committee of the Department of Psychology, University of Bologna.

We then used the same procedure as in the main experiment to divide our sample in three groups based on the median value of hunger rates (= 2) (Low-Hunger, Medium-Hunger, High-Hunger). Since only three participants had the hunger rating equal to the median, and since we did not obtain any significant results in the main experiment for the group with a medium level of hunger, here we tested only participants with a low level of hunger (lower than the median value of hunger rates) and a high level of hunger (higher than the median value of hunger rates) (Table 4). All demographic characteristics of subjects in these two groups (lower hunger and higher hunger) were matched with those of participants in the main experiment (lower hunger and higher hunger). Indeed, there were neither differences in age, years of education, hours of fasting, hunger level, and BMI, DEBQ, and BAS between the two lower hunger level groups [all Fs(1, 30), ps > 0,12], nor between the two higher hunger level groups [all Fs(1, 26), ps > 0,10].

Groups	Number of subjects	Hunger rating	Age (years)	Education (years)	BMI	DEBQ (external eating behavior)	BAS (tot)
Low-Hunger	18	-1.3 (0.5)	25 (1.2)	17 (0.4)	21 (1.5)	3.4 (0.1)	40 (1)
High-Hunger	16	4 (0.2)	24.5 (0.5)	17 (0.5)	20 (0.6)	3.6 (0.1)	40 (1)

Table 4. Participants' demographic data after being divided in three and then two groups. BMI = Body Mass Index; Bas (tot) = total score obtained at the Behavioral Activation Scale. Numbers in parenthesis are standard errors.

Food rating task

Participants underwent to a computerized Food rating task (carried out through E-Prime 1.0 software, Psychology Software Tools ©) in which they rated on a 11-points Likert scale (-5, 5) their hunger level at the time (anchoring labels 'not hungry at all' and 'very hungry'), and then, one at a time, they were asked several questions concerning six foods depicted in picture (the same as in the main experiment, see Figure 2). Participants rated on a 11-points Likert scale (-5, 5) how much they wanted that food at the moment ['wanting' process, indicating the incentive salience (e.g., Berridge, 2007, 2009) or the decision utility (Kahneman et al., 1997) of an outcome], how much they liked that food at the moment ['liking' process, indicating the hedonic pleasure of an outcome (Peciña et al, 2006; Berridge, 2009)], the perceived healthiness of that food, and how they felt angry, anxious, calm, disgusted, happy, sad, and surprised, with respect to that food. The order of blocks of ratings pertaining to different foods was randomly determined across participants, as well as ratings order within each block of food. To make sure that any result of the present experiment could have been explained with a difference in the rating Pre test between these participants and those in the main experiment, we compared scores at the question 'how appetizing do you find this food?' of the main experiment, with scores at the question 'how much do you want to eat this now?' ('wanting' rating scale) obtained in this experiment, for both general groups, and lower hunger groups and higher hunger groups. No significant difference emerged between all participants along the two experiments, neither for LEF [all Fs(1, 75), ps > 0.89] nor for HEF [all F(1, 75), p > 0.24]. The same results yielded for both lower hunger groups [LEF: all Fs(1, 30), ps > 0.62; HEF: all Fs(1, 30), ps > 0.80], and higher hunger groups [LEF: all Fs(1, 26), ps > 0.62; HEF: all Fs(1, 22), ps > 0.44].

Procedure

The whole experiment took place in a quiet room. After collecting participants' personal data, subjects completed the Food rating task. Then, the experimenter chose, individually for each participant, the two foods that obtained the highest score to the rating concerning the 'wanting' as stimuli for subsequent Stop-signal task (see the main experiment). Since the two most favourite foods often obtained a different evaluation, they were assigned in a counterbalanced order to the two different trial conditions of the Stop-signal task, so that, along participants, no difference in the attractiveness of one food over the other was detectable. For the whole duration of the Stop-signal task, no changes of cues were provided. After completed the Stop-signal task, participants underwent again to the Food rating task. At the end of this task, participants were administered the DEBQ (external eating behavior subscale, van Strien et al., 1986) and the BAS (Carver and White, 1994).

Results

Hunger rating

An ANOVA on rating scores about the perceived hunger level, with group (Low-Hunger, High-Hunger) as a between-subject factor, and time (Pre, Post Stop-signal task) as a within-subject factor, showed a significant effect of group [F(1, 32) = 33.10, p = 0.000002], no significant effect of time [F(1, 32) = 0.16, p = 0.70], and a significant group × time interaction [F(1, 32) = 7.93, p = 0.008]. Post hoc comparisons, performed with the Newman–Keuls test, showed that hunger ratings were overall lower for the Low-Hunger group as compared to the High-Hunger group (-0.61 vs. 3.56; p = 0.0001), and, while in the Low-Hunger group the hunger level significantly increased in the Post test as compared to the Pre test (-1.28 vs. 0.05; p = 0.03), in the High-Hunger group the hunger level tended to decrease, even if non significantly (4.10 vs. 3.06; p = 0.10), suggesting that someway, arguably due to energy depletion after the Stop-signal task, the sense of hunger increased for those participants who were not so much hungry at the beginning of the experiment, whereas the opposite trend is detectable in participants who were already quite hungry at that moment, suggesting that a different mechanism could have been acted on them.

Stop-signal task

Here we replicated results of the main experiment. An ANOVA with group (Low-Hunger, High-Hunger) as between subject factor, and with error likelihood (Low, High) and trial type (Go, Stop) as within subject factors was performed on the percentage of errors. This analysis evidenced a significant effect of error likelihood [F(1, 32) = 937.20, p = 0.000001], a significant effect of trial type [F(1, 32) = 428.70, p = 0.000001], and a significant interaction error likelihood × trial type [F(1, 32) = 1178.0, p = 0.000001]. No significant difference between groups or interaction with groups was found (all ps > 0.51). Post hoc comparisons, performed with the Newman-Keuls test, first of all showed that the percentage of errors was significantly higher during the High-Error condition than the Low-Error condition (30% vs. 12%; p = 0.0001), and that the number of errors committed during Stop trials was significantly higher than the number of errors committed during Go trials (34% vs. 7%; p = 0.0001). Moreover, while the percentage of errors committed during Go trials was the same along High- and Low-Error conditions (0.08 vs. 0.07; p = 0.25), the percentage of errors during Stop trials was significantly higher for the High-Error condition than the Low-Error condition (50% vs. 18%; p = 0.0001).

We then entered RTs for correct trials in an ANOVA with group (Low-Hunger, High-Hunger) as between subject factor, and with error likelihood (Low, High) and trial type (Go, Stop) as within subject factors. This analysis evidenced a significant effect of error likelihood [F(1, 32) = 45.32, p = 0.000001], a significant effect of trial type [F(1, 32) = 257.40, p = 0.000001], and a significant interaction error likelihood × trial type [F(1, 32) = 31, p = 0.000004]. No significant difference between groups or interaction with groups was found (all ps > 0.18). Post hoc comparisons, performed with the Newman-Keuls test, first of all showed that RTs were significantly higher (i.e., responses were slower) during the High-Error condition than the Low-Error condition (450 ms vs. 421.1 ms; p = 0.0001), and that RTs during Go trials were significantly higher than RTs during Stop trials (470 ms vs. 400 ms; p = 0.0001). Moreover, while RTs for correct responses during Go trials were the same along High-Error condition and Low-Error condition (466.40 ms vs. 474 ms; p = 0.13), RTs for incorrect responses during Stop trials were significantly higher for the High-Error condition than the Low-Error condition (423.53 ms vs. 376 ms; p = 0.0001).

Moreover, an ANOVA on SSRT values with group (Low-Hunger, High-Hunger) as between subject factor, and with error likelihood (Low, High) as within subject factor revealed a significant difference between High- and Low-Error likelihood [F(1, 32) = 412.1, p = 0.0000001], evidencing how inhibition was higher during Low-Error trials (because easier) rather than during High-Error trials (382.14 vs. 282.23), that is, participants were worse, as expected, during High-Error likelihood trials. No significant difference between groups or interaction with groups was found (all ps > 0.20).

These results support the validity of the paradigm of Stop-signal task in producing different patterns of errors for the Stop condition comparing to the Go condition, and for the High- versus Low-Error likelihood, replicating results of the main experiment. Indeed, participants clearly made a significantly higher number of errors during the High-Error condition only when performing Stop trials.

Food rating task

We started with a general ANOVA on rating scores with group (Low-Hunger, High-Hunger) as a between-subject factor, and type of food (LEF, HEF), time (Pre, Post), and type of judgement (desirability, pleasantness, healthiness, disgust, surprise, anger, anxiety, calmness, happiness, and sadness) as within-subject factors. This analysis yielded a marginally significant effect of group [F(1, 32) = 3.95, p = 0.05], and a significant effect of time [F(1, 32) = 7.82, p = 0.009]. Post hoc comparisons, performed with the Newman-Keuls test, showed that ratings were overall lower for the Low-Hunger group as compared to the High-Hunger group (-1.10 vs. -0.48; p = 0.05), and ratings in the Post test phase were overall lower than in the Pre test phase (-0.95 vs. 0.63; p = 0.007). Moreover, the principal analysis yielded a significant effect of type of judgement [F(9, 288) = 35.40, p = 0.000001], a significant group × type of judgement interaction [F(2, 288) = 1.95, p = 0.04], and a significant type of judgement × time interaction [F(9, 288) = 8.50, p = 0.000001]. This result is not surprising, since we were comparing very different judgements and emotions. No other significant results for this general analysis were found (all ps > 0.21). To investigate the main effect, avoiding possible confounding, we carried out separate analysis, one for each judgement at stake.

An ANOVA on desirability ratings with group (Low-Hunger, High-Hunger) as a between-subject factor, and type of food (LEF, HEF) and time (Pre, Post) as within-subject factors yielded a significant effect of group [F(1, 32) = 5.00, p = 0.03], a significant effect of time [F(1, 32) = 29.02; p = 0.000006], no significant effect of type of food [F(1, 32) =

2.30, p = 0.14], and a marginally significant group × time interaction [F(1, 32) = 4.20, p = 0.05]. No other significant results (all ps > 0.53). Post hoc comparisons, performed with the Newman–Keuls test, showed that ratings were overall lower for the Low-Hunger group as compared to the High-Hunger group (1.00 vs. 3.00; p = 0.03), and ratings in the Post test phase were overall lower than in the Pre test phase (3.00 vs. 0.80; p = 0.009). We also developed the group × time interaction, finding that the decrease in the rating for the Low-Hunger group was significantly more pronounced (2.44 vs. -0.50; p = 0.0001) than in the High-Hunger group (3.50 vs. 2.20; p = 0.06), suggesting that the Stop-signal task had a greater effect on the wanting system relative to both food in individuals not so much hungry, rather than in individuals with higher levels of hunger.

The same analysis on pleasantness ratings yielded a significant effect of group [F(1, 32) = 53.76, p = 0.006], and a significant effect of time [F(1, 32) = 11.76, p = 0.002]. No other significant results were found (all ps > 0.20). Newman–Keuls post-hoc test revealed that ratings were overall lower for the Low-Hunger group as compared to the High-Hunger group (1.46 vs. 3.05), and ratings in the Post test phase were generally lower than in the Pre test phase (2.80 vs. 1.62).

The analysis on anxiety yielded no significant effect of group [F(1, 32) = 1.60, p = 0.21], no significant effect of time [F(1, 32) = 3.57, p = 0.07], no significant effect of type of food [F(1, 32) = 0.001, p = 0.98], a significant group × time × type of food interaction [F(1, 32) = 4.50, p = 0.04], no significant group × time interaction [F(1, 32) = 0.03; p = 0.85], and no significant group × type of food interaction [F(1, 32) = 0.22, p = 0.64]. We developed the group × time × type of food interaction (Fig. 5), finding that, while for the Low-Hunger group the LEF in the Post test phase was rated as associated with the same level of anxiety as in the Pre test phase (-2.80 vs. -2.89; p = 0.75) whereas the HEF in the

Post test phase was rated as more associated with anxiety as in the Pre test phase (-2.11 vs. -3.33; p = 0.007), we found a different trend for the High-Hunger group. That is, both LEF (-1.10 vs. -2.10; p = 0.04) and HEF (-1.40 vs. -2.0; p = 0.03) were rated as producing more anxiety in the Post test as compared to the Pre test. Note that, since anxiety, as well as disgust, anger, and sadness are negative judgments, smaller negative values mean higher scores.

The analysis on calmness ratings revealed only a significant effect of group [F(1, 32) = 5.03, p = 0.03], with High-Hunger participants being less calm than Low-Hunger participants (-0.73 vs. 1). No other significant results were found (all ps > 0.21).

The analysis on disgust ratings revealed only a significant effect of time (F(1, 32) = 4.63, p = 0.04), with an increase in the disgust toward both foods after the Stop-signal task as compared to before the task (-2.85 vs. -3.72). No other significant results were found (all ps > 0.13).

The analysis on anger scores revealed no significant effects. Only the time factor was close to statistical significance [F(1, 32) = 3.72, p = 0.06], suggesting a tendency to increase the anger toward both foods after the Stop-signal task as compared to before the task (-2.50 vs. -3.32). No other significant results were found (all ps > 0.46).

The analysis on surprise ratings revealed a significant effect of time [F(1, 32) = 14.40, p = 0.0006], with an decrease in being surprised toward both foods after the Stop-signal task as compared to before the task (-2.00 vs. -0.12). No other significant results were found (all ps > 0.08). The same analysis on healthiness, happiness, and sadness yielded no significant results (p > 0.16; p > 0.10; p > 0.31 respectively).

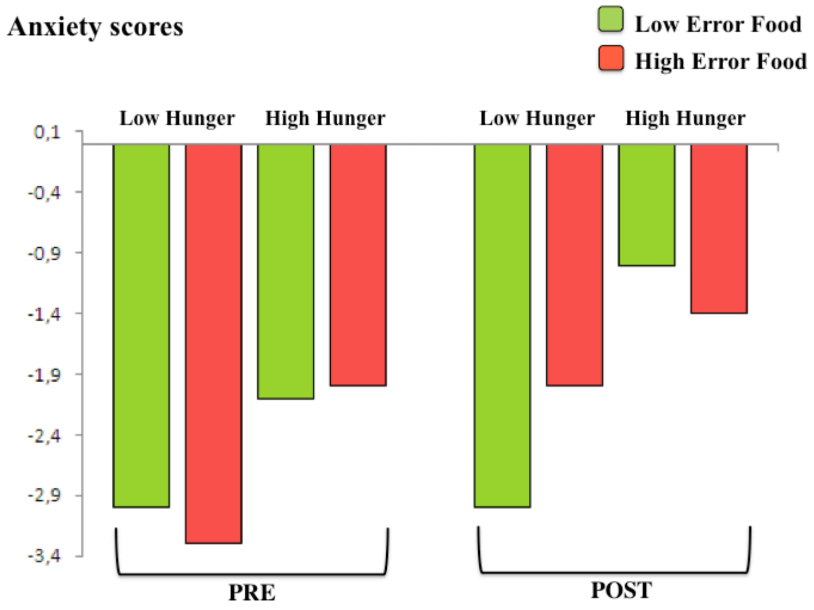

Figure 4. Anxiety scores Pre and Post test, separated by groups (Low Hunger, High Hunger), and error likelihood associated to foods (Low, High).

Discussion

The important finding here is that the Stop-signal task had a differential effect on self-report judgements about the two foods between groups only regarding the perceived anxiety.

Overall, participants with a lower hunger level had lower rating scores as compared to participants with a higher hunger level. Among the several judgements, the desirability decreased in the Post test phase as compared to the Pre test phase in both groups, more for the lower hunger group than for the higher hunger group, but without any difference between the two foods. This means that the wanting system (e.g., Berridge, 2007, 2009), that is, the incentive motivation, was affected in the same direction, even if in a more pronounced way for the former group. The same decrease was detectable for the perceived pleasantness, suggesting the same effect on the liking system (e.g., Berridge, 2009), that is, the hedonic pleasure. However, anxiety seems the only to have been influenced differently between the two groups concerning the two foods. Indeed, in individuals with a lower hunger level, the Stop-signal task increased the perceived anxiety only towards the food associated with a higher number of errors during the performance. Conversely, in individuals with a higher hunger level at the moment of the task, their attitude was characterised by more anxiety toward both foods. Finally, while the disgust and the anger experienced toward the two foods increased in the same way across groups in the Post error task as compared to the Pre test, surprise decreased, whereas all other judgements remained unaffected.

Anxiety is strictly related to arousal, and both should have changed, as they did, after the error task. However, as we suggested in the discussion of the main experiment, having a different motivational state related to food at the beginning of a task also related to food, influenced in a different way our participants' attitude. In a low level of hunger state, the aversive and arousing nature of mistakes has been correctly attributed (switched from errors) to one of the two foods, namely, the one toward subjects made more errors. Conversely, in individuals already hungry at the beginning of the task, the arousing quality of errors has been probably translated in hunger itself, increasing anxiety toward both foods. We will discuss these findings later.

General discussion

Consistent with our hypothesis, errors reduced impatient food decisions, indicating that the aversive quality of errors lessened the desirability of food. However, this occurred only in participants with a low hunger level. Conversely, in participants with a high hunger level, errors had the opposite effect, reducing participants' willingness to wait for future rewards. This suggests that, when individuals are not in a particular motivational state or need related to food, they are subjected to the negative conditioning, whereas this is not the case when they are in the opposite condition. Similarly to our dual result, Stafford and Scheffer (2008) found that participants in the pre-lunch time were slower to associate food with unpleasant words (implicit association test, IAT, Greenwald et al., 1998) as compared to participants in the post-lunch time, and Seibt and colleagues (2007) found that hungry individuals were influenced in the immediate evaluation of food items, rating them with a more positive valence. This is because food deprivation is associated with an increase in the reinforcing value of food (Lappalainen and Epstein, 1990; Epstein et al., 1996, 2003).

The finding that hungry participants behaved then more impulsively when choosing between immediate and future amounts of food suggests not only a failure in associating errors with food, but also that, in a state of hunger, the arousing quality of errors may be apparently misinterpreted as being related to food, thereby increasing immediate desire for this reward. Kavanagh and colleagues (2005), indeed, starting from the work of Schachter and Singer (1962; the same physiological arousal can have different cognitive labels) suggested that under particular conditions people can misattribute ambiguous internal states, as in Bauer and Kranzler (1994), where drug cravers' responses to erotic stimuli were apparently mistaken for responses to drug cues, or in Dutton and Aron (1974), where fear arousal appeared to be misattributed to sexual arousal in male subjects interviewed on a high suspension bridge from a female researcher (for other examples, see Ross et al., 1969; Storms and Nisbett, 1970; Zanna and Cooper, 1974). Deprivation itself induces desire (Jarvik et al., 1995; Jorenby et al., 1996), and the involvement of associational processes implies that desire may arise from salient but misleading attributions, so that the physiologic activation that does not arise from desire (e.g., sympathetic nervous system arousal associated with anxiety) can also be misattributed to desire (Kavanagh et al., 2005).

It is like to say that the negative emotion increased the awareness of deprivation (Kavanagh et al., 2005).

As said before, errors are considered aversive event, producing a negative neural wave (error-related negativity, ERN; Falkenstein et al., 1991; Gehring et al., 1995) generated in ACC (e.g., Miltner et al., 2003) when subject becomes aware of having committed a mistake, thus priming defensive motivation (Hajcak and Foti, 2008). When expectancy violations occurs, dopaminergic neurons projecting from the midbrain to ACC temporarily cease firing, resulting in the generation of the ERN that acts as a reinforcement learning signal (or prediction error) to adjust the ongoing behavior (Inzlicht and Al-Khindi, 2012; Holroyd and Coles, 2002). What we found in the control experiment is that self-rated anxiety toward the two foods differently changed between before and after the error task in the two groups. It seems that the Stop-signal task induced an increase in the physiological activation and consequently in anxiety toward the HEF only in participants free of food-related motivational state. Conversely, individuals in a state of need of food exhibited an increase in arousal and anxiety for both foods. This could explain why in the main experiment, participants with lower hunger differentiated between the two foods during the TD task, being less impulsive toward the HEF, whereas those with higher hunger had the opposite trend, even if non statistically significant. This also suggest that High-Hunger participants in the main experiment were someway aware of a difference between the two foods even if the increasing in the anxiety and arousal toward them was probably the same. Our result is completely in line with a recent study of Inzlicht and Al-Khindi (2012) suggesting that the ERN may partially reflect a distress response to errors. Their participants consumed a drink they believed would have either increased their anxiety or would have had no side effects, and then they completed a Stop-signal task. Results evidenced that subjects who were given the opportunity to misattribute arousal had a reduced ERN than participants who were not given any misattribution cues. This occurred despite no differences in performance on the error task, as for our participants. Moreover, correlations between the ERN and behavior were observed only for participants who did not misattribute their arousal to the placebo beverage. These findings suggest that the ERN is dissociable from cognitive performance but not from negative affect. Also, startle, that is a protective or defensive response that is reduced when appetitive stimuli are presented and augmented when aversive stimuli are showed (Lang et al., 1990; Lang, 1995; Bradley et al., 1999), has been found decreased in smokers as compared to non-smokers, during smoking cues (Geier et al., 2000).

Accumulating evidence indicates that dopamine signals are integrated with metabolic signals to guide reward search (in this case, food) in response to homeostatic state (e.g., Berridge, 2007; Schultz, 2007). Our suggestion, here, is that dopamine signals deriving from errors could have been misinterpreted as signals triggering consumption. Indeed, research showed that the experience of desire is qualitatively in subjective reports similarly across a range of rewards, including food, soft drinks, alcohol, and tobacco (May et al., 2004), relying in the commonality in the dopamine mesocorticolimbic pathways (Robinson and Berridge, 1993, 2003; Kavanagh et al., 2005). For instance, dopamine antagonists attenuate the incentive properties of food, water, and drugs in deprived animals (Nader et al., 1997).

It is worth to note that in our study we induced participants to associate a negative event with food and we did not prime them with an aversive event unrelated to food: This could have induced a negative mood influencing then spontaneous motivational tendencies toward edible stimuli (e.g., Wagner et al., 2012). However, even if this were our case, inducing negative affect and distress with a lot of mistakes in performance, our results are clearly different between less hungry participants and more hungry participants. Moreover, it is also important to say that even if we did not control for menstrual cycle in our subjects, we know that food intake fluctuates across hormonal phases in women. Specifically, women eat less food during the late follicular and periovulatory phases of the menstrual cycle, which are characterized by elevated levels of estrogen and low levels of progesterone, compared to the luteal phase, the only phase of the menstrual cycle in which progesterone is elevated (Lyons et al., 1989; Johnson et al., 1994; Pelkman et al., 2001; Reimer et al., 2005; Bryant et al., 2006). However, our initial purpose was to test subjects at least 2 hours fasted just to avoid them to have been in touch with food too recently, and the fasting that hours correlated with the hunger rating ($\beta = 0.41$, $p = 0.01$) suggests that hunger level in our participants was due to how long they have been without food.

Finally, we could also hypothesise that the Stop-signal task could have induced different levels of inhibition or cognitive control toward the two different foods. However, no significant differences were found between groups relative to this issue (as for instance in Hawk et al., 2004), and also this could have not explained the opposite result we found between Low-Hunger and High-Hunger participants. The same consideration is valid also if we hypothesised that during the Stop-signal task participants had someway to associate that, during High-Error trials, do not perform the action was rewarding as compared to do perform it, or that with a food, as compared to the other, they were required a higher effort to have success. Conversely, in a study in which our participants carried out a sustained attention task with food as cue (unpublished data), where the food appeared as reward only in correct trials, we found that the pleasantness associated with that food increased at the end of the task, suggesting that, in that case, we positively conditioned our participants.

Furthermore, since disordered eating have been recently consistently linked to drug addiction, sharing with it not only behavioral features like impulsivity and executive dysfunction, but also a documented dysregulation of the reward circuit (e.g., Avena et al., 2011; Gearhardt et al., 2011; Fortuna, 2012; Umberg et al., 2012), we could suggest to use the method here tested as a clinical training for people suffering from obesity and binge eating disorders (not related to pre-existent medical conditions).

Study V – The effect of aging on intertemporal choice

Introduction

The two causative studies I previously reported here (Study I, II-Part II) were based on the comparison between brain lesioned groups of patients and healthy groups of individuals, matched each other on sex, education, and age. Lesional studies, whose aim is to investigate how specific brain damage affects cognitive processes, require experimenters to collect data from patients with acquired lesions in a chronic phase, which is necessary to avoid confounding effects relative to the acute phase (e.g., spontaneous improvement of the disorder is highly likely; see Karnath et al., 2011 for an example). It turns out that the mean age of participants in the first lesional experiment here reported was about 58 years old, whereas in the second lesional study here reported was about 61 years old. However, when it comes to test healthy participants in behavioral or imaging studies, experimenters are used to recruit young subjects, especially at the University (that also means that they have at least several years of education). Among those trait variables influencing intertemporal decision-making in humans, age plays a prominent role. Are elderlies more wisdom than young individuals in making their intertemporal decisions? Or, have they a shorter horizon of future life to forecast about?

Contrasting findings arise from studies about this issue. For instance, evidence from Green and colleagues (1994, 1999) suggest that the older the subject the shallower the discount rate during intertemporal choice (Fig. 1).

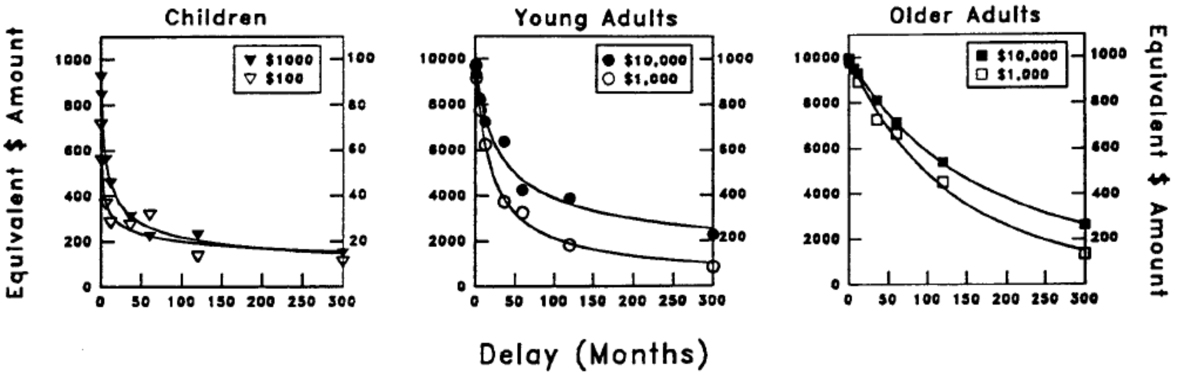

Figure 1. Mean hyperbolic discounting functions for children (mean age 12 years), younger (mean age 20 years), and elderly (mean age 68 years) (Adapted from Green et al., 1994).

Similarly, three recent studies (Reimers et al., 2009[1]; Löckenhoff et al., 2011[2]; Rhodes and Pivik, 2011[3]) found that impulsive intertemporal choices (gains but not losses) were associated with several demographics, like younger age, lower income, and lower education, and positive affect (e.g., liking for risky driving behaviors) more strongly predicted risky driving for teen and male drivers than for adult and female drivers. Conversely, other studies (Harrison et al., 2002[4]; Sozou and Seymour, 2003; Read and Read, 2004[5]) showed that individuals tend to become more patient with age, but only until adulthood, and then, elderly adults start to prefer again smaller sooner gains, behaving myopically, thereby suggesting that choosing a smaller but sooner reward is a warranty against an uncertain future, to maximize physiological conditions (Fig. 2).

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[1] participants aged 21-65; [2] participants aged 19-91; [3] teens aged 16-20 and adults aged 25-45; [4] participants aged 19-75; [5] younger mean age 25, middle-aged 44, and elderly 75.

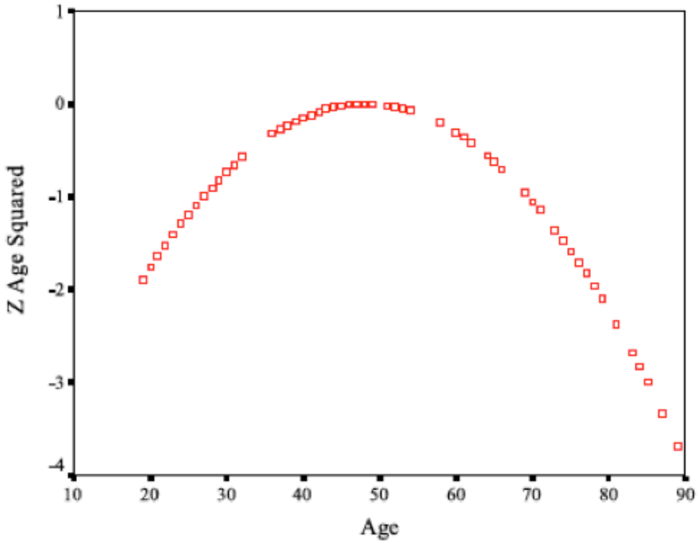

Figure 2. TD behavior changes with age (Adapted from Read and Read, 2004).

At the same time, however, it is well documented that the prefrontal cortex is among the brain regions most sensitive to the negative effects of aging (e.g., Lezak, 1995; West, 1996, 2000; Jahanshahi et al., 2000; Raz, 2000), even if with different outcomes on different areas. Several reviews (e.g., Carstensen and Mikels, 2005; Brown and Ridderinkhoff, 2009; Mohr et al., 2010) unanimously pointed out that, in the aging mind, while judgment, knowledge, and emotion regulation are relatively spared, processing capacity declines, with elderly performing overall less efficiently than younger participants, as demonstrated by the smaller total reward that the elderly acquired in lab tasks. For instance, Lamar and Resnik (2004[6]) found that tasks requiring a greater involvement of OFC appeared more sensitive to the effects of aging when directly compared to measures requiring a greater engagement of dlPFC. Similarly, Denburg and colleagues (2005) found that all their younger normal participants[7] performed in an advantageous manner on the

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[6] young participants aged 23-34, older participants aged 64-74; [7] aged 26-55.

Gambling task (the same task in which vmPFC patients were impaired in Bechara et al., 2000; see also Koenigs and Tranel, 2007, and Moretti et al., 2009 for other economics and social deficits following the disruption of vmPFC), while a subset of elderlies[8] performed abnormally on it, failing to shift their selections toward advantageous outcomes.

All these studies support the idea that the decision-making process is affected by neurocognitive changes due to age. However, while evidence clearly suggests that the smaller the age the larger the discount rate during pre-adolescent and adolescent age (e.g., Olson et al., 2008[9]), results are less clear for older people. We thereby decided to investigate if and how intertemporal choice behavior for hypothetical rewards is modulated by age in a group of Italian young participants and a group of Italian elderly individuals. For the first time, moreover, we assessed if and how age differently affected monetary and edible outcomes, both when an immediate option was offered and it when it was not.

Materials and methods

Participants

Forty healthy individuals participated in this study. Participants comprised twenty young adults and twenty elderlies (see Table 1 for demographics) who were not taking psychoactive drugs, and were free of current or past psychiatric or neurological illness as determined by history.

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[8] aged 56-85; [9] participants aged 9-23 years.

Groups	Sex (f/m)	Age (years)	Education
Young adults	10/10	21.7 (1.9)	13.6 (3.1)
Elderly	10/10	67.3 (9.7)	7.7 (2.4)

Table 1. Groups' demographic data. Values in parenthesis are standard deviations.

To ensure that all participants had intact cognitive functions, participants were submitted to several neuropsychological tests, commonly used in clinical practice. Both groups were assessed through the digit span (DS) forward and the DS backward. Elderlies were also submitted to the MMSE (Folstein et al., 1975) to evaluate language and visuo-spatial abilities (see Table 2). Even if the two groups differed in the education level ($p < 0.000001$), since it is quite difficult to find now elderly who gained high scholar degrees when they were young, all participants reached normal scores to neuropsychological tests corrected for their age. That is, even if groups differed in both the DS forward ($p < 0.00001$) and the DS backward ($p < 0.001$), their performance were in the normal range for their age (this held also for MMSE in elderlies).

Groups	DS forward	DS backward	MMSE
Young adults	7.3 (1.1)	6.5 (1.9)	-
Elderlies	4.8 (1.4)	4.3 (0.7)	26.8 (2.5)

Table 2. Mean values (corrected scores) for cognitive tests. Values in parenthesis are standard deviations. DS = digit span.

Procedure

After collecting demographic data (younger participants were also asked to report their height and weight to calculate their BMI; Smalley et al., 1990), both groups performed in a randomized order two TD tasks (Sellitto et al., 2010, see also Study I, II-Part II) based on two different reward types: in one we offered money amounts (Euro), and in the other we offered bites of food as reward. However, before starting the experiment, all participants chose their favourite food among four alternatives, which included two sweet snacks (cookie and chocolate bar), and two salty snacks (cracker and breadstick), to ensure motivation in the food TD task. Moreover, to avoid hunger confounding, all participants, before choosing among those four foods, rated their hunger level at the moment on a 6-points Likert scale (from 0, no hunger at all, to 5, very hungry). At the end of the second TD task, all participants were submitted to the BDI (Beck et al., 1961) to assess depression, and, only younger participants filled out both the BIS-11 (Fossati et al., 2001) and the BAS (Carver and White, 1994) scales to assess both inhibition and activation levels. Finally, the neuropsychological assessment was carried out. Groups did not differ on BDI scores ($p = 0.40$) and hunger levels ($p = 0.63$) at the moment of the experiment.

TD task procedure was the same we used in the study here reported in the Part II about insular cortex patients. That is, subjects performed intertemporal choices for both reward types along two different temporal conditions: one in which we provided an immediate option (Now condition), and one in which the sooner option was available only after 60 days (Not-now condition). Delays and titration procedure used to adjust sooner amounts based on participants' previous choice is the same we used in the Study I-Part II (Du et al., 2002; Sellitto et al., 2010). The whole experiment required about 40 minutes.

Results

To analyse data we used the same procedure as in Sellitto and colleagues (2010; see Part II). Since we found in all our previous studies that hyperbolic model was always superior to the exponential model, here we will analyse only hyperbolic k parameters, and no AUCs were calculated.

Figure 3 (a, b) shows TD curves by participant group and delay for both rewards, separately for Now and Not-now condition. The *k* value for each curve reflects the geometric mean of the group — which corresponds to mean of the log-transformed values — and thus provides a better measure of central tendency for positively skewed metrics, such as TD rates, than does the arithmetic mean. As is evident, TD curves were steeper for elderly individuals as compared to younger participants, suggesting that elderlies had an increased tendency to discount future rewards. Figure 3 (a, b) also highlights that TD of food was steeper than TD of money across both groups. These impressions were confirmed by statistical analyses. An ANOVA on log-transformed *k* values with group (Young adults and Elderlies) as a between-subject factor, and task (money and food) and temporal condition (Now and Not-now) as a within-subject factors yielded a significant effect of group [F(1, 38) = 4.48, p = 0.04]. Post hoc comparisons, performed with the Newman-Keuls test, showed that TD was steeper in Elderlies compared with Young adults (-1.59 vs. -2.01). Moreover, there was a significant effect of task [F(1, 38) = 6.38, p = 0.02], indicating that TD of food was steeper than TD of money (-1.65 vs. -1.95), and a significant effect of temporal condition [F(1, 38) = 12.32, p = 0.001], indicating that participants behaved less prudently when an immediate option was offered in the pair as compared to those trials in which no immediate option was provided (-1.68 vs. -1.92). Moreover, a significant task × temporal condition interaction was found [F(1, 38) = 5.76, p = 0.02], indicating that future food amounts in the Now condition were the most discounted as compared to future food amounts in the Not-now condition and future money amounts in both temporal conditions (all ps = 0.0001). This result was held for both young adults and elderlies. All other interactions did not reach statistical significance (all ps > 0.20).

Furthermore, BIS-11, BAS, and BMI values did not predict TD behavior in younger subjects (all ps > 0.63).

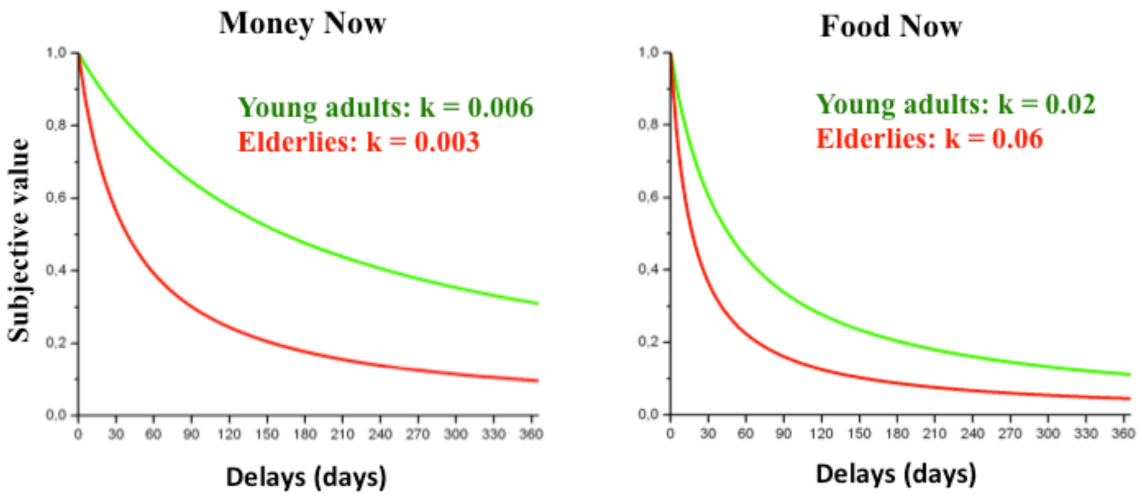

Figure 3a. TD functions by participant group (Young adults and Elderlies) and type of reward for the Now temporal condition. The hyperbolic curves describe the discounting of subjective value (expressed as a proportion of the delayed amount) as a function of time (days). The discounting parameter *k* reflects the geometric mean of the group (mean of the log-transformed values).

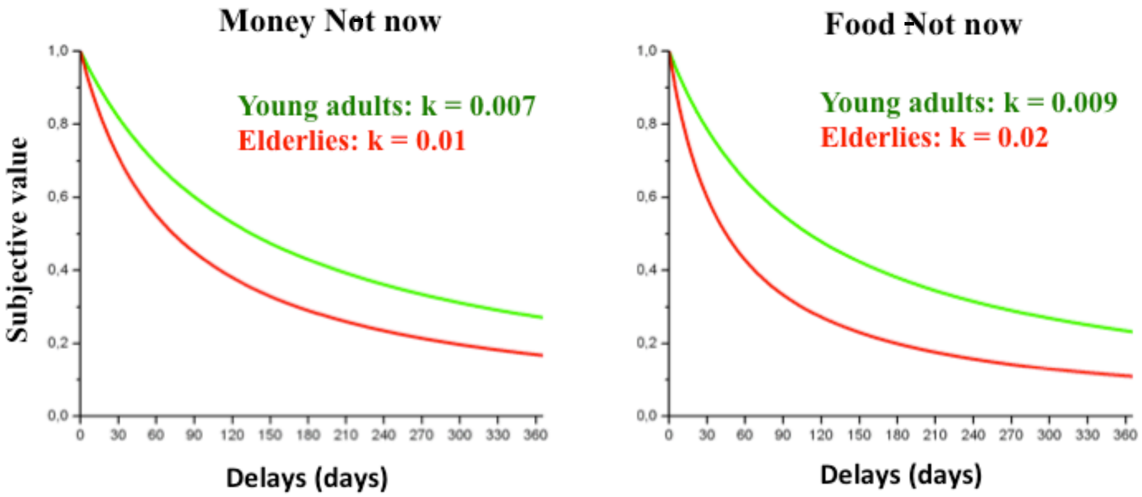

Figure 3b. TD functions by participant group (Young adults and Elderlies) and type of reward for the Not-now temporal condition. The hyperbolic curves describe the discounting of subjective value (expressed as a proportion of the delayed amount) as a function of time (days). The discounting parameter *k* reflects the geometric mean of the group (mean of the log-transformed values).

Discussion

Divergent trajectories characterize the aging mind: older adults evidence superior cognitive performance for emotional relative to non-emotional information, and age differences are most evident when the emotional content is positively as opposed to negatively valenced (Brown and Ridderinkhof, 2009). Overall, speaking specifically about outcome-based decision-making, it seems clear that aging has an effect on the subjective value computation. Accordingly, here we demonstrated that healthy elderly individuals had higher discount rates as compared to healthy younger participants when offered different gains attainable at different delays. This result held for both hypothetical money and food. However, as younger participants, elderly tended to prefer the sooner option significantly more frequently for primary than for secondary outcomes. Moreover, the tendency to behave more prudently when no immediate option was offered in the pair remained unaltered between the two groups.

Our finding that older people behave overall less patiently than younger people is in line with recent findings (Trostel and Taylor, 2001; Finkelstein et al, 2008; Chao et al., 2009) and also theories (e.g., Rae, 1834) suggesting that aging is associated with uncertainty of life, reduction in the ability to enjoy pleasure, and the discomfort from delaying gratification, resulting in a decline in people's ability to enjoy consumption, and higher discount rates. More precisely, our result is in agreement with the U-shaped relationship between age and discounting behavior, with individuals who tend to become more patient after adolescence (as for our younger participants), but only until adulthood, and then, elderly adults start to prefer again smaller sooner gains, behaving myopically like our elderlies, suggesting that choosing a smaller but sooner reward is a warranty against an uncertain future, to maximize physiological conditions (e.g., Read and Read, 2004).

Moreover, the fact that our older subjects lessened their impulsivity when faced with only delayed rewards (one sooner and one available later) suggests that, when nothing is accessible in the near time, choices are shifted toward the larger option, probably applying an heuristic of quantity.

However, this result does not reject older findings (e.g., Green et al., 1994, 1999) that suggest that older people are less impulsive during intertemporal choice because more wisdom and patient. In fact, most of those studies (e.g., Green et al, 1994, 1999) did not analysed participants as different groups but they only looked at age as a continuum, with the exception of Rhodes and Pivik (2011) who, however, did not test very old participants in their sample of elderly people (see Introduction).

Why people become more impulsive with age? Evolutionary theory posits that this behavior should be considered advantageous in light of increasing paucity of resources available in the future, for instance because with aging people are less able to find them (e.g., Rogers, 1994; Sozou and Seymour, 2003), maximizing their gains as they can. However, intertemporal decision-making is a complex process that need memory and computation capabilities, adequate visceral sensations translation (see Study II-Part II), correct selection of strategies among those acquired and/or learned in the past, emotion regulation, attention to social rules, intact affect forecast abilities and so on (e.g., Payne et al., 1992; Bechara, 2005). That said, it comes that we cannot overlook evidence about brain changes with aging. Indeed, cognitive decline with aging is well documented (e.g., Craik et al., 2006). Löckenhoff and colleagues (2011), for instance, suggested that the apparent paradox of age-related increments in processing speed but decrements in decision time highlights that people can decline in the ability to correctly estimate time intervals. According to them, age differences in the use of heuristic decision strategies might be a compensatory response to limitations in processing speed, but could also result from shifts in global time perspective that promote an affect-rich processing style. Similarly, effects of aging in correct affective forecasting and future anhedonia could result from a subjective compression of time perceptions, differences in the subjective speed of time, or deeper insights into one's emotional functioning in the face of limited future time horizons.

Our results can also be read in light of our previous findings about intertemporal choice in mOFC patients. Indeed, as our mOFC patients did, our elderlies showed an increased impulsivity towards future outcomes as compared to younger individuals, while maintaining unaltered the tendency to behave less prudently when tastes of food were available in the immediate present against larger but later amount of the same food. This result could suggest a dysfunction in the activity of mOFC in older people when processing intertemporal choice. A less effective activation of mOFC with aging, indeed, has been also suggested by Löckenhoff and colleagues (2011), together with a dysfunctioning of dlPFC during the experience of a conflict when engaged in difficult intertemporal decisions (Reuter-Lorenz et al., 2005; see also Figner et al., 2010; Essex et al., 2012; Roesch et al., 2012).

Moreover, taking into account the MTT manipulation we did in Study I-Part III (i.e., we made individuals who had just thought about events of their past, or imagined events of their probable future, as less shortsighted decision-makers when faced with monetary amounts), we can also read the present results in light of a study of Addis and colleagues (2009). They evidenced how older adults generated fewer episodic details than younger individuals for both past and future events. Indeed, our study supports the idea that aging affects the capacity to both recollect past events as well as imagine possible future scenarios (by affecting the same neural circuits involved in intertemporal choice), making thereby more difficult the act of envisage future selves projected in time receiving future monetary amounts (Ersner-Hershfield et al., 2009).

It is worth suggesting that neuroscientific research should consider the intertemporal choice and its modulation by aging, since mean lifespan of people is considerably rising. Indeed, most of the future decision-makers will be over 65 years old. Among older persons without dementia, a lower level of cognitive function, for instance, is associated with greater TD, having implications regarding the ability of older persons to make decisions that involve delayed rewards but maximize well-being (Boyle et al., 2012).

General discussion

People make decisions daily. Sometimes, these decisions appear to have a quite restrained impact, affecting, for instance, the course of a day when choosing how to spend free time. However, the overall impact of a choice may also have broader consequences, with important implications in the long term, requiring then a more careful consideration of all alternatives. Indeed, in a larger range, spending the free time out with friends, for example, can have a good impact on one's social life, health, and mood, discharging from working stress, and increasing knowledge, e.g., visiting a museum. Even more broadly, this can affect overall economy (buying the ticket at the museum), friends' mood (they will be happy to spend fun time together), and so on. However, one can decide to make an effort forgoing fun activities and remaining home working on a job application. Similarly, this will increase chances to be shortlisted, leading then to become, for instance, a good researcher, with a larger income, and so on. Such type of decisions, involving trade-offs between benefits and costs differing in the time of their occurrence, is commonly referred to as *intertemporal choices* (e.g., Frederick et al., 2002).

Economics and psychology have long established that humans and other animals tend to prefer smaller rewards with short-term availability over larger rewards that become available in the long run, even when waiting would yield larger payoffs than pursuing immediate feelings (Ainslie, 1974; Rosati et al., 2007). Preferring closer reward implies that the subjective value (i.e., utility depending on specific characteristics of a subject) of a future reward is weakened (discounted), as a function of the time until its delivery (e.g., Cardinal et al., 2001; Kalenscher et al., 2005; Myerson and Green, 1995). This phenomenon, known as delay or *temporal discounting* (TD, Ainslie, 1975; Samuelson, 1937), is usually considered a good measure of impulsivity (e.g., Takahashi, 2005). Individuals with greater discounting, indeed, are described as unable to wait for delayed rewards (i.e., impatience choices, Takahashi et al., 2007; Frederick et al., 2002) and may have impaired self-control (e.g., Takahashi et al., 2007), which is necessary to favour distant, more important goals (Shamosh and Gray, 2008). But, how do people make such decisions, and why do they all choose differently?

Neuroeconomics gives the opportunity to understand at neural level how people weight outcomes to choose and how they assign them a subjective value, appearing sometimes as irrational. As highlighted before, intertemporal decision-making is not a unitary process: Several mechanisms, including automatic and controlled processes, go beyond a coherent utility maximization, resulting in either patient or imprudent behaviors.

Extant functional neuroimaging evidence in humans converges to suggest that intertemporal choices are governed by a network of brain regions, including VS, mOFC, PCC, and lateral prefrontal cortex (e.g., McClure et al., 2004, 2007; Kable and Glimcher, 2007, 2010; Sellitto et al., 2011; Part I), whose specific role, however, is still unclear. Mainly, two different views emerge from previous studies. On the one hand, according to the dual model proposed by McClure and colleagues (2004, 2007, Part I), during intertemporal choice, the activation of the so-called impulsive ß-system, which includes VS, mOFC and mPFC, is preferentially activated when an immediate option is available, whereas activation of the so-called rational ∂-system, which includes lateral prefrontal cortex and PPC, is activated by all types of choice (Laibson, 1994, 1997; Loewenstein, 1996; McClure et al., 2004, 2007). The ß-system is thought to be responsible for impatient choices, driven by the desire for present outcomes (i.e., the ‘myopic doer’, Thaler and

Shefrin, 1981; Elster, 1985, 1986; Graham and Isaac, 2000). The ∂-system is thought to be responsible for prudent choices, emphasizing more the consequences of choosing delayed outcomes (i.e., the ‘farsighted planner’, Thaler and Shefrin, 1981). On the other hand, according to the unitary model proposed by Kable and Glimcher (2009, 2010, Part I), the activity in VS, mPFC and PCC tracks the subjective value of both immediate and delayed rewards, suggesting that these areas do not carry an impulsive signal that primarily values immediate rewards, but rather a value signal for delayed rewards as a function of sooner ones.

In Part II of this dissertation we provided new evidence about the neural bases of intertemporal choice both using a lesional approach and neuroimaging novel paradigms, which have important implications for understanding mechanisms regulating this neural network.

A proposed unitary neural model

Our lesional findings (Study I, II-Part II) supported the hypothesis of the unitary model proposed by Kable and Glimcher (2007, 2010; Peters and Büchel, 2009), according to which mOFC and adjacent mPFC, VS, and PCC represent the subjective value of all rewards at stake. On the one hand, the fact that damage to mOFC increased imprudent choices (Study I-Part II, Sellitto et al., 2010) does not support the idea that mOFC underlays the impulsive system, as suggested by the dual model of McClure and colleagues (2004, 2007). As discussed above, were this the case, damage to mOFC should have resulted in a weak ß-system overwhelmed by the ∂-system, and, consequently, in less impulsive choices. On the other hand, findings on patients with damage to the insular cortex (Study II-Part II, Sellitto et al., submitted), at odds with those obtained on patients with lesion in the mOFC (Study I, Sellitto et al., 2010), showed that lesion to insula decreases TD of future rewards. This allows us to add another tile to the architecture of the neural network underlying intertemporal choice. Within the proposed network, the mOFC and adjacent medial prefrontal regions are thought to weight the long-term prospects of a given choice (Schoenbaum et al., 2009; Sellitto et al., 2010), signaling the subjective value of expected outcomes during choice (Rudebeck et al., 2006; Schoenbaum et al., 2006, 2009; Murray et al., 2007; Rushworth et al., 2007; Talmi et al., 2009), by integrating different information (e.g., magnitude, delay; Ballard and Knutson, 2009) coming from different structures (e.g., amygdala, De Martino et al., 2006) into a 'common neural currency', namely, a common scale used to compare future actions and outcomes value (Montague and Berns, 2002). The insula, which possesses connections with both the vmPFC and the VS (Reynolds and Zahm, 2005), therefore may relay interoceptive inputs about need states and reward preference, possibly remapping changes in bodily states generated by the amygdala (Winston et al., 2002). This in turn will determine the strength with which one will pursue a reward option rather than the other (Weller et al., 2009). According to this model, damage to the mOFC would cause a problem envisioning future outcomes, leading to steep TD, whereas damage to the insula would lead to emotionally blunt intertemporal choices based on a heuristic of quantity, and therefore to a reduced discount rate.

Our preliminary imaging findings (Study III-Part II), on the one hand, partially replicated (univariate analysis) McClure and colleagues (2004, 2007)' results. Mainly, as in their studies, regions located in the medial frontal cortex (including ACC), PCC, the precuneus and the angular gyrus have been found activated when an immediate option was available, whereas the lateral prefrontal cortex, the anterior insula, and the occipital cortex have been found activated when no immediate option was offered. On the other hand, however, we found other areas clustering in the medial frontal gyrus and in the precuneus responding to both immediate and delayed rewards (as in Ballard and Knutson, 2009). Both these regions are included in the limbic system and involved in reward processing (Breiter and Rosen, 1999; Knutson et al., 2001b), but if they were underlaing the impulsive ß-system, as hypothesized in the dual model of McClure and colleagues (2004, 2007), they should not have been activated during choices in which both options were projected in the future. This suggestion is further supported by the novel carry-over effect analysis on the same data. We contrasted offers preceded by the same or a different type of offer (based on the availability or not of an immediate option). Activity in the insular cortex, the middle frontal gyrus, the superior temporal gyrus, and the putamen emerged when contrasting trials preceeded by the same type of trial against trials preceeded by a different type of trial (be an immediate option available or not). Activity in vmPFC, the superior frontal gyrus, the ACC and the temporal lobe emerged when contrasting trials preceeded by a different type of trial vs. trials preceeded by the same type of trial (whether an immediate option be available or not). These results strongly suggest that these regions participate in coding offers at all delays (both with and without an immediate outcome available), thus not supporting the dual model hypothesis of McClure and colleagues (2004, 2007), while in line with the proposed unitary model of Kable and Glimcher (2007, 2010; Peters and Büchel, 2010b). Our suggestion is that, on the one hand, during the computation of subjective value (univariate analysis), it has been given a special weight to the immediate option (i.e., the more tempting one) when available, whereas, when choices were more difficult (because both options were projected in future), more dorsolateral areas activity was required. On the other hand, however, when not distinguishing between offers with and without an immediate option (carry-over effect analysis), regions in the medial wall of the prefrontal cortex, the superior frontal cortex, the temporal lobe, and the insula were recruited to value outcomes at all delays.

Proposed mechanisms: prospect and valuation

We proposed (Sellitto et al., 2010, 2011; Ciaramelli and di Pellegrino, 2011) two possible mechanisms through which mOFC may influence evaluation and preference of future rewards: prospect and valuation. vmPFC regions, including mOFC, are at the core of a network of brain regions involved in self-projection, namely, the ability to shift perspective to alternatives other than the present, unbinding one from her sensorial self (Buckner and Carroll, 2006; Andrews-Hanna et al., 2010). During intertemporal choice, mOFC may allow individuals to anticipate future experiences associated with rewards, and modulate valuation of future outcomes based on the resulting (positive) affective states (Bechara, 2005). For instance, mOFC may subserve the ability to imagine and reproduce how one will feel tomorrow after collecting 20 €. Moreover, signals in ACC, coupled with hippocampus and amygdala, have been found to predict the degree to which future thinking modulated individual TD (Peters and Büchel, 2010a), suggesting a mechanism through which decision-making and prospection neural networks can interact to generate future-minded choice behavior. Our imaging data (Study III-Part II) showed that neural patterns in the medial temporal lobe and the parahippocampal gyrus are able to discriminate between offers with and without an immediate option, in line with the idea that affective reactions to stimuli can emerge from recall of personal emotional experiences, or from the imagination of hypothetical affective events, driving choices (somatic-marker hypothesis, Damasio, 1994; Bechara, 2005; Bechara and Damasio, 2005; Verdejo-García and Bechara, 2009; see also anticipatory-utility perspective, Rae, 1834; Frederick et al., 2002).

We further explored this possibility linking MTT to TD (Study I-Part III). MTT refers to human beings' capacity to both re-experience episodes from one's personal past, and pre-experience possible events that may occur in the future (Suddendorf and Corballis, 1997; Wheeler et al., 1997; Atance and O'Neill, 2001; Tulving, 2001; Suddendorf and Busby, 2003; Suddendorf, 2006; Botzung et al 2008). As Schacter and colleagues (2007) suggested, the brain areas included in the 'default mode', the same activated when projecting oneself in time, could be necessary to adaptively integrate information about relations and associations deriving from past experiences (memory retrieving) to construct mental simulations about possible future episodes (prospection and forecasting) (see Part I), so that one can recall memories of receiving a money amount to anticipate feelings associated with collecting 20 € tomorrow. Being engaged in MTT in prior to making intertemporal decisions reduced preferences for smaller immediate monetary amounts in our participants (Study I-Part III), suggesting that training to detach from one's present self and project it in time allow the system to more accurately evaluate time. Importantly, our data showed that thinking about future selves (e.g., Ersner-Hershfield et al., 2009) was not the only way to disengage one from her sensorial self: Also thinking about the past time had the same effect. Reduced impulsivity seemes thereby coming directly from moving oneself in a distant time.

The idea that mOFC enables one to envision future rewards (Ciaramelli and di Pellegrino, 2011) is not confined to intertemporal choice only, but is also supported by our findings about TD and moral judgment (Study II-Part III). We demonstrated that more impulsive individuals during intertemporal choices were also more impulsive when judging the moral valence of an action, being at the same time more willing to accept both immediate outcomes and moral violations. Lesional findings show not only that our mOFC patients were less willing to wait for larger delayed outcomes (Sellitto et al., 2010; Study I-Part II), but also that vmPFC patients (Ciaramelli et al., 2007) were less reluctant in accepting moral violation, suggesting a system dysregulation when faced with a conflict between emotional and utilitarian components. In both cases, being not able to anticipate emotions driving one's choices, based on previous experiences (probability) of feeling pleasure or pain as a consequence of an act, might be the general underpinning of impulsive behavior (e.g., Bechara 1994, 2005). If one is not efficient in envisioning future outcomes (i.e., a larger amount of money; no remorse for having violated a moral rule), poor representations of future goods will be underpowered to compete with salient, current rewards representations, so that imprudent choices will follow (Ciaramelli and di Pellegrino, 2011).

mOFC has also been proposed to enable more rational behavior by integrating emotional and cognitive information (De Martino et al., 2006). Indeed, mOFC is the target of top-down signals from lateral prefrontal cortex promoting 'rational' decision-making and self-control over immediate gratification (Christakou et al., 2009; Hare et al., 2009; Figner et al., 2010). Lateral cortices are involved in goal pursuing, future planning and implementation of cognitive control (e.g., Miller and Cohen, 2001; Knoch and Fehr, 2007; Figner et al., 2010; Essex et al., 2012), and neurophysiological studies suggest that the PFC is also important for the ability to prospectively activate long-term memories (Rainer et al., 1999; Tomita et al., 1999; Miller and Cohen, 2001). Based on findings reported in this dissertation, damage to the mOFC, therefore, would prevent lateral prefrontal signals from modulating the value signal influencing preferences, thus depriving patients of self-control during intertemporal decisions (Sellitto et al., 2010; Study I-Part II). Poor MTT (during both intertemporal choice and moral judgement) and/or poor self-control arguably result in problems anticipating, or adapting behavior to, the long-term consequences of decisions biasing choices towards closer rewards (i.e., 'myopia for the future'; Damasio, 1994, Bechara, 2005; Sellitto et al., 2010; Ciaramelli and di Pellegrino, 2011). This suggestion is compatible with a theory of impulse control proposed by Bechara (Bechara, 2005; Bechara and Van Der Linden, 2005), according to which regions in the vmPFC, including mOFC, weight the long-term prospect of a given choice during decision-making (Schoenbaum et al., 2009), while the amygdala and VS signal the immediate prospect of pain or pleasure (Bechara and Damasio, 2005; Kringelbach, 2005). Impulsive behavior would emerge as the result of an imbalance between competing signals, favoring valuation of immediate over future outcomes. Competing signals from insula and other somatosensory cortices, critical for representing patterns of emotional/affective states, and from dlPFC and the hippocampus, critical for memory and imagination (Damasio, 1994; Bechara, 2004), converge to vmPFC and mOFC: A disruption of these cortices might lead to the hypervaluation of immediate over future outcomes, as in our mOFC patients (Study I-Part II), or as in previous studies where, during the Iowa gambling task, mOFC patients made impulsive, shortsighted choices that warranted (monetary) gains in the short-term but proved disadvantageous losses in the long-term (Bechara et al., 1997; Berlin et al., 2004; Anderson et al., 2006).

As argued by Monterosso and Luo (2010), instead of describing intertemporal choice as governed by separate and competing value systems, the alternative hypothesis that it is guided by a single valuation system better fit with lesional and imaging evidence to date: Higher cognitive capacities leading to greater valuation of larger later alternatives affect intertemporal choice through mediation of (rather than competition with) older cortical and subcortical structures, core regions for reward and motivation (Monterosso and Luo, 2010).

Outcome representation

Humans have been found to discount at some degree all types of reward. Is there a way to reduce peoples' impulsivity during intertemporal choices, namely, to increase their willingness to wait for larger but later outcomes? In Study III (Part III) we explored the possibility of modulating the psychological distance between decision-makers and outcomes. In the self-control domain, being engaged in high levels of construal is thought to lead people having greater consistency between long-term goals value and behavior (Trope and Liberman, 2010; Fujita and Carnevale, 2012). We demonstrated that, removing objects from the self could affect objects' construals (i.e., representations): Increased spatial distance from outcomes made people thinking to more abstract properties (high level representations) of rewards in prior to choosing, leading to a decreased discount rate. Namely, participants were induced to be less concerned about the effort related to waiting longer for the larger outcome, thereby being more attracted by its greater magnitude. This result can also be thought in terms of MTT. Here, instead of projecting the self in the distant time to detach one from her sensorial self, we increased the psychological distance from the outcome by moving the outcome itself, making one less attracted by the low-level property of the reward (i.e., longer time to be waited). We could say that here the sensorial properties of outcomes have been removed from the decision-maker. Moreover, at the same time, we demonstrated that, by manipulating the perceived spatial position of monetary amounts, a reduced TD rate can be obtained making the larger later reward as more salient and concrete, increasing its appeal, instead of increasing the distance from objects to highlight their abstract and decontextualized representations (e.g., Leiser et al., 2008). When the immediate outcome was perceived as far away, but the future one was perceived as close, the attractiveness of the latter increased, shifting peoples' choices towards it. This further supports the idea that one can act on rewards' representations in order to drive choices. To make a general consideration, in order to guide decisions toward the optimal outcome, on the one hand, one's attention can be capitalized toward global, centre features of an event, undermining goals with short-lived effects, and, on the other hand, one's attention can be directed toward the larger (but later) outcome, making it more attractive (accompanied by lessening temptation associated with the smaller sooner outcome). Both these solutions imply acting on objects representations, as it is already done in advertisement and marketing.

Outcome value

When we applied the cognitive procedure of MTT with edible goods (Study I-Part III) we failed to bias choice behavior toward larger amounts. Are we so hopeless with food? As explained above, people face an even stronger conflict with primary rewards since stronger visceral sensations are called into play, for instance when craving for a tasty treat, consequently experiencing loss of self-control. Even the simple visual exposure to tempting foods is a powerful trigger for immediate consumption (Hawk et al., 2004; di Pellegrino et al., 2011), making higher-level intervention more difficult to succeed. We demonstrated that reducing impulsivity for food is thereby possible by conditioning individuals to associate it with aversive events (Study IV-Part III). Changing the value of a reward, at least with a short-term effect, allowed individuals to be more inclined in avoiding that object, moving it in the distant time in order to move away the negative emotion associated with it. This means that we can operate at a lower level, manipulating emotions influencing outcome representations in prior to making an intertemporal decision. Indeed, also an increased level of anxiety has been recorded after our manipulation. However, we obtained the desired effect only taking into account arousal and visceral feelings at the moment of decision: While not hungry individuals showed the expected reduced impulsivity, hungry individuals showed the opposite effect, leading us to suggest that, in a state of need (hunger), increased arousal can be misattributed to hunger itself (e.g., Kavanagh et al., 2005). Indeed, it seems that the temporal and physical proximity of the food that could have reduced the aversive arousal state (hunger) leaded thereby to a disproportionate, even if transient, increase in the attractiveness of that reward (Loewenstein, 1996). This finding has important implications in light of the modern western problem of obesity and binge eating disorders (e.g., Fortuna, 2012). Eating when moody or stressed, or eating because of a lack of self-control can be effectively reduced with a training similar to the one we proposed here. Abnormalities in OFC and ACC associated with craving (e.g., Gautier et al., 2000; Volkow and Fowler, 2000; Wang et al., 2004), together with dopamine dysregulation (Wang et al., 2001), have been reported in obese individuals, similar to those reported for addicted people. This suggests that increased salience attribution, enhanced motivation, and decreased inhibitory control drive drug/food-oriented behaviors (Volkow and Wise, 2005). Moreover, an inhibitory feedback circuit linking dlPFC and OFC in successful dieters in response to meal ingestion has been found (DelParigi et al., 2007), supporting the idea that the inhibition of food reward is probably the goal of this frontal loop as a peculiar case of OFC being the target of top-down signals from lateral prefrontal cortex, promoting ‘rational’ decision-making and self-control, necessary to override more valuable immediate gratification (Christakou et al., 2009; Hare et al., 2009; Figner et al., 2010; Essex et al., 2012). When the system is dysregulated, affecting emotions can drive one toward less prudent decisions. Even obese children were more likely to behave impulsively than children of normal weight (Braet et al., 2007). This suggest that, when one cannot switch her decision toward the optimal outcome based on its representation, affecting emotions can be an effective strategy to reduce impulsivity, taking into account the pre-existent arousal state.

The future of intertemporal choice

The finding that mOFC patients had steeper TD rates than controls (Study I-Part II), and that they were still able to make a difference between primary and secondary rewards are paralleled by our results on elderly healthy individuals (Study V-Part III). Indeed, while behaving less prudently than young adults, older individuals maintained unaltered youngers’ tendency to behave more patiently when faced with secondary rewards (i.e., money) as compared to edible ones. This supports recent research about negative effects of aging on mOFC and dlPFC: These regions activity resulted dysfunctional during both experiencing a conflict when engaged in difficult intertemporal decisions, and when shifting selections toward advantageous outcomes was required during a gambling task (Lamar and Resnik 2004; Denburg et al., 2005; Reuter-Lorenz et al., 2005; see also Figner et al., 2010; Löckenhoff and colleagues, 2011; Essex et al., 2012; Roesch et al., 2012). As highlighted before, signals conveyed to the mOFC (e.g., from VS, insula, and amygdala) are at the same time under the top-down regulation of lateral prefrontal cortex, and possibly the PPC (Kable and Glimcher, 2007, 2010; Hare et al., 2009; Figner et al., 2010; Christakou et al., 2009, 2011; Essex et al., 2012), coming into play especially if more self-control is required (e.g., when the choice is difficult; Figner et al., 2010; Essex et al., 2012; Study III-Part II). Once the mechanism becomes dysregulated due to aging, an increased TD rate is detectable, as in our mOFC patients.

Boyer (2008) proposed that the engagement with past and future events enriches them with motivational force: both memory and imagination may break impulsiveness or boost on patience by associating plans with non-opportunistic rewards. MTT would lead to activate stored knowledge against which to compare imagined future events, by passing current goals (Ciaramelli and di Pellegrino, 2011). This could be the best way to get adapted to new contingencies, escaping form errors made in the past, and then reducing TD rates. However, from an evolutionary perspective, impulsive behavior in elderly individuals (Study V-Part III) should be considered advantageous in light of increasing paucity of resources available in the future, for instance because with aging people are less able to find them (e.g., Rogers, 1994; Sozou and Seymour, 2003), maximizing their gains as they can. Taking into account these considerations, we cannot overlook the present increase in life expectancies: Most of the decision-makers in the near future, indeed, will be over 65 years old. Intertemporal decision-making is a complex process that need memory and computation capabilities, adequate visceral sensations translation (see Study II-Part II), correct selection of strategies among those acquired and/or learned in the past, emotion regulation, attention to social rules, intact affect forecast abilities and so on (e.g., Payne et al., 1992; Bechara, 2005). All these abilities are still required in old age, and looking at the evidence about brain changes with aging, a cognitive decline is well documented (e.g., Craik et al., 2006). Löckenhoff and colleagues (2011), for instance, suggested that the apparent paradox of age-related increments in processing speed but decrements in decision time highlights that people can decline in the ability to correctly estimate time intervals. According to them, age differences in the use of heuristic decision strategies might be a compensatory response to limitations in processing speed but could also result from shifts in global time perspective that promote an affect-rich processing style. Similarly, effects of aging in correct affective forecasting and future anhedonia could result from a subjective compression of time perceptions, differences in the subjective speed of time, or deeper insights into one's emotional functioning in the face of limited future time horizons (Löckenhoff et al., 2011). Taking into account all this evidence, together with our finding that old individuals reduced impulsivity during intertemporal choice when no immediate option was available, it opens up to the need of interventions and policies on elderlies, based, for instance, on the MTT training we used here (Study I-Part III). As suggested by Löckenhoff and colleagues (2011), in contrast to chronological age, affective forecasting and time horizons can be modified in different ways, like contextual and motivational manipulations (Löckenhoff and Carstensen, 2007). Being engaged in MTT, thinking about events occurred in the past or possible events coming in the future, led people to disconnect themselves from the present sensorial self, and project them in the distant time. This could help to more efficiently anticipate and forecast feeling associated with going for a future reward, especially if it requires an effort in waiting.

Concluding remarks

As is evident from this dissertation, neuroeconomics methods open the way to disentangle between different mechanisms regulating intertemporal decision-making at neural level. Not only lesional and imaging approaches add important information to the current knowledge about how people weight goods available with different timings, but also the TD procedure used along experiments in this dissertation offers the unique opportunity to measure directly and effortlessly how impulsivity is modulated during intertemporal choice. As extensively pointed out, making the optimal choice is necessary for humans to survive. When faced with intertemporal choices, apparently people are choosing for themselves. Frequently, however, they are also considering, for instance, their relatives and their ingroup in prior to deciding. In a broader range, and the current worldwide financial crisis is an example, whatever they choose will affect the overall economy of nations (Smith, 1776). In the domain of the social discounting (e.g., Yi et al., 2011), several behavioral studies have already been conducted looking at intertemporal choice in a more complex context, linking decision process to ingroup/outgroup, social distance, and prosociality effort, in both healthy (e.g., see Jones and Rachlin, 2006; Charlton et al., 2012; Ziegler and Tunner, 2012; Locey et al., 2013) and pathological populations characterized by steep TD (e.g., Bickel et al., 2012). The next step for neuroeconomics should be the effort in finding neuroscientific procedures that can account also for these variables that can no longer be underestimated.

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Appendices

A - Table 1

Example of a research in PubMed.gov database by using as search keywords ‘imaging OR fMRI AND intertemporal choice OR temporal discounting’; [1]fNIRS and fMRI; [2]Resting state; [3]DTI; [4]Meta-analysis.

Authors	*Journal*	*Year*	*Content*
Heinzel et al.[1]	*Neuroimage*	***2013***	Impulsivity-related personality traits
Jimura et al.	*J Neurosci*		Dynamic reward representations
Zhang and Hirsch	*Neuroimage*		Temporal derivative
Amlung et al.	*Addict Biol*	***2012***	Alcohol Use Disorder
Essex et al.	*J Neurosci*		PPC and dlPFC: long-term value
Gianotti et al.	*Front Neurosci*		Dorsal PFC, COMT genotype
Kayser et al.	*J Neurosci*		Dopa, Corticostriatal connectivity
Kim et al.	*Phil Trans R Soc B*		Cultural differences
Liu et al.	*Behav Brain Res*		Valuation, Choice
Liu and Feng	*Brain Res*		Valuation, Choice
Luo et al.	*Neuroimage*		Moderators
Luo et al.	*SCAN*		Emotional primes
MacKillop et al.	*Psychiatry Res*		Nicotine, money, cigarettes
Miedl et al.	*Arch Gen Psychiatry*		Gamblers, delay, probability
Murawski et al.	*PLoS One*		Brand logos, incidental decisions
Ripke et al.	*Brain Res*		Adult, adolescents, impulsivity
Yu	*PLoS One*		White matter
Albrecht et al.	*SCAN*	***2011***	Self, others
Benoit et al.	*J Neurosci*		Episodic prospection
Camchong et al.[2]	*Biol Psychiatry*		Hyperconnectivity, Cocaine
Christakou et al.	*Neuroimage*		Connectivity
Claus et al.	*Alcohol Clin Exp Res*		Alcohol
Samanez-Larkin et al.	*Front Neurosci*		Age, striatal sensitivity
Kable and Glimcher	*J Neurophysiol*	***2010***	Single valuation system
Luo et al.	*Drug Alcohol Depend*		Cigarette smokers
Marco-Pallarés et al.	*Brain res*		Conflict monitoring
Mitchell et al.	*J Cogn Neurosci*		Future thinking
Peters and Büchel[a]	*Neuron*		Episodic future thinking
Pine et al.	*J Neurosci*		DOPA
Sripada et al.	*Human Brain Map*		Impulsivity trait
Wittmann et al.	*J Neurosci Psychol Econ*		Immediate, delayed
Ballard and Knutson	*Neuroimage*	***2009***	Magnitude, delay

Bickel et al.	*J Neurosci*		Real and fictive, Gain and Loss
Clithero et al.	*Neuroimage*		Pattern classification
Ersner-Hersfield et al.	*SCAN*		Future self-continuity
Gregorios-Pippas et al.	*J Neurophysiol*		Short-term discounting
Luo et al.	*J Neurosci*		Incentive bias, intertemporal
Olson et al.[3]	*J Cogn Neurosci*		White matter
Peters and Büchel	*J Neurosci*		Risky choice, Intertemporal
Pine et al.	*J Neurosci*		Marginal utility
Plichta et al.	*Biol Psychiatry*		ADHD
Xu et al.	*Brain Res*		Gain, Loss
Bjork et al.	*Biol Psychiatry*		Frontal gray matter, cocaine
Hoffmann et al.	*Psychopharmachol*	***2008***	Metamphetamine dependent
Luhmann et al.	*J Neurosci*		Delay, Uncerteinty, Prospection
Shamosh et al.[4]	*Psychol Sci*		Intelligence
Weber and Huettel	*Brain Res*		Probabilistic, Intertemporal
McClure et al.	*J Neurosci*	***2007***	Primary reward
Boettiger et al.	*J Neurosci*		Genotype, Alcohol
Kable and Glimcher	*Nat Neurosci*		Single valuation system
Wittmann et al.	*Exp Brain Res*		Time perception
Hariri et al.	*J Neurosci*	***2006***	Off-line, VS
McClure et al.	*Science*	***2004***	Dual valuation system

B - Supplementary material

(Study I-Part II; Sellitto et al., 2010)

Inconsistent preferences: Count of any deviation from a monotonically decreasing function, regardless of the magnitude. As an additional measure of inconsistent preference, we counted the number of times the subjective value of the future outcome at a given delay was greater than that at the preceding delay, with no constrain on the magnitude of the difference between the subjective values at the two different delays. The mean number of such departures from a monotonically decreasing function was small, and comparable across participant groups [Money task: HC: 0.80, mOFC: 1.28, non-FC: 1.00, F (2,33) = 0.91, p = 0.40; Discount voucher task: HC: 0.90; mOFC: 1.14; non-FC: 1.00, F (2,33) = 0.25; p = 0.77; Food task: HC: 0.95; mOFC: 0.57; non-FC: 0.66, F (2,33) = 0.86; p = 0.43].

ANOVA analyses (food reward data removed). To make comparisons across money, discount vouchers, and food rewards possible, the same delays and amounts were used across types of reward. Although we took care that delays and amounts used were comparable with those used in previous experiments (Charlton and Fantino, 2008, Estle et al., 2007; Odum and Rainaud, 2003), it is possible that these were more suited for the assessment of TD of money and discount vouchers than for TD of food (Jimura et al., 2009). One may argue, for example, that 40 units of food (e.g., 40 chocolate bars) would reach saturation, and be therefore less appetitive than 40 units of money, leading to increased TD for food than money. Although this and other problems are somewhat intrinsic to the study of TD of food (see Charlton and Fantino, 2008 for a discussion), we also ran all our

ANOVA analyses including data for money and discount vouchers only (see Supplementary material). We confirmed our results.

k. An ANOVA on log-transformed *k* values with Group (mOFC, non-FC, and HC) as a between-subject factor, and Task (money, discount voucher) as a within-subject factor yielded a significant effect of Group [F(2, 33) = 9.02, p = 0.0007]. Post hoc comparisons, performed with the Newman-Keuls test, showed that TD was steeper in mOFC patients compared to non-FC patients (-1.08 vs. -2.15; p = 0.0004) and HC (-1.08 vs. -2.00; p = 0.0008), whereas no significant difference was detected between non-FC patients and HC (p = 0.54). There was no significant effect of Task (p = 0.36) or Group × Task interaction (p = 0.95).

AUC. An ANOVA on AUC scores with Group and Task as factors yielded a significant effect of Group [F(2, 33) = 5.13, p = 0.01]. Post hoc comparisons, performed with the Newman- Keuls test, showed that AUC was smaller (i.e., TD was steeper) in mOFC patients compared to non-FC patients (0.28 vs. 0.54; p = 0.004) and HC (0.28 vs. 0.48; p = 0.01), whereas no significant difference was detected between non-FC and HC (p = 0.41). There was no significant effect of Task (p = 0.88) or Group × Task interaction (p = 0.94).

Nonparametric Mann-Whitney U analyses. Due to the small sample size, and the presence of a few outliers (data points falling outside the 95% confidence limits) in the HC (1 subject had low TD rates for discount vouchers, 1 subject had low TD rates for food) and non-FC group (2 subjects had high TD rates for food), we also ran all our analyses using robust non-parametric tests. We confirmed our results.

k. Mann-Whitney U analyses on *k* values showed that TD for money was steeper in mOFC patients compared to non-FC (U = 9; p = 0.01) and HC (U = 23; p = 0.01), with no difference between non-FC and HC (p = 0.67). Similarly, TD for discount vouchers was steeper in mOFC patients compared to non-FC (U = 4; p = 0.003) and HC (U = 20; p = 0.005), with no difference between non-FC and HC (p = 0.37). Finally, TD for food was steeper in mOFC patients compared to non-FC (U = 8; p = 0.01) and HC (U = 25; p = 0.01), with no difference between non-FC and HC (p = 0.70).

AUC. Mann-Whitney U analyses on AUC scores showed that TD for money was steeper in mOFC patients compared to non-FC (U = 13; p = 0.05) and HC (U = 31; p = 0.03), with no difference between non-FC and HC (p = 0.57). Similarly, TD for discount vouchers was steeper in mOFC patients compared to non-FC (U = 11; p = 0.03) and HC (U = 33; p = 0.04), with no difference between non-FC and HC (p = 0.63). Finally, TD for food was steeper in mOFC patients compared to non-FC (U = 12; p = 0.03) and HC (U = 15; p = 0.002), with no difference between non-FC and HC (p = 0.77).

Corollary study: TD for real monetary rewards. We tested 3 mOFC patients (mean age = 61.3; SD= 10.01) and 11 healthy controls (mean age = 57.01; SD= 7.23) using real monetary rewards. The 3 mOFC patients and 6 of the 11 healthy controls had taken part in the primary study. Unfortunately, the other patients and controls involved in the primary study were no longer available for testing. The new investigation took part about 1.5 years after the primary study. The task assessing TD for money and the procedure to calculate *k* were the same as in the primary investigation. This time, however, participants were informed before testing that they would be awarded the outcome chosen in one randomly selected discounting trial.

Despite the very small sample size, the difference in *k* between mOFC patients, M = 0.04, SD = 0.04, and healthy controls, M = 0.01, SD = 0.008, approached statistical significance, Mann-Whitney U = 4, p = 0.051. These results confirm that mOFC patients have increased TD of monetary rewards compared to normal controls.

The use of real money did not change participants' behavior significantly. We compared the k value evinced by participants (3 mOFC patients and 6 healthy controls) in the real money vs. hypothetical money TD tasks using Wilcoxon Matched Pairs Tests. k values obtained with real money were not significantly different from those obtained with hypothetical monetary rewards, in both mOFC patients (k_{real}: M = 0.04, SD = 0.04, $k_{\text{hypothetical}}$: M = 0.05, SD = 0.08; Z = 0, p = 1.00) and healthy controls (k_{real}: M = 0.004, SD = 0.003, $k_{\text{hypothetical}}$: M = 0.01, SD = 0.01; Z = 0.73, p = 0.46).

Glossary

ACC	anterior cingulate cortex
AUC	area under the curve
BAS	behavioral activation scale
BDI	Beck depression inventory scale
BIS-11	Barratt impulsiveness scale
BMI	body mass index
BOLD	blood oxygenation level dependent
LEF	low-error likelihood food (Study IV-Part III
HEF	high-error likelihood food (Study IV-Part III)
CLT	construal level theory
COMT	catechol-*O*-methyltransferase
CNS	central nervous system
CT	computerized tomography
DA	dopamine
DEBQ	Dutch eating behavior questionnaire
dlPFC	dorsolateral prefrontal cortex
DU	discounted utility model
DS	digit span
DTI	diffusion tensor imaging
EPI	echo planar
ERN	error related negativity
EUD	expected utility model
fMRI	functional magnetic resonance imaging
fNIRS	functional near infrared spectroscopy
HRF	hemodynamic response function
GLM	general linear model
IAT	implicit association test
mOFC	medial orbitofrontal cortex
MMSE	mini mental state examination
MRI	magnetic resonance imaging

mrPFC	medial rostral prefrontal cortex
MTT	mental time travel
MVPA	multi voxel pattern analysis
NAcc	nucleus accumbens
OFC	orbitofrontal cortex
OMPFC	orbitomedial portions of the prefrontal cortex
PCC	posterior cingulate cortex
PFC	prefrontal cortex
PPC	posterior parietal cortex
ROCF	Rey-Osterrieth Complex Figure Test
rTMS	repetitive transcranial magnetic stimulation
RT	reaction time
SRS	self-regulation scale
SSD	stop-signal delay
SSRT	stop-signal reaction time
TD	temporal discounting
TE	echo time
TR	repetition time
vmPFC	ventromedial prefrontal cortex
VOI	volume of interest
VS	ventral striatum