The Role of Goal Proximity and Invested Effort for the Valuation of Expected Outcomes

An investigation with functional magnetic resonance imaging

Dissertation
zur Erlangung des Doktorgrades
der Naturwissenschaften

vorgelegt beim Fachbereich Psychologie und Sportwissenschaften
der Johann Wolfgang von Goethe - Universität
in Frankfurt am Main

von
Ruth Schmitt
aus Miltenberg am Main

Frankfurt 2011
D 30

Vom Fachbereich Psychologie und Sportwissenschaften der
Johann Wolfgang Goethe-Universität als Dissertation angenommen.

Dekan: Prof. Dr. Winfried Banzer

Gutachter: Prof. Dr. Christian Fiebach
Prof. Dr. Jochen Kaiser

Datum der Disputation: 25.05.2011

Danksagung

Meinem Betreuer Prof. Dr. Christian Fiebach danke ich für seine Unterstützung durch Diskussionen, zahlreiche Anregungen und wertvolles Feedback während der Entstehung der vorliegenden Arbeit.

Außerdem möchte ich Prof. Dr. Jochen Kaiser für seine Bereitschaft danken, diese Arbeit zu begutachten.

Ein Teil der fMRT Untersuchungen wurde am Ghent Institute for Functional and Metabolic Imaging of the Brain in Belgien durchgeführt. Dafür möchte ich mich herzlich bei Prof. Dr. Marcel Brass bedanken, der mir dies ermöglicht hat. Mein ganz besonderer Dank gilt zudem Egbert Hartstra für die tatkräftige und zeitaufwändige Unterstützung bei der Datenerhebung.

Meinen Kolleginnen Ulrike Basten, Dr. Andrea Gäbel und Dr. Christine Stelzel bin ich dankbar für die überaus angenehme Arbeitsatmosphäre, für Antworten auf unzählige Fragen und für vieles mehr.

Bedanken möchte ich mich außerdem bei meinen Freunden, besonders bei Anna Ropeter, für die kontinuierliche und ausdauernde Unterstützung während der letzten Jahre. Marco Muñoz danke ich für die wunderbare Ablenkung von dieser Arbeit und für seine unendliche Geduld.

Mein ganz besonderer Dank gilt meinen Eltern, Gisela und Heribert Schmitt, die mich stets in meinen Vorhaben unterstützt haben. Ohne Euch wäre das alles nicht möglich gewesen.

Table of Contents

Abstract

In human neuroscientific research, there has been an increasing interest in how the brain computes the value of an anticipated outcome. However, evidence is still missing about which valuation related brain regions are modulated by the proximity to an expected goal and the previously invested effort to reach a goal. The aim of this dissertation is to investigate the effects of goal proximity and invested effort on valuation related regions in the human brain.

We addressed this question in two fMRI studies by integrating a commonly used reward anticipation task in differential versions of a Multitrial Reward Schedule Paradigm. In both experiments, subjects had to perform consecutive reward anticipation tasks under two different reward contingencies: in the delayed condition, participants received a monetary reward only after successful completion of multiple consecutive trials. In the immediate condition, money was earned after every successful trial.

In the first study, we could demonstrate that the rostral cingulate zone of the posterior medial frontal cortex signals action value contingent to goal proximity, thereby replicating neurophysiological findings about goal proximity signals in a homologous region in non-human primates. The findings of the second study imply that brain regions associated with general cognitive control processes are modulated by previous effort investment. Furthermore, we found the posterior lateral prefrontal cortex and the orbitofrontal cortex to be involved in coding for the effort-based context of a situation.

In sum, these results extend the role of the human rostral cingulate zone in outcome evaluation to the continuous updating of action values over a course of action steps based on the proximity to the expected reward. Furthermore, we tentatively suggest that previous effort investment invokes processes under the control of the executive system, and that posterior lateral prefrontal cortex and the orbitofrontal cortex are involved in an effort-based context representation that can be used for outcome evaluation that is dependent on the characteristics of the current situation.

1 Introduction

It is a key focus of current research in cognitive neuroscience how the brain computes value. This is not surprising considering the fact that value computations build the fundaments for all kinds of voluntary choice behavior, ranging from basic animal foraging decisions to complex human decisions, such as trading in the stock market.

In a recent model of value-based decision making, Rangel and colleagues (Rangel, Camerer, & Montague, 2008) proposed two basic processes contributing to the computation of value. On the one hand, the brain needs to determine internal states of the organism (e.g., hunger level), as well as external states of the environment (e.g., the price range of available options), which might represent a reference frame for the evaluation of the expected outcome. Apart from this reference dependent valuation mechanism, the brain must process so-called decision variables such as benefits, costs and risks associated with each alternative in order to enable efficient selection between those alternatives. In general, most neuro-cognitive research on decision making is concerned with investigating the influence of decision variables like reward size, probability of reward, delay of reward, and expected effort, respectively. However, thus far, almost no evidence has been provided for the decision variables of increasing reward proximity and the previously invested effort to obtain a reward. This is surprising considering that a) monkeys' posterior medial frontal cortex (pMFC) was shown to be highly specialized in coding for increasing reward proximity (Shidara & Richmond, 2002), and that b) the increase in the subjective value perception due to previous effort expenditure is a common research objective in fields like social psychology (e.g., Arkes & Ayton, 1999; Strough, Mehta, McFall, & Schuller, 2008).

It is the aim of the present thesis to show for the first time that increasing goal proximity and previous effort investment can also modulate valuation related regions in the human brain. To this end, we conducted two functional imaging studies integrating a monetary delayed response task into different versions of a multitrial reward schedule paradigm. In the first study, we set out to replicate neurophysiological findings in monkeys about the role of the caudal motor area (CMA) in the pMFC in signaling increasing reward proximity. In the second study, we investigated the influence of previous effort investment on neuronal activity and behavioral performance. Through accordant modifications of the multitrial reward

schedule paradigm, we investigated the influence of previous workload both in terms of a decision variable accumulating over action steps as well as in terms of a reference frame for relative value computation.

In the following, I will first give an introduction in the concepts and neurobiology of reference dependent valuation mechanisms. Then I will shortly describe the experimental approaches and associated brain responses of frequently investigated decision variables. Afterwards I will introduce the concepts of goal proximity and invested effort together with their operationalization used in the present thesis to analyze their influence on neuronal activity and behavioral performance. In the following experimental sections, the two studies will be described in detail. In the last section, the findings from both studies will be summarized and critically discussed.

2 Theoretical Background

There are two processes that result in a representation of the desirability of an anticipated outcome. One is the valuation mechanism based on the context in which equivalent choices are presented. It is also referred to as reference dependent valuation mechanisms (Clithero & Smith, 2009). The other one is concerned with the so-called “decision variables” (Stephens & Krebs, 1986). Notably, the evaluation of expected outcomes is performed even in the absence of any immediate necessity to choose and in a way that is also relevant for free-choice trials (Berns, McClure, Pagnoni, & Montague, 2001).

2.1 Context Dependent Valuation

Although value has generally been viewed as an absolute measure (e.g., expected value, the summed product of objective decision variables reward size and probability), much evidence suggests that value is often computed in relative terms, i.e., with respect to a reference point, rather than in isolation. The susceptibility to such reference points can easily be demonstrated by questions like: “Would you be willing to pay more for a new television the same day you bought a new house?”, or similarly “Would you be more likely to purchase that television if it was marked on sale?”. Most individuals respond affirmatively to questions of this form, likely because they make use of contextual anchors to determine the value of an option.

2.1.1 Framing and Relative Value Coding

This aspect of human behavior is called “framing”. Framing describes the process whereby the choice made is influenced by the manner or context in which the choice is presented. Kahneman and Tversky (1979) originally described this context or reference dependent value computation as a key aspect of prospect theory, a model of choice that predicts different preferences for equivalent outcomes that are framed either as gains or as losses. More specifically, people are more motivated to avoid losses than to make gains,

indicating that they assign higher values to potential losses than to equivalent potential gains. This is why prospect theory is also known as "loss-aversion theory". Another paradigmatic example of reference dependent computation of value that has a dramatic impact on financial transactions within real markets is the endowment effect (Thaler, 1980). This phenomenon refers to an observation whereby subjects value a good they own substantially more than an identical good that is available for purchase. Taken together, people attribute value as a change from a set reference point, which means they commonly judge options and prices in relative terms (e.g., Seymour & McClure, 2008). Findings like these also stimulated research about mechanisms underlying value assignment in the brain.

Recent studies in neuroscience implicate regions in the orbitofrontal cortex (OFC), striatum and ventromedial prefrontal cortex (vmPFC) in the construction of relative value (Seymour & McClure, 2008). Particularly the orbitofrontal cortex has a well-studied role in general reward processing (Padoa-Schioppa & Assad, 2006). Initial evidence for relative value coding in this region came from a classic experiment by Tremblay and Schultz (1999), who presented monkeys with variously preferred juice rewards, and recorded from orbitofrontal neurons while presenting each juice, presented in blocks with one other juice. Critically, neuronal activity depended on whether or not the juice was the preferred one in that block, rather than its absolute value. Comparable findings have also been found in human medial orbitofrontal cortex, using an analogous design in an fMRI study (Elliot, Agnew, & Deakin, 2008). Furthermore, OFC activity declines for a reward (or cues that predict a reward) when an individual (human or monkey) is sated with that reward (Chritchley & Rolls, 1996; Gottfried, O'Doherty, & Dolan, 2003), analogous to the perceived subjective decline in value. The representation of value in the OFC is additionally sensitive to the available choices in a given context, i.e., to the range of values presented in a specific condition (Padoa-Schioppa, 2009), further underlining its crucial role in relative value coding.

2.1.2 Cognitive Representation of Context Information

Also from a cognitive perspective on adaptive and flexible behavior, it could be more beneficial to code each stimulus according to the context in which the stimulus is presented, than to code only its physical properties. Recent evidence amply demonstrates that neurons in the lateral prefrontal cortex (LPFC) are involved in coding the stimulus depending on the

context of the situation (Sakagami & Niki 1994; White & Wise 1999; Watanabe & Sakagami, 2007). For example, cognitive context-representing neuronal activities have been reported in a multitask situation, in which LPFC activity depended solely on which rule was currently in effect (Wallis, Anderson, & Miller, 2001). Also in human subjects, the posterior LPFC (post-LPFC) was related to the selection of task sets according to contextual signals (Brass & von Cramon, 2004). In line with this, according to a series of experiments by Koechlin and colleagues (Koechlin, Basso, Pietrini, Panzer, & Grafman, 1999; Koechlin, Ody, & Kouneiher, 2003; Kouneiher, Charron, & Koechlin, 2009), contextual control in humans is subserved by posterior LPFC regions (typically, Brodmann's areas (BAs) 9/44/45). In their opinion, the cognitive context effect, i.e., the context-dependent coding of stimuli, may result from the engagement of posterior LPFC regions in maintaining task sets in working memory over a temporal episode.

In monkeys' LPFC, there are also neurons that code stimuli on the basis of the motivational context. For example, Watanabe and Sakagami (2007) found that in response to an instruction cue indicating absence of reward, LPFC neurons not only predicted the absence of reward but also represented more specifically which kind of reward would be omitted in a given trial. These neurons seem to represent the motivational context information in differential baseline activities as a function of the reward context. Because the LPFC receives highly processed motivational information from the orbitofrontal cortex and highly processed cognitive information from the posterior association cortices (Barbas, 1993), the integration of cognitive and motivational context information might occur in the LPFC, and the integrated information might be used as a top-down signal for adaptive goal-directed behavior.

Taken together, while OFC is predominantly concerned with processing value with reference to the motivational context, LPFC seems to play important roles in integrating the cognitive and motivational context information in order to be able to select appropriate responses according to a given situation.

2.2 Common Decision Variables

2.2.1 Reward Size

Apart from the characteristics of the current situation, individuals are guided by the expected mean value of the potential outcomes when deciding between choice options (e.g., Schultz, 2004). Correspondingly, the most obvious variable influencing decisions is the reward size of the expected decision outcome. Neurons in several brain structures show stronger activation when comparing rewarded with unrewarded trials. These structures include the striatum (Hollerman, Tremblay, & Schultz, 1998; Knutson, Adams, Fong, & Hommer, 2001), the dorsolateral prefrontal cortex (Kobayashi, Lauwereyns, Koizumi, Sakagami, & Hikosaka, 2002), the medial prefrontal cortex (Matsumoto, Suzuki, & Tanaka, 2003), the orbitofrontal cortex (Trembley & Schultz, 2000), and the dopaminergic midbrain (Waelti, Dickinson, & Schultz, 2001; Kawagoe, Takikawa, & Hikosaka, 2004). Some neurons in motor regions of the frontal lobe, such as premotor cortex, frontal eye fields, and supplementary eye fields also show enhanced activity with increasing reward magnitude, which could be related to the movement changes induced by rewards (Roesch & Olson, 2003).

However, in decision making situations of everyday behavior, when we choose between options and engage in courses of actions, we do not only have to decide according to reward size, but also according to a variety of additional decision variables that mostly devalue the expected outcome. In the following, I will discuss alterations of the reward signals by temporal delay, probability, and expected effort concerning a reward. I will also review how these variables influence choice behavior, as the subjective values that decision makers assign to outcomes are measured objectively in choice preference. Despite the growing interest in the neural correlates of decision making, however, it is not fully clear how these three additional decision variables of interest are represented and to which extent they are encoded by distinct neuronal populations.

2.2.2 Probability

The expected mean values of decision outcomes are additionally influenced by their associated degrees of probability (e.g., Schultz et al., 2008). Current views distinguish two

forms of probability, namely “risk” und “ambiguity”, depending on whether the probability distributions of outcomes are known or unknown.

The most direct way to investigate neural coding of risk is by comparing responses to stimuli with different reward probabilities. Across numerous studies, key areas involved in risky decision making include lateral prefrontal cortex (Huettel, Stowe, Gordon, Warner, & Platt, 2006b), anterior cingulate cortex (ACC) (Behrens, Woolrich, Walton, & Rushworth, 2007), and posterior parietal cortex (Huettel, Song, & McCarthy, 2005; Huettel, 2006a). Fiorillo, Tobler, and Schultz (2003) showed that the responses of dopamine neurons to reward attainment monotonically decreased with increasing reward probability, and, conversely, responses to the predictive stimulus monotonically increased. In contrast to that, Hsu and colleagues (Hsu, Krajbich, Zhao, & Camerer, 2009) identified neuronal activity in the striatum during valuation of monetary gambles to be nonlinear at the extreme tails of a probability distribution. Also behaviorally, the commonly observed linearity in responses to probability breaks down for very high and low probabilities in a systematic manner (Tversky & Kahneman, 1992), i.e., small probabilities are overweighted while high probabilities are underweighted.

Another point that is still a matter of debate is whether or not there are brain regions capable of integrating reward size with risk. Recent findings suggest that a region in mid-dorsolateral prefrontal cortex aggregates risk and reward magnitude signals into a common value signal that even varied with subjective risk attitude of the participants naturally modulating value perception (Tobler, Christopoulos, O'Doherty, Dolan, & Schultz, 2009). Of note, the integrated reward signal was not restricted to choices, but occurred also in choice-free (imperative) situations.

A smaller set of studies have examined the effects of ambiguity, or unknown probabilities, upon decision making and the associated valuation process. The orbitofrontal and the dorsolateral prefrontal cortex are engaged in these situations. When Hsu, Bhatt, Adolphs, Tranel, & Camerer (2005) presented decision problems to participants in an fMRI experiment, they found that lateral orbitofrontal cortex exhibited significantly greater activation to decisions involving ambiguity compared to decisions involving risk. A similar approach was used by Huettel and colleagues (2006b) who observed ambiguity related activation in the post-LPFC. This activation was predicted by ambiguity preference and was negatively correlated with an independent clinical measure of behavioral impulsiveness. This led the

authors to the conclusion that this region implements contextual analysis and inhibits impulsive responses, in accordance with the demands of an ambiguous situation.

In many real-life problems of decision making under uncertainty, however, decision makers are required to adjust their decision making strategies based on the value of the outcomes of their previous choices. This adaptive process is formally accounted for by the reinforcement learning theory (Sutton & Barto, 1998). Value anticipation in this field represents the empirical estimates of possible outcomes expected from several previous actions. During a sequence of choices the value of the actions is continually updated according to the experience of the decision maker. Numerous studies imply that the anterior cingulate cortex has a special role in this respect. After an ACC lesion, only the outcome of the most recent trial exerts any influence over subsequent decisions (Kennerley, Walton, Behrens, Buckley, & Rushworth, 2006) and the decision parameter of uncertainty correlates with the BOLD response in the ACC at the time the new outcome is observed which is the crucial time for learning (Behrens et al., 2007).

2.2.3 Temporal Delay

Uncertainty can also be induced by increasing the delay before a reward is received, which also leads subjects to devalue potential rewards. The time-dependent valuation of rewards is typically investigated using intertemporal choice tasks in which subjects have to choose between options that vary according to reward size and associated delays. On the basis of choice preferences, person-specific discount functions are established, i.e., the rate at which the subjective reward value decreases as a function of the delay until the reward is given.

Typically, the subjective reward value declines in a hyperbolic manner during intertemporal choice tasks, i.e., it exhibits a rapid decay in the beginning and flattens gradually with increasing delay-to-reward (Schultz, 2010). Particularly the neuronal activity in the striatum seems to track the subjective value of a delayed monetary reward (Kable & Glimcher, 2007). Further brain regions involved in the temporal discounting of reward value include the principal reward structures, namely the dopamine system and orbitofrontal cortex (Cardinal, Pennicott, Sugathapala, Robbins, & Everitt, 2001; Roesch, Calu, & Schoenbaum, 2007a). In monkeys, also premotor cortical neurons show lower firing rates following visual cues indicating a delay in reward (Roesch & Olson, 2005). The decreases in premotor

responses also correlate well with slower behavioral reactions, indicating that the decrease in neuronal response may reflect a reduction in general motivation through delays, rather than reduced reward value per se.

A fraction of neurons in monkeys' dorsolateral prefrontal cortex also show delay related reductions in choice experiments (Kim, Hwang, Seo, & Lee, 2009). However, in humans, posterior LPFC activity in delayed-reward tasks does not vary with expected reward value in a simple way (Tanaka et al., 2004). Therefore, it may not be important for representing the distant reward value itself. Instead, posterior LPFC activity is thought to represent the environmental states, and uncertainty about those states, during progression toward a distant reward.

Aiming to distinguish neural responses categorically between immediate and later rewards, it was proposed that the temporal discounting of decision options reflects two processes: an impulsive system *(β)* that rapidly devaluates rewards that are not immediately attainable, and a patient system *(δ)* that exhibits much more gradual discounting (McClure, Laibson, Loewenstein, & Cohen, 2004). Moreover, relative activation of these two sets of brain regions can predict actual choice behavior (McClure, Ericson, Laibson, Loewenstein, & Cohen, 2007). The studies of McClure and colleagues suggest that the *β*-system comprises reward-related regions including the ventral striatum and the ventromedial prefrontal cortex, whereas the *δ*-system includes cognitive regions like lateral prefrontal and lateral parietal cortices, i.e., areas related to executive control (e.g., Owen, McMillan, Laird, & Bullmore, 2005; Wager, Jonides, & Reading, 2004) that are commonly associated with deliberative cognitive processes including future planning. Thus far, it has not been investigated whether or not these putatively distinct decision systems might also be involved in value representation when available options vary according to other motivational aspects than temporal delay.

Taken together, reward-related neuronal responses undergo temporal as well as probabilistic discounting in a number of brain structures, suggesting that reward coding might be a rather widespread phenomenon in many brain regions representing value information.

2.2.4 Expected Effort

Furthermore, human decision makers show a tendency to avoid making decisions that are computationally demanding and subjectively effortful (McGuire & Botvinick, 2010). Other species also seem to take energetic expenditure into account when making foraging decisions (Bautista, Tinbergen, & Kacelnik, 2001). The degree to which effortfully obtained rewards are devalued may depend on the ecological niche occupied by a particular species (Stevens, Rosati, Ross, & Hauser, 2005). Interestingly, a comparative study of primate species demonstrates that a willingness to tolerate delay costs does not correlate with an inclination to exert more effort, i.e., to travel farer to obtain greater reward (Long & Platt, 2005). This suggests that the two types of decision costs, i.e., delay and effort, are also represented by different cortical regions.

Aiming to distinguish the influence of temporal delay and expected effort on decision making, Rudebeck and colleagues (Rudebeck, Walton, Smyth, Bannerman, & Rushworth, 2006) found out that orbitofrontal cortical lesions affected how long rats decided to wait for rewards. Conversely, anterior cingulate cortex lesions affected how much effort rats decided to invest for rewards. Furthermore, top-down signals from ACC to nucleus accumbens and midbrain DA cells may be vital for overcoming effort-related response costs (Walton, Kennerley, Bannerman, Phillips, & Rushworth, 2006). Anterior cingulate cortex is implicated in the making of cost-benefit decisions also in humans. In a recent study (Croxson, Walton, O'Reilly, Behrens, & Rushworth, 2009) subjects were scanned while they performed a series of effortful actions to obtain rewards that varied in magnitude. The putamen and several premotor and motor regions in the posterior medial frontal cortex were influenced by effort expectation independent of reward magnitude. Only activity in the dorsal ACC (dACC) also reflected the interaction of both expected reward and expected effort costs. This is further underlining the region's crucial role in guiding effort-based cost-benefit valuation, which may be a consequence of its role in representing the relationship between actions and outcomes (Rushworth, Walton, Kennerley, & Bannerman, 2004).

While the ACC or OFC may be selectively concerned with the processing of delay or effort costs, respectively, neither type of decision depends on either frontal region in isolation. Kennerley and colleagues (Kennerley, Dahmubed, Lara, & Wallis, 2009a) simultaneously recorded the activity of multiple single neurons in the frontal cortex while monkeys made choices involving the payoff of a choice, the probability the choice will yield a particular

outcome, and the cost in time and effort to obtain an outcome. Neurons in the ACC, OFC, and DLPFC encoded the value related to all of these decision variables. There was no evidence that specific areas of the frontal cortex were specialized for processing specific decision variables. However, there was a specialization of function with relation to the number of decision variables encoded. Neurons that encoded a single decision variable were equally prevalent throughout the frontal cortex, whereas neurons that encoded two or more decision variables were significantly more common in the ACC compared to the OFC and LPFC.

In general, it is still a matter of debate whether or not value coding involves mechanisms that are specific to the type of decision variables that are evaluated. During decision making, valuation of different domains of decision variables may involve partially distinct, i.e., domain-specific, neural systems (Ballard & Knutson, 2009). On the other hand, efficient choice behavior potentially requires a common neural coding of stimulus value. In line with this, some researchers suggest a mechanism for the neural coding of subjective value in the human brain that is based on the combination of domain-specific and domain general valuation networks, with domain general activation networks being identified through overlapping activation in response to differential decision variables (Peters & Buchel, 2009).

2.3 The Influence of Goal Proximity and Invested Effort on Valuation

Reward size, probability, delay, and expected effort are the most frequently investigated decision variables in neuroscientific research. Relatively few evidence has been provided for two other variables influencing valuation-related processes, and consequently choice behavior, i.e., the proximity to the desired goal and the previously invested effort to attain that goal.

A paradigm only used in monkey thus far to investigate these variables is the multitrial reward schedule paradigm (Bowman, Aigner, & Richmond, 1996). In this paradigm, a sequence of identical actions is required to obtain reward, and a visual cue indicates how many action steps remain before a reward is delivered. When performing in such multitrial reward schedules, the error rate of monkeys is proportional to the number of unrewarded trials remaining before reward, indicating that the value of the trial is modified by knowing the

proximity to the desired goal. The behavioral modulation contingent to goal proximity is potentially based on accordant adjustments of valuation related brain regions. Shidara and Richmond (2002) identified neurons in the monkeys' CMA, the putative homologue of human rostral cingulate zone (RCZ; Picard & Strick, 2001) in posteromedial frontal cortex, that reflect goal-based valuation by coding the proximity to a rewarding outcome. These CMA neurons showed progressively increasing or decreasing response strengths while monkeys performed in schedules of multiple trials with a visual cue indicating reward proximity. Notably, neurons in striatum (Shidara, Aigner, & Richmond, 1998), dopaminergic midbrain (Ravel & Richmond, 2006), and orbitofrontal cortex (Simmons & Richmond, 2008) are also active as monkeys work their way through schedules of responses to obtain reward. CMA, however, is distinguished by the presence of single neurons showing increasing firing rates as animals progress through such schedules (Shidara & Richmond, 2002). So far, it is an open question which regions in the human brain mediate the influence of increasing reward expectation while working through routine actions towards an anticipated reward.

Furthermore, in monkeys, the value of the current trial in a multitrial reward schedule also seems to be modified by the number of trials already completed, i.e., the previously invested effort (La Camera & Richmond, 2008). Also in humans, previous effort investment has been shown to have a substantial influence on outcome evaluation in the research fields of social psychology and economics. For example, a known phenomenon in economic decision making is the so-called sunk-cost fallacy, i.e., the increased tendency to persist in an endeavor once an investment of money, effort, or time has been made. The effect is considered potentially maladaptive because only current costs and benefits, not past costs, should factor into rational decision-making (Navarro & Fantino, 2005). While some doubt that there are clear-cut instances of the sunk cost effect in non-human animals (Arkes & Ayton, 1999), it has been documented in numerous studies with humans (Arkes & Blumer, 1985; Staw & Hoang, 1995; Moon, 2001). The sunk cost phenomenon comes in different varieties and with different interpretations (to the point of having different names, like ‘‘Concorde effect,’’ ‘‘cognitive dissonance,’’ or ‘‘justification of effort’’) (Arkes & Ayton, 1999). Importantly, all of these interpretations are based on motivational context effects due to differential effort expenditure, i.e., the influence of previously invested effort is conceptualized as an instance of the above mentioned “framing” (section 2.1.1). Surprisingly, evidence of the influence of previous workload on neuronal systems concerned with goal-based valuation is still missing both in

humans and in non-human animals, despite the prominent role of this motivational variable in other research fields.

2.4 Aims of the present work

The aim of the present work is to investigate how reward proximity and invested effort influence behavioral performance and neuronal systems concerned with goal based valuation in humans. We addressed this question in two fMRI studies by integrating a non-choice reward anticipation task (Knutson et al., 2001) into different versions of a multitrial reward schedule paradigm (Shidara & Richmond, 2002; Ichihara-Takeda & Funahashi, 2006).

The first experiment is mainly concerned with the influence of goal proximity along with the previously invested effort on the activity of the human rostral cingulate zone in the posterior medial frontal cortex. The strong anatomical hypothesis was derived from a recent monkey study using a similar experimental design (Shidara & Richmond, 2002, section 2.3). If the RCZ is indeed underlying the increasing reward anticipation over action steps towards predicted outcome, as proposed by the study of Shidara and Richmond (2002), signals in this region should be directly related to goal proximity, i.e., they should change contingent to the progress through the schedule. In humans, like in monkeys, pMFC seems to be a promising site for such a reward-proximity signal, as it is related to the monitoring of performance in relation to anticipated rewards (Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004). Alterations of this progression could be the basis for the changes from normal that are reported in pMFC activity for obsessive-compulsive disorder and drug abuse, conditions characterized by dysfunctional persistence in behavior related to deficient outcome valuation (Shidara & Richmond, 2002).

The second experiment was designed to investigate the impact of invested effort on neuronal activity and behavior and was more explorative in nature concerning the related brain regions. Monkeys are willing to put more effort in a trial if the total effort to get there had been larger, even though this does not affect the upcoming reward (“schedule length effect”; La Camera & Richmond, 2008). Also in humans, previous effort investment has been shown to have a substantial influence on outcome evaluation in other research fields (e.g., Navarro & Fantino, 2005). Correspondingly, we hypothesized that effort expenditure must modulate neuronal systems concerned with processes of outcome valuation.

As in this experiment the number of action steps per schedule varied randomly, the action course towards reward was less routine bound compared to the first experiment, thus yielding an increase of general performance monitoring demands. First of all, we hypothesized that regions generally associated with cognitive control functions are involved in effort-based value representation, analogous to the concept of a patient δ-system being activated when rewards are not immediately attainable (section 2.2.3). Furthermore, a previous study of Kouneiher and colleagues (2009) suggested that functional connectivity between lateral and medial PFC regions mediates the relationships between cognitive demands and motivational incentives, i.e., different reward sizes, to assure appropriate distribution of cognitive control resources. We sought to investigate whether or not such a connectivity profile could also be found with invested effort as a motivational incentive. As a question related aside, we were interested whether or not activity in effort related brain regions would be modulated contingent to the amount of previous effort expenditure.

Second, the other main focus of this study was to find out which brain regions are involved in the implementation of the so called "sunk cost effect", i.e., a framing effect based on previous effort expenditure (see section 2.3). It can be argued that, in the reward schedule task, the cost of performing trials is a ''sunk'' cost, as the subjects had to start the schedule anew after each error trial. Accordingly, there should be brain regions concerned with maintaining a state representation given the context of an immediate vs. a delayed block, in which the risk of sinking costs is substantially higher. Recent evidence indicates that the posterior LPFC and OFC are involved in representing cognitive and motivational aspects of the current environment (section 2.1). Disorganization symptoms observed in schizophrenic patients are supposed to be related to impairments in processing such context information in LPFC (MacDonald et al., 2006).

3 Functional Magnetic Resonance Imaging

Functional magnetic resonance imaging (fMRI) measures local changes of cerebral blood flow. These changes are attributed to changes in neuronal activity and interpreted in terms of cognitive brain functions. Below, a brief introduction into the physical and physiological bases of functional magnetic resonance imaging (fMRI) is given. Of course, such an introduction can only give an outline of these bases. For a comprehensive treatment, the reader might want to consult the introduction to fMRI by Huettel, Song, and McCarthy (2004).

3.1 Physical Basis of fMRI

The body is largely composed of water molecules which each contain two hydrogen nuclei or protons. MRI primarily images the signals from these hydrogen nuclei.

Protons in anatomic nuclei spin about themselves (therefore they are also referred to simply as *spins*). Thus, as any rotating mass, they possess an angular momentum. But as protons not only have mass but also charge, protons also possess a magnetic moment. This magnetic moment can be described as a vector. When no external magnetic field is applied, the vectors are oriented randomly. However, when these spins are placed in a strong external magnetic field (e.g., when a human body is moved into an MRI scanner) they align in two directions with corresponding energy "eigenstates" along the direction of the magnetic field. Always a few more spins align in parallel (their low energy state) than in antiparallel direction (their high energy state). The magnetic moments of the *surplus* parallel protons add up along the magnetic field. This is the so-called longitudinal magnetization state of the net magnetization vector and it is due to the tiny excess of protons in the lower energy state. But only magnetization perpendicular to the external field can be measured with MRI scanners. To bring the magnetic vector to point into another direction, MRI makes use of another property of the protons. In addition to their rotating movement about themselves, they precess when placed inside the powerful magnetic field of the scanner. This means their axis of spins performs a rotation of itself. Thus, we have in fact two rotations. The proton rotates around its axis of spin and at the same time this axis of spin performs a small precession movement

around the vector representing the external magnetic field. The precession frequency depends on the strength of the externally applied magnetic field. The higher the strength, the higher the precession frequency. This frequency is called the Larmor frequency.

When a corresponding RF (radio frequency, a so-called 90°) pulse is applied, two things happen. First, the protons absorb energy and the proton magnetization vector starts to turn in the direction of the high-energy state (i.e. the antiparallel direction). This reduces the longitudinal magnetization. Second, the precession of the protons is synchronized; the spins now precess in phase with each other. This turns the net polarization vector sideways into a transverse magnetization and the spins to precess perpendicular to the external field.

Once the RF pulse is turned off, relaxation happens. The longitudinal magnetization recovers as spins return to their low-energy state. The important one for the fMRI, however, is the decay of the transverse magnetization as a consequence of the dephasing of spins. The corresponding signal is oscillating at resonance frequency and is due to variations of the transverse magnetization vector and can be described as an exponential curve.

Of course, when measuring MRI, not only the signal per se, but also the localization of the signal is of huge importance. Spatial localization in MRI is accomplished by a controlled manipulation of the magnetic field. Based on the equivalence between strength of the magnetic field and precession frequency mentioned above a spatially variant magnetic field will lead to a spatially variant distribution of resonant frequencies. Accordingly, magnetic field manipulations are induced that get the spins to vary in their precession frequency depending on their spatial location. With such a gradient superimposed on the original external field, it is possible to select a slice for imaging by applying the proper excitation pulse (that means that only in this slice the spins are turned and thus only they can contribute to the signal). For localization in 2D, which is simply an MR image, two more gradients must be applied in a precise sequence. A method that is commonly used in functional MRI to encode the object data in two dimensions is called Echo Planar Imaging (EPI).

3.2 Physiological Basis of fMRI

What kind of physiological signal is measured with fMRI?

As mentioned above the signal used in fMRI is based on the dephasing of the spins and the subsequent decay of transverse magnetization. Crucially, how fast the spins dephase depends on the magnetic properties of the environment depending on the oxygenation level of the surrounding blood. Early research on the MRI signal demonstrated that deoxygenated hemoglobin (hemoglobin that does not carry oxygen) is paramagnetic while oxygenated hemoglobin (hemoglobin that carries oxygen) is diamagnetic. The presence of paramagnetic oxygen leads to faster spin dephasing causing a more rapid decay of the MR signal.

And where is the relation to brain function?

When neurons of a particular brain site become active, energy is required (e.g., for ion transportation and neurotransmitter metabolism), which is partly provided by arterial blood supply of oxygenated hemoglobin. The increase in oxygenation usually even exceeds the actual demand in the respective brain region. Thus, there is more oxyhemoglobin during an active state than during a non-active state, which causes a differential MR signal. This signal is used for functional MRI. The dynamic regulation of blood flow is called HR (hemodynamic response) or BOLD (blood-oxygenation-level-dependent) response.

The BOLD response to neural activity is delayed and relatively slow compared to actual brain activity. It consists of a short onset delay, a rise to a peak after about 6 seconds, a return to baseline after about 12 seconds, and a prolonged undershoot. Amplitude and latency of the HR depend on the strength of the evoking stimulus on the one hand but also on the region where it is measured.

4 Imaging Study 1

4.1 Introduction

In this experiment, we set out to investigate goal proximity signals in humans. To this end, we measured BOLD signals while participants performed a classical reward anticipation task (Knutson et al., 2001) under delayed vs. immediate reward schedules (Ichihara-Takeda & Funahashi, 2006). In the delayed condition, participants received a monetary reward only after successful completion of four consecutive trials, while they received a smaller reward (1/4) for each successful trial in the immediate condition. This allowed us to distinguish brain regions sensitive to increasing reward proximity from regions that solely code the progress through a schedule, independent of reward.

In a neurophysiological study with monkeys, the CMA was identified to code for goal proximity (Shidara & Richmond, 2002). Accordingly, we expected that in humans the homologous region, i.e., the RCZ in the pMFC (Picard & Strick, 2001), would also exhibit a signal sensitive to goal proximity.

A parallel line of research has associated the pMFC with cost-benefit decision making, specifically with representing the integrated value of an action outcome in terms of anticipated benefits and effort that one has to invest (e.g., Rudebeck et al., 2006; Croxson et al., 2009). We therefore also varied reward magnitude, enabling us to examine the interaction of reward magnitude and goal proximity, and to compare the anticipation of identical rewards resulting from high as compared to no previously invested effort.

4.2 Materials and Methods

4.2.1 Participants

18 participants took part in this experiment (9 male; mean age, 23.1 years). Informed consent was obtained according to a protocol approved by the local ethics committee. All subjects had normal or corrected to normal vision. None of the subjects had a history of neurological, major medical, or psychiatric disorders, and all were right-handed, as assessed

by the Edinburgh Inventory (Oldfield, 1971). One subject was excluded due to poor experimental performance. Subjects took part in two separate fMRI sessions. Subjects were informed that they would receive monetary reward related to their performance.

4.2.2 Experimental Procedure

In the present experiment, we integrated a slightly modified Monetary Incentive Delay (MID) Task (Knutson et al., 2001; Fig. 1a) into a multitrial reward schedule paradigm adapted from Ichihara-Takeda and Funahashi (2006; Fig. 1b). The MID task is a commonly used delayed response task that is frequently used to identify neural systems involved in reward anticipation. In our version, each MID trial begins with a cue (250 ms) instructing subjects to prepare for a response with either the index or the middle finger. Then subjects fixated on a cross-hair for a variable delay interval (2000-2500 ms). As soon as a white target square appeared (222 – 341 ms) subjects had to respond as quickly as possible with the appropriate button press. Feedback (1500 ms) followed the target and notified participants whether or not they had reacted quickly enough. Target durations were adjusted such that participants succeeded on approximately 80% of responses, based on reaction times obtained during a practice session. Subjects were not informed that the practice session conducted in the MRI scanner before the main experiment would serve for setting an individual response time criterion. All stimuli were presented at the center of the screen.

Each multitrial reward schedule consisted of four MID Trials. In the delayed contingency condition, subjects received a reward only after successful completion of four consecutive trials. In the immediate condition, subjects earned a reward after every correct trial. In addition, we manipulated the magnitude of reward. In the low reward condition, subjects could earn 5 euro-cents per correct trial in the immediate condition and 20 euro-cents for four correct trials in the delayed condition. In the high reward condition, subjects earned 20 euro-cents per correct trial in the immediate condition and 80 euro-cents for four correct trials in the delayed condition. This resulted in a 2 x 2 x 4 factorial design in which one factor is contingency (2 levels: delayed and immediate), the other reward magnitude (2 levels: low and high reward), and the third one is position in schedule (4 levels). Contingency and reward magnitude of the upcoming schedule were indexed by both an instruction screen (2 s) at the beginning (“delayed high”/ “delayed low”/ “immediate high”/ “immediate low”) and a

corresponding, colored rectangular frame that was on the screen throughout the sequence of four trials. The mapping of colors to conditions was balanced across participants. In addition, feedback was given after every single trial and this feedback additionally informed concerning the experimental condition and the current position within a schedule (e.g., 20/20 at any position in the immediate-high-reward condition or 20/80 at the 1st position in the delayed-high-reward condition). The succession of the different contingency schedules was randomized.

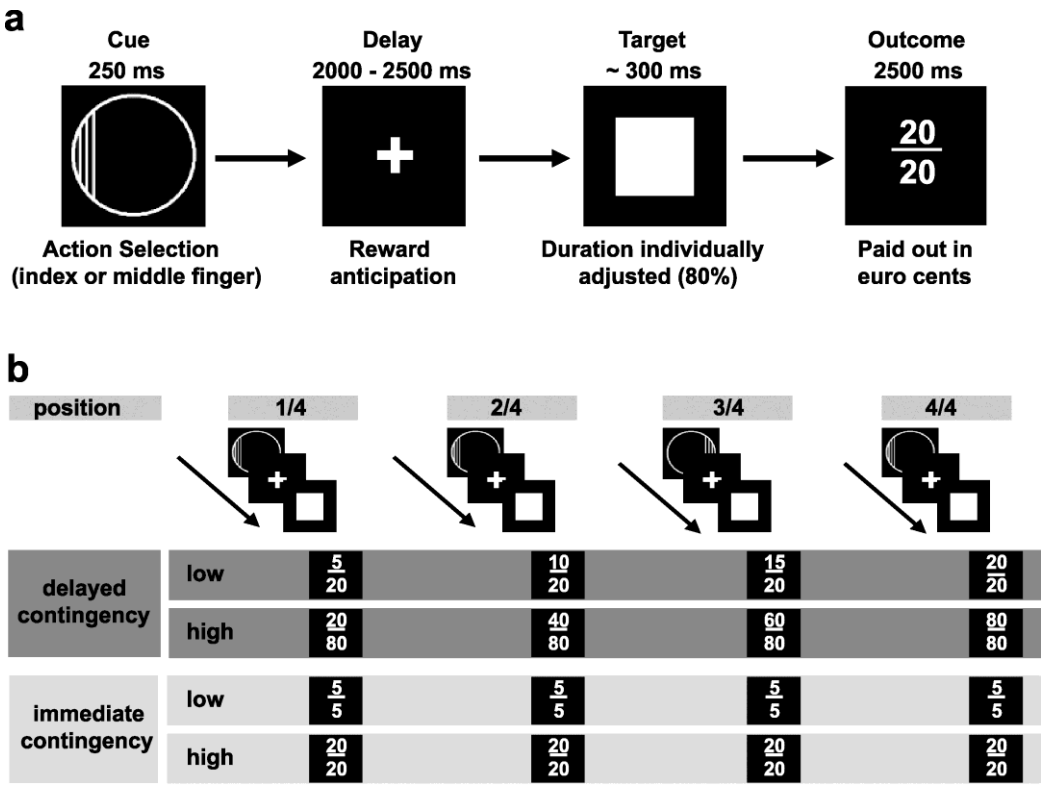

Figure 1. a, Sequence of stimulus events of the modified Monetary Incentive Delay (MID) task (Knutson et al, 2001). b, Multitrial reward schedules. Every schedule consisted of 4 MID trials. In the delayed contingency condition subjects received a reward only after the successful completion of 4 consecutive trials. In the immediate contingency condition subjects received a smaller monetary reward after every trial. In addition, we manipulated the magnitude of reward. Feedback was given after every single trial. This feedback additionally informed subjects concerning the experimental condition and the current position within a schedule.

Whenever participants made an error in any of the trials in the delayed contingency conditions, the schedule was aborted and no reward was given. Responding late, not

responding at all, and a wrong button press constituted an error. In the immediate condition, the trial sequence continued in case of an error. However, only completely correct schedules were included in the analyses. The main experiment consisted of 28 schedules for each contingency x reward magnitude combination (delayed low, delayed high, immediate low, immediate high), resulting in a total of 112 multitrial reward schedules. As each schedule consists of four MID trials there were also 28 trials of each trial type defined by contingency, reward magnitude, and position. Given that delayed multitrial schedules were aborted after incorrect responses, the actual number of trials within delayed schedules presented to the subjects varied dependent on the individual error rates (i.e., between 11 and 25). The mean number of trials within schedules that were included in the fMRI analyses varied across conditions (i.e., between 15.72 and 21.44) and is reported in the Results section.

The trial-to-trial interval (i.e., between trials, within schedule) varied between 3 and 7 s and was balanced across conditions. One block of four MID trials lasted between 38 and 42 s. After each schedule, a cross-hair was displayed for 14 s before the next schedule began. The experiment was acquired in two scanning sessions, each of which lasted about 60 minutes. Subjects were trained, without reward, for 15 minutes prior to scanning.

4.2.3 fMRI Procedure

Subjects were positioned head first and supine in the magnet bore. Images were collected with a 3T Trio MRI scanner system (Siemens Medical Systems, Erlangen, Germany). Prior to the functional runs of each session, a T1-weighted anatomical scan with the same spatial orientation and slice prescription as the functional data was acquired. Whole brain functional images were collected using a T2*-weighted echo-planar imaging sequence, sensitive to blood oxygen level dependent (BOLD) contrast (TR = 2000 ms, TE = 30 ms, image matrix = 64 x 64, FOV = 192 mm, flip angle = 80°, slice thickness = 3 mm, 1 mm interslice gap, in-plane resolution 3 mm x 3 mm, 32 oblique axial slices). A varying number of images were acquired per run due to varying numbers of abortions of the delayed contingency schedules. A T1-weighted, three-dimensional high-resolution magnetization-prepared (MP)-Rage scan was obtained after the functional scans.

4.2.4 fMRI Analysis

The fMRI data were analyzed with statistical parametric mapping, using the SPM5 software (Wellcome Department of Cognitive Neurology, London, UK). The first ten seconds of functional images were excluded from the analysis to minimize T1 relaxation artifacts. Separately for each session, a slice time correction was applied to correct for the temporal offset between the slices acquired in one scan. Then images were realigned using the first image of the first scan session as a reference and a mean image for all scan volumes was created. Thus, the realignment (which is based on a 2^{nd} degree B-Spline coregistration of each image to the reference image) effectively coregistered functional images from the two sessions. The high-resolution structural image was coregistered with the mean image of the EPI series and normalized to the Montreal Neurological Institute template. The normalization parameters were then applied to the EPI images to ensure an anatomically informed normalization. Voxels were resampled into a size of 2 x 2 x 2 mm and a spatial filter of 8 mm FWHM (full-width at half maximum) was applied. The time series data at each voxel were processed using a high-pass filter with a cut-off of 256 s to remove low-frequency drifts.

Subject-level statistical analyses were performed using the general linear model. The design matrix for event-related analysis was created using the canonical hemodynamic response function (HRF) as provided by SPM5, including the first derivative to account for variable delays. The main events of interest for the event-related analysis were the reward anticipation phases of each condition. We thus calculated a general linear model (GLM) for each subject that included separate predictors for the anticipation phase of each trial type. Thus, there were 16 different trial types that constituted the covariates of interest (defined by the combination of the two contingency levels, the two reward magnitude levels, and the four position levels).

To ascertain statistical independence of the results for the anticipation phase from activations related to the outcome phase of the task (that was not of interest in the present analysis), we modeled the outcome phases from correctly answered trials of all 16 trial types as a single predictor (which resulted in cross-correlation coefficients between anticipation and outcome phases ranging between 0.0684 and 0.2902). As covariates of no interest we further included the outcome phases from all incorrectly answered trial types, anticipation phases from incorrectly answered trials separately for immediate and delayed contingency, anticipation phases from incomplete schedules separately for immediate and delayed

contingency (i.e., trials from immediate contingency schedules in which at least one error occurred and trials from delayed contingency schedules that were later aborted due to an error), as well as one single predictor for outcome phases from incomplete schedules, and motion parameters derived from spatial realignment.

Subject-specific contrast images were constructed by linear combinations of the beta parameters resulting from the general linear model, and then entered into a random-effects model testing group effects by means of a one-sample *t*-test.

As the CMA in monkeys is the only region reported thus far containing single neurons that are progressively changing their activation strength contingent to increasing reward proximity, we confined our primary analyses of interest to the RCZ, the putative human homologue of monkeys' CMA (Picard & Strick, 2001). To capture the boundaries of the RCZ as precisely as possible, we generated an anatomical mask of the RCZ by performing an anatomical conjunction between (a) a standard mask comprising the cingulate gyrus and the anterior cingulate (as defined by the Talairach Daemon Labels Masks, Lancaster, Summerln Rainey, Freitas, & Fox, 1997; Lancaster et al., 2000; using the WFU Pick Atlas, Maldijan, Laurienti, Kraft, & Burdette, 2003) and (b) a self-generated anatomical box covering the previously published extension of RCZ in all three directions (i.e., from -20 to 20 in the x-direction, from 50 to -20 in the y-direction, and from 10 to 55 in the z-direction; Ridderinkhof et al., 2003, Fig. 1). The resulting anatomically derived mask is displayed in Figures presenting the results of respective ROI analyses (Figs. 3a, 5a, 6a).

To protect against false positive activations, we used a double-threshold approach that involves combining a voxel-based threshold with a minimum cluster size (Forman et al., 1995). This nonarbitrary cluster size was determined on the basis of a Monte Carlo simulation (1,000 iterations) determined with AFNI's AlphaSim tool (Ward, 2000; http://afni.nimh.nih.gov/afni). We determined the minimal cluster size for an individual voxel height threshold of $T > 3.65$ ($p < 0.001$, uncorrected) to ensure an overall image-wise false positive rate of 5%. This resulted in a cluster size threshold of 17 voxels for the anatomical mask of the RCZ. An additional Monte Carlo simulation (1,000 iterations) was conducted to determine cluster size thresholds for whole brain analyses. This yielded a cluster size of 91 voxels. Activations exceeding this threshold are considered to be activated at an experiment-wise threshold of $p < .05$, corrected for multiple comparisons.

The specific pattern of goal proximity signals (as defined by a contingency x position interaction) was examined by extracting mean parameter estimates from the beta images that were calculated during model estimation of the original general linear model, and by subjecting these to further analyses using standard statistics software. ROIs for these analyses were defined as peak voxels in three foci in the RCZ defined by previous analyses.

Furthermore, we assessed whether or not functional connectivities between brain regions were modulated by reward proximity. To this end, we conducted psychophysiological interaction analyses (PPI; Friston et al., 1997) with the posterior portion of the RCZ as individually determined seed region (cf. Results section). 14 participants were included in this analysis, as the remaining four subjects did not show significant univariate activation in or in the direct vicinity of the area of interest in the contrast delayed-4th position versus delayed-1st position (at thresholds as low as $p < 0.01$). For the PPI analysis, a novel GLM was set up that encompassed three regressors, i.e., the time series of individually determined peak voxels from the seed region as a physiological predictor (individual peak voxels ranging from 2 to 12 in the x-direction, from 0 to 12 in the y-direction, and from 42 to 50 in the z-direction; mean coordinates x = 7; y = 6; z = 43), the contingency (delayed vs. immediate) x position relative to the goal (i.e., close (4^{th} + 3^{rd}) vs. distant (2^{nd} + 1^{st})) interaction as psychological predictor, as well as the interaction of these two variables which served as the psychophysiological interaction term. The PPI analysis was thresholded at the whole brain level as described above.

4.3 Results

4.3.1 Behavioral Data

Subjects made relatively fewer errors under delayed contingency and under high reward magnitude (main effect of contingency: $F(1,17) = 13.1$, $p = 0.002$; main effect of reward magnitude: $F(1,17) = 26.84$, $p < 0.001$; cf. Fig. 2), but the two factors did not interact ($p = 0.467$). In addition, the percentage of errors did not vary over the different positions. In general, the performance in the experiment was slightly better compared to the practice session, which explains the error rates being below the intended 20 %. Delayed contingency and high reward expectation also reduced reaction times (delayed low 228 ms [SE 0.004]; delayed high 225 ms [SE 0.004]; immediate low 229 ms [SE 0.004]; immediate high 228 ms

[SE 0.004]; main effect of contingency: $F(1,17) = 4.13$, $p = 0.058$; main effect of reward magnitude : $F(1,17) = 10.1$, $p = 0.006$). Again the two factors did not interact ($p = 0.149$) and we did not find any significant effect over the positions.

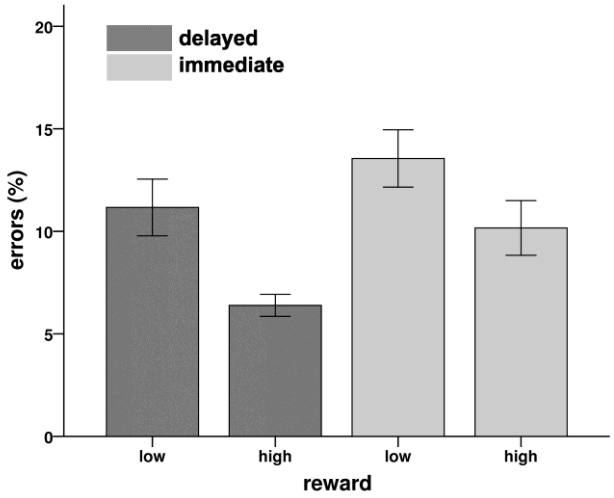

Figure 2. Behavioral performance is enhanced under delayed contingency and under high reward.

On average, participants performed without any error in 17.83 schedules (63.68% [SE 3.5]) in the delayed-low, in 21.44 schedules (76.57% [SE 2]) in the delayed-high, in 15.72 (56.14% [SE 3.4]) schedules in the immediate low, and in 18.28 schedules in the immediate high condition (65,29% [SE 3.7]; main effect of contingency: $F(1,17) = 26.7$, $p < 0.001$; main effect of reward magnitude: $F(1,17) = 22.2$, $p < 0.001$; interaction between contingency and reward magnitude: $F(1,17) = 0.74$, $p = 0.391$). Thus, performance was enhanced under delayed contingency and under high reward.

As single trial types (e.g., delay low, 3rd position) were only included in the analyses when the complete corresponding schedule (e.g., delayed low schedule) was performed without any error, the number of completely correct schedules corresponds to trial numbers (in the sense of numbers of trials per contingency, reward, and position) included in the analysis of reaction times and fMRI data.

4.3.2 fMRI Data

Neural Correlates of Goal Proximity: Contingency x Position Interaction

Our primary interest was the analysis of the interaction between contingency (delayed versus immediate) and position in schedule (4th position versus 1st position), collapsed across reward magnitudes, which should identify brain regions sensitive to increasing reward proximity during a sequence of actions. This analysis yielded activation foci in a posterior part of the RCZ (pRCZ; Fig. 3a; Table 1). The reverse contrast did not yield any significant activation. This result is consistent with previous reports of CMA activity in monkeys being related to the degree of reward expectancy (Shidara & Richmond, 2002). No other frontal region outside of the RCZ showed contingency x position interactions, when assessed in an explorative whole-brain analysis (but see Table 1 for areas outside of frontal cortex).

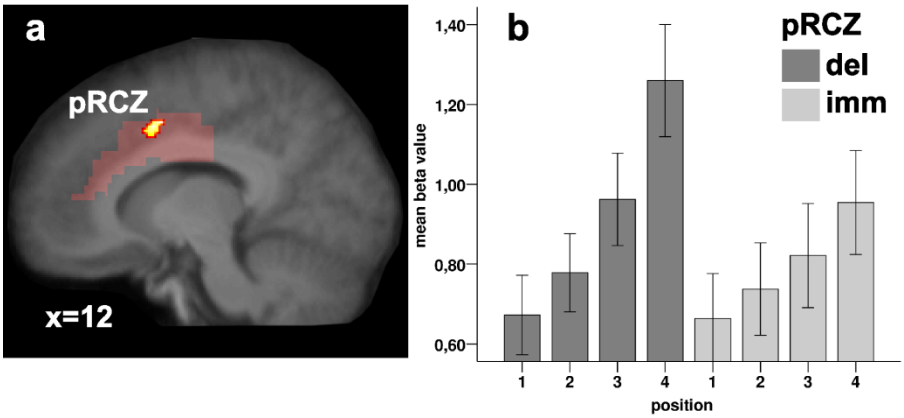

Figure 3. Group functional activation maps, overlaid on the average of the normalized structural images of the study participants. RCZ mask is visualized in transparent red, activations within the mask are thresholded at $p < 0.001$, $k > 17$ (cf. Methods and Materials). Parameter estimates are averaged across reward magnitude. a, Goal proximity effect in the posterior RCZ (pRCZ) identified using the contingency x position interaction contrast. b, Parameter estimates for pRCZ for each position and contingency condition. del, delayed; imm, immediate.

We next aimed at examining whether or not the pRCZ would indeed exhibit a stepwise increase or decrease of brain activity related to actual reward proximity as suggested by the non-human primate literature (while the interaction effects reported above could also result from different patterns of activation). To this end, we extracted mean parameter estimates for each subject, separately for each position and contingency condition, collapsed across reward magnitude. While this kind of analysis (i.e., testing the interaction in a cluster that was

identified in the whole brain analysis as showing an interaction) is potentially subject to non-independence error (Kriegeskorte, Simmons, Bellgowan, & Baker, 2009), we used it exclusively to resolve the whole-brain interaction effect, with the aim of better understanding the nature of the obtained interaction effect.

As expected, the ROI analysis replicated the significant modulation of position effects by contingency of the schedule (interaction effect position x contingency, $F(1,17) = 8.19$, $p < 0.001$). The pRCZ exhibited a steeper position-related increase of activity in the delayed contingency in comparison to the immediate contingency condition (Fig. 3b), which reflects the coding of the proximity to actual reward attainment in the delayed contingency condition. We also found significant main effects of position ($F(1,17) = 31.01$, $p < .001$), contingency ($F(1,17) = 8.10$, $p < 0.011$), and reward magnitude ($F(1,17) = 10.94$, $p = 0.004$). The remaining interaction effects were not significant (interaction effect contingency x reward $F(1,17) = 3.40$, $p = 0.081$; interaction effect position x reward $F(1,17) = 0.33$, $p = 0.803$; interaction effect contingency x position x reward $F(1,17) = 0.56$, $p = 0.644$).

Table 1. Proximity Effect: Activation for the interaction contrast contingency x position.

		Peak voxel (in mm)			
Brain region	**cluster size**	**x**	**y**	**z**	**voxel T**
[1]Posterior Rostral Cingulate Zone (pRCZ)	59	12	4	46	4.92
[2]Middle Temporal Gyrus	134	48	-24	-6	6.03
[2]Inferior Parietal Cortex	132	40	-32	24	5.84

[1] ROI analysis restricted to RCZ mask.

[2] Explorative whole brain analysis.

Functional Connectivity of the Rostral Cingulate Zone

If the pRCZ truly has a crucial role in governing goal-directed behavior during a series of action steps towards a predicted outcome, we furthermore hypothesized that the pRCZ should be more strongly coupled with regions related to motor functions when the individual is getting closer to the goal, i.e., during the last trials as compared to the first trials of a multitrial schedule. Importantly, this goal proximity effect on functional pRCZ connectivity should be more prominent under delayed than under immediate contingency. To explore the functional connectivity pattern of the pRCZ, we applied psychophysiological interaction analysis (PPI; Friston et al., 1997) to the interaction between contingency (delayed vs. immediate) and position. The physiological predictor was the time series from the peak voxel of the seed region, i.e., pRCZ. It was modulated by the interaction of contingency and position (psychological predictor), thus testing a 3-way psycho-physiological interaction. Significant PPI effects were observed in the premotor cortex, putamen, thalamus, and cerebellum (Fig. 4; Table 2).

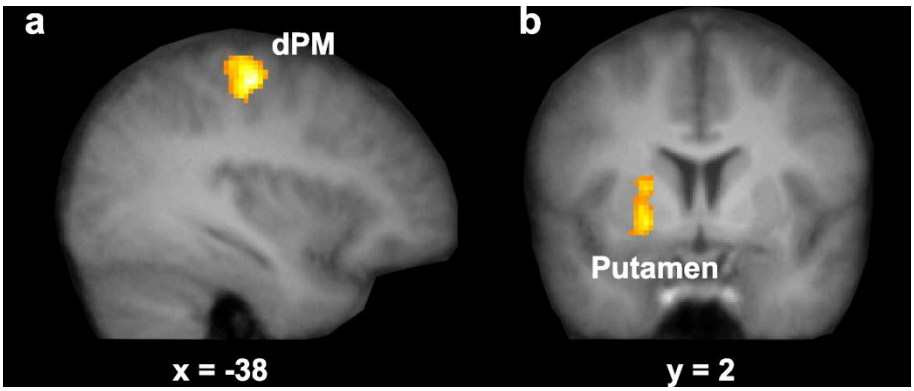

Figure 4. Goal proximity effect on functional pRCZ connectivity. While working towards a delayed reward, pRCZ (see Fig. 3a) exhibited an increased coupling with dorsal premotor cortex (a, dPM) and putamen (b). Images are thresholded at $p < 0.001$, $k > 91$.

Table 2. Areas showing a reward proximity effect (i.e., contingency x position interaction) in the psycho-physiological interaction analysis with pRCZ seed.

		Peak voxel (in mm)			
Brain region	**cluster size**	**x**	**y**	**z**	**voxel T**
Dorsal Premotor Cortex (dPM)	349	-38	-20	58	8.53
Basal ganglia (putamen)	262	-22	2	-2	6.16
Thalamus	291	-6	-12	2	6.17
Cerebellum	135	24	-46	-28	5.95

Effects of Reward Magnitude

In numerous studies RCZ was additionally found to code choice outcomes in terms of expected costs and reward magnitude (Rushworth & Behrens, 2008; Kennerley et al., 2009a; Kennerley & Wallis, 2009b). In the current study, we were also able to assess these variables. In the delayed contingency condition, monetary reward was only administered after the 4th position. Given that the size of the actually administered reward, after the 4th trial, differed between the delayed and the immediate conditions, we compared the effect of reward magnitude separately for the delayed and immediate contingency condition.

The contrast of differential reward magnitude after equal effort expenditure in the delayed contingency condition (i.e., delayed-high-4th position > delayed-low-4th position) identified a region in the anterior RCZ (aRCZ; Fig. 5a; Table 3). Whole-brain analyses additionally showed a reward magnitude effect (delayed contingency) in dopaminergic midbrain. No area showed significantly greater activation for high as compared to low reward under immediate contingency.

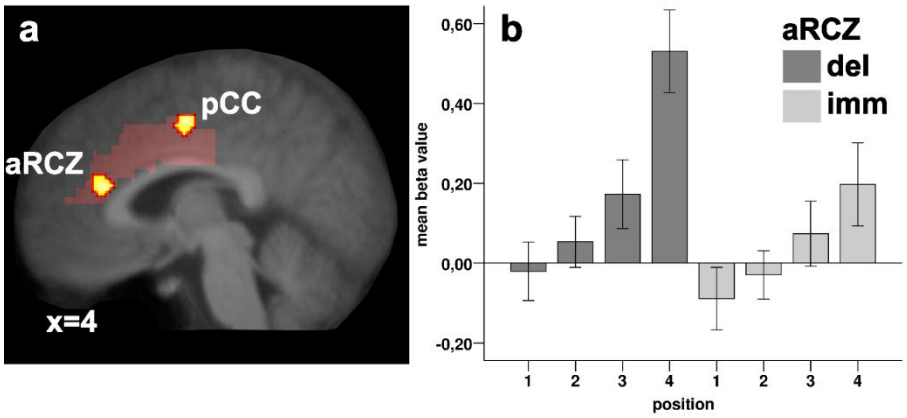

Figure 5. Group functional activation maps, overlaid on the average of the normalized structural images of the study participants. RCZ mask is visualized in transparent red, activations within the mask are thresholded at $p < 0.001$, $k > 17$ (cf. Methods and Materials). Parameter estimates are averaged across reward magnitude. a, Activations in the anterior RCZ (aRCZ) and posterior cingulate cortex (pCC) for the contrast of differential reward magnitude after equal effort expenditure. b, Parameter estimates for aRCZ for each position and contingency condition revealing that aRCZ shows a significant contingency x position interaction. del, delayed; imm, immediate.

Examination of parameter estimates in the aRCZ revealed a proximity effect comparable to pRCZ, i.e., significantly steeper activation increase during delayed as compared to immediate reward contingency (interaction effect contingency x position, $F(1,17) = 5.04$, $p = 0.04$; Fig 5c). The region further displayed significant main effects of contingency ($F(1,17) = 15.49$, $p = 0.001$) and position ($F(1,17) = 19.86$, $p < 0.001$), and a significant interaction effect of reward and contingency ($F(1,17) = 11.43$, $p = 0.004$). Importantly, reward magnitude per se did not modulate aRCZ activity (main effect reward magnitude ($F(1,17) = 2.03$, $p = 0.172$), thus indicating that this aRCZ subregion integrates information about reward magnitude and contingency.

Table 3. Reward Magnitude Effect: Activation for delayed high 4th position versus delayed low 4th position.

		Peak voxel (in mm)			
Brain region	**cluster size**	**x**	**y**	**z**	**voxel T**
[1]Anterior Rostral Cingulate Zone (aRCZ)	74	6	30	18	4.74
[1]Posterior Cingulate Cortex (pCC)	154	6	-6	46	4.94
[2]Posterior Cingulate Cortex (pCC)	152	14	-24	42	4.83
[2]Superior Temporal Gyrus	117	-48	8	4	4.90
[2]Superior Parietal Cortex	331	-20	-56	66	6.19
[2]Occipital Cortex	107	4	-82	18	5.49
[2]Substantia Nigra	189	8	-18	-10	5.49
[2]Cerebellum	1311	20	-50	-20	6.35
[2]Posterior Insula	173	-36	-10	-2	5.6
[2]Anterior Insula	533	30	8	-18	5.20

[1] ROI analysis restricted to RCZ mask.

[2] Explorative whole brain analysis.

Differential Effort for Equal Reward Magnitude

By defining the costs of an action as effort already invested, we additionally examined how brain activations were modulated by previously invested effort given the expectation of constant reward magnitude (i.e., delayed-low-4th position > immediate-high-4th position). In both of these conditions, subjects expected a reward of 20 euro-cents. The only difference between these two conditions lies in the effort participants had invested to gain the predicted

reward, prior to the current trial. More specifically, under delayed contingency, participants had successfully completed the three preceding trials of the multi-trial schedule, while the three preceding trials were of no relevance for the current outcome in the immediate condition. Accordingly, an additional cost variable inherent to this comparison was the risk of potential loss of previously invested effort in case of an error. The analysis yielded a significant effect of previously invested effort in the anterior portion of the RCZ (Fig. 6a; x=-14, y=34, z=22; T = 5.20; k = 71). No brain regions outside cingulate cortex showed an effort related modulation.

An ROI analysis of the aRCZ yielded a modulation of position effects by contingency of the schedule (interaction effect position x contingency, $F(1,17) = 4.44$, $p = 0.008$; Fig. 6c). Further significant effects were found for contingency ($F(1,17) = 8.75$, $p = 0.009$) and position ($F(1,17) = 22.68$, $p < 0.001$; all effects concerning reward magnitude $F > 2.07$; $p > 0.167$).

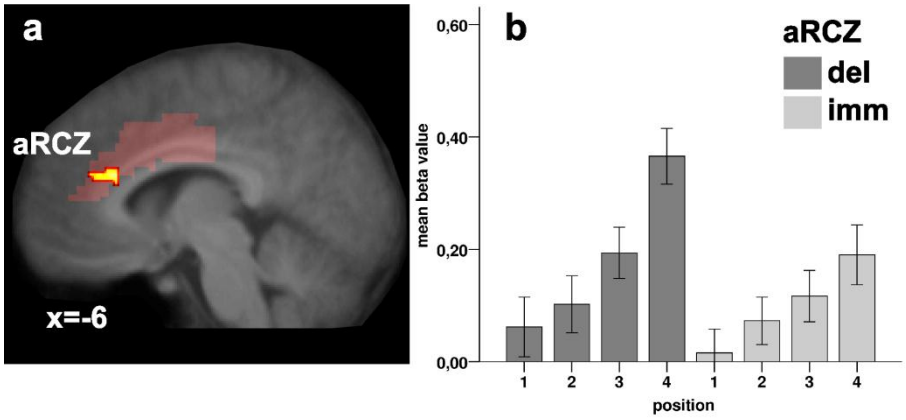

Figure 6. Group functional activation maps, overlaid on the average of the normalized structural images of the study participants. RCZ mask is visualized in transparent red, activations within the mask are thresholded at $p < 0.001$, $k > 17$ (cf. Methods and Materials). Parameter estimates are averaged across reward magnitude. a, The contrast of differential effort for equal reward magnitude yielded another activation focus in the aRCZ. b, This region also shows a significant contingency x position interaction. del, delayed; imm, immediate.

4.4 Discussion

The present study shows that the medial prefrontal area RCZ codes the proximity to an expected reward. Functional connectivity analyses demonstrate that the reward proximity

signal in RCZ covaries with activity in motor-related regions. Thus, RCZ seems to be involved in governing behavior directed towards a delayed reward over several action steps. Furthermore, two separable anterior RCZ regions represent the anticipated reward magnitude and the effort that was previously invested to reach a given reward. Of note, they also show a proximity modulated activity pattern over action steps toward the predicted outcome. In the following, we will discuss the contribution of the RCZ to the performance of action sequences directed towards attaining a delayed goal together with the region's potential role of a continuous updating of action values over a course of actions.

4.4.1 The Role of the Rostral Cingulate Zone for the Integration of Reward Information over Several Actions

Several monkey neurophysiology studies revealed that the CMA is implicated in behavior directed toward distant rewards (Procyk & Joseph, 2001; Shidara & Richmond, 2002; Amiez, Joseph, & Procyk, 2005; Hoshi, Sawamura, & Tanji, 2005). Previous human neuroimaging research has also demonstrated that RCZ integrates information across multiple actions, e.g., the number of preceding negative feedback trials (Jocham et al., 2009a; Jocham, Neumann, Klein, Danielmeier, & Ullsperger, 2009b). Most direct evidence comes from the demonstration that after an ACC lesion, only the outcome of the most recent trial exerts any influence over subsequent decisions (Kennerley et al., 2006). Our results are in line with these findings, as the multitrial sequences of the present experiment require that the participants encode successive elements of sequential behavior and integrate information over several action steps. The general activation increase of RCZ across positions, that is visible in our data independent of contingency, confirms its role in this regard. It is also in line with reports about the general mediation of serial order behavior in this region (Procyk, Tanaka, & Joseph, 2000), as well as throughout the frontal cortex (Berdyyeva & Olson, 2010). The additional modulation of the position related increase in neuronal activity by reward contingency, however, is the critical result of our study and provides the ultimate evidence that the RCZ has the additional crucial role of mediating behavior directed towards delayed goals also in humans.

4.4.2 Goal Proximity versus Representation of the Subjective Goal Value

More generally, the pMFC was suggested to represent an integrated signal necessary for determining the overall value of actions or decision outcomes (Rushworth & Behrens, 2008). Importantly, the representation of single decision components that alter the value of a trial seems to be more typical for pMFC than for other prefrontal brain regions such as orbitofrontal or lateral prefrontal cortex (Kennerley et al., 2009a). For instance, pMFC activity was found to code for decision costs in terms of the amount of work that is necessary to earn an expected payoff, but also for the perceived likelihood and the magnitude of a successful outcome (Croxson et al., 2009; Kennerley & Wallis, 2009b; Knutson, Taylor, Kaufman, Peterson, & Glover, 2005). In the present study, we support this model of multiple value representations in pMFC, and show that distinct RCZ subregions are modulated by the costs that result from already invested effort, and by reward magnitude, respectively. Of note, aRCZ subregions modulated by previous effort and magnitude also showed a goal proximity related activation profile. In sum, our data indicate that in humans as in non-human primates, the RCZ is critical for accumulating distinct aspects of reward information over multiple action steps.

As of now, it is still an open question which specific type of information is accumulated by the pMFC contingent to reward proximity. In monkey neurophysiology, goal proximity modulations of neural activity (Bowman et al., 1996; Shidara & Richmond, 2002; Ichihara-Takeda & Funahashi, 2006) are interpreted as directly reflecting of the amount of work that is needed until reception of reward. Our results, particularly for the posterior RCZ, are consistent with this interpretation.

However, in the present experiment, the likelihood of actual goal attainment – combined with the risk of the potential loss of already invested effort – changed with each action step. As outlined above, pMFC codes probability estimates and reward sizes of expected outcomes (e.g., Kennerley et al., 2009a). These representations are thought to contribute to a computation of expected value (EV), i.e., an integration of reward magnitude and probability of an anticipated reward. The goal proximity contingent activation profile of RCZ subregions, rather than reflecting a representation of proximity as such, could therefore reflect a continuous updating of the net value of the upcoming action outcome. In line with this, EV-computing regions in the pMFC show increasing activity during the anticipation of large-magnitude, high-probability gains (Knutson et al., 2005). Further evidence that pMFC could

track action values during sequential actions comes from reports of a gradual increase of activation in this region that coincides with effort expenditure (Croxson et al., 2009).

Within this conceptual framework, reward proximity signals could also be interpreted as an additional factor modulating expected reward value. A more radical interpretation of the present data, which would be fully compatible with the assumption of ACC as an integrator of multiple cost and benefit components of decisions (Rushworth & Behrens, 2008), would suggest that goal proximity as such is not represented in the brain, but a result of cost benefit computations involving expected as well as already invested effort, both of which modulate the value of a distant reward. Future work will be needed to explore the relationship between goal proximity signals and cost-benefit calculations in pMFC.

In contrast to a devaluation when anticipating costs, as often shown in discounting paradigms (e.g., Kable & Glimcher, 2007; Croxson et al., 2009), already invested effort seems to enhance the subjective value of the expected outcome. This bears obvious analogies to cognitive dissonance theory in psychology (Festinger, 1957), according to which humans attempt to justify additional effort for an equal reward by assigning greater value to outcomes following greater effort (Aronson & Mills, 1959).

We conclude that the RCZ represents the expected value (reward magnitude x probability of loss of invested effort) of a reward integrated with proximity to the anticipated action goal. Given the specific activation pattern observed, we speculate that anterior and posterior portions of RCZ both contribute to this function, however possibly with a relative emphasis on reward proximity (pRCZ) versus reward magnitude and effort representation (aRCZ), respectively. Based on our functional connectivity results, we can in addition conclude that RCZ modulates behavior, contingent to reward proximity, by relaying reward-related information onto regions involved in action generation.

4.4.3 A Network for Assuring Goal Achievement

We assume that the sequentially modulated response pattern of RCZ areas identified here is functionally relevant for assuring persistence in goal pursuit when working through series of routine actions towards distant goals (Pears, Parkinson, Hopewell, Everitt, & Roberts, 2003). The pMFC is anatomically and functionally ideally suited to fulfill this general role in

goal achievement (Shima & Tanji, 1998; Ito, Stuphorn, Brown, & Schall, 2003; Matsumoto, Suzuki, & Tanaka, 2003; Matsumoto, Matsumoto, Abe, & Tanaka, 2007; Gehring & Taylor, 2004), as it has extensive connections with brain areas involved in the control of cognitive and motor processes and with areas that process reward information (Van Hoesen, Morecraft, & Vogt, 1993; Paus, 2001; Morecraft et al., 2007). More specifically, the extensive connections of the cingulate motor areas include the dorsolateral prefrontal cortex (Bates & Goldman-Rakic, 1993; Lu, Preston, Strick, 1994) and the brainstem monoamine nuclei (Paus, 2001), as well as lateral premotor cortex (Barbas & Pandya, 1987; Luppino, Govoni, Matelli, 1998; Beckmann, Johansen-Berg, & Rushworth, 2009) and the anterior striatum (incl. putamen; Takada et al., 2001; Haber, Kim, Mailly, & Calzavara, 2006). Our analysis of functional connectivities has shown that the coupling with the latter two regions was increased (a) under delayed contingency and (b) when getting closer to the goal.

The striatum is an important part of the circuitry mediating influences of reward expectation on performance. It was suggested that the ventral striatum supports keeping track of the progress through learned behavioral sequences (Bowman & Brown, 1998; Shidara et al., 1998). While our connectivity analysis yielded a coupling between pRCZ and putamen, not ventral striatum, we speculate that the reward proximity modulation of RCZ-putamen coupling likely mediates the motor control of reward seeking behavior, as previous work showed that the neuronal response in the putamen to financial reward is additionally enhanced when a movement is required (Elliott, Newman, Longe, & Deakin, 2004). The functional connectivity of RCZ with premotor cortex putatively reflects the increasing degree of motivation contingent to actual reward delivery (Roesch & Olson, 2004), which further renders this circuit optimally suitable for action readiness through facilitating action preparation.

5 Imaging Study 2

5.1 Introduction

The first imaging study provided evidence that the decision variable of increasing reward proximity might gradually enhance the valuation of expected outcomes. Furthermore, the study indicated that the widely acknowledged role of RCZ in action valuation (Rushworth & Behrens, 2008) also encompasses the representation of already invested effort intrinsic to the actions. The second imaging study was designed to investigate neuronal and behavioral effects of previously invested effort in more detail. This was motivated by the fact that, to our knowledge, the effect of previously invested effort on the valuation of future outcomes has not been investigated systematically in the field of cognitive neuroscience thus far. However, previous effort investment has been shown to influence error rates in monkeys performing in multitrial reward schedules (La Camera & Richmond, 2008). Also in other research fields, previous workload is investigated with respect to the upvaluation of expected outcomes (Arkes & Ayton, 1999; Navarro & Fantino, 2005).

To investigate the neuronal signals related to previous effort expenditure, we again measured BOLD activity while participants performed an MID task (for a detailed description see section 4.2.2) under delayed vs. immediate contingency. Critically, in this experiment we varied the number of action steps (i.e., the workload) that participants had to perform in order to obtain reward. In the delayed condition, participants received a monetary reward after successful completion of one, two, or three consecutive trials, while they received a reward of equal magnitude for each successful trial in the immediate condition.

Due to these variable schedule lengths, the action course towards the reward was less-routine bound in comparison to the first study, which resulted in a higher cognitive control demand. It has been argued in numerous studies investigating the interaction between cognitive control and reward size that higher levels of motivation might act to increase cognitive control in order to sustain attention and prevent interference, thus maximizing reward (Small et al., 2005; Adcock, Thangavel, Whitfield-Gabrieli, Knutson, & Gabrieli, 2006; Krawczyk, Gazzaley, & D'Esposito, 2007; Locke & Braver, 2008). As effort investment obviously also results in an increase in subjective value (Arkes & Ayton, 1999),

we hypothesized cognitive control regions to be modulated through previous effort investment when engaging in a series of non-routine actions towards reward. Furthermore, such an involvement could also be seen in analogy to a patient δ-decision making system comprising higher cognitive control regions that mediates the choices in favor of rewards that are more valuable, but not immediately attainable (McClure et al., 2004, 2007).

Another interesting question in this respect is whether or not previously invested effort can modulate functional coupling between pMFC and LPFC. In our first study, we showed that RCZ represents the expected value of a reward integrated with the previously invested effort to obtain that reward. In an elegant study, Kouneiher and colleagues (2009) could show that the RCZ regulates the allocation of cognitive control resources by mid-LPFC according to potential rewards and penalties at stake. Given the assumption that, in the present study, the variability of schedule lengths leads to an increase in overall cognitive control demands, we hypothesized that an enhanced connectivity between RCZ and mid-LPFC can also be found depending on previously invested effort acting as a motivational incentive. Furthermore, the variable schedule lengths allowed us to investigate whether or not brain regions exist that change their activity contingent to the previous workload.

Another difference to the first experiment is the block-wise presentation of delayed versus immediate contingency schedules. This is due to the fact that several researchers have shown that people value choice alternatives in relative terms, for example with respect to the price range of available options serving as a contextual frame for relative outcome evaluation (Padoa-Schioppa, 2009). Importantly, this relative value coding seems only to be determinable between, and not within, blocks (Tremblay & Schultz, 1999; Seymour & McClure, 2008). In delayed blocks, the risk of sinking cost, i.e., the contextual frame based on higher effort expenditure that should set the reference point for outcome evaluation, is substantially higher than in immediate blocks. Accordingly, the blockwise presentation of schedules that consisted of only one action allowed us to investigate which brain regions are concerned with maintaining this context representation in absence of other valuation-related processes. Recent evidence indicates that the posterior LPFC (Watanabe & Sakagami, 2007) and the OFC (Padoa-Schioppa, 2009) are involved in coding the value dependent of the cognitive and motivational context of the current environment. However, it is an open question whether or not they are also underlying the representation of the contextual frame itself that is based on previous workload.

5.2 Material and Methods

5.2.1 Participants

18 participants took part in this experiment (7 male; mean age, 20.2 years). Informed consent was obtained according to a protocol approved by the local ethics committee. All subjects had normal or corrected to normal vision. None of the subjects had a history of neurological, major medical, or psychiatric disorders, and all were right-handed, as assessed by the Edinburgh Inventory (Oldfield, 1971). Subjects took part in two separate fMRI sessions. Subjects were informed that they would receive monetary reward related to their performance.

5.2.2 Experimental Procedure

We again integrated the slightly modified Monetary Incentive Delay (MID) Task (Knutson et al., 2001; see section 4.2.2; Fig. 1a) into a multi-trial reward schedule paradigm. An individual response time criterion was set on the basis of each participant's response times to ensure that participants would succeed on ~80 % of the trials. In the present experiment, we adapted the multi-trial reward schedule paradigm from Shidara and Richmond (2002; Fig. 7).

The length of schedules varied from one to three consecutive MID Trials. Reward schedules were again embedded in a delayed or an immediate contingency condition. In the delayed contingency condition, subjects received a monetary reward of 18 euro-cents only after successful completion of all consecutive trials within one schedule. In the immediate condition, subjects earned a reward of 18 euro-cents after every correct trial. This resulted in a design with three factors, i.e., contingency (2 levels: delayed and immediate), schedule length (3 levels: 1, 2, or 3 MID trials), and position within schedule (number of positions depending on schedule length).

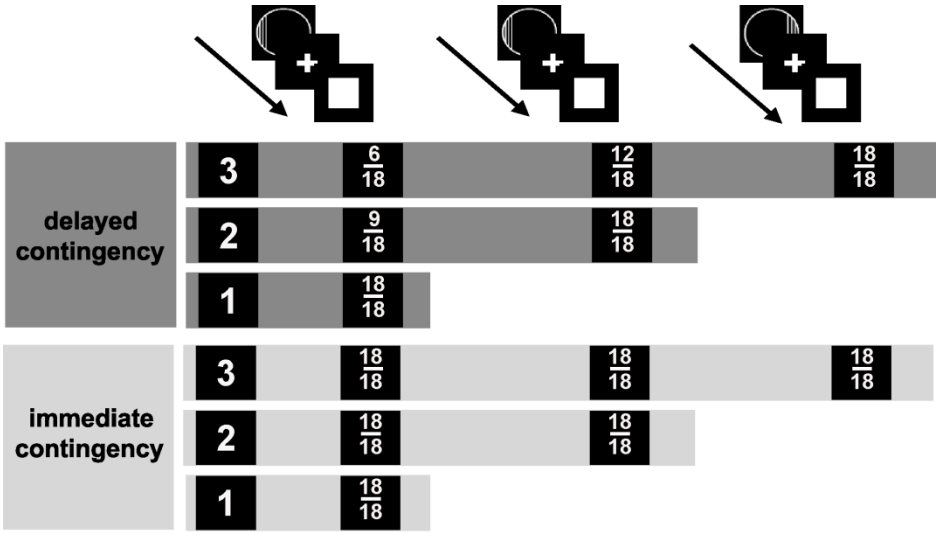

Figure 7. Multitrial reward schedules. Schedules consisted of 1 to 3 MID trials. In the delayed contingency condition, subjects received a reward of 18 euro-cents only after the successful completion of the whole schedule. In the immediate contingency condition, subjects received a reward of 18 euro-cents after every trial. An instruction screen at the beginning of each schedule notified participants about the number of MID trials in the current schedule. Feedback was given after every single trial. Delayed and immediate contingency were presented block-wise.

Contingency was indexed by both an instruction screen (2 s; "delayed" / "immediate") at the beginning of each contingency block and a corresponding, colored rectangular frame. Prior to the beginning of each reward schedule a second instruction screen (2 s) informed participants about the number of MID trials of the current schedule ("1" / "2" / "3"). The colored rectangular frame corresponding to the current contingency condition was on the screen throughout the sequence of MID trials. The mapping of colors to conditions was balanced across participants. In addition, feedback was given after every single trial, and this feedback screen additionally informed concerning the contingency condition and the current position within a schedule (e.g., 18/18 at any position in the immediate condition, or 6/18 at the 1st position in the delayed 3-action-schedule, or 9/18 at the 1st position in the delayed 2-action-schedule). Delayed and immediate contingency blocks were presented alternately with a duration of approximately four minutes each, comprising between 9 and 17 reward schedules per block. The number of reward schedules per block varied according to the relative distribution of reward schedules with longer and shorter schedule lengths. The

number of MID trials within one reward schedule (schedule length) was randomized within the contingency blocks.

Whenever participants made an error in any of the trials in the delayed contingency conditions, the schedule was aborted and no reward was given. Participants were informed that no substitutional reward schedules would be presented for aborted schedules, to prevent them from intentionally skipping schedules of three actions (as they were less profitable in comparison to 2-action-schedules and 1-action-schedules). Without the participants' knowledge, however, after an error additional reward schedules were added to the end of a contingency block until the block length of approximately four minutes was completed, with the aim of assuring sufficient trial numbers. Responding late, not responding at all, and a wrong button press constituted an error. In the immediate condition, the trial sequence continued in case of an error. Only completely correct schedules were included into the fMRI analyses.

Averaged across participants the experiment consisted of 50.20 schedules in the delayed contingency conditions (i.e., averaged over delayed schedules with a length of 1, 2, or 3 actions) and 43.95 schedules in the immediate contingency condition (i.e., averaged over immediate schedules with a length of 1, 2, or 3 actions). Given that delayed multitrial schedules were aborted after incorrect responses and that only completely correct schedules were included, the actual number in the fMRI analyses varied between 20.89 and 38.39 per single condition, i.e., per contingency, schedule length and position in schedule (e.g., delayed, schedule length of 3 actions, 2^{nd} position; cf. Results section).

Between contingency blocks a white crosshair was displayed for 12 s. The trial-to-trial intervals within contingency blocks varied between 3 and 7 s and were randomized across conditions. After each schedule, a small cross-hair was displayed before the next schedule began. The experiment was acquired in two scanning sessions, each of which lasted about 60 minutes. Subjects were trained, without reward, for 15 minutes prior to scanning.

5.2.3 fMRI Procedure

The experiment was carried out on a 3T scanner (Siemens Medical Systems, Erlangen, Germany). Subjects were positioned head first and supine in the magnet bore. First, 176 high-

resolution anatomical images were acquired using a T1-weighted 3D MPRAGE sequence (TR = 2530 ms, TE = 2.58 ms, image matrix = 256 x 256, FOV = 220 mm, flip angle = 7°, slice thickness = 0.90 mm, voxel size = 0.9 x 0.86 x 0.86 mm (resized to 1 x 1 x 1 mm)). Whole brain functional images were collected using a T2*-weighted echo-planar imaging sequence, sensitive to blood oxygen level dependent (BOLD) contrast (TR = 2000 ms, TE = 35 ms, image matrix = 64 x 64, FOV = 224 mm, flip angle = 80°, slice thickness = 3 mm, voxel size 3.5 x 3.5 . 3 mm, 30 axial slices). On average, 410 images were acquired per run.

5.2.4 fMRI Analysis

Preprocessing, subject-level statistical analyses, and the calculation of subject-specific contrast images of fMRI data were performed analogous to Experiment 1. The main events of interest for the event-related analysis were again the reward anticipation phases of each condition. We calculated a general linear model (GLM) for each subject that included separate predictors for the anticipation phase of each trial type, as defined by contingency and position in the respective schedule consisting of one, two, or three trials. The outcome phases of all trial types were again modeled as a single predictor. In this experiment the cross-correlation coefficients between anticipation and outcome phases ranged between 0.0897 and 0.2643.

Resulting group SPMs were thresholded at $t > 3.65$ ($p < 0.001$, uncorrected). To protect against false positive activations, we used the double-threshold approach combining the voxel-based threshold with a minimum cluster size (Forman et al., 1995). This nonarbitrary cluster size was again determined on the basis of a Monte Carlo simulation (1,000 iterations) using AFNI's AlphaSim tool (Ward, 2000; http://afni.nimh.nih.gov/afni). This yielded a cluster size of 91 voxels. Activations exceeding this threshold are considered to be activated at an experiment-wise threshold of $p < .05$, corrected for multiple comparisons. Results are again displayed on an average image of the study participants' brain.

To identify effects of previously invested effort on both behavioral performance and neuronal activity, we compared the last actions of 2-action schedules and 3-action schedules with respect to delayed and immediate contingency conditions. In this comparison, the anticipated reward size (i.e., 18 euro-cents) and the position in schedule are held constant, with the only difference being the amount of previously invested effort. To check for the

influence of the motivational context on error rates and brain activity, we compared the 1-action schedules between the differential contingency conditions. Importantly, these trials are completely identical with the exception of the experimental context in which they are presented, i.e., an immediate reward vs. a delayed reward context, in which the risk of sinking costs, i.e., loosing previously invested effort, is substantially higher.

Furthermore, we assessed whether or not functional connectivities between brain regions were modulated by previously invested effort. To this end, we conducted psychophysiological interaction analyses (Friston et al., 1997) with mid-LPFC as a seed region (cf. Results section). The seed region was the same for all participants and was defined with the contrast delayed versus immediate contingency, averaged across positions and schedule lengths, with a threshold of $p = 0.99$. For the PPI analysis, a novel GLM was set up that encompassed three regressors, i.e., the time series from the seed region as a physiological predictor, the previously invested effort (delayed versus immediate last actions of multitrial reward schedules) as psychological predictor, as well as the interaction of these two variables which served as the psychophysiological interaction term. The second-level random effects analysis of the psychophysiological interaction term was thresholded at the whole brain level as described above.

As we had strong hypotheses concerning a contribution of the RCZ to effort-related coupling with our seed region we additionally looked specifically for effects in this area. To this end, we used the same anatomical mask of the RCZ as in our previous study. The minimal cluster size to ensure an overall image-wise false positive rate of 5% for an individual voxel height threshold of $T > 3.65$ ($p < 0.001$, uncorrected) was any activation exceeding a size of 17 voxels.

5.3 Results

5.3.1 Behavioral Data

On average, participants performed without any error in 25.94 (51.69% [SE 3.6]) delayed-3-action-schedules, in 31.44 (62.66% [SE 3.6]) delayed-2-action schedules and in 38.39 (78.90% [SE 2.2]) trials of the delayed-1-action-schedules. In the immediate contingency condition schedules were performed without errors in 20.89 (46.85% [SE 3.3]) 3-action-

schedules, in 27.50 (62.18% [SE 3.5]) 2-action-schedules, and 34.06 (78.00% [SE 2.5]) 1-action schedules. As single trial types (e.g., delayed, schedule length of three trials, 3rd position) were only included in the analyses when the complete corresponding schedule (e.g., delayed 3-action-schedule) was performed without any error, the number of correctly completed schedules corresponds to trial numbers (in the sense of numbers of trials per contingency, schedule length, and position) included in the analysis of reaction times and fMRI data. The analysis of percentage of fully completed multitrial reward schedules revealed an inherent main effect of schedule length ($F(1,17) = 113.7$, $p < 0.001$). Furthermore, subjects tended to perform better in delayed as compared to immediate schedules (main effect of contingency ($F(1,17) = 3.7$, $p = 0.072$), but the two factors did not interact (interaction effect between schedule length and contingency ($F(1,17) = 1.2$, $p = 0.309$).

Our main focus of interest was the comparison of percentage of errors between the final trials of multi-trial reward schedules (i.e., 2nd trial in 2-actions-schedules and 3rd trial in 3-actions schedules) with respect to the different contingency conditions (delayed vs. immediate contingency). Under both delayed and immediate contingency subjects expected a reward of 18 euro-cents after completion of the last action with the only difference being the previously invested effort to obtain this reward. Analysis of variance revealed that error rates differed with respect to the factor contingency ($F(1,17) = 14.2$, $p = 0.002$; cf. Fig. 8), but were neither modulated by schedule length in isolation ($F(1,17) = 0.1$, $p = 0.723$) nor by the interaction between contingency and schedule length ($F(1,17) = 3.1$, $p = 0.098$). This indicates that the previous invested effort in general leads to a performance enhancement, while the manipulation of the amount of effort expenditure (2 vs. 3 action steps towards the goal) did not affect performance significantly.

When averaging across the single positions in the schedules, we found that subjects made relatively fewer errors under delayed as compared to immediate reward contingency (main effect of contingency: $F(1,17) = 6.4$, $p = 0.022$), even though the net reward that could be gained under delayed contingency was smaller. Error rates were not significantly influenced by schedule length ($F(1,17) = 0.1$, $p = 0.901$) and the two factors did not interact ($F(1,17) = 1.0$, $p = 0.387$).

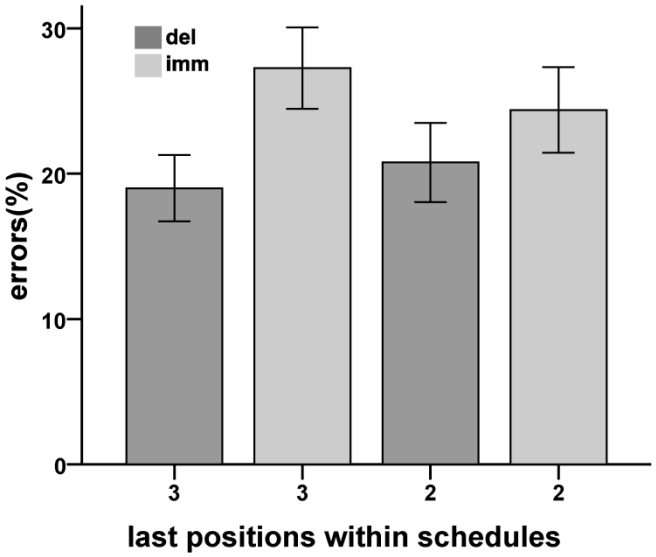

Figure 8. Error rates (%) in the last actions of 3-action schedules and 2-action schedules. Performance is enhanced under delayed contingency, i.e., after higher effort expenditure, but independent of the amount of previously invested effort. del, delayed; imm, immediate.

The only significant reaction time effect was reached in the main effect of position in the 2-action-schedule ($F(1,17) = 22.3$, $p < 0.001$). All other reaction time analysis yielded a $p > 0.1$, which is probably due to the reduced variance in reaction times due to the individually set response time criterion.

We conclude that performance was in general enhanced after previously invested effort. At the same time error rates were not modulated by the amount of effort invested (i.e., schedule length). In addition, we found a decrease in error rates under delayed as compared to immediate contingency, while the experimental context itself (i.e., the comparison between the delayed 1-action schedule and the immediate 1-action schedules) did not seem to influence behavioral performance.

5.3.2 fMRI Data

Neuronal Correlates of Differential Effort for Equal Reward Magnitude

Our primary interest lies in the effect of previously invested effort on the valuation of an outcome given the expectation of equal reward magnitude. To this end, we contrasted the

delayed and immediate multi-trial reward schedules only with respect to the anticipation phases of their final trials. On the basis of the behavioral results (cf. Behavioral Data), we collapsed our analysis across the amount of effort expenditure (i.e., 2nd trials in 2-actions-schedules and 3rd trials in 3-actions schedules for both immediate and delayed contingency condition). In these conditions, subjects invariably expected a reward of 18 euro-cents. The only difference between delayed and immediate conditions lies in the effort participants had invested to gain the predicted reward, prior to the current trial. More specifically, under delayed contingency, participants had successfully completed the one (or two) preceding trials of the multitrial schedule, while the one (two) preceding trials were of no relevance for the current outcome in the immediate condition. An additional variable inherent to this comparison was the risk of potential loss of previously invested effort in case of an error.

The analysis identified several activation cluster associated with general cognitive processing (Wager et al., 2004; Owen et al., 2005) including several regions in the lateral prefrontal cortex (Brodmann area 9 (BA9), BA44, BA45, and BA10) and posterior medial frontal cortex (comprising wide parts of the rostral cingulate zone [RCZ], and pre-supplementary [pre-SMA] and supplementary motor areas [SMA]; Fig. 9; Table 4). Additionally we found activation in bilateral posterior parietal cortex, anterior Insula, and the head of the caudate nucleus.

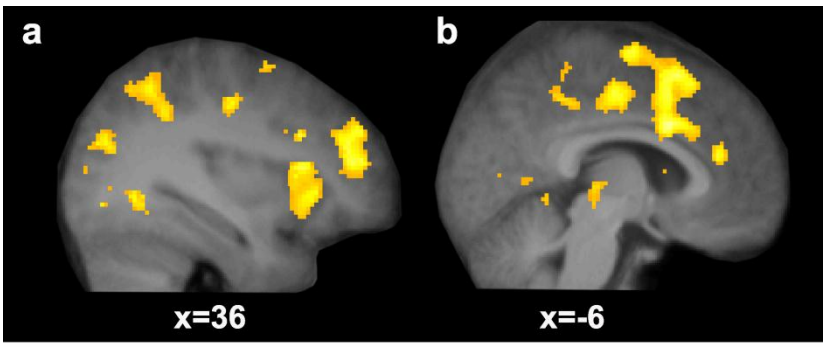

Figure 9. Group functional activation maps, overlaid on the average of the normalized structural images of the study participants. The contrast of differential effort expenditure for equal reward magnitude revealed a widespread network of activation clusters in the (a) lateral prefrontal cortex, posterior parietal cortex, anterior insula, and in the (b) rostral cingulate zone, supplementary, and pre-supplementary motor areas. Images are thresholded at $p < .001$, $k > 91$.

Table 4. MNI coordinates and anatomical locations of the peak activations for the contrast of differential effort expenditure to obtain a reward of equal magnitude.

		Peak voxel (in mm)			
Brain region	**cluster size**	**x**	**y**	**z**	**voxel T**
Mid-Lateral Prefrontal Cortex (mid-LPFC) (BA 9/10)	447	34	46	16	5.63
[1] Precentral Gyrus	2269	50	-8	50	6.41
[1] Posterior Lateral Prefrontal Cortex (post-LPFC) (BA 44/45)		44	14	24	5.82
Inferior Frontal Gyrus (BA 45)	297	-34	34	4	6.29
[2] Rostral Cingulate Zone (RCZ)	1652	6	12	32	5.94
[2] Supplementary Motor Area (SMA)		0	-8	70	5.70
[2] Pre-Supplementary Motor Area		6	18	58	5.59
Posterior Cingulate Gyrus	812	16	16	48	5.56
Precuneus	241	10	-38	64	5.28
Superior Parietal Lobe	1436	28	-68	44	5.84
Insula	231	-42	8	16	5.64
Nucleus Caudatus	151	-6	6	6	4.82
Thalamus	91	0	-28	2	5.44
Occipital Cortex	141	40	-84	6	5.04
Occipital Cortex	870	-22	-66	10	4.73

[1] wide network in the lateral frontal cortex. [2] wide network in the medial frontal cortex.

Functional Connectivity of the Mid-LPFC

We next aimed at examining whether or not the manipulation of effort expenditure would also influence the functional connectivity between lateral and medial frontal regions (cf. Kouneiher et al, 2009). Accordingly, we explored the functional connectivity pattern of the mid-LPFC, a region that showed a clear effort related effect in both hemispheres and is more generally associated with the integration of reward expectation and the selection and preparation of actions during the pursuit of behavioral goals (Ramnani & Miall, 2003; Ramnani & Owen, 2004). We applied psychophysiological interaction analysis (Friston et al., 1997) to the contrast of differential invested effort for equal reward magnitude. The physiological predictor was the time series from the seed region, i.e., the mid-LPFC activation cluster that responded stronger to higher previous invested effort. It was modulated by the contrast of differential invested effort for equal reward magnitude (i.e., psychological predictor). Analysis of the psychophysiological interaction term, which reflects the effort related change in functional coupling with the mid-LPFC seed region (x,y,z =34,46,16; Fig. 10a), revealed an effect in the SMA (x,y,z =-6,-8,60; Fig. 10b) and in the thalamus (x,y,z = 16,-14,6). In addition, we expected an effect in the RCZ both due to literature (Kouneiher et al., 2009) and due to findings in our first study concerning the crucial role of the RCZ in effort-based valuation. Accordingly, we focused on this area in a ROI analysis using the same RCZ mask as in the previous study. Corresponding to our hypothesis, we found significant effects in the pRCZ (x,y,z = 10,8,-42; x,y,z =8,-8,38; Fig. 10c).

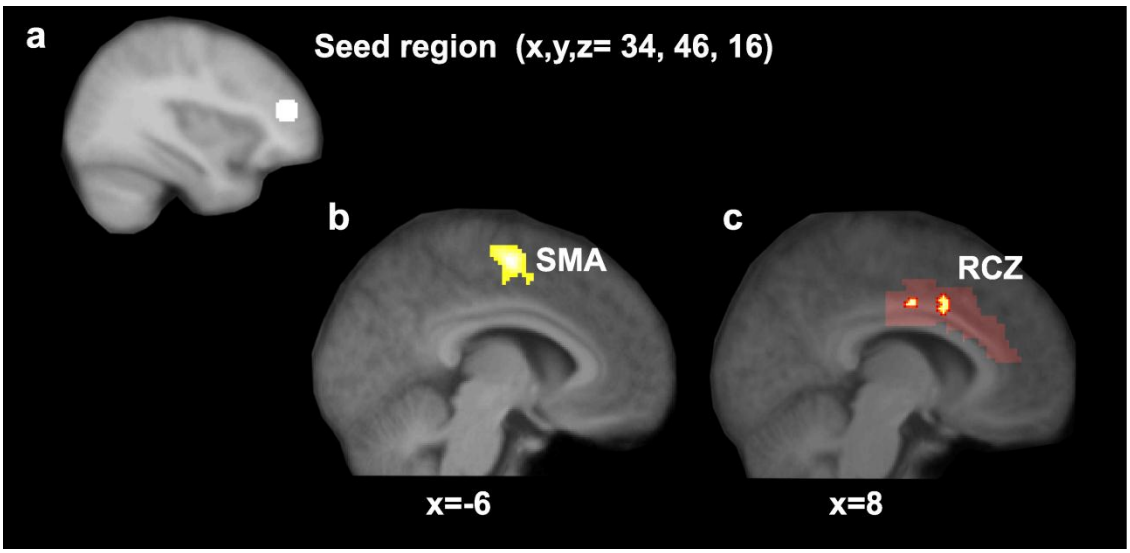

Figure 10. The seed region in the mid-LPFC (a) exhibited an increased functional connectivity to supplementary motor area (b, SMA, thresholded at $p < 0.001$, $k > 91$) and rostral cingulate zone (c, RCZ) after higher previous effort investment. RCZ mask is visualized in transparent red, activations within the mask are thresholded at $p < 0.001$, $k > 17$.

No Differential Effect of the Amount of Previously Invested Effort

Furthermore, we were interested whether or not there was a neuronal effect of the amount of previous effort expenditure. Analogous to the analysis of the behavioral data, we compared the final trials of multi-trial reward schedules (i.e., 2nd trial in 2-actions-schedules and 3rd trial in 3-actions schedules) with respect to the different contingency conditions (delayed vs. immediate contingency) on the whole brain level. If one region is modulated through the amount of previously invested effort to obtain a reward of equal magnitude, it should exhibit a significant interaction between contingency and schedule length. Actually, no region displayed such a significant interaction effect under the chosen significance criterion. This corresponds to the behavioral results, where also no sensitivity to the amount of invested effort as operationalized in the present study could be identified.

Representation of the Experimental Context

By contrasting the anticipation phases of 1-action schedules, we additionally examined how the brain represents the motivational context of a situation. As the 1-action-schedules

consist of only one MID Trial, they are completely identical under both contingency conditions. The only difference is the experimental context they are embedded in (delayed vs. immediate contingency block). The comparison yielded exactly two activation foci in left orbitofrontal cortex (BA10 ; x,y,z =-38,48,-2) and left posterior LPFC (BA9; x,y,z =-46,16,30) (Fig. 11).

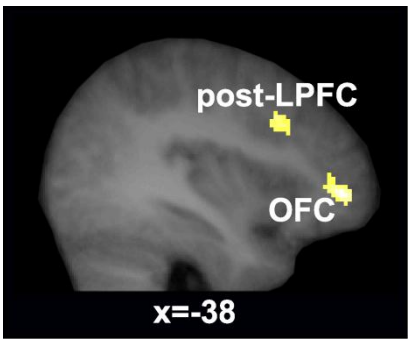

Figure 11. Group functional activation map, overlaid on the average of the normalized structural images of the study participants. Activation in posterior lateral prefrontal cortex (post-LPFC) and orbitofrontal cortex (OFC) in the contrast of 1-action schedules that were embedded in the delayed vs. the immediate contingency context. The image is thresholded at $p < 0.001$, $k > 91$.

5.4 Discussion

The present study examined behavioral and neural responses to previously invested effort in a multitrial reward schedule paradigm. We found that the fraction of correctly completed trials to obtain a reward of equal magnitude was increased after higher effort expenditure. Accordingly, invested effort influenced the motivational values of action outcomes.

We furthermore identified a wide network of brain regions previously shown to be engaged in cognitive control functions that was modulated after a prior investment has been made. This could indicate that previous effort investment acts on cognitive control processes concerned with optimal task performance. More precisely, invested effort potentially influences the allocation of cognitive control resources into task performance through an enhanced connectivity between mid-lateral prefrontal cortex and medial frontal cortex regions, i.e., SMA and RCZ. In addition, posterior lateral prefrontal cortex and orbitofrontal cortex seem to represent the contextual frame based on the risk of loosing already invested effort that could be used for reference-dependent outcome evaluation.

5.4.1 Invested Effort Engages a Network Associated with Executive Control Functions

In a recent behavioral study with non-human primates, La Camera and Richmond (2008) found a significant tendency for errors to decrease with the trials already performed, at equal proximity to reward. Also in the present study, the previous invested effort led to a performance enhancement as measured in the final trials of multitrial reward schedules that varied according to the number of actions until reward attainment. This phenomenon is referred to as "schedule length effect". As performance accuracy in general is guided by the motivational value of an anticipated outcome and given that all other operant demands of the last actions between schedules under delayed or immediate contingency are constant, the schedule length effect can be taken as a direct consequence of motivational value modulation due to previous workload.

As neuronal underpinnings of the schedule length effect we observed an activation of several regions in the lateral prefrontal cortex, posterior medial frontal cortex, supplementary motor areas, parietal cortex, and insular cortex, all regions commonly associated with higher level cognitive functions (Wager et al., 2004; Owen et al., 2005). The present study provides the first evidence that the previously invested effort can elicit processes concerned with general cognitive processing and future planning. However, it was not designed to address the question whether the identified areas may code for an effort-based value representation or whether their activity is due to a general effect of motivation increasing task-specific activity in order maximize reward attainment. As can be seen from the following sections both interpretations are feasible.

One the one hand, it is a known fact that executive functions must intersect with functions that determine value for the organism. In line with this, functional imaging work in humans (Small et al., 2005; Adcock et al., 2006; Krawczyk et al, 2007; Locke & Braver, 2008) and single-unit recording in non-human primates (Kennerley & Wallis, 2009c) provide evidence that changes in motivational state may modulate performance through activity in task-related cognitive control regions.

Interestingly, on the other hand, McClure and colleagues (2004, 2007) identified a comparable network contributing to the value determination of time-discounted rewards. More precisely, they found that the degree of engagement of a wide part of this network,

namely several regions in the DLPFC (BAs 9, 44, 46, and 10), bilateral parietal cortex, and anterior insula predict deferral of gratification during intertemporal choices. The increased activity of this so-called *δ*-decision making system in response to the selection of a later/larger reward is consistent with a key role of this network for cognitive processes such as general reasoning, abstract problem solving, and exertion of control in favor of long-term goals (Miller & Cohen, 2001). These processes putatively underlie the uniquely human capacity for future planning. Damage to these areas in humans produces a pattern of short-sighted nondeliberative behavior termed "reward-dependency syndrome" (Lhermitte, 1986). Notably, this network was previously not only identified in the context of time discounting, but also during the valuation of probabilistic decision options (Peters & Buchel, 2009), potentially indicating that the identified regions are engaged in a domain-general analysis of economic options and the valuation of future reward.

While the same general δ-regions may be involved in a variety of functions (Shallice, 1982; Miller & Cohen, 2001) limbic reward-related *β*-areas seem to be more stimulus or task specific. The specific subregions of the limbic *β*-decision system were shown to be sensitive to different aspects of common decision variables as for example the person-specific scaling of delayed decision options (Kable & Glimcher, 2007), and the tracking of a reward-probability functions (Hsu et al., 2009). It is an open question if limbic subregions also show a graded sensitivity with respect to invested effort as opposed to the putative binary coding in domain general cognitive control regions identified in the present study.

5.4.2 Invested Effort Enhances Functional Connectivity between Medial and Lateral Frontal Regions

As mentioned above, previously invested effort induces a modulation of potentially cognitive control-related neuronal activity. In the present study, we could show that RCZ and SMA exhibit an increased functional connectivity to mid-LPFC in the face of higher effort expenditure. This is similar to the connectivity profile shown by Kouneiher and colleagues (2009) varying as a function of reward magnitude when participants performed a cognitive demanding task. Following their argumentation, RCZ and SMA could provide an effort-based cost-benefit analysis used for the regulation of task-dependent cognitive control resources by the mid-LPFC. In line with this, the mid-LPFC has been associated with a variety of cognitive

control processes subserving the pursuit of hierarchical goals (e.g., Ramnani & Owen, 2004). For example, the mid-LPFC has been implicated in subgoal processing, i.e., taking a larger goal and breaking it down into smaller goals (Koechlin et al., 1999; Braver & Bongiolatti, 2002). The execution of a varying number of action steps, i.e., subgoals, towards a delayed reward, i.e., the hierarchically larger goal, might have been governed by exactly this type of cognitive control process. Also anatomically, the mid-LPFC seems to be ideally suited to govern cognitive processes according to the values of expected outcomes. It receives input from orbitofrontal cortex, cingulate cortex, and dopaminergic midbrain (Ilinsky, Jouandet, & Goldman-Rakic, 1985; Preuss & Goldman-Rakic, 1989; Ungerleider, Gaffan, & Pelak, 1989; Petrides & Pandya, 2002), all regions from where value information could arrive. In turn, it projects to dorsolateral prefrontal and premotor regions, and could, thus, influence behavioral output (Preuss & Goldman-Rakic, 1989; Petrides & Pandya, 2002).

On the other hand, in a recent study, it was argued that mid-LPFC represents a combined value signal integrating reward size, risk, and even personal risk attitudes of the decision maker (Tobler et al., 2009). In the last actions of the delayed contingency condition, the risk of loosing previously invested effort is substantially higher than in the immediate contingency condition. Furthermore, the RCZ was shown in our first study to represent the expected reward value integrated with the previously invested effort to obtain that reward. Therefore, this connectivity could also enable a combined value representation in the mid-LPFC based on the risk of loosing previously invested effort. As indicated by the behavioral manifestations of potential sunk-cost situations, the prevention of loosing previously invested effort is a strong motivational factor in peoples' decisions (Arkes & Ayton, 1999). Thus, together with the increased coupling to the SMA, the connectivity profile could also indicate an enhanced degree of motivation reflected by an increased level of motor readiness and movement preparation (Pears et al., 2003; Roesch & Olson, 2007b).

Taken together, both the widespread activation of brain regions and the increased functional coupling due to increased effort expenditure are potentially related to the enhanced behavioral task performance after higher effort expenditure. More general, they might also underlie the behavioral manifestation of the sunk cost effect, i.e., the increased motivation to spend resources in a course of actions once an investment of effort has been made. However, whether this is due to the additional allocation of task-related resources or the integration of effort based value information recruiting the same brain regions as typical cognitive control tasks is behind the scope of the present study.

5.4.3 Previous Effort Investment Serves as a Contextual Frame Used for Outcome Evaluation

The sunk cost fallacy is uniformly seen as a contextual framing effect based on previous effort expenditure, eventually resulting in the differential valuation of potentially equivalent decision options. We found the posterior LPFC and the OFC to be concerned with maintaining such a context representation. Importantly, by comparing 1-action schedules with respect to contingency conditions, this context representation could be investigated in the absence of other valuation-related processes. As the risk of sinking costs is substantially higher in the delayed contingency context, the higher activation in the posterior LPFC and lateral OFC in this condition could represent the contextual frame itself used as a reference point for relative outcome valuation.

In general, both human neuroimaging and monkey neurophysiological studies clearly indicate that the posterior LPFC plays significant roles in processing cognitive context information (Koechlin et al., 2003; Brass & Cramon, 2004; Watanabe & Sakagami, 2007). For instance, primate caudal LPFC neurons seem to be involved in cognitive context-dependent stimulus coding, e.g., by responding differently to an identical stimulus according to the current task situation (Watanabe & Sakagami, 2007). Also in the human brain, post-LPFC was associated with the selection of task-relevant information indicated by changing contextual cues (Brass & von Cramon, 2004).

Furthermore, in addition to encoding the cognitive context of the environment, the posterior lateral prefrontal cortex might represent the utilities or values associated with various states of the environment, thus also coding the stimuli on the basis of the motivational context (Lee, Rushworth, Walton, Watanabe, & Sakagami 2007; Watanabe & Sakagami, 2007). This has previously also been suggested in fMRI studies with human subjects where the motivational context varied according to the probability of rewarding outcomes (Tanaka et al., 2004; Huettel et al., 2006b). In the present study, the risk of sinking cost might be processed in the posterior LPFC as a strong incentive to select and maintain the accordant task representation, i.e., which button to press as soon as the target appears.

Also the OFC was significantly activated when comparing delayed with immediate 1-action schedules. In contrast to the posterior LPFC, the OFC seems to be predominantly involved in coding for motivational context information (Watanabe & Sakagami, 2007). The

increased activity in the OFC might therefore represent the frame, i.e., the reference point itself, and through this might also underlie the subjective evaluation of an equal reward after differential effort expenditure. This fits well with various reports about relative value coding in the OFC, which activity adapts to the range of values available in a given context (e.g., Tremblay & Schultz, 1999; Ursu & Carter, 2005).

6 General Discussion

In the theoretical background section of the present thesis, previous research on valuation related processes and the role of associated brain regions has been introduced. This review of the literature showed that most of the present research in this field pertains to absolute value representations modulated by decision variables like reward size (e.g., Hollerman et al., 1998), probability (e.g., Huettel et al., 2005), temporal delay (e.g., McClure et al., 2004), and expected effort (e.g., Croxson et al., 2009). A parallel line of evidence is concerned with the investigation how value is computed relatively, i.e., with respect to the current context of the situation. In these studies, contextual attributes of a situation modulating the evaluation of a decision option are, for example, the price range of the available options (Padoa-Schioppa, 2009) or the satiety state of the individual (Gottfried et al., 2003).

The present thesis focused on the influence of goal proximity and invested effort as decision variables modulating the estimation of value, and, in the case of invested effort, also as a contextual anchor for value evaluation. Thus far, at least in the field of human cognitive neuroscience, these variables have not been investigated systematically. In the following sections, the results of the two studies comprising the present thesis will be summarized. Furthermore, some suggestions will be made on how the present experiment on effort expenditure can be continued to further specify the role of the associated brain regions.

6.1 Summary of the Behavioral Results

In both studies reported here, performance was enhanced under delayed contingency, even though this did not lead to an increase in reward size. While in the first study the contingency conditions did not differ with respect to the overall net reward, in the second study, the net reward that could be gained under delayed contingency was even smaller than under immediate contingency. In addition, subjects made less errors in a trial if the total effort to get there had been larger, even though this does not affect the upcoming reward (“schedule length effect”). This indicates that participants were differentially motivated depending on previous workload when facing a situation with identical reward/cost ratio. This proves that the

performance of humans in the reward schedule task is influenced by valuation related processes based on invested effort.

Taken together, these results suggest that the participants did not only strive for maximizing the overall reward/cost ratio when performing in multitrial reward schedules, as commonly assumed in rational theories of decision making (La Camera & Richmond, 2008). Conversely, a number of experiments have supported the notion that the avoidance of wasting cost already is a strong motivating factor in people's decision (Arkes & Ayton, 1999). Correspondingly, the present behavioral effects could be due to an inherent aversion to loss, as in the delayed contingency condition, the risk of sinking already invested resources is substantially higher than in the immediate condition, and the degree to which already invested resources would be lost varies according to the effort already invested.

In line with this, aversion to loss has been observed in other situations, in which subjects do not evaluate options in a rational, absolute way. For example, some researchers proposed that the endowment effect, i.e., the tendency to weigh products for sale more heavily than products for buy, results from the subjective impression of loosing the sold product (Kahneman, Knetsch, & Thaler 1990, 1991). Also prospect theory, a successful behavioral model of decision-making under risk (Kahneman & Tversky, 1979) explains risk aversion in gambles using the concept of loss aversion: People are more sensitive to the possibility of loosing money than they are to the possibility of gaining the same amount of money. Thus far, this is the first study in humans using multitrial reward schedule paradigms showing that also increasing goal proximity and invested effort can produce effects explainable with loss aversion. Reasonably, also the behavioral manifestation of the sunk cost fallacy, i.e., the increased motivation to persist in a course of actions once an investment of effort has been made, results from the aversion of loss that obviously drives human choice behavior.

6.2 Summary of the Neuronal Results

According to the two experiments of the present thesis, reward proximity and invested effort influence neural systems concerned with goal based valuation mainly in the prefrontal cortex. In general, over the past decade, much research has been done in the field of decision making and associated valuation-related processes. It has become clear that reward signals are ubiquitous in the frontal lobe (Schultz, 2010), which is not surprising given that a central goal

of behavior is to obtain rewards of all kinds. In the following, the results of the two imaging studies will be repeated. Based on the results of the first study, the role of the RCZ with respect to valuation based processes will be specified. Furthermore, potential criticism and unclarities about the precise functionality of brain regions identified in the second study will be addressed.

6.2.1 RCZ Represents Action Values based on Goal Proximity

In line with our hypothesis, the first experiment demonstrated that the human pRCZ is, like the CMA in monkeys, highly specialized in value representation contingent to the proximity of the expected outcome in a series of routine actions leading to a delayed reward. According to studies trying to specify the role of pMFC regions in outcome evaluation, value representation in the RCZ is putatively based on the calculation of the value of the action producing a certain outcome (for a review see Rushworth et al., 2004; Rushworth, Buckley, Behrens, Walton, & Bannerman, 2007). Also our functional connectivity analysis, demonstrating that the reward proximity signal in the pRCZ covaries with activity in motor-related regions, and, more generally, the anatomical finding that much of the primate medial frontal cortex projects to cortical and subcortical areas with motor functions (Dum & Strick, 1991) provides evidence that the activity of the RCZ is modulated primarily with regard to the rewarding values of actions, thus enabling efficient action selection. In line with this, lesions in the pMFC impair rodents' ability to combine information about the costs and benefits associated with alternative actions (Rudebeck et al., 2006). Thus, in sum, the results of our first imaging study show for the first time that the role of the human RCZ in representing action values can be extended to the continuous updating of action values over a routine action course with regards to the proximity to the expected goal.

6.2.2 The Neuronal Effects of Invested Effort

Importantly, in multitrial reward schedules, previously invested effort influences two kinds of valuation related process. On the one hand, invested effort can function as a decision variable accumulating over action steps towards the predicted outcome. On the other hand, invested effort can be conceptualized as a reference point for relative outcome evaluation.

Neuronal correlates of the schedule length effect. In both studies of the present thesis, we measured the influence of invested effort in terms of a decision variable that accumulates over action steps by comparing the final trials of the delayed as compared to the immediate multitrial reward schedules. This comparison is also referred to as "schedule length" effect.

In the first study, when investigating the schedule length effect after the execution of routine actions towards reward, we found an anterior part of the RCZ to code for previous effort expenditure. This result suggests that the RCZ integrates action values also with respect to the workload already invested, which is furthermore in line with the finding that RCZ codes for a higher number of decision variables than any other regions in the frontal cortex (Kennerley et al., 2009a).

In the second study, we extended our findings about the neuronal underpinnings of the schedule length effect towards the execution of non-routine action sequences. In line with our hypothesis, we found a broad network of cognitive control regions changing their activity dependent on previous effort expenditure to obtain a reward of equal magnitude. However, on the basis of the second study, we were not able to further disentangle the precise functionality of the identified regions in effort based valuation. For example, we could not find a variation in any of these regions dependent on the amount of previous effort investment. Also behaviorally, the amount of effort expenditure did not yield a significant effect. This could be due to the fact that the differentiation of previous workload as operationalized in the present study, i.e., 2 vs. 3 action steps towards the reward, does not make a difference for the scaling mechanism implemented in the human brain for the computation of value based on differential effort expenditure. Additionally, as in the second study delayed and immediate contingency conditions were not balanced according to reward magnitude, we were not able to investigate whether or not the activity in any of the effort-related brain regions also shows goal proximity-based valuation effects. This could have revealed which of the identified brain regions is specifically activated in response to previously invested effort, and which brain regions code for the expected value also with respect to goal proximity, thus in a more domain general way.

An alternative interpretation of the neuronal correlates of the schedule length effect is that a general increase in motivation due to previous effort investment modulated task-related activity in classical cognitive control regions. Admittedly, this conclusion has a major weakness. For proving that invested effort can influence executive processes it would be

necessary to show that it modulates the representation of information related to executive control, thereby ensuring the efficient allocation of cognitive resources. However, as executive control demands and previous effort investment did not vary independently from each other in the second study, we could not investigate whether or not there are brain regions changing their activity both due to manipulations of cognitive load and the motivational incentive due to effort investment. Conversely, we could only speculate that a higher performance monitoring demand, requiring a higher degree of executive control, was present in the delayed as compared to immediate multitrial reward schedules, potentially resulting from the higher necessity to monitor action steps leading to a delayed reward compared to actions leading immediately to a reward.

Taken together, a parsimonious interpretation of our results is that the encoding of invested effort invoked processes related to the executive system. This could be due to an effort based value representation recruiting the same brain regions as typical cognitive control tasks. In line with this, some studies identified a comparable network contributing to the value determination of time-discounted rewards and to the valuation of probabilistic decision options (McClure et al., 2004, 2007; Peters & Buchel, 2009). An alternative interpretation is that invested effort interacts with task-related processes, thereby assuring efficient allocation of cognitive resources (e.g., Locke & Braver, 2008). In line with this, the sunk-cost literature has focused on resource allocation dependent on previous effort expenditure as one variation of this phenomenon (Navarro & Fantino, 2005). A suggestion to clarify the role of brain regions concerned with effort based valuation in a sequence of non-routine actions will be addressed in the "outlook" section of the present thesis.

The role of the posterior lateral prefrontal cortex and orbitofrontal cortex in context-dependent outcome valuation. As expected on the basis of the work discussed in the theoretical background section, we also found the post-LPFC and the OFC to be involved in another crucial component of outcome valuation. More precisely, we could identify the representation of the experimental context itself, i.e., the risk of sinking already invested effort, that could be used as a reference frame for relative value computation, in the absence of other motivational variables modulating the anticipated outcome.

The post-LPFC is unequivocally associated with maintaining both cognitive (e.g., Brass & von Cramon, 2004) and motivational (Tanaka et al., 2004; Huettel et al, 2006b) state

representations in order to identify optimal actions in a given environment (Lee et al., 2007). This suggests that, in the second study, a lateral prefrontal representation of the task context could have led to a more precise action preparation during the anticipation phase of the MID task in the delayed contingency condition.

The exact role of the OFC, however, in attributing value as a change from a set reference point is still under debate. Interestingly, in a recent functional imaging study (De Martino, Kumaran, Seymour, & Dolan, 2006) the ability to resist to framing effects was linked to the activation of the OFC. Following this interpretation, the OFC could account for the lacking behavioral effects of the comparison between delayed and immediate 1-action schedules in the second experiment. This resistance is of high importance in the real world, as the inability to resist irrelevant cues, like previous workload in outcome evaluation, can potentially lead to maladaptive economic behavior as can be seen, for example, in the development of the Concorde. The plane's vague financial prospects were known long before the plane was completed, but the two governments financing the project decided to continue anyway on the grounds that they had already invested a lot of money. In short, they had "too much invested to quit" (Teger, 1980).

Contrary to this, for many everyday decisions, perhaps a fast and frugal heuristic like "Past investment predicts future benefits" is a serviceable substitute for the computationally more demanding rules (Gigerenzer, Czerlinski, & Martignon, 1999). In evolutionary terms, these context- or framing-dependent evaluation mechanism may even confer a strong advantage, because contextual cues may carry useful, if not critical, motivational information (Pompilio, Kacelnik, & Behmer, 2006), and these mechanisms only fail in circumstances in which additional resources do not result in an increase in future benefits. However, given that past investment is typically correlated with prospective value, perhaps the cost of vulnerability to the sunk cost fallacy is not as great as the benefits gained from use of such a computationally cheap rule.

6.3 Conclusion

The aim of the present thesis was to investigate for the first time which valuation related brain regions in humans are modulated by the proximity to the expected goal and the

previously invested effort, two variables not addressed thus far in numerous human neuroimaging studies concerned with decision making and goal-based valuation.

We could demonstrate that the RCZ of the pMFC signals increasing reward expectation contingent to goal proximity, thereby replicating neurophysiological findings about goal proximity signals in a homologous region in non-human primates. Through this, we could extend the role of the human RCZ in outcome evaluation to include also the continuous updating of action values over a course of routine action steps based on the proximity to the expected reward.

We further tentatively suggest that increased effort investment in order to obtain a reward of equal magnitude invokes processes related to the executive system, while the degree of invested effort does not necessarily influence the degree to which control systems are engaged. Additionally, we report for the first time that the posterior lateral prefrontal cortex and orbitofrontal cortex are concerned with maintaining a context representation based on the risk of sinking already invested effort which could serve as reference frame for relative value computation.

6.4 Outlook

The present experiments used fMRI to investigate which brain regions are modulated by goal proximity and invested effort. The results that were reported here led to the conclusion that, in a sequence of routine actions, RCZ represents action values based on goal proximity and previous effort expenditure.

Furthermore, we provided evidence that in a course of non-routine actions, invested effort evokes processes related the executive system. However, the precise roles of the regions responding to increased effort expenditure need further clarification.

One of our hypotheses states that the identified areas could be concerned with an effort-based evaluation of an option, in analogy to a highly deliberative δ-decision making system mediating the selection of temporally delayed, but larger monetary reward (McClure et al., 2004, 2007). However, additional evidence is needed to further underline the putative involvement of the classical cognitive control regions comprising the δ-decision making

system in processes concerned with effort based valuation. To this end, one could investigate whether or not these regions also predict the choice of options that are associated with a comparably higher previous effort investment in a decision making experiment. In general, to further specify regions involved in effort based value computation, behaviorally derived preference curves analogous to decision making experiments concerned with temporal discounting (Kable & Glimcher, 2007) could be established. These preference curves should be based on effort-based choices, i.e., they should depict how the subjective value of a decision option varies with effort expenditure for each individual. Through this, it would be possible to identify neural activity that correlates with the effort-based subjective value. Furthermore, they could indicate according to which function invested effort modulates the evaluation of outcomes, i.e., which amount of effort investment makes a difference for subjective outcome evaluation, as well as for effort based value computation in the brain, respectively.

Experimentally, it is not trivial how to convert choice behavior into how hard subjects will work for an option. Practically, in order to investigate effort-based choice behavior, the multitrial reward schedule task could be transformed into a free choice task in which each transition to the next action step is subjected to the decision whether or not the participant is sufficiently motivated to act or not. How hard subjects are willing to work for a certain amount of money, i.e., the number of actions steps until they decide to abandon a course of actions leading to a prespecified reward, should reflect the subjective effort-based reward value. Hereby, if the hypothesis proves correct, the decision to continue to invest should be governed by cognitive control regions associated with the δ-decision making system. Additionally, an experiment like this would provide other valuable evidence concerning the neuronal underpinnings of the sunk cost effect, as the literature has focused on the persistence in goal pursuit as another variation of this phenomenon next to increased allocation of resources (Fantino, 2004).

Another hypothesis concerning the role of the regions activated after increased effort expenditure in the second study is that they reflect a facilitation of cognitive processes required for goal achievement of the current task. To find additional evidence for this hypothesis, one could investigate how subjects perform a typical cognitive control task, e.g., a working memory tasks (e.g., Stelzel, Basten, Montag, Reuter, & Fiebach, 2009) under differential expectancies of monetary rewards for correct performance. Critically, these rewards should be associated with differential effort expenditure, for example in a practice

session before the experiment, such that two factors, i.e., (a) memory load and (b) motivational incentive due to previous effort expenditure can be orthogonally varied. The main effects could demonstrate whether or not effort-based incentives recruit some of the same neural networks that underlie the working memory task. Through the identification of areas of interaction evidence could be provided whether or not previous effort investment can modulate task related activity to assure goal achievement.

Deutsche Zusammenfassung

Theoretischer Hintergrund

Derzeit besteht im Bereich der Neurowissenschaften ein großes Interesse daran aufzuklären, auf welche Weise verschiedene Variablen die Wertigkeit eines erwarteten Handlungsziels beeinflussen bzw. welche Hirnregionen an der Kodierung der Wertigkeit eines Handlungsziels beteiligt sind. Die Wertigkeit eines Handlungsziels ist beispielsweise immer dann relevant, wenn eine Entscheidung zwischen zwei Handlungsoptionen getroffen werden muss.

Prinzipiell können an der Zuschreibung von Wertigkeit zwei unterschiedliche Einflussfaktoren beteiligt sein. Zum einen kommt es darauf an, in welchem Kontext Handlungsoptionen präsentiert werden. Die Tendenz kontextuelle Merkmale, das heißt Merkmale der aktuellen Situation, in den Bewertungsprozess mit einzubeziehen kann man sich leicht vor Augen führen indem man sich die folgenden Fragen stellt: „Würde es mir leichter fallen, einen neuen Fernseher zu kaufen, wenn ich an dem gleichen Tag schon ein neues Haus gekauft hätte?“ oder „Würden ich diesen Fernseher eher kaufen, wenn er als heruntergesetzt gekennzeichnet wäre?“. Die meisten Menschen bejahen solche Fragen, was zeigt, dass Optionen weniger absolut, sondern eher *relativ* in Abhängigkeit des jeweiligen Bezugsrahmens bewertet werden. Studien weisen darauf hin, dass der orbitofrontale Cortex (OFC; Watanabe & Sakagami, 2007) und der laterale präfrontale Cortex (LPFC; Padoa-Schioppa, 2009) an der Repräsentation des wahrgenommenen Wertes in Abhängigkeit von Merkmalen der Situation beteiligt sind.

Unabhängig von den Merkmalen der jeweiligen Situation wird die wahrgenommene Wertigkeit einer Entscheidungsoption auch *absolut* durch Parameter beeinflusst wie den erwarteten Geldbetrag (die „Belohnungshöhe“), die Wahrscheinlichkeit, mit der ein bestimmtes Ereignis eintritt, die Dauer bis zur Belohnung, und die Anstrengung, die man aufbringen muss, um etwas zu erhalten. Diese Parameter werden unter dem Begriff „Entscheidungsvariablen“ zusammengefasst. Hirnregionen, die an der Kodierung von Wertigkeit anhand dieser Entscheidungsvariablen beteiligt sind, sind klassische belohnungs-assoziierte Areale wie das dopaminerge Mittelhirn (Waelti et al, 2001), das Striatum (Hollerman et al., 1998) und der orbitofrontale Cortex (Trembley & Schultz, 2000). Weitere

beteiligte Regionen sind der posteriore mediale präfrontale Cortex (pMFC; Walton et al., 2006), der laterale PFC (Kim et al., 2009) sowie prämotorische Areale (Roesch & Olson, 2003). Die meisten neurowissenschaftlichen Studien zur neuronalen Repräsentation der Wertigkeit eines Handlungsziels beziehen sich auf diese Entscheidungsvariablen. Bisher liegen jedoch kaum neuronale Untersuchungen vor bezüglich zweier anderer Variablen, die ebenfalls den erwarteten Wert eines Handlungsergebnisses beeinflussen. Das sind (a) die Nähe zu dem erwarteten Ziel und (b) die bisher investierte Anstrengung, um ein Ziel zu erreichen. Die bisher investierte Anstrengung kann sowohl als Entscheidungsvariable gesehen werden, die den erwarteten Wert absolut verändert, als auch als ein kontextuelles Merkmal der Situation, das als Bezugsrahmen für eine relative Zuschreibung von Wertigkeit dient. Das Ziel der vorliegenden Arbeit ist es zu untersuchen, wie die Nähe zum Ziel und die bisher investierte Anstrengung Gehirnregionen beeinflussen, die mit der Repräsentation von Wertigkeit im Zusammenhang stehen. Dazu führten wir zwei fMRT-Studien durch, in denen wir eine klassische Belohnungs-Antizipationsaufgabe (Monetary Incentive Delay (MID) - Aufgabe; Knutson et al., 2001) in zwei unterschiedliche Versionen eines „Multitrial Reward Schedule“ Paradigmas integriert haben (Shidara & Richmond, 2002; Ichihara-Takeda & Funahashi, 2006).

Studie 1 – Die neuronale Repräsentation der Zielnähe

Zur Untersuchung der Zielnähe mussten die Probanden jeweils vier aufeinanderfolgende MID-Aufgaben pro Reward Schedule durchführen. Das bedeutet, dass ein Multitrial Reward Schedule immer aus vier MID-Aufgaben bestand. Der kritische Unterschied zwischen den Multitrial Reward Schedules bestand darin, dass sie unter zwei unterschiedlichen Belohnungskontingenzen dargeboten wurden: In dem verzögerten Schedule erhielten die Probanden eine Belohnung nach der erfolgreichen Bearbeitung von vier aufeinanderfolgenden MID-Aufgaben, in dem direkten Schedule dagegen nach jeder korrekten MID-Aufgabe innerhalb einer vierer Sequenz (siehe Abbildung 1, Kapitel 4.2.2). Wurde in einem verzögerten Schedule ein Fehler gemacht, so wurde die MID-Aufgaben Sequenz abgebrochen, und es erfolgte keine monetäre Belohnung. In einem direkten Schedule wurde lediglich die aktuelle MID-Aufgabe nicht belohnt, der Schedule an sich lief danach mit der nächsten MID-Aufgabe weiter. Zusätzlich manipulierten wir die Belohnungshöhe. In der niedrigen Belohnungsbedingung konnten die Probanden entweder 5 Euro-Cents pro korrekter MID-Aufgabe (direkte Kontingezbedingung) oder 20 Euro-Cents nach vier korrekten MID-

Aufgaben (verzögerte Kontingenzbedingung) bekommen. In der hohen Belohnungsbedingung konnten sie sich 20 Euro-Cents pro korrekter MID-Aufgabe (direkte Kontingezbedingung) und 80 Euro-Cents für vier korrekte MID-Aufgaben (verzögerte Kontingenzbedingung) verdienen. Daraus resultierte ein 2 x 2 x 4 Paradigma (verzögerte vs. direkte Kontingenz; hohe vs. niedrige monetäre Belohnung; 4 Positionen pro Schedule).

Effekte der Zielnähe wurden identifiziert über eine Interaktionsanalyse zwischen Kontingenz- und Positionseffekten, das heißt über die Identifikation von Arealen, die eine stärker ansteigende Aktivität über die Positionen in der verzögerten im Vergleich zur direkten Bedingung aufwiesen. Shidara und Richmond (2002) hatten zuvor in einer Studie mit einem ähnlichen Design Neurone im caudalen motor Areal (CMA) bei Affen gefunden, dessen Aktivität über die einzelnen Handlungsschritte hinweg durch die Nähe zum Ziel moduliert wurde. Aufgrund dieses Befundes erwarteten wir, Effekte der Zielnähe in der rostralen cingulären Zone (RCZ) zu finden, die das homologe menschliche Areal zur CMA von Affen ist (Picard & Strick, 2001).

Hypothesenkonform zeigte sich für die RCZ eine signifikante Interaktion zwischen Kontingenz und Position, genauer eine sukzessiv ansteigende Aktivität über die Positionen hinweg, das heißt in Abhängigkeit der Nähe zum verzögerten Ziel. Weiterhin zeigte sich, dass die RCZ kontingent zur Zielnähe eine erhöhte Konnektivität zu motorisch-relatierten Arealen wie dem dorsalen prämotorischen Cortex und dem Putamen aufweist.

Weiterhin wurde geprüft, welches Hirnareal auf die Erwartung eines identischen Geldbetrages nach hoher versus keiner investierten Anstrengung reagiert. Dies war möglich durch einen Vergleich der vierten Position in dem niedrig belohnten verzögerten Schedule mit der vierten Position in dem hoch belohnten direkten Schedule (verzögert niedrig 4. Position vs. direkt hoch 4. Position). In diesen Bedingungen erwarteten die Probanden jeweils eine Belohnung von 20 Euro-Cents. Der einzige Unterschied war die Anzahl der bisherigen Handlungen, d. h. die bisher investierte Anstrengung, die nötig war, um die 20 Euro-Cents zu erhalten. In der verzögerten Bedingung war die korrekte Ausführung der drei vorangegangenen Handlungen die Voraussetzung für den Erhalt der Belohnung. In der direkten Bedingung spielten die vorangegangenen MID-Aufgaben keine Rolle für den Erhalt der Belohnung. Dieser Vergleich ergab einen Aktivitätsunterschied in einem weiter anterior gelegenen Teilbereich der rostralen cingulären Zone. Interessanterweise zeigte dieses Areal in einer Region of Interest Analyse ebenfalls eine signifikante Interaktion zwischen Kontingenz

und Position, das heißt einen parametrischen Anstieg der Aktivität in Abhängigkeit zur Zielnähe.

Insgesamt weisen diese Befunde darauf hin, dass die RCZ eine entscheidende Rolle innehat für die Kontrolle sequenzieller Handlungsstufen, die auf eine verzögerte Belohnung ausgerichtet sind. Dies erreicht diese Region unter anderem durch das Vermitteln von belohnungsbezogener Information an motorische Regionen, die für die Handlungsvorbereitung zuständig sind. Diese Kontrollfunktion scheint auf der kontinuierlichen Aktualisierung des Wertes einer Handlungsstufe in der RCZ zu basieren, der sowohl von der aktuellen Zielnähe als auch von der bisher investierten Anstrengung bestimmt wird.

Studie 2 – Die neuronale Repräsentation der bisher investierten Anstrengung

Die erste Studie ergab zum ersten Mal Hinweise darauf, wie die bereits investierte Anstrengung im Hinblick auf ein Handlungsziel im menschlichen Gehirn repräsentiert wird. Demgegenüber wurde in anderen Forschungsfeldern wie in der Sozialpsychologie schon häufig gezeigt, dass die bisher investierte Anstrengung einen substantiellen Einfluss auf die Evaluation eines erwarteten Handlungsergebnisses ausübt (Arkes & Ayton, 1999; Navarro & Fantino, 2005). Da bisher kaum Evidenz vorliegt, welche Hirnregionen durch die vorher investierte Anstrengung beeinflusst werden, hatten wir in Studie 2 das Ziel dies genauer zu untersuchen. Bisher deutete neben den Befunden aus Studie 1 außerdem eine reine Verhaltensstudie mit Affen darauf hin, dass der wahrgenommene Wert einer Handlung innerhalb eines Multitrial Reward Schedules von den bisher abgeschlossenen Handlungen, also der bereits investierten Anstrengung, beeinflusst wird (La Camera & Richmond, 2008).

Wie in Studie 1 wurden MID-Aufgaben in verzögerte und direkte Multitrial Reward Schedules integriert. Der kritische Unterschied zur ersten Studie bestand darin, dass die Schedules aus einer variierenden Anzahl von MID-Aufgaben bestanden. In der verzögerten Bedingung erhielten die Probanden eine monetäre Belohnung von 18 Euro-Cents nach der fehlerfreien Ausführung von einer, zwei oder drei aufeinanderfolgenden MID-Aufgaben. In der direkten Bedingung erhielten sie 18 Euro-Cents nach jeder fehlerfreien MID-Aufgabe,

unabhängig von der Anzahl der MID-Aufgaben pro Schedule (siehe Abbildung 7, Kapitel 5.2.2).

Die variable Länge der Schedules hatte im Vergleich zur ersten Studie, in der immer vier Handlungsschritte auf dem Weg zur Zielerreichung ausgeführt werden mussten, eine erhöhte Anforderung an allgemeine kognitive Kontrollfunktionen zur Folge. In vielen Studien zum Zusammenhang zwischen Belohnungshöhe und kognitiver Kontrolle wurde festgestellt, dass eine höhere Belohnungserwartung während der Bearbeitung von kognitiv anspruchsvollen Aufgaben die Performanz verbessert und die Aktivität in aufgabenbezogenen Arealen erhöht (z. B. Small et al., 2005; Adcock et al., 2006; Krawczyk et al., 2007; Locke & Braver, 2008). Da die investierte Anstrengung ebenfalls die subjektive Belohnungserwartung erhöht (Arkes & Ayton, 1999), erwarteten wir, dass typische kognitive Kontrollregionen wie der laterale präfrontale Cortex, der posteriore mediale frontale Cortex und der parietale Cortex (Wager et al., 2004; Owen et al., 2005) bei dem Vergleich zwischen hoher und keiner investierten Anstrengung bei der Erwartung einer identischen Belohnungshöhe signifikant erhöht sind. Der Einfluss der bisher investierten Anstrengung wurde analog zur Studie 1 untersucht, indem die letzten Handlungen der verzögerten mit den letzten Handlungen der direkten Multitrial Reward Schedules miteinander verglichen wurden. Wie in der ersten Studie spielten die vorangegangenen Handlungen in den direkten Schedules keine Rolle für den Erhalt der Belohnung. In der verzögerten Bedingung war die korrekte Ausführung der vorangehenden MID-Aufgaben die Voraussetzung für den Erhalt der Belohnung. Das bedeutet, dass sich die letzten Handlungen in beiden Kontingenzbedingungen nur durch die bisher investierte Anstrengung eine Belohnung von 18 Euro-Cents zu verdienen unterschieden.

Entsprechend unserer Hypothesen fanden wir eine Modulation durch die bisher investierte Anstrengung in einem weit verzweigten Netzwerk an kortikalen Regionen, die klassischerweise mit kognitiven Kontrollfunktionen in Zusammenhang gebracht werden. Dazu gehörte der LPFC (BA9, BA44, BA45, BA10), der posteriore mPFC inklusive der RCZ und das supplementär-motorische Areal. Zusätzlich war die Aktivität im parietalen Cortex und der anterioren Insula erhöht.

Ein weiterer Unterschied zur ersten Studie bestand darin, dass verzögerte und direkt belohnte Multitrial Reward Schedules in Blöcken von jeweils etwa vier Minuten präsentiert wurden. Diese geblockte Darbietungsweise ermöglichte es uns weiterhin, verzögerte und direkte Multitrial Reward Schedules miteinander zu vergleichen, die jeweils aus nur einer

MID-Aufgabe bestanden. Diese unterschieden sich also lediglich bezüglich des Kontextes, in dem sie präsentiert wurden. Genauer gesagt ist das Risiko Kosten zu versenken, das heißt bisher investierte Anstrengung zu verlieren, höher im verzögerten als im direkten Kontext. Mit diesem Vergleich sollte demnach geprüft werden, ob der posteriore LPFC und der OFC, zwei Areale die schon zuvor mit der Repräsentation von kontextabhängiger Wertigkeit in Verbindung gebracht wurden (Watanabe & Sakagami, 2007; Padoa-Schioppa, 2009), auch an der Kodierung des Kontextes selbst auf der Basis der bisher investierten Anstrengung beteiligt sind.

Der Vergleich von einzelnen Handlungen, die entweder im verzögerten oder im direkten Kontext präsentiert wurden, erzielte eine hypothesenkonforme Aktivierung im posterioren LPFC und im OFC.

Die Befunde der zweiten Studie lassen darauf schließen, dass sich die investierte Anstrengung im Hinblick auf ein Handlungsziel auf die Bereitstellung von allgemeinen kognitiven Ressourcen auswirkt. Außerdem scheinen der posteriore LPFC und der OFC die motivationalen Kontextmerkmale einer Situation auch dann zu repräsentieren, wenn sich diese auf das Risiko des Verlustes von bisher investierter Anstrengung beziehen.

Zusammenfassende Diskussion

Die vorliegenden Studien befassten sich mit dem Einfluss der Zielnähe und der bisher investierten Anstrengung im Hinblick auf die neuronale Repräsentation der Wertigkeit eines Handlungsziels. Außerdem wurde untersucht, inwieweit das Risiko die bisher investierte Anstrengung zu verlieren als motivationales Merkmal der Situation neuronal kodiert wird.

Entsprechend der vorab formulierten Hypothesen zeigte sich, dass die rostrale cinguläre Zone, analog zum caudalen motorischen Areal im Affen, den erwarteten Wert kontingent zur Nähe zum Ziel in einer Sequenz von Routinehandlungen repräsentiert. Neuere Studien, die die Rolle der RCZ bezüglich der Bewertung eines Handlungsergebnisses zu spezifizieren versuchen, schlagen vor, dass diese auf der Berechnung des Wertes der spezifischen Handlung beruht, mit der ein Ergebnis erzielt werden kann (für einen Überblick siehe Rushworth et al., 2004). Die schrittweise ansteigende Aktivität der RCZ könnte damit funktionell relevant sein für die Absicherung der Persistenz in einem

Routinehandlungsverlauf, der auf eine verzögerte Belohnung ausgerichtet ist (Pears et al., 2003).

Die bisher investierte Anstrengung kann auf zwei verschiedene Arten den erwarteten Wert einer Handlung beeinflussen. Auf der einen Seite kann die bisher investierte Anstrengung im Sinne einer Entscheidungsvariable den wahrgenommenen Wert einer identischen Belohnung verändern. Im Rahmen von routinemäßigen Handlungssequenzen scheint die Aktivität der rostralen cingulären Zone die Wertigkeit nicht nur kontingent zur Zielnähe, sondern auch in Abhängigkeit der bisher investierten Anstrengung zu kodieren. Dieser Befund stimmt mit der Annahme überein, dass die RCZ eine höhere Anzahl von Entscheidungsvariablen (wie bspw. die Belohnungshöhe, oder die Wahrscheinlichkeit, mit der ein bestimmtes Belohnung eintritt) kodiert als jede andere Regionen im frontalen Cortex (Kennerley et al., 2009a). In einer Sequenz von einer variablen Anzahl von Handlungen bis zur Zielerreichung scheint sich die bisher investierte Anstrengung im Sinne einer gesteigerten allgemeinen Handlungskontrolle auszuwirken. Es sind jedoch weitere Studien nötig, um alternative Interpretationsmöglichkeiten ausschließen zu können.

Das Risiko des Verlustes der bisher investierten Anstrengung kann außerdem ein kontextuelles Merkmal der Situation darstellen, das als Bezugsrahmen für eine relative Evaluation des erwarteten Wertes dient. Der orbitofrontale Cortex und der posteriore dorsolaterale Cortex scheinen an der Aufrechterhaltung dieses Bezugsrahmens beteiligt zu sein. Interessanterweise wurde der OFC kürzlich auch mit der Fähigkeit in Verbindung gebracht, einer relativen Wertzuschreibung entgegenzuwirken. Diese Fähigkeit ist potentiell von hoher Wichtigkeit in realen Entscheidungssituationen, da die zu hohe Anfälligkeit für ökonomisch irrelevante Entscheidungskriterien schwerwiegende Konsequenzen haben kann. Ein Beispiel hierfür scheint der Bau der Concorde zu sein. Offensichtlich waren die damit verbundenen mittelmäßigen finanziellen Aussichten schon vor Beendigung der Konstruktion bekannt. Allerdings entschloss man sich nichtsdestotrotz den Bau fortzusetzen, da man schon „zu viel investiert hatte“ um das Projekt wieder abzubrechen und damit den Verlust von bisherigen Investitionen zu riskieren (Teger, 1980).

References

Adcock, R. A., Thangavel, A., Whitfield-Gabrieli, S., Knutson, B., & Gabrieli, J. D. (2006). Reward-motivated learning: mesolimbic activation precedes memory formation. *Neuron, 50*(3), 507-517.

Amiez, C., Joseph, J. P., & Procyk, E. (2005). Anterior cingulate error-related activity is modulated by predicted reward. *European Journal of Neuroscience, 21*(12), 3447-3452.

Arkes, H. R., & Ayton, P. (1999). The Sunk Cost and Concorde Effects: Are Humans Less Rational Than Lower Animals? *Psychological Bulletin, 125*(5), 591-600.

Arkes, H. R., & Blumer, C. (1985). The psychology of sunk cost. *Organizational Behavior and Human Decision Processes, 35,* 124–140.

Aronson, E., & Mills, J. (1959). The effect of severity of initiation on liking for a group. *Journal of Abnormal & Social Psychology, 59,* 177-181.

Ballard, K., & Knutson, B. (2009). Dissociable neural representations of future reward magnitude and delay during temporal discounting. *NeuroImage, 45*(1), 143-150.

Barbas, H. (1993). Architecture and cortical connections of the prefrontal cortex in the rhesus monkey. In P. Chauvel & A. V. Delgado-Escueta (Eds.), *Advances in neurology* (Vol. 57, pp. 91-115). New York: Raven Press.

Barbas, H., & Pandya, D. N. (1987). Architecture and frontal cortical connections of the premotor cortex (area 6) in the rhesus monkey. *Journal of Comparative Neurology, 256*(2), 211-228.

Bautista, L. M., Tinbergen, J., & Kacelnik, A. (2001). To walk or to fly? How birds choose among foraging modes. *Proceedings of the National Academy of Sciences, 98*(3), 1089-1094.

Beckmann, M., Johansen-Berg, H., & Rushworth, M. F. (2009). Connectivity-based parcellation of human cingulate cortex and its relation to functional specialization. *Journal of Neuroscience, 29*(4), 1175-1190.

Behrens, T. E., Woolrich, M. W., Walton, M. E., & Rushworth, M. F. (2007). Learning the value of information in an uncertain world. *Nature Neuroscience, 10*(9), 1214-1221.

Berdyyeva, T. K., & Olson, C. R. (2010). Rank signals in four areas of macaque frontal cortex during selection of actions and objects in serial order. *Journal of Neurophysiology, 104*(1), 141-159.

Berns, G. S., McClure, S. M., Pagnoni, G., & Montague, P. R. (2001). Predictability modulates human brain response to reward. *Journal of Neuroscience, 21*(8), 2793-2798.

Bowman, E. M., Aigner, T. G., & Richmond, B. J. (1996). Neural signals in the monkey ventral striatum related to motivation for juice and cocaine rewards. *Journal of Neurophysiology, 75*(3), 1061-1073.

Bowman, E. M., & Brown, V. J. (1998). Effects of excitotoxic lesions of the rat ventral striatum on the perception of reward cost. *Experimental Brain Research, 123*(4), 439-448.

Bates, J. F., & Goldman-Rakic, P. S. (1993). Prefrontal connections of medial motor areas in the rhesus monkey. *Journal of Comparative Neurology, 336*(2), 211-228.

Brass, M., & von Cramon, D. Y. (2004). Selection for cognitive control: a functional magnetic resonance imaging study on the selection of task-relevant information. *Journal of Neuroscience, 24*(40), 8847-8852.

Braver, T. S., & Bongiolatti, S. R. (2002). The role of frontopolar cortex in subgoal processing during working memory. *NeuroImage, 15*(3), 523-536.

Cardinal, R. N., Pennicott, D. R., Sugathapala, C. L., Robbins, T. W., & Everitt, B. J. (2001). Impulsive choice induced in rats by lesions of the nucleus accumbens core. *Science, 292*(5526), 2499-2501.

Clithero, J. A., & Smith, D. V. (2009). Reference and preference: how does the brain scale subjective value? *Frontiers in Human Neuroscience, 3*, 11.

Critchley, H. D., & Rolls, E. T. (1996). Hunger and satiety modify the responses of olfactory and visual neurons in the primate orbitofrontal cortex. *Journal of Neurophysiology, 75*(4), 1673-1686.

Croxson, P. L., Walton, M. E., O'Reilly, J. X., Behrens, T. E., & Rushworth, M. F. (2009). Effort-based cost-benefit valuation and the human brain. *Journal of Neuroscience, 29*(14), 4531-4541.

De Martino, B., Kumaran, D., Seymour, B., & Dolan, R. J. (2006). Frames, biases, and rational decision-making in the human brain. *Science, 313*(5787), 684-687.

Dum, R. P., & Strick, P. L. (1991). The origin of corticospinal projections from the premotor areas in the frontal lobe. *Journal of Neuroscience, 11*(3), 667-689.

Durston, S., Thomas, K. M., Worden, M. S., Yang, Y., & Casey, B. J. (2002). The effect of preceding context on inhibition: an event-related fMRI study. *NeuroImage, 16*(2), 449-453.

Elliott, R., Agnew, Z., & Deakin, J. F. (2008). Medial orbitofrontal cortex codes relative rather than absolute value of financial rewards in humans. *European Journal of Neuroscience, 27*(9), 2213-2218.

Elliott, R., Newman, J. L., Longe, O. A., & William Deakin, J. F. (2004). Instrumental responding for rewards is associated with enhanced neuronal response in subcortical reward systems. *NeuroImage, 21*(3), 984-990.

Fantino, E. (2004). Behavior-analytic approaches to decision making. *Behavioural Processes, 66*(3), 279-288.

Festinger, L. (1957). *A theory of cognitive dissonance*. Stanford, CA: Stanford University Press.

Fiorillo, C. D., Tobler, P. N., & Schultz, W. (2003). Discrete coding of reward probability and uncertainty by dopamine neurons. *Science, 299*(5614), 1898-1902.

Forman, S. D., Cohen, J. D., Fitzgerald, M., Eddy, W. F., Mintun, M. A., & Noll, D. C. (1995). Improved assessment of significant activation in functional magnetic resonance imaging (fMRI): use of a cluster-size threshold. *Magnetic Resonance in Medicine, 33*(5), 636-647.

Friston, K. J., Buechel, C., Fink, G. R., Morris, J., Rolls, E., & Dolan, R. J. (1997). Psychophysiological and modulatory interactions in neuroimaging. *NeuroImage, 6*(3), 218-229.

Gehring, W. J., & Taylor, S. F. (2004). When the going gets tough, the cingulate gets going. *Nature Neuroscience, 7*(12), 1285-1287.

Gigerenzer, G., Czerlinski, J., & Martignon, L. (1999). How good are fast and frugal heuristics? In J. Shanteau, B. Mellers, & D. Schum (Eds.), *Decision science and technology: Reflections on the contributions of Ward Edwards* (pp. 81-102). Norwell, MA: Kluwer Academic.

Gottfried, J. A., O'Doherty, J., & Dolan, R. J. (2003). Encoding predictive reward value in human amygdala and orbitofrontal cortex. *Science, 301*(5636), 1104-1107.

Haber, S. N., Kim, K. S., Mailly, P., & Calzavara, R. (2006). Reward-related cortical inputs define a large striatal region in primates that interface with associative cortical connections, providing a substrate for incentive-based learning. *Journal of Neuroscience, 26*(32), 8368-8376.

Hollerman, J. R., Tremblay, L., & Schultz, W. (1998). Influence of reward expectation on behavior-related neuronal activity in primate striatum. *Journal of Neurophysiology, 80*(2), 947-963.

Hoshi, E., Sawamura, H., & Tanji, J. (2005). Neurons in the rostral cingulate motor area monitor multiple phases of visuomotor behavior with modest parametric selectivity. *Journal of Neurophysiology, 94*(1), 640-656.

Hsu, M., Bhatt, M., Adolphs, R., Tranel, D., & Camerer, C. F. (2005). Neural systems responding to degrees of uncertainty in human decision-making. *Science, 310*(5754), 1680-1683.

Hsu, M., Krajbich, I., Zhao, C., & Camerer, C. F. (2009). Neural response to reward anticipation under risk is nonlinear in probabilities. *Journal of Neuroscience, 29*(7), 2231-2237.

Huettel, S. A. (2006a). Behavioral, but not reward, risk modulates activation of prefrontal, parietal, and insular cortices. *Cognitive, Affective, and Behavioral Neuroscience, 6*(2), 141-151.

Huettel, S. A., Song, A. W., & McCarthy, G. (2004). *Functional Magnetic Resonance Imaging.* Sunderland, MA: Sinauer Associates.

Huettel, S. A., Song, A. W., & McCarthy, G. (2005). Decisions under uncertainty: probabilistic context influences activation of prefrontal and parietal cortices. *Journal of Neuroscience, 25*(13), 3304-3311.

Huettel, S. A., Stowe, C. J., Gordon, E. M., Warner, B. T., & Platt, M. L. (2006b). Neural signatures of economic preferences for risk and ambiguity. *Neuron, 49*(5), 765-775.

Ichihara-Takeda, S., & Funahashi, S. (2006). Reward-period activity in primate dorsolateral prefrontal and orbitofrontal neurons is affected by reward schedules. *Journal of Cognitive Neuroscience, 18*(2), 212-226.

Ilinsky, I. A., Jouandet, M. L., & Goldman-Rakic, P. S. (1985). Organization of the nigrothalamocortical system in the rhesus monkey. *Journal of Comparative Neurology, 236*(3), 315-330.

Ito, S., Stuphorn, V., Brown, J. W., & Schall, J. D. (2003). Performance monitoring by the anterior cingulate cortex during saccade countermanding. *Science, 302*(5642), 120-122.

Jocham, G., Klein, T. A., Neumann, J., von Cramon, D. Y., Reuter, M., & Ullsperger, M. (2009a). Dopamine DRD2 polymorphism alters reversal learning and associated neural activity. *Journal of Neuroscience, 29*(12), 3695-3704.

Jocham, G., Neumann, J., Klein, T. A., Danielmeier, C., & Ullsperger, M. (2009b). Adaptive coding of action values in the human rostral cingulate zone. *Journal of Neuroscience, 29*(23), 7489-7496.

Kable, J. W., & Glimcher, P. W. (2007). The neural correlates of subjective value during intertemporal choice. *Nature Neuroscience, 10*(12), 1625-1633.

Kahneman D., & Tversky, A. (1979). Prospect theory: An analysis of decision under risk. *Econometrica, 47*(2), 263-291.

Kahneman, D., Knetsch, J. L., & Thaler, R.H. (1990). Experimental tests of the endowment effect and the Coase Theorem. *Journal of Political Econonomy, 98,* 1325–1348.

Kahneman, D., Knetsch, J. L., & Thaler, R.H. (1991). Anomalies: The endowment effect, loss aversion, and status quo bias. *Journal of Economics Perspectives 5,* 193–206.

Kawagoe, R., Takikawa, Y., & Hikosaka, O. (2004). Reward-predicting activity of dopamine and caudate neurons--a possible mechanism of motivational control of saccadic eye movement. *Journal of Neurophysiology*, *91*(2), 1013-1024.

Kennerley, S. W., Dahmubed, A. F., Lara, A. H., & Wallis, J. D. (2009a). Neurons in the frontal lobe encode the value of multiple decision variables. *Journal of Cognitive Neuroscience, 21*(6), 1162-1178.

Kennerley, S. W., & Wallis, J. D. (2009b). Evaluating choices by single neurons in the frontal lobe: outcome value encoded across multiple decision variables. *European Journal of Neuroscience, 29*(10), 2061-2073.

Kennerley, S. W., & Wallis, J. D. (2009c). Reward-dependent modulation of working memory in lateral prefrontal cortex. *Journal of Neuroscience, 29*(10), 3259-3270.

Kennerley, S. W., Walton, M. E., Behrens, T. E., Buckley, M. J., & Rushworth, M. F. (2006). Optimal decision making and the anterior cingulate cortex. *Nature Neuroscience, 9*(7), 940-947.

Kim, S., Hwang, J., Seo, H., & Lee, D. (2009). Valuation of uncertain and delayed rewards in primate prefrontal cortex. *Neural Networks, 22*(3), 294-304.

Knutson, B., Adams, C. M., Fong, G. W., & Hommer, D. (2001). Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *Journal of Neuroscience, 21*(16), RC159.

Knutson, B., Taylor, J., Kaufman, M., Peterson, R., & Glover, G. (2005). Distributed neural representation of expected value. *Journal of Neuroscience, 25*(19), 4806-4812.

Kobayashi, S., Lauwereyns, J., Koizumi, M., Sakagami, M., & Hikosaka, O. (2002). Influence of reward expectation on visuospatial processing in macaque lateral prefrontal cortex. *Journal of Neurophysiology, 87*(3), 1488-1498.

Koechlin, E., Basso, G., Pietrini, P., Panzer, S., & Grafman, J. (1999). The role of the anterior prefrontal cortex in human cognition. *Nature, 399*(6732), 148-151.

Kouneiher, F., Charron, S., & Koechlin, E. (2009). Motivation and cognitive control in the human prefrontal cortex. *Nature Neuroscience, 12*(7), 939-945.

Koechlin, E., Ody, C., & Kouneiher, F. (2003). The architecture of cognitive control in the human prefrontal cortex. *Science, 302*(5648), 1181-1185.

Krawczyk, D. C., Gazzaley, A., & D'Esposito, M. (2007). Reward modulation of prefrontal and visual association cortex during an incentive working memory task. *Brain Research, 1141*, 168-177.

Kriegeskorte, N., Simmons, W. K., Bellgowan, P. S., & Baker, C. I. (2009). Circular analysis in systems neuroscience: the dangers of double dipping. *Nature Neuroscience, 12*(5), 535-540.

La Camera, G., & Richmond, B. J. (2008). Modeling the violation of reward maximization and invariance in reinforcement schedules. *PLoS Computational Biology, 4*(8), e1000131.

Lancaster, J. L., Summerln, J. L., Rainey, L., Freitas, C. S., Fox, P. T., & . (1997). The Talairach Daemon, a database server for Talairach Atlas Labels. *NeuroImage, 5*, S633.

Lancaster, J. L., Woldorff, M. G., Parsons, L. M., Liotti, M., Freitas, C. S., Rainey, L., et al. (2000). Automated Talairach atlas labels for functional brain mapping. *Human Brain Mapping, 10*(3), 120-131.

Lee, D., Rushworth, M. F., Walton, M. E., Watanabe, M., & Sakagami, M. (2007). Functional specialization of the primate frontal cortex during decision making. *Journal of Neuroscience, 27*(31), 8170-8173.

Lhermitte, F. (1986). Human autonomy and the frontal lobes. Part II: Patient behavior in complex and social situations: the "environmental dependency syndrome". *Annals of Neurology, 19*(4), 335-343.

Locke, H. S., & Braver, T. S. (2008). Motivational influences on cognitive control: behavior, brain activation, and individual differences. *Cognitive, Affective, and Behavioral Neuroscience, 8*(1), 99-112.

Long, A., & Platt, M. (2005). Decision making: the virtue of patience in primates. *Current Biology, 15*(21), R874-876.

Lu, M. T., Preston, J. B., Strick, P. L. (1994). Interconnections between the prefrontal cortex and the premotor areas in the frontal lobe. *Journal of Comparative Neurology, 341,* 375-392.

Luppino, G., Govoni, P., Matelli, M. (1998). Prefrontal and cingulate afferents to the rostral premotor areas in the macaque monkey. *Society for Neuroscience Abstract, 24,* 257.211.

MacDonald, A. W., 3rd, Carter, C. S., Kerns, J. G., Ursu, S., Barch, D. M., Holmes, A. J., et al. (2005). Specificity of prefrontal dysfunction and context processing deficits to schizophrenia in never-medicated patients with first-episode psychosis. *American Journal of Psychiatry, 162*(3), 475-484.

Maldjian, J. A., Laurienti, P. J., Kraft, R. A., & Burdette, J. H. (2003). An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *NeuroImage, 19*(3), 1233-1239.

Matsumoto, M., Matsumoto, K., Abe, H., & Tanaka, K. (2007). Medial prefrontal cell activity signaling prediction errors of action values. *Nature Neuroscience, 10*(5), 647-656.

Matsumoto, K., Suzuki, W., & Tanaka, K. (2003). Neuronal correlates of goal-based motor selection in the prefrontal cortex. *Science, 301*(5630), 229-232.

McClure, S. M., Ericson, K. M., Laibson, D. I., Loewenstein, G., & Cohen, J. D. (2007). Time discounting for primary rewards. *Journal of Neuroscience, 27*(21), 5796-5804.

McClure, S. M., Laibson, D. I., Loewenstein, G., & Cohen, J. D. (2004). Separate neural systems value immediate and delayed monetary rewards. *Science, 306*(5695), 503-507.

McGuire, J. T., & Botvinick, M. M. (2010). Prefrontal cortex, cognitive control, and the registration of decision costs. *Proceedings of the National Academy of Sciences, 107*(17), 7922-7926.

Matsumoto, K., Suzuki, W., & Tanaka, K. (2003). Neuronal correlates of goal-based motor selection in the prefrontal cortex. *Science, 301*(5630), 229-232.

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*, 167-202.

Moon, H. (2001). Looking forward and looking back: Integrating completion and sunk-cost effects within an escalation-of-commitment progress decision. *Journal of Applied Psychology, 86,* 104–113.

Morecraft, R. J., McNeal, D. W., Stilwell-Morecraft, K. S., Gedney, M., Ge, J., Schroeder, C. M., et al. (2007). Amygdala interconnections with the cingulate motor cortex in the rhesus monkey. *Journal of Comparative Neurology, 500*(1), 134-165.

Navarro, A. D., & Fantino, E. (2005). The sunk cost effect in pigeons and humans. *Journal of the Experimental Analysis of Behavior, 83*(1), 1-13.

Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-back working memory paradigm: a meta-analysis of normative functional neuroimaging studies. *Human Brain Mapping, 25*(1), 46-59.

Padoa-Schioppa, C. (2009). Range-adapting representation of economic value in the orbitofrontal cortex. *Journal of Neuroscience, 29*(44), 14004-14014.

Padoa-Schioppa, C., & Assad, J. A. (2006). Neurons in the orbitofrontal cortex encode economic value. *Nature, 441*(7090), 223-226.

Padoa-Schioppa, C., & Assad, J. A. (2008). The representation of economic value in the orbitofrontal cortex is invariant for changes of menu. *Nature Neuroscience, 11*(1), 95-102.

Paus, T. (2001). Primate anterior cingulate cortex: where motor control, drive and cognition interface. *Nature Reviews Neuroscience, 2*(6), 417-424.

Pears, A., Parkinson, J. A., Hopewell, L., Everitt, B. J., & Roberts, A. C. (2003). Lesions of the orbitofrontal but not medial prefrontal cortex disrupt conditioned reinforcement in primates. *Journal of Neuroscience, 23*(35), 11189-11201.

Peters, J., & Buchel, C. (2009). Overlapping and distinct neural systems code for subjective value during intertemporal and risky decision making. *Journal of Neuroscience, 29*(50), 15727-15734.

Petrides, M., & Pandya, D. N. (2002). Comparative cytoarchitectonic analysis of the human and the macaque ventrolateral prefrontal cortex and corticocortical connection patterns in the monkey. *European Journal of Neuroscience, 16*(2), 291-310.

Picard, N., & Strick, P. L. (2001). Imaging the premotor areas. *Current Opinion in Neurobiology, 11*(6), 663-672.

Pochon, J. B., Levy, R., Fossati, P., Lehericy, S., Poline, J. B., Pillon, B., et al. (2002). The neural system that bridges reward and cognition in humans: an fMRI study. *Proceedings of the National Academy of Sciences, 99*(8), 5669-5674.

Pompilio, L., Kacelnik, A., & Behmer, S. T. (2006). State-dependent learned valuation drives choice in an invertebrate. *Science, 311*(5767), 1613-1615.

Preuss, T. M., & Goldman-Rakic, P. S. (1989). Connections of the ventral granular frontal cortex of macaques with perisylvian premotor and somatosensory areas: anatomical evidence for somatic representation in primate frontal association cortex. *Journal of Comparative Neurology, 282*(2), 293-316.

Procyk, E., & Joseph, J. P. (2001). Characterization of serial order encoding in the monkey anterior cingulate sulcus. *European Journal of Neuroscience, 14*(6), 1041-1046.

Procyk, E., Tanaka, Y. L., & Joseph, J. P. (2000). Anterior cingulate activity during routine and non-routine sequential behaviors in macaques. *Nature Neuroscience, 3*(5), 502-508.

Ramnani, N., & Miall, R. C. (2003). Instructed delay activity in the human prefrontal cortex is modulated by monetary reward expectation. *Cerebral Cortex, 13*(3), 318-327.

Ramnani, N., & Owen, A. M. (2004). Anterior prefrontal cortex: insights into function from anatomy and neuroimaging. *Nature Reviews Neuroscience, 5*(3), 184-194.

Rangel, A., Camerer, C., & Montague, P. R. (2008). A framework for studying the neurobiology of value-based decision making. *Nature Reviews Neuroscience, 9*(7), 545-556.

Ravel, S., & Richmond, B. J. (2006). Dopamine neuronal responses in monkeys performing visually cued reward schedules. *European Journal of Neuroscience, 24*(1), 277-290.

Ridderinkhof, K. R., Ullsperger, M., Crone, E. A., & Nieuwenhuis, S. (2004). The role of the medial frontal cortex in cognitive control. *Science, 306*(5695), 443-447.

Roesch, M. R., Calu, D. J., & Schoenbaum, G. (2007a). Dopamine neurons encode the better option in rats deciding between differently delayed or sized rewards. *Nature Neuroscience, 10*(12), 1615-1624.

Roesch, M. R., & Olson, C. R. (2007b). Neuronal activity related to anticipated reward in frontal cortex: does it represent value or reflect motivation? *Annals of the New York Academy of Sciences, 1121*, 431-446.

Roesch, M. R., & Olson, C. R. (2003). Impact of expected reward on neuronal activity in prefrontal cortex, frontal and supplementary eye fields and premotor cortex. *Journal of Neurophysiology, 90*(3), 1766-1789.

Roesch, M. R., & Olson, C. R. (2004). Neuronal activity related to reward value and motivation in primate frontal cortex. *Science, 304*(5668), 307-310.

Roesch, M. R., & Olson, C. R. (2005). Neuronal activity dependent on anticipated and elapsed delay in macaque prefrontal cortex, frontal and supplementary eye fields, and premotor cortex. *Journal of Neurophysiology, 94*(2), 1469-1497.

Rudebeck, P. H., Walton, M. E., Smyth, A. N., Bannerman, D. M., & Rushworth, M. F. (2006). Separate neural pathways process different decision costs. *Nature Neuroscience, 9*(9), 1161-1168.

Rushworth, M. F., Buckley, M. J., Behrens, T. E., Walton, M. E., & Bannerman, D. M. (2007). Functional organization of the medial frontal cortex. *Current Opinion in Neurobiology, 17*(2), 220-227.

Rushworth, M. F., & Behrens, T. E. (2008). Choice, uncertainty and value in prefrontal and cingulate cortex. *Nature Neuroscience, 11*(4), 389-397.

Rushworth, M. F., Walton, M. E., Kennerley, S. W., & Bannerman, D. M. (2004). Action sets and decisions in the medial frontal cortex. *Trends in Cognitive Sciences, 8*(9), 410-417.

Sakagami, M., & Niki, H. (1994). Encoding of behavioral significance of visual stimuli by primate prefrontal neurons: relation to relevant task conditions. *Experimental Brain Research, 97*(3), 423-436.

Schultz, W. (2004). Neural coding of basic reward terms of animal learning theory, game theory, microeconomics and behavioural ecology. *Current Opinion in Neurobiology, 14*(2), 139-147.

Schultz, W. (2010). Subjective neuronal coding of reward: temporal value discounting and risk. *European Journal of Neuroscience, 31*(12), 2124-2135.

Schultz, W., Preuschoff, K., Camerer, C., Hsu, M., Fiorillo, C. D., Tobler, P. N., et al. (2008). Explicit neural signals reflecting reward uncertainty. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences, 363*(1511), 3801-3811.

Seymour, B., & McClure, S. M. (2008). Anchors, scales and the relative coding of value in the brain. *Current Opinion in Neurobiology, 18*(2), 173-178.

Shallice, T. (1982). Specific impairments of planning. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences, 298*(1089), 199-209.

Shidara, M., Aigner, T. G., & Richmond, B. J. (1998). Neuronal signals in the monkey ventral striatum related to progress through a predictable series of trials. *Journal of Neuroscience, 18*(7), 2613-2625.

Shidara, M., & Richmond, B. J. (2002). Anterior cingulate: single neuronal signals related to degree of reward expectancy. *Science, 296*(5573), 1709-1711.

Shima, K., & Tanji, J. (1998). Role for cingulate motor area cells in voluntary movement selection based on reward. *Science, 282*(5392), 1335-1338.

Simmons, J. M., & Richmond, B. J. (2008). Dynamic changes in representations of preceding and upcoming reward in monkey orbitofrontal cortex. *Cerebral Cortex, 18*(1), 93-103.

Small, D. M., Gitelman, D., Simmons, K., Bloise, S. M., Parrish, T., & Mesulam, M. M. (2005). Monetary incentives enhance processing in brain regions mediating top-down control of attention. *Cerebral Cortex, 15*(12), 1855-1865.

Staw, B. M., & Hoang, H. (1995). Sunk costs in the NBA: Why draft order affects playing time and survival in professional basketball. *Administrative Science Quarterly,40,* 474–494.

Stelzel, C., Basten, U., Montag, C., Reuter, M., & Fiebach, C. J. (2009). Effects of dopamine-related gene-gene interactions on working memory component processes. *European Journal of Neuroscience, 29*(5), 1056-1063.

Stephens, D. W., & Krebs, J. R. (1986). *Foraging Theory*. Princeton: Princeton University Press.

Stevens, J. R., Rosati, A. G., Ross, K. R., & Hauser, M. D. (2005). Will travel for food: spatial discounting in two new world monkeys. *Current Biology, 15*(20), 1855-1860.

Strough, J., Mehta, C. M., McFall, J. P., & Schuller, K. L. (2008). Are older adults less subject to the sunk-cost fallacy than younger adults? *Psychological Science, 19*(7), 650-652.

Sugrue, L. P., Corrado, G. S., & Newsome, W. T. (2004). Matching behavior and the representation of value in the parietal cortex. *Science, 304*(5678), 1782-1787.

Sutton, R., & Barto, A. G. (Eds.). (1998). *Reinforcement learning: An introduction*. Cambridge: MA: MIT Press.

Tanaka, S. C., Doya, K., Okada, G., Ueda, K., Okamoto, Y., & Yamawaki, S. (2004). Prediction of immediate and future rewards differentially recruits cortico-basal ganglia loops. *Nature Neuroscience, 7*(8), 887-893.

Takada, M., Tokuno, H., Hamada, I., Inase, M., Ito, Y., Imanishi, M., et al. (2001). Organization of inputs from cingulate motor areas to basal ganglia in macaque monkey. *European Journal of Neuroscience, 14*(10), 1633-1650.

Teger, A. I. (1980). *Too much invested to quit.* New York: Pergamon.

Thaler, R. (1980). Toward a positive theory of consumer choice. *Journal of Economic Behavior and Organization, 1*, 39–60.

Tobler, P. N., Christopoulos, G. I., O'Doherty, J. P., Dolan, R. J., & Schultz, W. (2009). Risk-dependent reward value signal in human prefrontal cortex. *Proceedings of the National Academy of Sciences, 106*(17), 7185-7190.

Tremblay, L., & Schultz, W. (1999). Relative reward preference in primate orbitofrontal cortex. *Nature, 398*(6729), 704-708.

Tremblay, L., & Schultz, W. (2000). Reward-related neuronal activity during go-nogo task performance in primate orbitofrontal cortex. *Journal of Neurophysiology, 83*(4), 1864-1876.

Tversky, A., & Kahneman, D. (1992). Advances in Prospect Theory: Cumulative Representation of Uncertainty. *Journal of Risk and Uncertainty, 5*, 297-323.

Ungerleider, L. G., Gaffan, D., & Pelak, V. S. (1989). Projections from inferior temporal cortex to prefrontal cortex via the uncinate fascicle in rhesus monkeys. *Experimental Brain Research, 76*(3), 473-484.

Ursu, S., & Carter, C. S. (2005). Outcome representations, counterfactual comparisons and the human orbitofrontal cortex: implications for neuroimaging studies of decision-making. *Brain Res Cognitive Brain Research, 23*(1), 51-60.

Van Hoesen, G. W., Morecraft, R. J., & Vogt, B.A. (1993) Connections of the monkey cingulate cortex. In B. A. Vogt & M. Gabriel (Eds.), *Neurobiology of cingulate cortex and limbic thalamus*. Boston: Birkhauser.

Waelti, P., Dickinson, A., & Schultz, W. (2001). Dopamine responses comply with basic assumptions of formal learning theory. *Nature, 412*(6842), 43-48.

Wager, T. D., Jonides, J., & Reading, S. (2004). Neuroimaging studies of shifting attention: a meta-analysis. *NeuroImage, 22*(4), 1679-1693.

Wallis, J. D., Anderson, K. C., & Miller, E. K. (2001). Single neurons in prefrontal cortex encode abstract rules. *Nature, 411*(6840), 953-956.

Walton, M. E., Kennerley, S. W., Bannerman, D. M., Phillips, P. E., & Rushworth, M. F. (2006). Weighing up the benefits of work: behavioral and neural analyses of effort-related decision making. *Neural Networks, 19*(8), 1302-1314.

Ward, B. D. (2000). Simultaneous inference for fMRI data. From http://afni.nimh.nih.gov/pub/dist/doc/manual/AlphaSim.pdf.

Watanabe, M., & Sakagami, M. (2007). Integration of cognitive and motivational context information in the primate prefrontal cortex. *Cerebral Cortex, 17 Suppl 1*, i101-109.

White, I. M., & Wise, S. P. (1999). Rule-dependent neuronal activity in the prefrontal cortex. *Experimental Brain Research, 126*(3), 315-335.

Lebenslauf

Persönliche Informationen

Name	Ruth Schmitt
Geburtsdatum	05.04.1980
Geburtsort	Miltenberg, Bayern

Berufliche Erfahrung

02/2007 – 09/2010	**Universität Heidelberg**, Doktorandin in der Arbeitsgruppe „Kognitive Neurowissenschaften“ von Prof. Dr. C. Fiebach ▪ Thema der Doktorarbeit: The Role of Goal Proximity and Invested Effort for the Valuation of Expected Outcomes
seit 01/2011	**Psychiatrische Klinik, Universität Heidelberg**, wissenschaftliche Mitarbeiterin

Hochschulbildung

04/2003 – 01/2007	**Universität Leipzig**, Hauptstudium Psychologie Diplom ▪ Thema der Diplomarbeit: Neuronale Korrelate des Handlungsverständnisses
10/2000 – 03/2003	**Philipps-Universität Marburg**, Grundstudium Psychologie Vordiplom

Schulbildung

1990 – 1999	**Johannes Butzbach Gymnasium Miltenberg** Abitur

Berufliche Weiterbildung

01/2008 – 12/2010	**Internationale Gesellschaft für systemische Therapie e.V. (IGST)** 3-jährige Weiterbildung in systemischer Therapie und Beratung

Praktische Erfahrungen

04/2009 - 04/2010	**Universität Heidelberg** Teilnahme am Seminar „Coaching von Studierenden für Studierende“
07/ 2004 – 10/ 2004	**Tagesklinik für kognitive Neurologie, Universität Leipzig** Praktikum
07/2003 – 12/2006	**Max-Planck-Institut für Kognitions- und Neurowissenschaften, Leipzig** studentische Hilfskraft

Lehrerfahrung

10/2008 - 02/2009	**Universität Heidelberg** Seminar „Neuronale Grundlagen zielgerichteten Verhaltens“

Publikationen

Brass, M., **Schmitt, R.M.**, Spengler, S., & Gergely, G. (2007). Investigating action understanding: inferential processes versus action simulation. *Current Biology 17 (24*): 2117-21.

Schmitt, R.M., Gäbel A., & Fiebach, C.J. (under revision) Human Rostral Cingulate Zone codes goal proximity and invested effort in action sequences.

Poster

Brass, M., **Schmitt, R.M.**, Spengler, S., & Gergely, G. (2007, May). Understanding action understanding. Poster session at the 14th annual meeting of the Cognitive Neuroscience Society, San Francisco, USA.

Schmitt, R.M., Gäbel A., & Fiebach, C.J. (2009, March). Neuronal representation of goal proximity in a multitrial reward schedule. Poster session at the 16th annual meeting of the Cognitive Neuroscience Society, San Francisco, USA.

Schmitt, R.M., Gäbel A., & Fiebach, C.J. (2009, March). Die neuronale Repräsentation der Zielnähe. Poster session at the 51th Tagung experimentell arbeitender Pschologen, Jena, Germany.

Heidelberg, im Februar 2011