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Neural Foundations of Risk Processing and Decision Making under Risk in Young Adulthood and Old Age

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Eidesstattliche Erklärung

Hiermit erkläre ich an Eides statt,

- dass ich die vorliegende Arbeit selbstständig und ohne unerlaubte Hilfe verfasst habe,
- dass ich mich nicht bereits anderwärts um einen Doktorgrad beworben habe und keinen Doktorgrad in dem Promotionsfach Psychologie besitze und
- dass ich die zugrunde liegende Promotionsordnung vom 02.12.2008 kenne.

Berlin, 02.07.2010 Peter N.C. Mohr

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Zusammenfassung

In vielen Situationen des Alltags, wie beispielsweise bei der Wahl einer privaten Altersvorsorge, müssen Entscheidungen unter Risiko getroffen werden. Diese können, wie im Falle von Altersvorsorgeentscheidungen, die den Lebensstandard im Alter beeinflussen, weitreichende Konsequenzen für das weitere Leben haben. Zum heutigen Zeitpunkt ist allerdings weitestgehend unklar wie Menschen Risiko verarbeiten und wie sie Entscheidungen unter Risiko treffen. Das Ziel der vorliegenden Arbeit war es daher, die Mechanismen von Risikoverarbeitung und Entscheidungen unter Risiko näher zu untersuchen. Hierzu wurde zunächst eine Meta-Analyse von fMRT-Studien zur Risikoverarbeitung (Projekt I) durchgeführt. Ziel der Studie war es herauszufinden, wie die neurale Verarbeitung von Risiko durch Emotionen, potentielle Verluste und Kontext beeinflusst wird. Die gefundenen Aktivationen in der anterioren Insula, einer Hirnregion, die mit der Verarbeitung aversiver Emotionen wie Furcht, Enttäuschung oder Bedauern assoziiert wird, deuten darauf hin, dass Risikoverarbeitung von Emotionen beeinflusst wird. Die anteriore Insula war allerdings vorwiegend aktiv, wenn Verluste möglich waren. Dies deutet darauf hin, dass Verluste einen Einfluss auf die Art der Risikoverarbeitung haben. Weiterhin waren der dorsolaterale präfrontale Kortex und der parietale Kortex nur im Kontext von in Entscheidungssituationen aktiv, nicht aber in Situationen, in denen keine Entscheidung zu treffen war, was nahe legt, dass Risikoverarbeitung kontextabhängig ist.

In den meisten Entscheidungen unter Risiko, wie beispielweise beim Roulette, sind alle möglichen Konsequenzen und zugehörigen Wahrscheinlichkeiten bekannt. Bei Anlageentscheidungen unterliegen die möglichen Renditen von Wertpapieren allerdings in der Regel stetigen Verteilungen. Es ist daher nahezu unmöglich alle möglichen Renditen und Wahrscheinlichkeiten in die Bewertung des Wertpapiers einzubeziehen. Unklar ist daher wie Menschen Anlageentscheidungen treffen. Die Ergebnisse aus Projekt II zeigen, dass Risiko-Gewinn Modelle Entscheidungen auf Verhaltensebene gut erklären können und dass die Komponenten dieser Modelle (Wert, Risiko und Risikoeinstellung) während einer Entscheidung im Gehirn repräsentiert werden. Insbesondere die Repräsentation des Risikos in der anterioren Insula spricht eher für Risiko-Gewinn Modelle als für nutzenbasierte Modelle, da Risiko eine explizite Komponente von Risiko-Gewinn Modellen, nicht aber von nutzenbasierten Modellen ist.

In Projekt III werden mithilfe einer Literaturanalyse das dopaminerge und das serotoninerge Hirnsystem als wichtige Neurotransmittersysteme im Kontext ökonomischer Entscheidungen identifiziert. Beide sind bekannt dafür, sich im Verlauf der Lebensspanne Veränderungen zu unterziehen. Ebenso ändert sich das ökonomische Verhalten während der Lebenszeit. Zusammengenommen deuten diese Erkenntnisse auf einen triadischen Zusammenhang zwischen (a) ökonomischen Entscheidungen, (b) dopaminerger und serotoninerger Neuromodulation und (c) Altern hin.

Summary

In our everyday life we often have to make decisions with uncertain consequences, for instance in the context of retirement savings. Although these decisions can have important consequences (i.e., they can have an effect on our living standard in old age) it is still not fully understood how individuals process risk and how they make decisions under risk. In the context of this dissertation I have investigated three main questions all related to the topic risky decision making, namely (a) how neural processing of risk is influenced by emotions, context, and potential losses, (b) how individuals value choice options with continuous outcome distributions, and (c) how age-related changes in economic decision making are related to neurobiological changes during the adult life span.

By showing in Project I that risk is consistently represented in the anterior insula, a brain region known to process aversive emotions like anxiety, disappointment, or regret, I provide evidence that risk processing is influenced by emotions. Further, the results show risk-related activity in the dorsolateral prefrontal cortex and the parietal cortex in choice situations but not in situations were no choice is involved or a choice has already been made. The anterior insula was predominantly active in the presence of potential losses, indicating that potential losses modulate risk processing. The results thus provide evidence that neural processing of risk is influenced by emotions, context, and potential losses.

In Project II I can show that risk-return models can explain choices behaviorally and that the components of risk-return models (value, risk, and risk attitude) are represented in the brain during choices. Most importantly, the observed correlation between risk and brain activity in the anterior insula during choices supports risk-return models more than utility-based models in the case of continuous outcome distributions because risk is an explicit component of risk-return models but not of the utility-based models.

In Project III I identify the dopaminergic and serotoninergic brain systems as key neurotransmitter systems involved in economic behavior. Both are known to be prone to significant changes during the adult life span. Similarly, economic behavior undergoes significant age-related changes over the course of the adult life span. Consequently, I propose a triadic relationship between (a) economic decision making, (b) dopaminergic and serotoninergic neuromodulation, and (c) aging.

List of original publications

This dissertation is based on the following original research articles:

Project I

Mohr, P. N., Biele, G., & Heekeren, H. R. (2010). Neural processing of risk. *J Neurosci, 30*(19), 6613-6619, DOI: 10.1523/JNEUROSCI.0003-10.2010.

Project II

Mohr, P. N. C., Biele, G., Krugel, L. K., Li, S. C., & Heekeren, H. R. (2010). Neural foundations of risk-return trade-off in investment decisions. *Neuroimage, 49*(3), 2556-2563, DOI: 10.1016/j.neuroimage.2009.10.060.

Project III

Mohr, P. N., Li, S. C., & Heekeren, H. R. (2010). Neuroeconomics and aging: neuromodulation of economic decision making in old age. *Neurosci Biobehav Rev, 34*(5), 678-688, DOI: 10.1016/j.neubiorev.2009.05.010.

List of abbreviations

aINS	Anterior Insula
ALE	Activation Likelihood Estimation
BOLD	Blood Oxygen Level Dependent
CRUNCH	Compensation-Related Utilization of Neural Circuits Hypothesis
DLPFC	Dorsolateral Prefrontal Cortex
DMPFC	Dorsomedial Prefrontal Cortex
EUT	Expected Utility Theory
EV	Expected Value
EVT	Expected Value Theory
FDR	False Discovery Rate
fMRI	Functional Magnetic Resonance Imaging
IGT	Iowa Gambling Task
lOFC	Lateral Orbitofrontal Cortex
MNI	Montreal Neurological Institute
mOFC	Medial Orbitofrontal Cortex
MPFC	Medial Prefrontal Cortex
MRI	Magnetic Resonance Imaging
MVM	Mean-Variance Model
NACC	Nucleus Accumbens
PCC	Posterior Cingulate Cortex
PET	Positron Emission Tomography
PR	Perceived Risk
PRRM	Psychological Risk-Return Model
PT	Prospect Theory
RPID	Risk Perception and Investment Decision
rTMS	Repetitive Transcranial Magnetic Stimulation
SD	Standard Deviation
SER	Subjective Expected Return
SMH	Somatic Marker Hypothesis
SPECT	Single Photon Emission Computed Tomography
SV	Subjective Value

VLPFC	Ventrolateral Prefrontal Cortex
VMPFC	Ventromedial Prefrontal Cortex
VST	Ventral Striatum

1. Introduction

In our everyday life we often have to make decisions with uncertain consequences. Choosing a job, a partner to marry, or a form of private retirement saving are prominent examples of decisions with uncertain consequences. Such decisions are usually referred to as decisions under risk by decision scientists. Especially retirement saving decisions have become more and more important in Germany over the last years. Due to demographic changes the public pension system is no longer able to ensure the living standard for older adults. Therefore everybody is recommended to invest in private retirement plans. Although we have to make decisions under risk throughout our everyday life and although these decisions can have important consequences (e.g., they can affect the living standard in old age) it is still not fully understood how individuals process risk and how they make decisions under risk. It further remains unclear how risk processing and decision making under risk might change across the lifespan, influencing especially retirement saving decisions that individuals have to make throughout the entire adult lifespan.

Traditional research in risk processing and decision making under risk focused on observable choice behavior neglecting the underlying processes. Technological and conceptual advancements in the last two decades offered new methods to investigate these underlying processes. Especially, the advancement of functional magnetic resonance imaging (fMRI) offered a new tool that contributed significantly to the understanding of human cognition. The new field of neuroeconomics uses neuroscientific methods and psychological concepts to investigate the underlying processes of economically relevant behavior, including risk processing and decision making under risk. The aim of this dissertation is to close some of the gaps in research on risk processing and decision making under risk and to advance knowledge in these domains by following the neuroeconomics approach.

This dissertation is organized as follows. In chapter 2 the theoretical background of risk processing and decision making under risk will be discussed. Here, I will introduce some concepts of risk, models of decision making under risk and behavioral findings regarding age-related changes in economic decision making. I will further describe the current knowledge regarding the neural foundations of risk processing and decision making under risk as well as age-related changes in the neuromodulation of dopamine and serotonin. Based on this theoretical background and the current state of the art I will formulate the research questions that should be targeted in this dissertation in chapter 3. In chapter 4, I

will then describe the methods that I used to answer these questions, followed by brief summaries of the results of the different projects I conducted. Finally, I will discuss the results of the different projects and integrate them into a novel neural model of risky decision making in chapter 6. Chapter 7 concludes by summing up the main findings of this dissertation.

2. Theoretical and empirical foundations

2.1. Risk

2.1.1. Concepts of risk

Risk is a concept that is defined differently in different scientific disciplines. Most of these disciplines define risk in relation to an unwanted or hazardous outcome. In engineering, for example, risk is usually defined as the probability of an accident times the losses per accident. In decision theory, however, risk is usually defined as a form of uncertainty. But even in decision sciences risk is often not clearly defined and used ambiguously. Basically, there are three forms of risk in decision sciences that are distinguishable though they are highly related to each other: (a) *risk as a state*, (b) *risk as variance*, and (c) *perceived risk*.

In an early approach, economics distinguished three states in which a gamble can occur: (a) certainty, (b) risk, and (c) ambiguity (Camerer & Weber, 1992; Ellsberg, 1961; Knight, 1921). These states can be characterized by two dimensions. The outcome(s) of a gamble can be either certain or uncertain and the probabilities in which specific outcomes occur can also be either certain or uncertain. The first dimension specifies whether outcomes are probabilistic or certain. The second dimension determines whether the probabilities (e.g., 100% in the case of certain outcomes) are known or unknown. The first dimension is object-related whereas the second one is subject-related. Certainty is defined by a certain (non-probabilistic) outcome that is also known to be certain (i.e., to have a probability of 100%). Risk refers to a probabilistic outcome of which the probabilities associated with the different possible outcomes are known. Ambiguity reflects all cases in which probabilities are unknown, independent of whether the outcomes are certain or probabilistic. In this approach risk is defined as a state which is either present or not. It has, however, no dimension and thus cannot be high or low.

The definition of *risk as variance* has overcome this shortcoming. Here, risk was defined from a slightly different perspective. It was no longer defined as a state, but as a metric that can be measured or computed (Markowitz, 1952). The variance of possible outcomes (or the standard deviation as the square root of the variance) was chosen as a metric for risk as it reflects the spread of the outcome distribution around its mean. The logic behind this approach is that a lower variance increases the certainty that the outcome of a gamble will be close to the mean and thus decreases the uncertainty regarding the outcome. The definition of *risk as variance* is, however, only object-related. Following this definition it

makes no difference whether probabilities and/or outcomes are known to a potential decision maker. The gamble either contains a specific amount of risk or not (the special case when the variance is equal to zero).

Psychology, in contrast, took a different route and defined risk as a purely subjective construct. *Risk perception* is thus only determined by the individual's subjective perception (Weber & Milliman, 1997). This perception is affected by a variety of different factors. One line of research focused on systematic object-related influences on *risk perception*. *Perceived risk* usually increases with variance (standard deviation) (Keller, Sarin, & Weber, 1986). Most individuals, however, care more about downside variability (i.e., outcomes that are worse than the average) than upside variability. Oftentimes, individuals do not consider upside variability risky at all, even though there might be uncertainty involved (Weber, Anderson, & Birnbaum, 1992). Similarly, *perceived risk* usually increases with increasing probability of a loss and increasing expected loss (expected value of possible losses). Furthermore, *perceived risk* usually decreases if a constant positive amount is added to all outcomes (i.e., the mean outcome increases). In line with this observation is the coefficient of variation (standard deviation divided by the mean) better able to predict choices in humans and animals than the standard deviation (Weber, Shafir, & Blais, 2004). Finally, skewed outcome distributions are usually perceived as more risky than corresponding symmetric gambles with equal mean and variance (Keller, et al., 1986).

Although most of these object-related factors are highly related to each other, there are huge inter-individual differences in the strength of the specific influences. This is due to the fact that risk is at least partly a learned concept. The *risk perception* of an investment broker who has learned the concept of *risk as variance* will likely be more closely related to the variance than the *risk perception* of an insurance broker who usually focuses more on potential losses. Similarly, *risk perception* also has a cultural component, indicated by significant cross-cultural differences in *risk perceptions* between the USA, Germany, Poland, and China (Weber & Hsee, 1998). But *risk perception* does not only differ between individuals. Even within individuals *risk perception* changes depending on prior experiences (e.g., winning or losing) (Weber & Milliman, 1997), depends on the time horizon (Klos, Weber, & Weber, 2005), and differs with the framing of the risky object. *Risk perceptions* of investments, for example, are significantly different when presented either as bar charts of past returns or as continuous distributions of possible returns (e.g., inferred from past returns) (Weber, Siebenmorgen, & Weber, 2005).

Another important inter-individual difference in *risk perception* is domain specificity (Blais & Weber, 2006; Weber, Blais, & Betz, 2002; Weber & Milliman, 1997). The way an individual perceives risk in the financial domain is usually not related to her concept of risk in the health domain. This finding could (at least) be partly explained by another line of research that investigates the psychological dimensions of *risk perceptions*. It turned out that *risk perceptions* of various hazards are related to dread and controllability, qualitative experiences associated with risk that are not captured by probabilities and magnitudes of outcomes (Fischhoff, Watson, & Hope, 1984; Slovic, Fischhoff, & Lichtenstein, 2000). Recently the importance of the dread dimension was replicated for *risk perception* in the financial domain (Holtgrave & Weber, 1993). Different domains could, thus, differ in the importance of these two dimensions resulting in different *risk perceptions*.

But most importantly, these findings indicate that emotions might play an important role in *risk perceptions* and that one needs both cognitive and affective components to fully capture individuals' *risk perception* (Loewenstein, Weber, Hsee, & Welch, 2001; Slovic, Finucane, Peters, & MacGregor, 2004; Slovic, Peters, Finucane, & Macgregor, 2005). Emotions are, however, hard to investigate with self-report measures, as these are highly dependent on the introspective abilities of individuals. It thus remains unclear if emotions are indeed implicated in risk processing and how they influence *risk perceptions*.

2.1.2. Neural representations of risk

Risk has frequently been investigated with neuroscientific methods (e.g., fMRI in humans and single cell recording studies in monkeys). Although only few studies defined risk explicitly, two lines of research can be distinguished. The first line implicitly uses the definition of *risk as a state,* whereas the other line of research implicitly builds on the assumption that risk is a metric, and is thereby more in line with the definitions of *risk as variance* and *risk perception*.

Due to the implicit definition of *risk as a state*, the first line of research compares risky situations with safe situations (e.g., risky choices vs. safe choices). A typical task used to compare risky with safe situations is the Risky-Gains Task (Paulus, Rogalsky, Simmons, Feinstein, & Stein, 2003). In this task, subjects are presented with three numbers in ascending order (20, 40, and 80). Each number is presented on the screen. The subjects are informed that 20 represents a safe outcome, whereas for both 40 and 80 points there is a chance that a 40 or an 80 in red color may appear which signals that the subject loses 40 or

80 points. Subjects further knew the probabilities in which a red 40 or 80 appears, which was set such that the expected value of all gambles was equal (20 points). By comparing risky (waiting for the 40 or 80 points option) and safe choices (taking the safe 20 points) it is possible to identify brain regions that are active in the presence of risk.

Studies that compared risky with safe situations identified a wide network of brain regions implicated in processing risky situations. These included the anterior insula (aINS), the ventral striatum (VST), the medial prefrontal cortex (MPFC), and the dorsolateral prefrontal cortex (DLPFC) (Hsu, Bhatt, Adolphs, Tranel, & Camerer, 2005; Matthews, Simmons, Lane, & Paulus, 2004; Paulus, et al., 2001; Paulus, et al., 2003; Tobler, O'Doherty, Dolan, & Schultz, 2007; Weber & Huettel, 2008).

The other line of research investigates which brain regions code for the degree of riskiness of a situation thereby building on the definitions of *risk as a metric (risk as variance* or *perceived risk)*. The studies that followed this approach either compared high risk with low risk situations or correlated brain activity with the degree of riskiness. A typical task that allows to correlate brain activity with the degree of riskiness is the Card Gambling Task (Preuschoff, Bossaerts, & Quartz, 2006). On each trial of this task two cards are drawn (without replacement within each trial) from a deck of ten cards, numbered from 1 to 10. Before seeing either card subjects have to place a bet (usually 1$) on one of the two options, “second card higher” or “second card lower” (than first card shown). Subjects can earn the amount betted if they guessed right and lose it if they were wrong. The number on the first card determines the probabilities for winning and losing the bet, which can be used to compute the risk of the respective situation (in this case the variance of possible outcomes). By comparing high risk with low risk situations or correlating brain activity with risk, it is possible to identify brain regions in which brain activity co-varies with risk. Not all studies, however, specified *risk as variance* but used metrics (e.g., increasing reward probability for $p<0.5$) that are usually highly correlated with the variance (e.g., Huettel, Song, & McCarthy, 2005).

Studies that followed this approach identified several brain regions as sensitive to the present degree of riskiness. These included the aINS, the VST, the midbrain, the MPFC, and the DLPFC (Behrens, Woolrich, Walton, & Rushworth, 2007; Critchley, Mathias, & Dolan, 2001; Huettel, 2006; Huettel, et al., 2005; Kuhnen & Knutson, 2005; Preuschoff, et al., 2006; Preuschoff, Quartz, & Bossaerts, 2008; Rolls, McCabe, & Redoute, 2008; Volz, Schubotz, & von Cramon, 2003, 2004; Yoshida & Ishii, 2006).

The results of both lines of research are highly consistent with each other, as they revealed similar networks of brain regions coding for risk either defined as a state or a metric. A comparison between a situation with a certain outcome and a situation with a probabilistic outcome is, however, not sufficient to distinguish between the definition of *risk as a state* and definitions of *risk as a metric*. The probabilistic situation is not only risky following the risk as state definition (and therefore differs from the certain situation) but is also more risky than the certain situation following the risk as metrics definition. The results of the first line of research thus provide no evidence in favor of the definition of *risk as a state* over the definitions of *risk as a metric*. But as the results of the second line of research may distinguish between the two (classes of) definitions and indicate that the aINS, the VST, the MPFC, and the DLPFC co-vary with risk following the *risk as a metric* definitions, it is likely that they code for a risk metric. Nevertheless, there might also be brain regions that code the pure presence of uncertainty in the sense of *risk as a state*.

Risk processing can also be differentiated further. It can be performed during or before choice (decision risk) and after or without a choice (anticipation risk). The crucial difference between the two is that the risk information is likely used to guide behavior in the context of decision risk but not in the context of anticipation risk. To date, however, little is known if risk is processed differently during decisions compared with pure outcome anticipation.

2.2. Decision making under risk

2.2.1. Models of decision making under risk

Individuals are not only exposed to situations with uncertain outcomes, but also they often have to make decisions regarding choice alternatives which outcomes are (at least partly) uncertain. These types of decisions are often referred to as decisions under risk based on the definition of *risk as a state*.

During the 17th century classical economics started out with a very simple but elegant model of risky decision making. The *Expected Value Theory (EVT)* assumes that individuals make risky decisions on the basis of the objective expected value of a gamble X.

$$EV(X) = \sum_{x} p(x) \cdot x \qquad (1)$$

Individuals are thought to always choose the alternative that offers a higher expected value. *EVT* formed the basis for most modern models of risky decision making and influenced models in several other domains. Modern reinforcement learning models for example still assume that decisions are based on expected values and describe how these could be learned from past outcomes (Sutton & Barto, 1981). *EVT*, however, has two important shortcomings, namely (a) that it does not allow for inter-individual differences, and (b) that it fails to predict a number of observable choice patterns, including the so-called St. Petersburg Game, where individuals are only willing to pay a small price for the privilege of playing a game with a highly skewed payoff distribution that has an infinite expected value. It turned out that both shortcomings are related to risk (either defined as a state or as a metric) and individuals' attitudes towards risk.

	Utility-based Models	**Risk-Return Models**
Normative Economic Models	***Expected Utility Theory***	***Mean-Variance Model***
Descriptive Psychological Models	***Prospect Theory***	***Psychological Risk-Return Model***

Fig. 1. *Classification of different models of decision making under risk.*

Modern models of decision making under risk therefore implemented individuals' reactions to risk. These models can be characterized by two dimensions: (a) the way they incorporate the influence of risk, and (b) their origin and scientific orientation (cf. **Fig. 1**). The way these models incorporate risk is highly dependent on the underlying definition of risk (see chapter 2.1.1). Utility-based models implicitly use the *risk as a state* definition

and incorporate risk indirectly by assuming that outcomes and/or probabilities are non-linearly transformed, whereas risk-return models use definitions of *risk as a metric* (*risk as variance* or *perceived risk*) and assume that risk directly linearly influences the overall subjective value of a choice option. The normative economic models have their origins in economics/finance and describe optimal behavior under certain circumstances. Descriptive psychological models, in contrast, aim to describe actual choice behavior without any normative constraints and take psychological factors and limitations into account.

Expected Utility Theory (EUT) proposes that individuals do not maximize their *expected value*, but behave *as if* they would maximize their *expected utility* (von Neumann & Morgenstern, 1953).

$$EU(X) = \sum_{x} p(x) \cdot u(x) \qquad (2)$$

Utility in this case was defined as a function of objective wealth states. Individuals are assumed to have hidden preferences for wealth states that can be described by the utility function. *EUT*, however, remains agnostic regarding the actual decision-making process. It only claims that preferences can be described by expected utility, but not that individuals in fact maximize this metric during the decision making process.

Importantly, it can be shown analytically that the existence of a certain utility function is formally equivalent with following a small set of axioms related to the rationality of an individual. This axiomatic foundation gave *EUT* its character as a normative model of decision making under risk.

As a utility-based model of decision making under risk, *EUT* does not directly model the influence of risk on decisions. This influence is modeled through the curvature of the utility function. For concave utility functions the *expected utility* of a risky gamble is always lower than the *expected utility* of a certain outcome with the same *expected value.* In this case individuals are characterized as *risk averse* (cf. **Fig. 2**). In convex utility functions this relation is reversed, resulting in higher expected utilities for risky gambles. Thus, individuals with convex utility functions are characterized as *risk seeking*. In the case of linear utility functions, where preferences are equivalent to *EVT*, individuals are described as *risk neutral*.

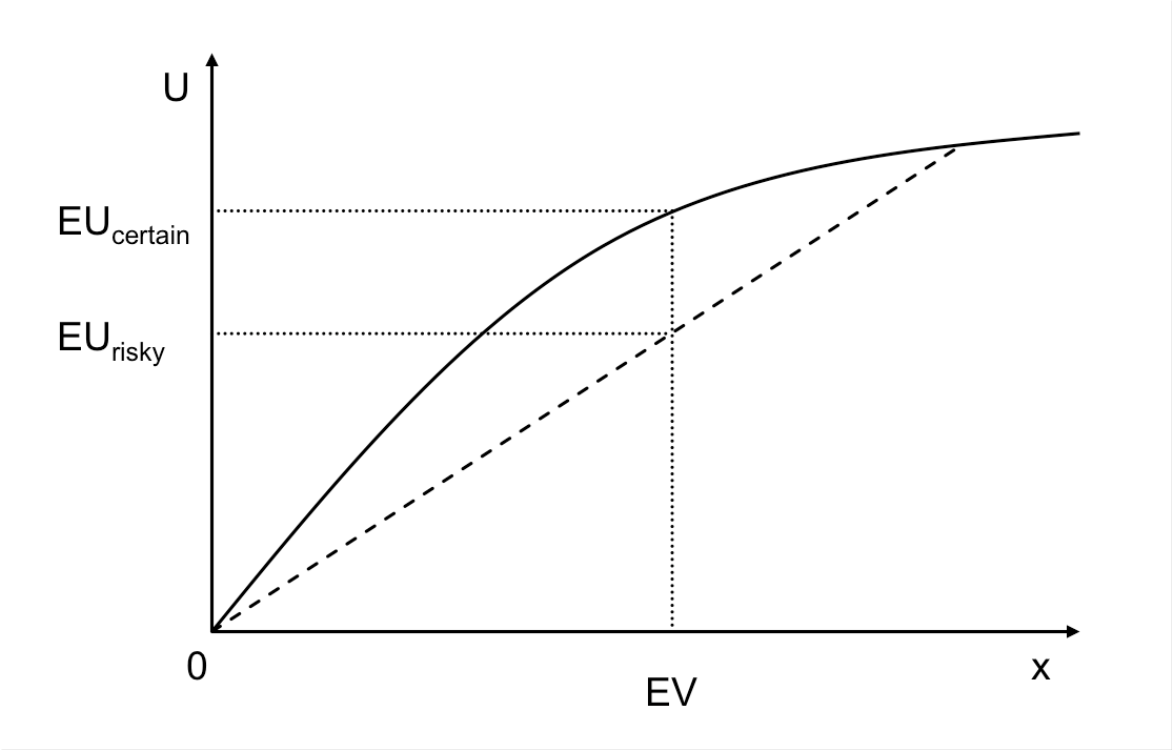

Figure 2. *Relationship between curvature of the utility function and risk attitude*. In the case of concave utility functions (solid line), the expected utility (EU) of a risky choice alternative (dashed line) is always lower than the utility function itself. As the EU of a certain choice alternative lies on the utility function, it is always higher than the EU of a risky choice alternative that offers the same expected value (EV). Individuals with concave utility functions can thus be characterized as risk averse. For convex utility functions this relation is reversed. Consequently, individuals with convex utility functions are characterized as risk seeking.

In parallel to the development of modern *EUT,* finance scholars proposed another normative economic model of decision making under risk: The *Mean-Variance Model (MVM;* also called *normative Risk-Return Model)* is based on the idea of a *risk premium* (Markowitz, 1952). To be equally attractive, a risky choice option has to offer a higher expected value compared to a safe choice option.

$$SV(X) = EV(x) - b \cdot SD(x) \qquad (3)$$

The *MVM* proposes that the subjective value (SV) of a choice option is determined by the expected value of possible outcomes (EV) minus its standard deviation (SD) (or variance) linearly weighted with a factor b. This factor represents the risk attitude in the *MVM* and determines the *risk premium.* If b is positive, risk (measured as the SD) reduces the SV of a choice option and the individual is characterized as *risk averse*. Similarly, individuals can be described as *risk neutral* if b is equal to zero (reducing the *MVM* to *EVT*) and as *risk seeking* if b is negative.

The *MVM* is highly related to *EUT* and therefore is also regarded as a normative model of decision making under risk. For the special case of quadratic utility functions it can be shown analytically that the expected utility of a choice option can be re-described in the form of the *MVM* (see **Appendix**). Furthermore, utility functions can be approximated by means of a second-order Taylor series expansion, that is the sum of an infinite number of statistical moments (e.g., expected value, variance, skewness, etc.) of the utility function (d'Acremont & Bossaerts, 2008). Taking the first two statistical moments (expected value and variance) results in a formulation of expected utility that is similar to the *MVM.*

As both, *EUT* and the *MVM*, are normative economic models of decision making under risk they have proven very useful in economics, where predictions often have to be made on an aggregate macroeconomic level, but they have failed to accurately describe the full range of individual behaviors. Psychologists showed that the rationality axioms on which *EUT* (and also the *MVM,* as a special case of *EUT)* was built are frequently violated even in decisions between simple gambles (Allais, 1953; Ellsberg, 1961). For example, Allais (1953) showed that individuals are often risk averse with regard to gains, but risk seeking when faced with potential losses.

On the basis of these findings psychologists further developed *EUT* and the *MVM,* thereby taking a descriptive rather than a normative route. *Prospect Theory (PT)* took basically the same utility-based approach as *EUT* but revised it in three substantial parts (Kahneman & Tversky, 1979; Tversky & Kahneman, 1992). First, *PT* proposes that the choice option is edited before it is evaluated. Important editing steps are, for example, the simplification of the choice options in the sense that probabilities and/or outcome magnitudes are rounded and the elimination of dominated choice options. Second, *PT* proposes to transform not only outcome magnitudes but also probabilities.

$$SV(X) = \sum_{x} w(p(x)) \cdot v(x) \qquad (4)$$

The subjective value of a choice option in *PT* is determined by the weighted sum of transformed outcomes. The weights in this case are determined by a function of (cumulative) probabilities. Third, *PT* proposes that outcome magnitudes are not transformed on the basis of the resulting wealth levels (as in *EUT*), but on the basis of deviations from a reference point. This reference point is not formally described, as it is assumed to be influenced by the specific object, individual, and context in which the decision should be made. *PT* further assumes that the value function of individuals (which is equivalent to the utility function in *EUT*) is concave in the gain domain (in relation to the reference point) and convex but steeper in the loss domain. This reflects the behaviorally observed tendency of individuals to be risk averse regarding gains and risk seeking regarding losses as well as the general tendency of individuals to be loss averse (Kahneman & Tversky, 1979).

The *psychological Risk-Return Model (PRRM)* took a different route to account for these phenomena (Weber & Johnson, 2009). It generalized the intuitively appealing idea of the *MVM* to trade off risk and return, reflecting positive and negative characteristics of the choice options. Based on findings that risk is often perceived differently from the variance (see chapter 2.1.1), the *PRRM* defines risk and return as subject-related variables.

$$SV(X) = SER(x) - b \cdot PR(x) \qquad (5)$$

In the *PRRM* the SV of a choice option is defined by the difference between subjective expected return (SER) and weighted perceived risk (PR). Similarly to the *MVM* the trade-off factor b reflects the risk attitude of the individual (in this case perceived risk attitude). Whereas observed risk attitudes are highly dependent on individual and contextual factors in *EUT*, *PT*, and the *MVM*, perceived risk attitudes are constant within individuals for certain choice domains (Weber, et al., 2002; Weber & Milliman, 1997).

2.2.2. Neural basis of decision making under risk

Decision making under risk is usually seen as a type of value-based decision making (but see (Brandstatter, Gigerenzer, & Hertwig, 2006), where the values of different actions are first compared, and the action selected is the one that corresponds to the highest value. All models presented in chapter 2.2.1 of this dissertation follow this approach. But as value predictions of all presented models are usually highly correlated with each other, to date, no study explicitly related predicted values to brain activity.

Some studies, however, investigated the neural correlates of value in situations in which no risk was involved (e.g., intertemporal decision making and consumer choices). One study investigated the value of monetary rewards during intertemporal choice (Kable & Glimcher, 2007). In this study, the subjective value of delayed monetary rewards was modeled with a hyperbolic function and was significantly correlated with the blood oxygen level dependent (BOLD) response in the ventromedial prefrontal cortex (VMPFC), posterior cingulate cortex (PCC), and VST. Another study investigated the value of food products in a consumer choice paradigm (Plassmann, O'Doherty, & Rangel, 2007). Determined by the willingness-to-pay, the subjective value of the food products correlated with the BOLD signal in the medial orbitofrontal cortex (mOFC) and the DLPFC. These results were supported by a study using a similar consumer choice paradigm that found representations of value in mOFC and VMPFC (Hare, O'Doherty, Camerer, Schultz, & Rangel, 2008). Thus, although these studies did not investigate the value of risky choice alternatives they indicate that value is represented in mOFC, VMPFC, DLPFC, and VST.

Studies that investigated the neural basis of decision making under risk focused on representations of basic choice parameters (e.g., magnitudes and probabilities of rewards) and behavioral choice phenomena (e.g., loss aversion). These were mainly investigated using simple gambling tasks with probabilistic outcomes (e.g., Tom, Fox, Trepel, & Poldrack, 2007) or cued reaction time tasks where outcomes are determined by reaction times faster or slower than an adaptive threshold (e.g., Knutson, Taylor, Kaufman, Peterson, & Glover, 2005).

Several studies investigated the magnitudes and/or probabilities of possible rewards before they were actually obtained. The magnitude of possible gains usually correlates with ventral striatal activations including the nucleus accumbens (NACC) (Knutson, Adams, Fong, & Hommer, 2001; Knutson, et al., 2005; Tobler, et al., 2007; Tom, et al., 2007).

Potential losses are also represented in the VST (Tom, et al., 2007) although another study failed to find any loss-related activations in this region (Knutson, et al., 2001).

Representations of reward probability were found in the VST as well as in the VMPFC (Knutson, et al., 2005; Abler, Walter, Erk, Kammerer, & Spitzer, 2006; Tobler, et al., 2007). Similarly, these studies found representations of expected value, which integrates magnitudes and probabilities into one single metric, in these same brain regions (Knutson, et al., 2005; Tobler, et al., 2007). These results are in line with *EVT* (compare section 6.2.1), as they found representations of all parameters (magnitude, probability, and expected value) specified in this model. They are, however, also in line with *EUT* and *PT* of which *EVT* can be seen as a special case.

Another line of research aimed to differentiate between *EUT* and *PT* within the class of utility-based models of decision making under risk. This line of research targeted the special assumptions and psychological phenomena implemented in *PT*. Three of these psychological phenomena, namely reference dependence, framing, and loss aversion are highly interrelated, as the categorization of outcomes as gains and losses differs between different reference points and different forms of framing. There is, however, only one study directly investigating the assumption that individuals are loss averse, meaning that potential losses have a greater impact on the overall subjective value of an action than potential gains (Tom, et al., 2007). In this study participants made several decisions whether to accept a mixed gamble offering a 50% chance of gain and loss, respectively, or not. The authors found that the decrease of ventral striatal activity for losses was steeper than the increase in activity for gains, reflecting loss aversion, as implemented in *PT*.

Another study manipulated the framing of choice options in a decision task in which participants chose between a sure outcome and a gamble after receiving an initial endowment (De Martino, Kumaran, Seymour, & Dolan, 2006). The initial endowment was manipulated such that the gamble was either a loss or a gain compared to the endowment, although offering exactly equal final wealth states. The authors found that amygdala activity was associated with the dominant choices, with increased activity for sure choices in the gain frame and risky choices in the loss frame whereas the dorsomedial prefrontal cortex (DMPFC) showed the opposite pattern across conditions.

Reference-dependence was mostly investigated in the context of market transactions. One study used consumer decisions in which no risk was involved (Weber, et al., 2007). During decisions whether to accept the price for a consumer good or not the reference point was

manipulated by sometimes providing the original store price of the good which was always higher than the offered price. Activity in the VMPFC and mOFC was higher in the condition where (higher) original store prices were shown, indicating that these regions track a reference-dependent value-signal. Together these results provide evidence for a neural basis of loss aversion in combination with reference-dependence and framing, although they provide no clear picture with regard to the underlying processes of these psychological phenomena.

A further aspect that distinguishes *PT* from *EUT* is probability weighting. *EUT* assumes that outcomes are linearly weighted with their probability of occurrence whereas *PT* assumes that probabilities are weighted with a probability weighting function, usually overweighting low probabilities and underweighting high probabilities (Kahneman & Tversky, 1979; Tversky & Kahneman, 1992). Neuroscience usually did not investigate neural representations of probabilities including probabilities near zero or one (Knutson, et al., 2005; Abler, et al., 2006; Tobler, et al., 2007). Therefore, they only investigated a nearly linear part of the probability weighting function assumed by *PT*. One study explicitly investigated probabilities near the endpoints and found that brain activity in the VST indeed follows an S-shaped function, overweighting probabilities near zero and underweighting probabilities near one (Hsu, Krajbich, Zhao, & Camerer, 2009). Together these findings indicate that the brain processes risky alternatives at least partly as proposed by *PT*, although the exact processes remain unclear.

Another line of research investigated the basic choice parameters of risk-return models, namely risk and return of possible outcomes. Studies that solely investigated risk found neural representations in aINS, DLPFC, DMPFC, and VST (see chapter 2.1.2). But more importantly, some studies investigated neural representations of risk and expected value simultaneously. Two studies used a card game to manipulate variance and expected value of possible outcomes (Preuschoff, et al., 2006; Preuschoff, et al., 2008). In this game individuals initially have to state in each trial whether they think the second of two cards that will be drawn is higher or lower than the first one. If the participant is right she gets a fixed amount of money. After the first card is drawn, variance and expected value are fixed as winning probabilities are known. During this time period (after first card and before second card) both studies found that the variance correlates with brain activity in the aINS and VST as well as the expected value correlates with the BOLD signal in the VST. The variance-related BOLD response in the VST was, however, one second delayed. Another

study that conducted two experiments with simple gambles found that both expected value and variance covary with brain activity in the ventrolateral prefrontal cortex (VLPFC) (Tobler, Christopoulos, O'Doherty, Dolan, & Schultz, 2009).

There is, thus, also evidence that the brain processes risky alternatives by trading off risk and return and it therefore remains a puzzle how the valuation process is actually implemented in the brain. Further, studies to date only used simple gambles with a limited number of known probabilities and outcomes to investigate the neurobiological basis of risky decision making. The outcomes of real-life choice alternatives (e.g., stocks), however, often follow continuous distributions. Thus, to date it remains also unclear if the outcome distribution influences the valuation process of risky choice alternatives.

2.3. Aging

2.3.1. Age-related changes in economic decision making

Most economic decisions, such as buying a lottery ticket or investing money for retirement saving, can be seen as decisions under risk. Economic preferences are quite stable in the short term. If you actually prefer, for example, a specific kind of meal (e.g., Lasagne) over another meal (e.g., Pizza), your preference will likely also hold next week or in a few months. It is, however, assumed that value (utility) functions change over the long run, that is, over the adult lifespan (Rogers, 1994; Trostel & Taylor, 2001). Your actual preference for Lasagne over Pizza might thus chnage in five or ten years. Economic preferences are also influenced by situational, environmental, and biological factors. A woman, for example, who has just become a mother will likely have different economic preferences than she had a few years earlier. Similarly, a newly retired man may also have different financial considerations than before the retirement. Age is a descriptive variable for many changes that might cause changes in risky decision making in general and specifically in economic behavior over the adult life span.

One study that used data from a large representative sample found that age has a significant effect on the willingness to take risks (Dohmen, et al., 2005). The applied scale was validated in a sub-sample by showing that it predicts actual risk-taking behavior in a lottery game where subjects repeatedly had to choose between safe gains and risky lotteries. Thus, the authors conclude that risk-taking behavior decreases over the adult lifespan. An experimental study using a gambling task supported this finding (Deakin,

Aitken, Robbins, & Sahakian, 2004). In each trial of the gambling task, subjects receive a certain amount of points. In the following they can freely distribute the amount of points between two different option (e.g., half of the points for option 1 and half of the points for option 2). In one option, points were kept safe, whereas they were exposed to lottery risk in the other. The authors observed that the mean proportion of available points that a subject staked on each trial was significantly lower in older adults than in younger adults, that is, older adults showed less risky behavior.

Further support for the hypothesis that economic behavior changes over the adult lifespan comes from experimental studies that used the Iowa Gambling Task (IGT) (Bechara, Damasio, Tranel, & Damasio, 1997), which has been used in numerous studies to investigate individuals' ability to make favorable choices (Bechara, Damasio, & Damasio, 2000; Maia & McClelland, 2004). In the IGT subjects have to choose repeatedly between four decks of cards without any knowledge about possible outcomes (i.e., reward magnitude and probability). Two of these card decks are "bad decks" in the sense that they result on average in a loss. The other two decks ("good decks") have a positive expected reward. Usually, individuals start with preferring the bad decks, which have higher gains but also much higher losses compared to the good decks, and then switch to the good decks.

In one study, both younger and older subjects started with the usual pattern to choose the bad card decks (Denburg, Tranel, & Bechara, 2005). Whereas the younger subjects then gradually shifted towards the good card decks as the game progressed, the older subjects did not demonstrate this shift, staying with the bad card decks, indicating an impaired ability to identify favorable options in the long run. Two other studies also found that older adults perform less advantageously in the IGT compared to younger adults (Fein, McGillivray, & Finn, 2007; Zamarian, Sinz, Bonatti, Gamboz, & Delazer, 2008). Zamarian et al. (2008) compared the performance of younger and older adults in the IGT with their performance in another task that, in contrast to the IGT, provides the subjects with full information about the lotteries (probabilities and magnitudes of associated gains and losses). Older adults showed poor performance in the IGT relative to younger adults, indicating difficulty in making advantageous decisions under ambiguous conditions. In contrast, older adults performed as well as younger adults in the other task, demonstrating their ability to make decisions in situations where they are given full information about the problem. However, despite substantial evidence for age-related differences in the

performance of the IGT, it should be noted that there is also one study using a variant of the IGT (only two card decks) to compare the economic behavior of younger and older adults that did not find any significant differences between the age groups (Kovalchik, Camerer, Grether, Plott, & Allman, 2005).

Indirect support for the hypothesis that economic behavior changes over the adult lifespan can be derived from age-comparative studies related to second-order factors influencing economic decision making. Working memory capacity and processing speed both decline during the course of normal aging (e.g., Bäckman, Small, Wahlin, & Larsson, 1999; Baltes & Lindenberger, 1997; Dobbs & Rule, 1989; Li, et al., 2008; Salthouse & Babcock, 1991; Schmiedek, Li, & Lindenberger, 2009) and thus likely influence economic behavior and decision making in general. In one study, that investigated the effect of aging on the adaptive selection of decision strategies, older adults with lower working memory capacity and lower processing speed tended to look up less information, took longer to process it, and used simpler, less cognitively demanding strategies (Mata, Schooler, & Rieskamp, 2007).

Thus, many studies have identified age-related differences in economic behavior, specifically in risk-taking behavior, delay discounting, and the ability to make advantageous decisions in the IGT. These studies, however, provide no evidence for the underlying mechanisms that drive age-related changes in economic decision making.

2.3.2. Neurobiological changes during healthy aging

Brain aging involves neurofunctional, neuroanatomical, and neurochemical changes as well as dynamic interactions between these changes (Cabeza, Nyberg, & Park, 2005; Lindenberger, Li, & Backman, 2006). As individuals get older their brains become subject to significant changes (Reuter-Lorenz & Lustig, 2005). Structural imaging and postmortem studies indicate a general loss of brain tissue (white matter and gray matter). However, some brain regions are more affected by these losses than others. Especially, prefrontal grey matter volume seems to be more strongly negatively influenced by age than other brain areas (Raz, et al., 2004).

On the level of brain activation initial neuroimaging studies of cognitive aging reported activations in older adults in brain regions not activated by younger adults. In some studies these overactivations co-occur with underactivations in other brain regions (Reuter-Lorenz

& Lustig, 2005, for review). The terms overactivation and underactivation in this context are purely relative, referring to higher or lower activations in older adults compared to younger adults. Overactivation is often observed in prefrontal brain regions that mirror activation patterns in younger adults, but in the opposite hemisphere (Cabeza, Anderson, Locantore, & McIntosh, 2002). This pattern of reduced asymmetry in older adults has been referred to as hemispheric asymmetry reduction in older age (short HAROLD) (Cabeza, et al., 2002).

Age-related underactivations are typically interpreted as a sign of impairment, for example due to structural changes such as atrophy. In the case of an overactivation an interpretation is less straight forward. To date it remains unclear whether overactivations are beneficial, detrimental, or inconsequential to cognitive functioning (Reuter-Lorenz & Lustig, 2005, for review).

Two explanations for the observed over- and underactivation patterns were proposed in the literature – dedifferentiation and compensation. The first explanation proposed – dedifferentiation – is based on the differentiation-dedifferentiation hypothesis of lifespan intelligence (Baltes, Cornelius, Spiro, Nesselroade, & Willis, 1980). This hypothesis states that the functional organization of cognitive processes is rather undifferentiated in childhood, undergoes differentiation during child development, and becomes relatively dedifferentiated again during aging. This means that different measures of cognition (e.g., working memory, processing speed, etc.) show stronger correlations between each other in older adults and children compared to young adults. Applied to the neurobiological level, this means that brain regions are less functionally distinct in old age, resulting in more diffuse activation patterns (Reuter-Lorenz & Lustig, 2005). A study regarding the ventral visual cortex found evidence for this hypothesis (Park, et al., 2004). Unlike younger adults, who show discrete, anatomically and functionally separable activation peaks for faces, places, and words, older adults show less differentiated activation patterns, recruiting all regions-of-interest, regardless of stimuli category.

The compensation hypothesis assumes that overactive brain regions in older adults are "working harder" than corresponding regions in younger adults. There are several reasons why a brains region needs to "work harder" in older adults. One reason is that overactivation compensates for the declining efficiency of the overactivated brain region. Another reason might be that overactivation compensates for degraded or compromised inputs from other brain regions (Reuter-Lorenz & Lustig, 2005). Compensation, however,

usually works only to a certain degree. Consequently, overactivations were usually reported for relatively low task demands. As task difficulty increases older adults tend to show a more constrained BOLD response than younger adults (Nagel, et al., 2009; Nyberg, Dahlin, Stigsdotter Neely, & Backman, 2009). These findings are in line with the Compensation-related Utilization of Neural Circuits Hypothesis (CRUNCH) (Reuter-Lorenz & Capell, 2008). According to the CRUNCH, processing inefficiencies cause the aging brain to recruit more neural resources to achieve a computational output equivalent to that of younger adults. Compensatory activation is effective at lower levels of task demand. At higher load, activation cannot be further increased, leading to an insufficient processing and a compromised BOLD response.

During the course of normal aging, dopaminergic systems undergo substantial decline. Much of the work on the relationship between aging and dopamine neurotransmission has focused on the caudate and the putamen, two major nuclei in the striatal complex with dense dopaminergic innervation from the substantia nigra. Thus, the conditions for reliable analyses of dopamine biomarkers are particularly favorable in the striatum. There is strong evidence for age-related losses of pre- and postsynaptic biochemical markers of the nigrostriatal dopamine system. Regarding presynaptic mechanisms, both positron emission tomography (PET) and single photon emission computed tomography (SPECT) studies (Erixon-Lindroth, et al., 2005; Mozley, Gur, Mozley, & Gur, 2001) indicate marked age-related losses of the dopamine transporter in the striatum, with the average decline estimated to be 5-10% per decade from early to late adulthood. For postsynaptic mechanisms, molecular imaging work reveals age-related losses of both striatal D1 (Suhara, et al., 1991; Wang, et al., 1998) and D2 (Antonini & Leenders, 1993) receptor densities of comparable magnitude, as found for the dopamine transporter.

A similar downward age trajectory is observed for the mesocortical and mesolimbic dopaminergic pathways. Thus, marked age-related losses in D2 receptor binding have been observed throughout the neocortex as well as in the hippocampus, the amygdala, and the thalamus (Inoue, et al., 2001; Kaasinen & Rinne, 2002). The fact that similar age patterns can be observed for the dopamine transporter and postsynaptic markers suggests that the expression of transporters and receptors may reflect adaptation of major components of the dopaminergic pathways. One possibility derived from work on knockout mice is that the loss of the dopamine transporter initially results in increased dopamine concentrations; increased dopamine levels may subsequently lead to down regulation of neurotransmission

in postsynaptic neurons (Shinkai, Zhang, Mathias, & Roth, 1997; Zhang, Ravipati, Joseph, & Roth, 1995).

Various neurocomputational models have been proposed to link aging-related decline in dopaminergic neuromodulation to behaviorally observed cognitive deficits. One of these models relates weakened phasic activity of the mesencephalic dopamine system with aging-related deficits in detecting performance errors (Nieuwenhuis, et al., 2002). Another model focuses on capturing the effect of deficient dopaminergic neuromodulation on compromised prefrontal cortex functions, such as cognitive control (Braver, et al., 2001). A third model captures the effects of deficient neuromodulation on processing variability and the distinctiveness of memory and goal representations in more general terms (Li, Lindenberger, & Sikstrom, 2001).

Compared to dopamine there is limited data in the literature that deals with changes in the serotonin system during normal aging. Several post-mortem studies have reported a reduction in the number of serotonin binding sites with age in the frontal lobe, occipital lobe, and hippocampus (Arranz, Eriksson, Mellerup, Plenge, & Marcusson, 1993; Cheetham, Crompton, Katona, & Horton, 1988; Gross-Isseroff, Salama, Israeli, & Biegon, 1990; Marcusson, Oreland, & Winblad, 1984; Marcusson, Morgan, Winblad, & Finch, 1984; Sparks, 1989). A PET study provided in vivo evidence for an age-related decline in cortical serotonin binding sites (Wong, et al., 1984). Further, abnormalities of the serotoninergic nervous system are well documented in studies of Alzheimer's disease, and there is evidence suggesting that changes in this system occur in association with non-disease aging (McEntee & Crook, 1991).

In sum, separate lines of research have found evidence for age-related changes in economic decision making and dopaminergic and serotoninergic brain systems over the adult life span. To date it remainsunclear, however, how changes in economic decision making can be attributed to neurobiological changes during healthy aging.

3. Research questions

3.1. Neural processing of risk

Traditional models of risky decision making implicitly assume that the characteristics of a choice option (e.g., magnitude of possible outcomes) are evaluated cognitively. In the framework of *EUT* people's willingness to take risk depends on the concavity of the utility function, and in *EUT's* popular relative *PT* it additionally depends on the shape of the probability weighting function (e.g., Bossaerts, Preuschoff, & Hsu, 2009; Fox & Poldrack, 2009, for reviews). Recent approaches, however, highlighted the role of emotions in decision making. Based on psychological and neuroscientific research, theories like the affect heuristic (Slovic, et al., 2004), the Risk-as-feelings hypothesis (Loewenstein, et al., 2001), and the Somatic Marker Hypothesis (SMH) (Damasio, Tranel, & Damasio, 1991), claim that emotions interact with a cognitive evaluation of the choice problem to guide behavior. To date, however, it remains unclear if risk processing is specifically influenced by emotions.

Traditional models of risky decision making further often assume that risk is a context-independent function of the variability of possible outcomes (e.g., variance) (Markowitz, 1952). Research on the perception of risk, however, indicates that risk perception is neither context-independent nor a pure measure of outcome variability (Weber, et al., 2002). One can distinguish risk processing during or before choice (decision risk) and risk processing after or without a choice (anticipation risk). The crucial difference between the two is that the risk information is likely used to guide behavior in the context of decision risk but not in the context of anticipation risk. Furthermore, research has shown, that individuals' judgments of perceived risk are more sensitive to downside variability and losses than to upside variability, indicating that risk might be processed differently if losses are possible (Weber, et al., 1992).

***Research question 1**:*

How is neural processing of risk influenced by emotions, context, and potential losses?

3.2. Valuation of choice options with continuous outcome distributions

Various models have aimed to describe decision making under risk. Utility-based models as well as risk-return models have proven biologically plausible when using simple gambles with limited pairs of outcomes and probabilities. It therefore remains a puzzle how the valuation process is actually implemented in the brain. As individuals are limited in their processing capacity, one criterion, by which different models might be assigned to different types of decisions, is the amount of information processing required by each. In investment decisions individuals are usually faced with investments where returns follow continuous distributions (e.g., stocks); thus they are faced with an infinite number of potential outcomes and probabilities. While the amount of required computations stays constant in risk-return models (calculation of risk, return, and value), it increases with the amount of outcome-probability pairs in *EUT* and *PT*. That is, in *EUT* and *PT* each outcome and each probability (in the case of *PT*) first needs to be transformed before they are combined to derive the value of a choice option. Although this indicates that individuals use risk-return models in this case, it remains unclear how they actually value choice options with continuous outcome distributions.

Research question 2:

How do individuals value choice options with continuous outcome distributions?

3.3. Neural foundations of age-related changes in risky economic decision making

Many developed countries are now faced with aging populations, due to an increase in average life expectancy and a decrease in birth rate (Beddington, et al., 2008). The prosperity of societies generally depends heavily on its ability to profit from the cognitive resources of its constituent members, both economically and socially. Thus, in aging societies it is crucial to understand how brain mechanisms that affect cognitive abilities and decision making change over the adult lifespan to guide strategies for cognitive interventions at the individual level and social policies at the societal level.

It was recently suggested that risky economic decision making is influenced by two neurotransmitter systems, namely dopamine and serotonin, which are known to be prone to significant changes during the adult lifespan. It remains unknown, however, how changes

in these neurotransmitter systems are related to changes in economic behavior during healthy aging.

Research question 3:

How are age-related changes in risky economic decision making related to neurobiological changes during the adult life span?

4. General methodology

All three studies were based on fMRI data: Project I was a quantitative meta-analyses of fMRI studies on risk processing, Project II was an fMRI study on investment decisions, and Project III was a review of fMRI studies on age-related changes in economic decision making. FMRI is a method to study brain activity non-invasively (Logothetis, 2008) for review). It is important to emphasize that fMRI does not measure neuronal activity directly. FMRI employs the BOLD contrast to indicate local changes in neural activity (Kwong, et al., 1992; Ogawa, Lee, Kay, & Tank, 1990). Neural activity associated with information processing leads to metabolic changes including increased oxygen consumption in the respective brain regions. Mediated by physiological mechanisms that are still not completely understood, this increased oxygen consumption leads to an increase of local blood volume and a large rise in local blood flow, the so-called luxury perfusion (Fox & Raichle, 1986; Fox, Raichle, Mintun, & Dence, 1988). As a result of this increased blood flow, vessels in activated brain regions contain an over-supply of oxygenated blood and consequently a relatively low amount of de-oxygenated blood. Because deoxyhemoglobin has paramagnetic features, its presence leads to local inhomogeneities of the magnetic field. Inhomogeneities lead to a faster decay of the MRI signal. Therefore, active brain regions which exhibit a relatively low amount of deoxyhemoglobin show a slower decay of the MRI signal than non-activated brain regions resulting in an increased BOLD signal. In brief, fMRI measures the relative absence of deoxyhemoglobin in a given brain region which, mediated over hemodynamic coupling and the associated BOLD response, is an indicator of local neural activity (Logothetis & Wandell, 2004). In contrast to electroencephalography (EEG), fMRI offers a very good spatial resultion which depends on the magnetic field strength of the applied MRI scanner (Logothetis, 2008). Although still an issue of intense research, the BOLD contrast is assumed to reflect mainly neuronal input and local integration processes within a brain region associated with pre- and postsynaptic currents and to a lesser degree neuronal output of a brain region related to action potentials in projection neurons (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001; Viswanathan & Freeman, 2007). There are, however, also other mechanisms that might elicit significant BOLD responses, that are not related to stimuli or task demands (Logothetis, 2008). Increases of the BOLD signal may for example occur as a result of balanced proportional increases in the excitatory and inhibitory conductances (Logothetis, 2008).

The time course of the BOLD response to stimulation is called the hemodynamic response function (HRF). Whereas the neuronal response to the stimulus rises quickly and ends a few hundred ms post-stimulus, the typical BOLD response only begins to rise at about 2 s and reaches a maximum at 5–9 s after stimulus onset and then slowly returns to baseline (Logothetis and Wandell, 2004, for review). In some instances the BOLD response has an initial dip and a post-stimulus undershoot. The slow HRF causes the relatively poor temporal resolution of fMRI. The exact form of the HRF differs across brain regions and between subjects as well as tasks. It also depends on the stimulus duration. To model brain activity in fMRI analyses usually a canonical HRF is used (Friston, et al., 1996). Depending on the degree of spatial smoothing applied, the spatial resolution of fMRI is relatively highlies usually between 4 and 12 mm^2. For group analyses, functional maps are normalized to a structural brain template using coordinates according to the Talairach or the Montreal Neurological Institute standards (Talairach & Tournoux, 1988). For illustration purposes, the relatively low-resolution functional activation maps are usually super-imposed on high-resolution structural MRI images.

5. Dissertation projects

5.1. Project I: Neural processing of risk

In Project I I investigated, how neural processing of risk is influenced by emotions, context, and potential losses (Research Question 1). To answer these questions I conducted quantitative meta-analyses on studies that investigate risk in the brain. By using the Activation Likelihood Estimation (ALE) approach we can base our argumentation not only on a single study or a qualitative view on several studies but on a quantitative integration of many studies investigating risk. ALE is a quantitative meta-analysis technique that compares activation likelihoods calculated from observed activation foci with a null distribution of randomly generated activation likelihoods. In ALE, peak activation coordinates from a number of studies investigating similar effects are pooled (Chein, Fissell, Jacobs, & Fiez, 2002; Laird, et al., 2005; Turkeltaub, Eden, Jones, & Zeffiro, 2002). These coordinates are generally published relative to Talairach or Montreal Neurological Institute (MNI) space and have to be spatially renormalized to a single template.

The resulting coordinates are used to generate "activation likelihoods" for each voxel in the brain. For each focus, ALE scores each voxel as a function of its distance from that focus using a three-dimensional Gaussian probability density function centered at the coordinates of the focus. As a result, ALE gets vectors of values for each voxel representing probabilities to belong to specific foci. These values are assumed to be independent (the existence of one focus gives no information about whether another focus will occur) and are combined with the addition rule for probabilities, yielding so-called ALE statistics. The ALE statistic represents the probability of a certain voxel to belong to any of the included foci.

To test for significance the ALE statistic in each voxel is compared with a null distribution, generated via repeatedly calculating ALE statistics out of random activation foci (same number as included in the study). This null distribution is then used to estimate the threshold that results for a given false discovery rate (FDR). Finally, a cluster threshold (minimum spatial extend of significant clusters) can be applied.

The ALE meta-analysis can also be used to contrast two independent meta-analyses. In this case the ALE statistic in each voxel is calculated as the difference in ALE values between the two meta-analyses. Whereas ALE values can only be positive in a single ALE meta-

analysis they can be negative as well in a contrast of ALE meta-analyses. The null distribution is calculated accordingly via calculating the differences between ALE statistics of randomly generated foci (again same number of foci as included in the respective studies). Further steps of the analysis equal the procedure used for a single ALE meta-analysis described above.

I identified a network including bilateral aINS, dorsomedial Thalamus, posterior Thalamus, DMPFC, right DLPFC, and right parietal cortex for processing risk. The aINS was active for both decision risk and anticipation risk but predominantly when individuals were faced with potential losses. The aINS is regarded as a key brain region in emotion processing and arousal (Quartz, 2009) but also in the mapping of internal bodily states (Craig, 2009; Critchley, 2005). Several studies related activity in the aINS especially to aversive emotions such as fear, sadness, disgust, or anxiety (Paulus & Stein, 2006; Phan, Wager, Taylor, & Liberzon, 2002; for reviews). Thus, our results clearly support the hypothesis that aversive emotions are implicated in risk processing independent of the context but predominantly (not solely) when individuals are faced with potential losses.

The Thalamus is one of the most ignored brain regions in functional neuroimaging. Although most of the studies included in our meta-analyses found risk representations in the Thalamus, none of the studies discussed them. I found representations of risk in posterior and dorsomedial Thalamus. The posterior Thalamus was found to be active in the processing of emotions like regret (Chandrasekhar, Capra, Moore, Noussair, & Berns, 2008) and showed stronger activity for losses compared to gains (Xu, Liang, Wang, Li, & Jiang, 2009). The dorsomedial Thalamus is part of the striatal loop and reflects information about reward magnitudes (Glimcher & Lau, 2005). Thus, both parts of the Thalamus likely process important aspects of a risky stimulus.

The DMPFC was active during decision risk and anticipation risk as well as in both domains (gains+losses and gains). It was, however, more likely to be active during decision risk compared to anticipation risk. Activity in the DMPFC was found in a variety of different tasks related to the cognitive processing of stimuli. These studies included investigations of response conflict, error monitoring, decision making, as well as strategy selection (Venkatraman, Payne, Bettman, Luce, & Huettel, 2009); (Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004) for review).

I further found that both the right DLPFC and parietal cortex were active for decision risk but not for anticipation risk. Both brain regions were usually observed in the context of

decision making (Heekeren, Marrett, & Ungerleider, 2008, for review). In the context of reward-based decision making, activity in the right DLPFC is related to valuing choice options (Camus, et al., 2009; Mohr, Biele, Krugel, Li, & Heekeren, 2009). These results indicate that DLPFC and parietal cortex do not play a general role in risk processing but a specific role in risk processing during decision making.

In sum, our finding of insula activity supports the hypothesis that emotions are implicated in risk processing. The differential activation patterns for decision risk vs. anticipation risk and for the gain vs. gain+loss domain suggest that risk processing on the neural level is context dependent and specifically influenced by potential losses (note though, that context and domain are not fully independent in the fMRI studies I found).

5.2. Project II: Neural foundations of risk-return trade-off in investment decisions

In Project II we investigated how do individuals value choice options with continuous outcome distributions (Research question 2). Two classes of risky decision making models have been proposed that can be applied to investment decisions in general, one based on a transformation of outcomes and/or probabilities (*EUT* and *PT*) (Kahneman & Tversky, 1979; von Neumann & Morgenstern, 1953) and the other based on a risk-return trade-off (risk-return models) (Sarin & Weber, 1993; Weber & Johnson, 2009).

To be superior to other models, a better model should, in the best case, explain behavioral and neural data better than the other models. As value- and choice predictions of both classes of models are usually highly consistent with each other (Bossaerts, et al., 2009; d'Acremont & Bossaerts, 2008), here I focused on the question which class of models better describes the valuation process. In this case fMRI data can serve as a tiebreaker, because they provide additional insight into the neurobiological processes that sub-serve the cognitive processes, which ultimately lead to decisions. As previous research found neurobiological support for both classes of models we suggest to associate both classes of models with certain types of decisions, environments, or decision contexts in which different strategies are appropriate. One criterion by which different models can be assigned to different types of decisions is the amount of information processing required by each. In investment decisions, where investment returns often follow continuous distributions, both classes of models differ significantly with regard to this criterion.

To investigate the brain processes associated with investment decisions I used a novel investment decision task in an fMRI experiment. Each trial of the *Risk Perception and Investment Decision (RPID) task* consisted of two phases: the presentation of a return stream, followed by a decision or subjective judgment task. In investment situations investors are often confronted with past performance data of possible investments. To mimic this situation, in the first phase we sequentially presented a stream of ten returns from an investment (each presented for 2 sec). These ten returns provided information about the past performance of a given investment. In the experiment, each return stream was independent of the others and described a new investment option. We varied the mean and the standard deviation of the return streams parametrically with 3 means (6%, 9%, and 12%) and 3 standard deviations (1%, 5%, and 9%), resulting in 9 different combinations of means and standard deviations.

In the second phase, subjects performed one of three possible tasks in each trial (each 7 sec) without knowing in advance which one they would have to perform after the stream. The goal of these three tasks was to investigate choices as well as perceived risk and subjective expected return, as specified in the psychological risk-return models (see chapter 2.2.1). In the decision task the subjects had to make a choice between an investment with 5% fixed return (safe investment) and the investment represented by the return stream they saw before (risky investment). In the other two tasks subjects reported their subjective expected return and perceived risk of the investment represented by the return stream. Subjects indicated subjective expected return on a scale ranging from -5% to +15% and perceived risk on a scale ranging from 0 (no risk) to 100 (maximum risk; (Klos, et al., 2005). Subjects performed each task (decision, subjective expected return, perceived risk) twenty-seven times (81 trials in total). Before the experiment subjects completed four training trials, knowing that the standard deviations in the experiment would be in the same range as in the training trials. But no information with regard to the distribution of returns was given to the participants.

Using the RPID task, which mimics real-life investment decisions by providing subjects with past returns of investments, I found that value and return covaried with brain activity in bilateral DLPFC, PCC, VLPFC, and MPFC. Activation in these regions has usually been observed in the context of value and reward. Changes in the BOLD signal in these regions correlate with the magnitude of experienced and anticipated rewards as well as with the subjective value of (delayed) rewards and the willingness to pay for consumer

goods (Amiez, Joseph, & Procyk, 2006; Kable & Glimcher, 2007; Kennerley, Dahmubed, Lara, & Wallis, 2009; Knutson, et al., 2005; Kuhnen & Knutson, 2005; Markowitz, 1952; Plassmann, et al., 2007; Tom, et al., 2007).

I found that *perceived risk* correlated significantly with the BOLD signal in the aINS. Risk-related brain activity in the aINS was observed in a variety of studies (Critchley, et al., 2001; Grinband, Hirsch, & Ferrera, 2006; Huettel, et al., 2005; Paulus, et al., 2003; Preuschoff, et al., 2006; Preuschoff, et al., 2008; Rolls, et al., 2008). None of these studies, however, used lotteries with continuous distributions. Thus, our finding supports the results of previous studies and extends them by showing that risk is represented in the aINS in situations where subjects have to make a choice between two independent alternatives where one alternative is described by a continuous distribution of possible outcomes. Most importantly, the existence of a neural representation of risk during choices offers neural support for risk-return models because in the case of *EUT* and *PT* one would not expect a neural representation of risk whereas risk is explicitly specified in risk-return models.

I further found that inter-individual differences in decision-related brain activity in lOFC and PCC covaried with inter-individual differences in risk attitudes derived from the psychological risk-return model, which provides additional support for this model. The more risk averse a participant was, the greater was her decision-related brain activity in lOFC and PCC (independent of current risk and value). Our results support the findings from a recent study that found correlations between risk attitude and risk-related brain activity in lateral OFC for risk averse individuals and in medial OFC for risk seeking individuals (Tobler, et al., 2007).

In sum, I found support for the hypothesis of a risk-return trade-off in investment decisions. I extended existing evidence regarding the neurobiological basis of risky decision making (a) by predicting both behavioral data and neuroimaging data with the same choice model (risk-return model), (b) by showing that (perceived) risk and risk attitude do not only influence the value signal but are represented independently in the aINS (perceived risk) and the lOFC (risk attitude), and (c) by showing that risk and value are not only represented in the brain during choices between simple gambles with discrete outcome distributions but especially during choices where outcomes follow continuous distributions (like stocks usually do).

5.3. Project III: Neuroeconomics and aging: Neuromodulation of economic decision making in old age

In Project III I investigated how age-related changes in risky economic decision making are related to neurobiological changes during the adult life span? Risky economic decision making is a complex process of integrating and comparing various aspects of economically-relevant choice options. Most models of risky decision making are based on reward and risk, which is explicitly defined in risk-return models (Bell, 1995; Sarin & Weber, 1993) and implicitly influences the value of an alternative in utility-based models via the curvature of the utility function and additionally in the case of *PT* via the curvature of the probability weighting function (Kahneman & Tversky, 1979; von Neumann & Morgenstern, 1953). Importantly, however, a third factor influences the value of a choice alternative, namely the possible delay between action and reward delivery, which is specified in models of intertemporal choice (Ainslie, 1974; Kirby, 1997; Laibson, 1997).

Neuroeconomics has made important progress in grounding these aspects of decision making in neural systems and the neurotransmitters therein. Evidence from a range of fMRI studies indicates that the ventral striatum (VST) and the ventromedial prefrontal cortex (VMPFC) are implicated in the representations of reward (Delgado, Nystrom, Fissell, Noll, & Fiez, 2000; Elliott, Friston, & Dolan, 2000; Elliott, Newman, Longe, & Deakin, 2003). In the context of risk processing, many studies have shown two key regions to be involved – the ACC and the aINS (see section 9.1). Some recent studies have also investigated the effect of delayed rewards and showed that the subjective value of delayed rewards covaries with brain activity in VST, VMPFC, and PCC (Ballard & Knutson, 2009; Kable & Glimcher, 2007; McClure, Ericson, Laibson, Loewenstein, & Cohen, 2007; McClure, Laibson, Loewenstein, & Cohen, 2004)

The dopaminergic and serotoninergic brain systems have been identified as key neurotransmitter systems involved in economic behavior influencing all three aspects of economic decision making discussed above (reward, risk, and delay). Whereas dopamine and serotonin separately influence both reward - and risk processing (Tobler, Fiorillo, & Schultz, 2005) (Fiorillo, Tobler, & Schultz, 2003; Talbot, Watson, Barrett, & Cooper, 2006) they are also assumed to interact in implementing prediction signals that reflect the temporal information about the outcome (Denk, et al., 2005; Tanaka, et al., 2007)

Both neurotransmitters are known to be prone to significant changes during the adult life span. Regarding presynaptic mechanisms, both PET and SPECT studies (Erixon-Lindroth,

et al., 2005; Mozley, et al., 2001) indicate marked age-related losses of the dopamine transporter in the striatum, with the average decline estimated to be 5-10% per decade from early to late adulthood. For postsynaptic mechanisms, molecular imaging work reveals age-related losses of both striatal D1 (Suhara, et al., 1991; Wang, et al., 1998) and D2 (Antonini & Leenders, 1993) receptor densities of comparable magnitude, as found for the dopamine transporter. Several post-mortem studies have further reported a reduction in the number of serotonin binding sites with age in the frontal lobe, occipital lobe, and hippocampus (Arranz, et al., 1993; Cheetham, et al., 1988; Gross-Isseroff, et al., 1990; J. Marcusson, et al., 1984; J. O. Marcusson, et al., 1984; Sparks, 1989).

Similarly, economic behavior undergoes significant age-related changes over the course of the adult life span. Several studies indicate that older adults are more risk averse than younger adults (Deakin, et al., 2004; Dohmen, et al., 2005; Green, Fry, & Myerson, 1994) and that discount rates increase with age. These changes were reflected in changes in activation patterns observed while individuals make economic decisions. Although older adults show intact striatal activation during gain anticipation, one can observe a relative reduction in activation during loss anticipation (Samanez-Larkin, et al., 2007). They also show higher activations in the aINS when choosing risky choice alternatives, indicating that they perceived the alternative as more risky compared to younger adults.

In sum, I suggest, based on the reviewed evidence, a triadic relationship between (a) economic decision-making, (b) dopaminergic and serotoninergic neuromodulation, and (c) aging.

6. General discussion

In our everyday life we frequently have to make decisions under risk. Choosing a job, a partner to marry, or a form of private retirement saving are prominent examples of decisions with uncertain consequences. Although we have to make decisions under risk throughout our everyday life and although these decisions can have important consequences (e.g., they can affect the living standard in old age) it is still not fully understood how individuals process risk and how they make decisions under risk. It further remains unclear how risk processing and decision making under risk might change across the lifespan, influencing especially retirement saving decisions that individuals have to make throughout the entire adult lifespan.

In the context of this dissertation I investigated three main questions all related to risky decision making, namely (a) how neural processing of risk is influenced by emotions, context, and potential losses, (b) how individuals value choice options with continuous outcome distributions, and (c) how age-related changes in economic decision making are related to neurobiological changes during the adult life span. All of these questions can be addressed in the framework of neuroeconomics.

6.1. Why neuroeconomics?

Neuroeconomics (a convenient shorthand for "decision neuroscience") seeks to integrate ideas from different disciplines that investigate decision making in general, namely psychology, economics, and neuroscience (Sanfey, Loewenstein, McClure, & Cohen, 2006). In fact, neuroeconomics emerged when two lines of research met, that followed already interdisciplinary ideas – behavioral economics and cognitive neuroscience (Glimcher, Camerer, Fehr, & Poldrack, 2009). Behavioral economics aims to integrate ideas from psychology and economics to provide a better understanding of economic behavior. Cognitive neuroscience, in contrast, aims to integrate ideas from psychology and neuroscience to investigate the biological substrates of cognition. Neuroeconomics consequently tries to ground economic behavior in neural mechanisms thereby getting insights on the processes underlying economic decision making (Camerer, 2007). It can therefore be seen as a subfield of both behavioral economics and cognitive neuroscience. These two, however, constitute two different views on neuroeconomics. Behavioral economics aims to use neuroscientific methods as a tool to both test economic models of decision making and develop alternatives to classical revealed preference models (e.g.,

EUT). Cognitive neuroscience in contrast uses economic models as a tool to test and develop algorithmic models of the neural hardware of choice.

But whereas the neuroeconomics approach, that is, investigating the neural processes underlying economic behavior, is widely accepted in psychology and neuroscience, it is met with more skepticism in economics and received substantial criticism especially from economics scholars (Gul & Pesendorfer, 2008). The main argument of these scholars is that evidence from neuroscience cannot falsify economic theories as they make no claims regarding the psychological and neurological processes involved in economic decision making. Following this argument behavioral data are both necessary and sufficient to evaluate the validity of economic models. This is obviously correct, as economic models usually make "as if" statements. *EUT* for example proposes that individuals behave "as if" they would maximize their expected utility, implying that they behave "as if" a metric like utility would actually exist. The weakness of this argument is, however, that a variety of studies already provided behavioral data that questioned the predictive power of *EUT* or *PT* (e.g., Allais, 1953; Birnbaum, 2008).

The goal of neuroeconomics is, thus, not to falsify any model of individual decision making, as this has in most cases already been done (Clithero, Tankersley, & Huettel, 2008). The role of neuroeconomics in decision sciences lies mostly in its potential to guide and constrain the development of new hypotheses and models. Without this guidance and these constraints, research has to test in its extreme all plausible influencing factors on economic decision making to form the basis for a comprehensive model. This is of course highly impractical. No collection of researchers can obtain all possible data about all possible behaviors. An understanding of the neural processes underlying economic decision making can indicate which possible factors are more likely and which are less likely to influence economic behavior. Neural and behavioral studies should interact to identify interesting phenomena, to suggest mechanisms that underlie those phenomena, and to map out the biological substrates that support those mechanisms.

Aside from generating new hypotheses neurobiological data can also introduce constraints. Psychological research has already turned to focus not only on predicting and explaining choices, that is, the outcome of a decision process, but tries to develop process models that include testable hypotheses regarding the underlying processes of decision making (e.g., Weber & Johnson, 2009, for review). By virtue of hypothesizing a series of psychological processes that precede decisions, process models make predictions about intermediate

states of the decision maker, between the start and the end of the decision. Process models can, thus, improve model selection because they consider more variables and add multiple constraints. Following the same logic the neuroeconomics approach can add neurobiological constraints to models of decision making. In addition, neurobiological data can serve to test the biological plausibility of these models.

In this dissertation I took the neuroeconomics approach to contribute to a better understanding of risk processing and risky economic decision making. In the case of risk processing (Project I) several behavioral findings indicate that it is influenced by emotions, context, and potential losses (see chapter 2.1.1). By providing neurobiological data on risk processing we can strengthen behavioral findings and test the biological plausibility of recent approaches on risk perception. In the case of risky decision making choice predictions of competing theories are highly consistent with each other. Neuroeconomics has already provided neurobiological data that so far did not question the biological plausibility of these theories in simple gambles, that is, found support for risk-return models and utility-based models of risky decision making (see chapter 2.2.2). Prior studies have, however, neglected the biological plausibility of these models for gambles with continuous outcome distributions. Consequently, I tested which of the proposed models is biologically more plausible in this special case (Project II). Furthermore, behavioral research has identified several changes in economic decision making across the adult lifespan. However, the reasons for these changes are still debated. By reviewing parallels in behavioral changes and changes in dopaminergic and serotoninergic neuromodulation (Project III), which are implicated in economic decision making, I can guide hypothesis testing by suggesting new research agendas.

6.2. The role of emotions in risk processing and risky decision making

One central question of this dissertation was if and how emotions influence risk processing and risky decision making. In Project I, I identified the aINS as a key brain region in risk processing. It was found to be active in the context of risk across a wide range of tasks and experiments, including experiments where risk was processed in non-choice situations and during risky decision making. Consequently, I found a representation of perceived risk in the aINS also in Project II.

The aINS is regarded as a key brain region in emotion processing and arousal (Quartz, 2009) but also in the mapping of internal bodily states (Craig, 2009; Critchley, 2005).

These bodily states range from changes in the internal milieu and viscera that may not be perceptible to an external observer (e.g., heart rate) to changes in muscoloskeletal system that may be obvious to an external observer (e.g., facial expression) and play an important role in the generation of emotions (Bechara & Damasio, 2005).

Several studies related activity in the aINS especially to aversive emotions such as fear, sadness, disgust, or anxiety (Paulus & Stein, 2006; Phan, et al., 2002; for reviews). In the context of risky decision making, activity in the aINS was recently found to be implicated in outcome-related processing of disappointment and regret (Chua, Gonzalez, Taylor, Welsh, & Liberzon, 2009). Singer et al. proposed a model of insula functioning, in which the insula integrates external sensory and internal physiological signals with computations about their uncertainty (Singer, Critchley, & Preuschoff, 2009). According to this model the integration is expressed as a dominant feeling state that influences social and motivational behavior. A study on temporal discounting indicates that this feeling state might be stronger when making intertemporal decisions in the loss domain compared to the gain domain (Xu, et al., 2009). Thus, our results so far clearly support the hypothesis that aversive emotions are implicated in risk processing.

Standing alone, this conclusion is based on reverse inference (Poldrack, 2006), and needs to be qualified as the aINS is also active in a variety of tasks not explicitly related to emotions (e.g., Yang et al., 2009). Still, additional evidence comes from behavioral research on the influence of emotions on decision making. Several studies demonstrated that incidental emotions (i.e., emotions not related to the decision problem) significantly influence judgment and decision making. Risk judgments, for example, change if individuals perceive fear or anger (Lerner & Keltner, 2000). Together with these behavioral findings our results strongly indicate that emotions influence risk processing.

6.3. Complexity as determinant of decision strategy

Two classes of risky decision making models have been proposed, one based on a transformation of outcomes and/or probabilities (*EUT* and *PT*) (Kahneman & Tversky, 1979; von Neumann & Morgenstern, 1953) and the other based on a risk-return trade-off (risk-return models) (Sarin & Weber, 1993; Weber & Johnson, 2009).

To be superior to other models, a better model should, in the best case, explain behavioral and neural data better than the other models. Value- and choice predictions of both classes

of models are, however, usually highly consistent with each other (Bossaerts, et al., 2009; d'Acremont & Bossaerts, 2008). In this case fMRI data can serve as a tiebreaker, because they provide additional insight into the neurobiological processes that sub-serve the cognitive processes, which ultimately lead to decisions.

Recent research has found neural support for both classes of models. Some studies found representations of magnitudes and probabilities (supporting utility-based models) (e.g., Knutson, et al., 2005) whereas others found representations of risk and return (supporting risk-return models) (e.g., Preuschoff, et al., 2006; Tobler, et al., 2009). It has to be emphasized, however, that representations of magnitudes and probabilities, could also be attributed to the return component of risk-return models, as they form the (subjective) expected return of a choice option. But all of these studies used gambles with discrete outcome distributions. In investment decisions, however, outcomes are usually continuously distributed. Consequently, I investigated in Project II which class of models is better able to describe the underlying neural processes in this case.

By showing (a) that risk-return models can explain choices behaviorally and (b) that the components of risk-return models (value, risk, and risk attitude) are represented in the brain during choices, I provide evidence that risk-return models describe the neural processes underlying investment decisions well. Most importantly, the observed correlation between risk and brain activity in the aINS during choices supports risk-return models more than utility-based models because risk is an explicit component of risk-return models but not of the utility-based models. But this finding does not generally speak against utility-based models which were shown to be biologically plausible in the case of simple gambles (e.g., Tom, et al., 2007). In contrast, it remains possible that both classes of models are able to describe the processes underlying risky decision making.

One way to reconcile this apparent conflict is to assume that the return component of risk-return models follows a function similar to the expected utility in the framework of *EUT* or the value in the framework of *PT*. Another possibility is to associate both classes of models with certain types of decisions, environments, or decision contexts in which different strategies are appropriate. One criterion by which different models can be assigned to different types of decisions is the amount of information processing required by each. Individuals are limited in their processing capacity and therefore need to be selective in how to use information and under what conditions (Weber & Johnson, 2009). If one assumes that the return component of risk-return models does not follow a function like in

EUT or *PT*, but is computed simply as the mean of all possible returns of the choice option, the amount of required computations stays constant in risk-return models (calculation of risk, return, and value). In contrast, it increases with the amount of outcome-probability pairs in *EUT* and *PT*. That is, in *EUT* and *PT* each outcome and each probability (in the case of *PT*) first needs to be transformed before they are combined to derive the value of a choice option.

Thus, our findings indicate that the underlying processes of risky decision making might change depending on the complexity of the decision problem. The more complex a decision problem, the more likely it is that individuals use strategies like the risk-return trade-off or simple heuristics (e.g., Gigerenzer, Todd, & ABC Research Group, 1999, for an overview), which limit the amount of information processing.

6.4. The correlative triad of economic decision making, dopaminergic and serotoninergic neuromodulation, and aging

The dopaminergic system and the serotoninergic system interact in value-based decision making like decision making under risk as well as in reward-based learning. Both are known to influence reward, risk, and delay of reward, and undergo significant changes during the adult lifespan. These changes are paralleled by changes in economic behavior, specifically in risk taking, delay discounting, and reward-based learning. The neuroeconomics approach has already helped to identify age-related differences in activation patterns associated with reward processing, indicating that older adults have problems forming correct stimulus reward associations (Cox, Aizenstein, & Fiez, 2008; Marschner, et al., 2005; Schott, et al., 2007). One reason for these problems might be a higher temporal variability in the BOLD signal, which has been shown to mediate age-related suboptimal risk-taking in the case of the VST (Samanez-Larkin, Kuhnen, Yoo, & Knutson, 2010). Importantly, one reason for higher temporal variability in the BOLD signal could be lower levels of dopamine expression in dopamine-sensitive brain regions such as the NACC or the prefrontal cortex. This notion is based on the more general hypothesis that dopamine influences the signal-to-noise ratio of information processing, thereby influencing the distinctiveness of representations in the brain and ultimately performance (Li, et al., 2001).

Given the known relationships between reward, risk, and delay of reward and dopamine and serotonin on the one hand and dopamine and serotonin with aging on the other hand, it can be hypothesized that the observed age-related changes in reward processing are caused by declines in the dopaminergic and serotoninergic systems. A recent study found support for this view.

Consequently, I propose in Project III, where I review the evidence described above, a triadic relationship between economic decision making, dopaminergic and serotoninergic neuromodulation, and aging. To date however, no study took the full triade into account to fully discover the underlying mechanisms. Thus, future research should apply paradigms that include age differences as well as other individual differences that affect the functionality of the relevant transmitter systems.

Currently, there are two complementary approaches to investigate effects of neuromodulation on cognition in general and on decision making in particular: pharmacological intervention and genetics. In the case of a pharmacological intervention, one group of subjects is given a drug that increases or decreases dopamine or serotonin availability whereas another group receives a placebo, leaving availability unchanged. In case of genetics studies, subjects are chosen according to a genetic polymorphism that is known to influence the level of dopamine or serotonin (e.g., the catechol-O-methyltransferase Val^{158}Met polymorphism). But one should note that the effects are much stronger for pharmacological interventions, and that individuals that have lower levels of dopamine or serotonin due to a genetic polymorphism might already have compensated for this difference (e.g., by recruiting additional brain resources).

Most studies have, thus, only included one of these two approaches. A few exceptions took either a pharmacoimaging approach (Mattay, et al., 2003) or a behavioral genetic age comparative approach (Nagel, et al., 2008), which allowed direct investigations of the effects of genetic-based and age-related differences in neuromodulation and their interactions on cognitive and brain functions (Lindenberger, et al., 2008). Along these lines, future combined age comparative pharmacoimaging studies could shed light on the triadic relationship between (a) economic decision-making, (b) dopaminergic and serotoninergic neuromodulation, and (c) aging.

6.5. An integrated neural model of risky decision making

Several studies to date have investigated the neural foundations of risk processing and risky decision making in humans. The results of these studies reveal that both are highly complex processes that (a) are influenced by several factors and (b) recruit a network of different brain regions. Studies using simple gambles with discrete outcome distributions usually identified representations of reward magnitude and probability in VST, VMPFC, and VLPFC (Knutson, et al., 2001; Knutson, et al., 2005; Tobler, et al., 2007). Both were, however, found to be nonlinearly represented in the VST. The decrease of ventral striatal activity for losses is steeper than the increase in activity for gains, reflecting loss aversion (Tom, et al., 2007). Further probability-related activity in the VST follows an S-shaped function, overweighting probabilities near zero and underweighting probabilities near one (Hsu, et al., 2009). Similarly, the VST, VMPFC, and VLPFC all code the expected and subjective value of simple gambles (Tobler, et al., 2007; Tom, et al., 2007). In addition to VST, VMPFC, and VLPFC, also the DLPFC might play an important role in valuing choice options. Compared with a control condition, application of repetitive transcranial magnetic stimulation (rTMS) to the right DLPFC decreases values assigned to the stimuli (Camus, et al., 2009).

In Project II I did not find any representations of expected or subjective value in VST or VMPFC in the case of more complex gambles with continuous outcome distributions. But I found representations of expected and subjective value in VLPFC, DLPFC, and DMPFC, suggesting that the underlying processes of risky decision making at least partly change if individuals have to deal with abstract in contrast to concrete reward information. They further stress the important role of DLPFC and VLPFC in value computations.

Although risk is not directly implicated in utility-based models of risky decision making several studies found representations of risk during decision making. In Project I, I integrated this evidence and identified the neural underpinnings of risk processing during decision making independent of complexity. I found neural representations of risk especially in aINS, Thalamus, DLPFC, DMPFC, and parietal cortex.

Together, these findings suggest the following neural mechanism of risky decision making (cf. **Fig. 3**): When individuals observe a risky stimulus such as a gamble with uncertain outcomes or an investment option, two parallel processes are induced, a return process and a risk process. Both contain two sub-processes, an emotional and a cognitive process. During emotional return processing VST and VMPFC reflect both the magnitude and the

probability of potential outcomes. These are, however, not necessarily linearly represented in VST and VMPFC, but could, for example, differ between gains and losses or follow an S-shaped function of probabilities. VST and VMPFC also integrate the information regarding magnitude and probability and form an emotional estimate of the rewarding potential of the stimulus. The DMPFC evaluates the return of the stimulus on a cognitive level, for instance calculating the expected value of potential outcomes, thereby using the information from the VST and the VMPFC as a starting point. During this process information is repeatedly exchanged between DMPFC on the one hand and VST and VMPFC on the other hand, updating the emotional reward expectation, which in turn informs the cognitive return computation. If the risky stimulus is highly complex, as for example in the case of continuous outcome distributions, the brain is unable to represent all possible magnitudes and probabilities of outcomes. Return processing is in this case performed predominantly on the cognitive level in the DMPFC, thereby only roughly estimating the expected return in contrast to an exact computation.

Risk processing is performed by a similar interaction of emotional and cognitive processes. On the emotional level, activity in the aINS initially serves as a fast and rough estimate for the potential of the stimulus to result in an unwanted outcome (e.g., a loss). At the same time, this signal prepares the organism to take action to avoid the unwanted outcome. Activity in the Thalamus could thereby reflect anticipation of regret in response to possible outcomes of the risky stimulus. The DMPFC evaluates the risk of the stimulus on a cognitive level, for instance computing the variance of outcomes or the probability of a loss, thereby using the information from the aINS and the Thalamus as a first estimate for the riskiness of the stimulus. During this process information is also repeatedly exchanged between DMPFC on the one hand and aINS and Thalamus on the other hand, updating the emotional response to the stimulus, which in turn informs the cognitive processing of risk.

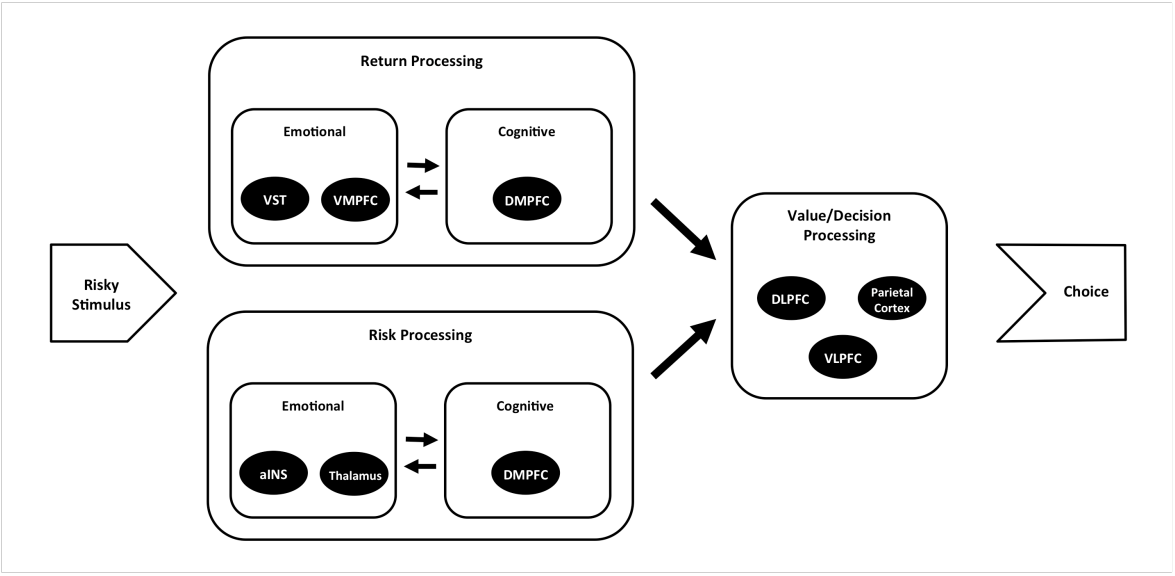

Figure 3. *A potential mechanism of risky decision making*. A risky stimulus such as a gamble with uncertain outcomes or a choice menu with different financial investments is evaluated by trading off return and risk. Both, during risk processing and during return processing, the risky stimulus is evaluated on an emotional level as well as a cognitive level. These two levels interact to determine the return and the risk of the stimulus. Return and risk are then traded off against each other to determine the value of the risky stimulus. A decision is formed by comparing the values of different choice alternatives.

After return and risk processing have concluded, risk and return are traded off against each other in the DLPFC, VLPFC, and parietal cortex to determine the value of a choice option. A decision is then made by comparing the values of different choice alternatives. The described process follows the general idea of a risk-return trade-off and is compatible with the general approach of the risk-as-feelings hypothesis (Loewenstein, et al., 2001). It reflects, however, only the level of brain activity. As described in section 2.5 the neurotransmitters dopamine and serotonin were already shown to influence return (reward) and risk processing. The exact relationship between levels of dopamine and serotonin and changes in activity in certain brain areas remains, however, unclear. Future studies should therefore directly target this obvious lack of research.

7. Conclusion

The results of this dissertation contribute to the existing literature on risk processing and risky decision making by suggesting that:

- The aINS plays a central role in risk processing, indicating that risk processing is influenced by emotions.
- The emotional influence on risk processing is especially high when losses are possible.
- The complexity of the choice problem likely influences the decision strategy, favoring risk-return models in more complex situations compared to utility-based models.
- There might be a triadic relationship between economic decision making, dopaminergic and serotoninergic neuromodulation, and aging.

Literature

Abler, B., Walter, H., Erk, S., Kammerer, H., & Spitzer, M. (2006). Prediction error as a linear function of reward probability is coded in human nucleus accumbens. *Neuroimage, 31*(2), 790-795.

Ainslie, G. W. (1974). Impulse Control in Pigeons. *Journal of the Experimental Analysis of Behavior, 21*, 485-489.

Allais, M. (1953). Le comportement de l'omme rationel devant le risque, critique des postulates et axiomes de l'école americaine. *Econometrica, 21*, 503-546.

Amiez, C., Joseph, J. P., & Procyk, E. (2006). Reward encoding in the monkey anterior cingulate cortex. *Cereb Cortex, 16*(7), 1040-1055.

Antonini, A., & Leenders, K. L. (1993). Dopamine D2 receptors in normal human brain: effect of age measured by positron emission tomography (PET) and [11C]-raclopride. *Ann N Y Acad Sci, 695*, 81-85.

Arranz, B., Eriksson, A., Mellerup, E., Plenge, P., & Marcusson, J. (1993). Effect of aging in human cortical pre- and postsynaptic serotonin binding sites. *Brain Res, 620*(1), 163-166.

Bäckman, L., Small, B. J., Wahlin, A., & Larsson, A. (1999). Cognitive functionling in very old age. In F. I. Craik & T. A. Salthouse (Eds.), *Handbook of Aging and Cognition* (pp. 499-558). Mahwah: Erlbaum.

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

Baltes, P. B., Cornelius, S. W., Spiro, A., Nesselroade, J. R., & Willis, S. L. (1980). Integration Versus Differentiation of Fluid/Crystallized Intelligence in Old Age. *Developmental Psychology, 16*(6), 625-635.

Baltes, P. B., & Lindenberger, U. (1997). Emergence of a powerful connection between sensory and cognitive functions across the adult life span: a new window to the study of cognitive aging? *Psychol Aging, 12*(1), 12-21.

Bechara, A., & Damasio, A. R. (2005). The somatic marker hypothesis: A neural theory of economic decision. *Games and Economic Behavior, 52*, 336-372.

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

Bechara, A., Damasio, H., Tranel, D., & Damasio, A. R. (1997). Deciding advantageously before knowing the advantageous strategy. *Science, 275*(5304), 1293-1295.

Beddington, J., Cooper, C. L., Field, J., Goswami, U., Huppert, F. A., Jenkins, R., et al. (2008). The mental wealth of nations. *Nature, 455*(7216), 1057-1060.

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

Bell, D. E. (1995). Risk, Return, and Utility. *Management Science, 41*(1), 23-30.

Birnbaum, M. H. (2008). New paradoxes of risky decision making. *Psychol Rev, 115*(2), 463-501.

Blais, A.-R. e., & Weber, E. U. (2006). A Domain-Specific Risk-Taking (DOSPERT) scale for adult populations. *Judgment and Decision Making, 1*(1), 33-47.

Bossaerts, P., Preuschoff, K., & Hsu, M. (2009). The Neurobiological Foundations of Valuation in Human Decision Making Under Uncertainty. In P. W. Glimcher, C. F. Camerer, E. Fehr & R. A. Poldrack (Eds.), *Neuroeconomics. Decision Making and the Brain* (pp. 353-366). London et al.: Elsevier.

Brandstatter, E., Gigerenzer, G., & Hertwig, R. (2006). The priority heuristic: making choices without trade-offs. *Psychol Rev, 113*(2), 409-432.

Braver, T. S., Barch, D. M., Keys, B. A., Carter, C. S., Cohen, J. D., Kaye, J. A., et al. (2001). Context processing in older adults: evidence for a theory relating cognitive control to neurobiology in healthy aging. *J Exp Psychol Gen, 130*(4), 746-763.

Cabeza, R., Anderson, N. D., Locantore, J. K., & McIntosh, A. R. (2002). Aging gracefully: compensatory brain activity in high-performing older adults. *Neuroimage, 17*(3), 1394-1402.

Cabeza, R., Nyberg, L., & Park, D. C. (Eds.). (2005). *Cognitive neuroscience of aging*: Oxford University Press.

Camerer, C., & Weber, M. (1992). Recent developments in modeling preferences: uncertainty and ambiguity. *Journal of Risk and Uncertainty, 5*, 325-370.

Camerer, C. F. (2007). Neuroeconomics: Using Neuroscience to Make Economic Predictions. *Economic Journal, 117*(519), C26-C42.

Camus, M., Halelamien, N., Plassmann, H., Shimojo, S., O'Doherty, J., Camerer, C., et al. (2009). Repetitive transcranial magnetic stimulation over the right dorsolateral prefrontal cortex decreases valuations during food choices. *Eur J Neurosci*.

Chandrasekhar, P. V., Capra, C. M., Moore, S., Noussair, C., & Berns, G. S. (2008). Neurobiological regret and rejoice functions for aversive outcomes. *Neuroimage, 39*(3), 1472-1484.

Cheetham, S. C., Crompton, M. R., Katona, C. L., & Horton, R. W. (1988). Brain 5-HT2 receptor binding sites in depressed suicide victims. *Brain Res, 443*(1-2), 272-280.

Chein, J. M., Fissell, K., Jacobs, S., & Fiez, J. A. (2002). Functional heterogeneity within Broca's area during verbal working memory. *Physiol Behav, 77*(4-5), 635-639.

Chua, H. F., Gonzalez, R., Taylor, S. F., Welsh, R. C., & Liberzon, I. (2009). Decision-related loss: Regret and disappointment. *Neuroimage*.

Clithero, J. A., Tankersley, D., & Huettel, S. A. (2008). Foundations of neuroeconomics: from philosophy to practice. *PLoS Biol, 6*(11), e298.

Cox, K. M., Aizenstein, H. J., & Fiez, J. A. (2008). Striatal outcome processing in healthy aging. *Cogn Affect Behav Neurosci, 8*(3), 304-317.

Craig, A. D. (2009). How do you feel--now? The anterior insula and human awareness. *Nat Rev Neurosci, 10*(1), 59-70.

Critchley, H. D. (2005). Neural mechanisms of autonomic, affective, and cognitive integration. *J Comp Neurol, 493*(1), 154-166.

Critchley, H. D., Mathias, C. J., & Dolan, R. J. (2001). Neural activity in the human brain relating to uncertainty and arousal during anticipation. *Neuron, 29*(2), 537-545.

d'Acremont, M., & Bossaerts, P. (2008). Neurobiological studies of risk assessment: A comparison of expected utility and mean-variance approaches. *Cogn Affect Behav Neurosci, 8*(4), 363-374.

Damasio, A. R., Tranel, D., & Damasio, H. (1991). Somatic markers and guidance of behaviour:theory and preliminary testing. In H. S. Levin, H. M. Eisenberg & A. L. Benton (Eds.), *Frontal lobe function and dysfunction*. New York: Oxford University Press.

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.

Deakin, J., Aitken, M., Robbins, T., & Sahakian, B. J. (2004). Risk taking during decision-making in normal volunteers changes with age. *J Int Neuropsychol Soc, 10*(4), 590-598.

Delgado, M. R., Nystrom, L. E., Fissell, C., Noll, D. C., & Fiez, J. A. (2000). Tracking the hemodynamic responses to reward and punishment in the striatum. *J Neurophysiol, 84*(6), 3072-3077.

Denburg, N. L., Tranel, D., & Bechara, A. (2005). The ability to decide advantageously declines prematurely in some normal older persons. *Neuropsychologia, 43*(7), 1099-1106.

Denk, F., Walton, M. E., Jennings, K. A., Sharp, T., Rushworth, M. F., & Bannerman, D. M. (2005). Differential involvement of serotonin and dopamine systems in cost-benefit decisions about delay or effort. *Psychopharmacology (Berl), 179*(3), 587-596.

Dobbs, A. R., & Rule, B. G. (1989). Adult Age-Differences in Working Memory. *Psychology and Aging, 4*(4), 500-503.

Dohmen, T., Falk, A., Huffman, D., Sunde, U., Schupp, J., & Wagner, G. G. (2005). Individual Risk Attitudes: New Evidence from a Large, Representative, Experimentally-Validated Survey, *IZA Discussion Paper Series*. Bonn.

Elliott, R., Friston, K. J., & Dolan, R. J. (2000). Dissociable neural responses in human reward systems. *J Neurosci, 20*(16), 6159-6165.

Elliott, R., Newman, J. L., Longe, O. A., & Deakin, J. F. (2003). Differential response patterns in the striatum and orbitofrontal cortex to financial reward in humans: a parametric functional magnetic resonance imaging study. *J Neurosci, 23*(1), 303-307.

Ellsberg, D. (1961). RISK, AMBIGUITY, AND THE SAVAGE AXIOMS. *Quarterly Journal of Economics, 75*(4), 643-669.

Erixon-Lindroth, N., Farde, L., Wahlin, T. B., Sovago, J., Halldin, C., & Backman, L. (2005). The role of the striatal dopamine transporter in cognitive aging. *Psychiatry Res, 138*(1), 1-12.

Fein, G., McGillivray, S., & Finn, P. (2007). Older adults make less advantageous decisions than younger adults: cognitive and psychological correlates. *J Int Neuropsychol Soc, 13*(3), 480-489.

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

Fischhoff, B., Watson, S. R., & Hope, C. (1984). Defining risk. *Policy Science, 17*, 123-139.

Fox, P. T., & Poldrack, R. A. (2009). Prospect Theory and the Brain. In P. W. Glimcher, C. F. Camerer, E. Fehr & R. A. Poldrack (Eds.), *Neuroeconomics. Decision Making and the Brain* (pp. 145-173). London et al.: Elsevier.

Fox, P. T., & Raichle, M. E. (1986). Focal physiological uncoupling of cerebral blood flow and oxidative metabolism during somatosensory stimulation in human subjects. *Proc Natl Acad Sci U S A, 83*(4), 1140-1144.

Fox, P. T., Raichle, M. E., Mintun, M. A., & Dence, C. (1988). Nonoxidative glucose consumption during focal physiologic neural activity. *Science, 241*(4864), 462-464.

Friston, K. J., Price, C. J., Fletcher, P., Moore, C., Frackowiak, R. S., & Dolan, R. J. (1996). The trouble with cognitive subtraction. *Neuroimage, 4*(2), 97-104.

Gigerenzer, G., Todd, P. M., & Group, A. R. (Eds.). (1999). *Simple heuristics that make us smart*. Cambridge, Mass: MIT Press.

Glimcher, P. W., Camerer, C. F., Fehr, E., & Poldrack, R. A. (2009). Introduction: A brief History of Neuroeconomcis. In P. W. Glimcher, C. F. Camerer, E. Fehr & R. A. Poldrack (Eds.), *Neuroeconomics. Decision Making and the Brain* Lonson et al.: Elsevier.

Glimcher, P. W., & Lau, B. (2005). Rethinking the thalamus. *Nat Neurosci, 8*(8), 983-984.

Green, L., Fry, A. F., & Myerson, J. (1994). Discounting od Delayed Rewards: A Life-Span Comparison *Psychological Science, 5*(1), 33-36.

Grinband, J., Hirsch, J., & Ferrera, V. P. (2006). A neural representation of categorization uncertainty in the human brain. *Neuron, 49*(5), 757-763.

Gross-Isseroff, R., Salama, D., Israeli, M., & Biegon, A. (1990). Autoradiographic analysis of [3H]ketanserin binding in the human brain postmortem: effect of suicide. *Brain Res, 507*(2), 208-215.

Gul, F., & Pesendorfer, W. (2008). The case for mindless economics. In A. Caplin & A. Schotter (Eds.), *Foundation of positive and normative economics, methodologies of modern economics* (pp. 3-39). Oxford: Oxford university Press.

Hare, T. A., O'Doherty, J., Camerer, C. F., Schultz, W., & Rangel, A. (2008). Dissociating the role of the orbitofrontal cortex and the striatum in the computation of goal values and prediction errors. *J Neurosci, 28*(22), 5623-5630.

Heekeren, H. R., Marrett, S., & Ungerleider, L. G. (2008). The neural systems that mediate human perceptual decision making. *Nat Rev Neurosci, 9*(6), 467-479.

Holtgrave, D., & Weber, E. U. (1993). Dimensions of risk perception for financial and health safety risks. *Risk Analysis, 13*, 553-558.

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. *J Neurosci, 29*(7), 2231-2237.

Huettel, S. A. (2006). Behavioral, but not reward, risk modulates activation of prefrontal, parietal, and insular cortices. *Cogn Affect Behav Neurosci, 6*(2), 141-151.

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

Inoue, M., Suhara, T., Sudo, Y., Okubo, Y., Yasuno, F., Kishimoto, T., et al. (2001). Age-related reduction of extrastriatal dopamine D2 receptor measured by PET. *Life Sci, 69*(9), 1079-1084.

Kaasinen, V., & Rinne, J. O. (2002). Functional imaging studies of dopamine system and cognition in normal aging and Parkinson's disease. *Neurosci Biobehav Rev, 26*(7), 785-793.

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

Kahneman, D., & Tversky, A. (1979). Prospect Theory: An Analysis of Decisison under Risk. *Econometrica, 47*(2), 263-291.

Keller, L. R., Sarin, R. K., & Weber, M. (1986). Empirical Investigation of Some Properties of the Perceived Riskiness of Gambles. *Organizational Behavior & Human Decision Processes, 38*(1), 114.

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

Kirby, K. N. (1997). Bidding on the Future: Evidence against normative dicounting of delayed rewards. *Journal of Experimental Psychology: General, 126*(1), 54-70.

Klos, A., Weber, E. U., & Weber, M. (2005). Investment Decisions and Time Horizon: Risk Perception and Risk Behavior in Repeated Gambles. *Management Science, 51*(12), 1777-1790.

Knight, F. H. (1921). *Risk, uncertainty and profit*. Boston: Houghton Mifflin.

Knutson, B., Adams, C. M., Fong, G. W., & Hommer, D. (2001). Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *Journal of Neuroscience, 21*(RC159), 1-5.

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

Kovalchik, S., Camerer, C. F., Grether, D. M., Plott, C. R., & Allman, J. M. (2005). Aging and decision making: a comparison between neurologically healthy elderly and young individuals. *Journal of Economic Behavior & Organization, 58*(1), 79-94.

Kuhnen, C. M., & Knutson, B. (2005). The neural basis of financial risk taking. *Neuron, 47*(5), 763-770.

Kwong, K. K., Belliveau, J. W., Chesler, D. A., Goldberg, I. E., Weisskoff, R. M., Poncelet, B. P., et al. (1992). Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proc Natl Acad Sci U S A, 89*(12), 5675-5679.

Laibson, D. (1997). Golden Eggs and Hyperbolic Discounting. *Quarterly Journal of Economics, 112*(2), 443-477.

Laird, A. R., Fox, P. M., Price, C. J., Glahn, D. C., Uecker, A. M., Lancaster, J. L., et al. (2005). ALE meta-analysis: controlling the false discovery rate and performing statistical contrasts. *Hum Brain Mapp, 25*(1), 155-164.

Lerner, J. S., & Keltner, D. (2000). Beyond valence: Toward a model of emotion-specific influences on judgement and choice. *Cognition and Emotion, 14*(4), 473-493.

Li, S.-C., Schmiedek, F., Huxhold, O., Röcke, C., Smith, J., & Lindenberger, U. (2008). Working memory plasticity in old age: Practice gains, transfer, and maintenance. *Psychology and Aging, 23*(731-742).

Li, S. C., Lindenberger, U., & Sikstrom, S. (2001). Aging cognition: from neuromodulation to representation. *Trends Cogn Sci, 5*(11), 479-486.

Lindenberger, U., Li, S. C., & Backman, L. (2006). Special Issue: Brain behavior dynamics across the lifespan. *Neuroscience & Behavioral Reviews, 30*, 713-885.

Lindenberger, U., Nagel, I. E., Chicherio, C., Li, S. C., Heekeren, H. R., & Backman, L. (2008). Age-related decline in brain resources modulates genetic effects on cognitive functioning. *Front Neurosci, 2*(2), 234-244.

Loewenstein, G. F., Weber, E. U., Hsee, C. K., & Welch, N. (2001). Risk as feelings. *Psychol Bull, 127*(2), 267-286.

Logothetis, N. K. (2008). What we can do and what we cannot do with fMRI. *Nature, 453*(7197), 869-878.

Logothetis, N. K., Pauls, J., Augath, M., Trinath, T., & Oeltermann, A. (2001). Neurophysiological investigation of the basis of the fMRI signal. *Nature, 412*(6843), 150-157.

Logothetis, N. K., & Wandell, B. A. (2004). Interpreting the BOLD signal. *Annu Rev Physiol, 66*, 735-769.

Maia, T. V., & McClelland, J. L. (2004). A reexamination of the evidence for the somatic marker hypothesis: what participants really know in the Iowa gambling task. *Proc Natl Acad Sci U S A, 101*(45), 16075-16080.

Marcusson, J., Oreland, L., & Winblad, B. (1984). Effect of age on human brain serotonin (S-1) binding sites. *J Neurochem, 43*(6), 1699-1705.

Marcusson, J. O., Morgan, D. G., Winblad, B., & Finch, C. E. (1984). Serotonin-2 binding sites in human frontal cortex and hippocampus. Selective loss of S-2A sites with age. *Brain Res, 311*(1), 51-56.

Markowitz, H. (1952). Portfolio Selection. *Journal of Finance, 7*(1), 77-91.

Marschner, A., Mell, T., Wartenburger, I., Villringer, A., Reischies, F. M., & Heekeren, H. R. (2005). Reward-based decision-making and aging. *Brain Res Bull, 67*(5), 382-390.

Mata, R., Schooler, L. J., & Rieskamp, J. (2007). The aging decision maker: cognitive aging and the adaptive selection of decision strategies. *Psychol Aging, 22*(4), 796-810.

Mattay, V. S., Goldberg, T. E., Fera, F., Hariri, A. R., Tessitore, A., Egan, M. F., et al. (2003). Catechol O-methyltransferase val158-met genotype and individual variation in the brain response to amphetamine. *Proc Natl Acad Sci U S A, 100*(10), 6186-6191.

Matthews, S. C., Simmons, A. N., Lane, S. D., & Paulus, M. P. (2004). Selective activation of the nucleus accumbens during risk-taking decision making. *Neuroreport, 15*(13), 2123-2127.

McClure, S. M., Ericson, K. M., Laibson, D. I., Loewenstein, G., & Cohen, J. D. (2007). Time discounting for primary rewards. *J Neurosci, 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.

McEntee, W. J., & Crook, T. H. (1991). Serotonin, memory, and the aging brain. *Psychopharmacology (Berl), 103*(2), 143-149.

Mohr, P. N., Biele, G., Krugel, L. K., Li, S. C., & Heekeren, H. R. (2009). Neural foundations of risk-return trade-off in investment decisions. *Neuroimage*. *49(3)*, 2556-2563.

Mozley, L. H., Gur, R. C., Mozley, P. D., & Gur, R. E. (2001). Striatal dopamine transporters and cognitive functioning in healthy men and women. *American Journal of Psychiatry, 158*, 1492-1499.

Nagel, I. E., Chicherio, C., Li, S. C., von Oertzen, T., Sander, T., Villringer, A., et al. (2008). Human aging magnifies genetic effects on executive functioning and working memory. *Front Hum Neurosci, 2*, 1.

Nagel, I. E., Preuschhof, C., Li, S. C., Nyberg, L., Backman, L., Lindenberger, U., et al. (2009). Performance level modulates adult age differences in brain activation during spatial working memory. *Proc Natl Acad Sci U S A, 106*(52), 22552-22557.

Nieuwenhuis, S., Ridderinkhof, K. R., Talsma, D., Coles, M. G., Holroyd, C. B., Kok, A., et al. (2002). A computational account of altered error processing in older age: dopamine and the error-related negativity. *Cogn Affect Behav Neurosci, 2*(1), 19-36.

Nyberg, L., Dahlin, E., Stigsdotter Neely, A., & Backman, L. (2009). Neural correlates of variable working memory load across adult age and skill: dissociative patterns within the fronto-parietal network. *Scand J Psychol, 50*(1), 41-46.

Ogawa, S., Lee, T. M., Kay, A. R., & Tank, D. W. (1990). Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proc Natl Acad Sci U S A, 87*(24), 9868-9872.

Park, D. C., Polk, T. A., Park, R., Minear, M., Savage, A., & Smith, M. R. (2004). Aging reduces neural specialization in ventral visual cortex. *Proc Natl Acad Sci U S A, 101*(35), 13091-13095.

Paulus, M. P., Hozack, N., Zauscher, B., McDowell, J. E., Frank, L., Brown, G. G., et al. (2001). Prefrontal, parietal, and temporal cortex networks underlie decision-making in the presence of uncertainty. *Neuroimage, 13*(1), 91-100.

Paulus, M. P., Rogalsky, C., Simmons, A., Feinstein, J. S., & Stein, M. B. (2003). Increased activation in the right insula during risk-taking decision making is related to harm avoidance and neuroticism. *Neuroimage, 19*(4), 1439-1448.

Paulus, M. P., & Stein, M. B. (2006). An insular view of anxiety. *Biol Psychiatry, 60*(4), 383-387.

Phan, K. L., Wager, T., Taylor, S. F., & Liberzon, I. (2002). Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage, 16*(2), 331-348.

Plassmann, H., O'Doherty, J., & Rangel, A. (2007). Orbitofrontal cortex encodes willingness to pay in everyday economic transactions. *J Neurosci, 27*(37), 9984-9988.

Poldrack, R. A. (2006). Can cognitive processes be inferred from neuroimaging data? *Trends Cogn Sci, 10*(2), 59-63.

Preuschoff, K., Bossaerts, P., & Quartz, S. R. (2006). Neural differentiation of expected reward and risk in human subcortical structures. *Neuron, 51*(3), 381-390.

Preuschoff, K., Quartz, S. R., & Bossaerts, P. (2008). Human insula activation reflects risk prediction errors as well as risk. *J Neurosci, 28*(11), 2745-2752.

Quartz, S. R. (2009). Reason, emotion and decision-making: risk and reward computation with feeling. *Trends Cogn Sci, 13*(5), 209-215.

Raz, N., Gunning-Dixon, F., Head, D., Rodrigue, K. M., Williamson, A., & Acker, J. D. (2004). Aging, sexual dimorphism, and hemispheric asymmetry of the cerebral cortex: replicability of regional differences in volume. *Neurobiol Aging, 25*(3), 377-396.

Reuter-Lorenz, P. A., & Capell, K. (2008). Neurocognitive aging and the compensation hypothesis. *Current Directions in Psychological Science, 18*(3), 177-182.

Reuter-Lorenz, P. A., & Lustig, C. (2005). Brain aging: reorganizing discoveries about the aging mind. *Curr Opin Neurobiol, 15*(2), 245-251.

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.

Rogers, A. R. (1994). Evolution of time preference by natural selection. *American Economic Review, 84*, 460-481.

Rolls, E. T., McCabe, C., & Redoute, J. (2008). Expected value, reward outcome, and temporal difference error representations in a probabilistic decision task. *Cereb Cortex, 18*(3), 652-663.

Salthouse, T. A., & Babcock, R. L. (1991). Decomposing Adult Age-Differences in Working Memory. *Developmental Psychology, 27*(5), 763-776.

Samanez-Larkin, G. R., Gibbs, S. E., Khanna, K., Nielsen, L., Carstensen, L. L., & Knutson, B. (2007). Anticipation of monetary gain but not loss in healthy older adults. *Nat Neurosci, 10*(6), 787-791.

Samanez-Larkin, G. R., Kuhnen, C. M., Yoo, D. J., & Knutson, B. (2010). Variability in Nucleus Accumbens Activity Mediates Age-Related Suboptimal Financial Risk Taking. *J Neurosci, 30*(4), 1426-1434.

Sanfey, A. G., Loewenstein, G., McClure, S. M., & Cohen, J. D. (2006). Neuroeconomics: cross-currents in research on decision-making. *Trends Cogn Sci, 10*(3), 108-116.

Sarin, R. K., & Weber, M. (1993). Risk-value models. *European Journal of Operational Research, 70*(2), 135-149.

Schmiedek, F., Li, S.-C., & Lindenberger, U. (2009). Interference and facilitation in spatial working memory: Age-related differences in lure effects in the N-back paradigm. *Psychology and Aging, 24*, 203-210.

Schott, B. H., Niehaus, L., Wittmann, B. C., Schutze, H., Seidenbecher, C. I., Heinze, H. J., et al. (2007). Ageing and early-stage Parkinson's disease affect separable neural mechanisms of mesolimbic reward processing. *Brain, 130*(Pt 9), 2412-2424.

Shinkai, T., Zhang, L., Mathias, S. A., & Roth, G. S. (1997). Dopamine induces apoptosis in cultured rat striatal neurons; possible mechanism of D2-dopamine receptor neuron loss during aging. *J Neurosci Res, 47*(4), 393-399.

Singer, T., Critchley, H. D., & Preuschoff, K. (2009). A common role of insula in feelings, empathy and uncertainty. *Trends in Cognitive Science*.

Slovic, P., Finucane, M. L., Peters, E., & MacGregor, D. G. (2004). Risk as analysis and risk as feelings: some thoughts about affect, reason, risk, and rationality. *Risk Anal, 24*(2), 311-322.

Slovic, P., Fischhoff, B., & Lichtenstein, S. (2000). Facts and Fears: Understanding Perceived Risk. In P. Slovic (Ed.), *The Perception of Risk*. London: Earthscan.

Slovic, P., Peters, E., Finucane, M. L., & Macgregor, D. G. (2005). Affect, risk, and decision making. *Health Psychol, 24*(4 Suppl), S35-40.

Sparks, D. L. (1989). Aging and Alzheimer's disease. Altered cortical serotoninergic binding. *Arch Neurol, 46*(2), 138-140.

Suhara, T., Fukuda, H., Inoue, O., Itoh, T., Suzuki, K., Yamasaki, T., et al. (1991). Age-related changes in human D1 dopamine receptors measured by positron emission tomography. *Psychopharmacology (Berl), 103*(1), 41-45.

Sutton, R. S., & Barto, A. G. (1981). Toward a modern theory if adaptive networks: expectation and prediction. *Psychological Review, 88*, 135-170.

Talairach, P., & Tournoux, J. (1988). *A Stereotactic Coplanar Atlas of the Human Brain*: Stuttgart:Thieme.

Talbot, P. S., Watson, D. R., Barrett, S. L., & Cooper, S. J. (2006). Rapid tryptophan depletion improves decision-making cognition in healthy humans without affecting reversal learning or set shifting. *Neuropsychopharmacology, 31*(7), 1519-1525.

Tanaka, S. C., Schweighofer, N., Asahi, S., Shishida, K., Okamoto, Y., Yamawaki, S., et al. (2007). Serotonin differentially regulates short- and long-term prediction of rewards in the ventral and dorsal striatum. *PLoS ONE, 2*(12), e1333.

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. *Proc Natl Acad Sci U S A, 106*(17), 7185-7190.

Tobler, P. N., Fiorillo, C. D., & Schultz, W. (2005). Adaptive coding of reward value by dopamine neurons. *Science, 307*(5715), 1642-1645.

Tobler, P. N., O'Doherty, J. P., Dolan, R. J., & Schultz, W. (2007). Reward value coding distinct from risk attitude-related uncertainty coding in human reward systems. *J Neurophysiol, 97*(2), 1621-1632.

Tom, S. M., Fox, C. R., Trepel, C., & Poldrack, R. A. (2007). The neural basis of loss aversion in decision-making under risk. *Science, 315*(5811), 515-518.

Trostel, P. A., & Taylor, G. A. (2001). A theory of time preference. *Economic Inquiery, 39*(3), 379-395.

Turkeltaub, P. E., Eden, G. F., Jones, K. M., & Zeffiro, T. A. (2002). Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. *Neuroimage, 16*(3 Pt 1), 765-780.

Tversky, A., & Kahneman, D. (1992). Advances in prospect theory - cumulative representation of subjective probability. *Journal of Risk and Uncertainty, 5*, 297-323.

Venkatraman, V., Payne, J. W., Bettman, J. R., Luce, M. F., & Huettel, S. A. (2009). Separate neural mechanisms underlie choices and strategic preferences in risky decision making. *Neuron, 62*(4), 593-602.

Viswanathan, A., & Freeman, R. D. (2007). Neurometabolic coupling in cerebral cortex reflects synaptic more than spiking activity. *Nat Neurosci, 10*(10), 1308-1312.

Volz, K. G., Schubotz, R. I., & von Cramon, D. Y. (2003). Predicting events of varying probability: uncertainty investigated by fMRI. *Neuroimage, 19*(2 Pt 1), 271-280.

Volz, K. G., Schubotz, R. I., & von Cramon, D. Y. (2004). Why am I unsure? Internal and external attributions of uncertainty dissociated by fMRI. *Neuroimage, 21*(3), 848-857.

von Neumann, J., & Morgenstern, O. (1953). *Theory of Games and Economic Behavior* (Vol. 3.). Princton.

Wang, Y., Chan, G. L., Holden, J. E., Dobko, T., Mak, E., Schulzer, M., et al. (1998). Age-dependent decline of dopamine D1 receptors in human brain: a PET study. *Synapse, 30*(1), 56-61.

Weber, B., Aholt, A., Neuhaus, C., Trautner, P., Elger, C. E., & Teichert, T. (2007). Neural evidence for Reference-dependence in real-market-transactions. *Neuroimage, 35*(1), 441-447.

Weber, B. J., & Huettel, S. A. (2008). The neural substrates of probabilistic and intertemporal decision making. *Brain Res, 1234*, 104-115.

Weber, E. U., Anderson, C. J., & Birnbaum, M. H. (1992). A theory of perceived risk and attractiveness. *Organizational Behavior and Human Decision Processes, 52*(3), 492-523.

Weber, E. U., Blais, A.-R. e., & Betz, N. E. (2002). A domain-specific risk-attitude scale: Measuring risk perceptions and risk behaviors. *Journal of Behavioral Decision Making, 15*(4), 263-290.

Weber, E. U., & Hsee, C. (1998). Cross-cultural Differences in Risk Perception, but Cross-cultural Similarities in Attitudes Towards Perceived Risk. *Management Science, 44*(9), 1205-1217.

Weber, E. U., & Johnson, E. J. (2009). Decisions Under Uncertainty: Psychological, Economic, and Neuroeconomic Explanations of Risk Preference. In P. W. Glimcher, C. F. Camerer, E. Fehr & R. A. Poldrack (Eds.), *Neuroeconomics. Decision Making and the Brain* (pp. 127-144). London et al.: Elsevier.

Weber, E. U., & Johnson, E. J. (2009). Mindful judgment and decision making. *Annu Rev Psychol, 60*, 53-85.

Weber, E. U., & Milliman, R. (1997). Perceived risk attitudes: relating risk perception to risky choices. *Management Sci., 43*, 122-143.

Weber, E. U., Shafir, S., & Blais, A. R. (2004). Predicting risk sensitivity in humans and lower animals: risk as variance or coefficient of variation. *Psychol Rev, 111*(2), 430-445.

Weber, E. U., Siebenmorgen, N., & Weber, M. (2005). Communicating asset risk: how name recognition and the format of historic volatility information affect risk perception and investment decisions. *Risk Anal, 25*(3), 597-609.

Wong, D. F., Wagner, H. N., Jr., Dannals, R. F., Links, J. M., Frost, J. J., Ravert, H. T., et al. (1984). Effects of age on dopamine and serotonin receptors measured by positron tomography in the living human brain. *Science, 226*(4681), 1393-1396.

Xu, L., Liang, Z. Y., Wang, K., Li, S., & Jiang, T. (2009). Neural mechanism of intertemporal choice: from discounting future gains to future losses. *Brain Res, 1261*, 65-74.

Yoshida, W., & Ishii, S. (2006). Resolution of uncertainty in prefrontal cortex. *Neuron, 50*(5), 781-789.

Zamarian, L., Sinz, H., Bonatti, E., Gamboz, N., & Delazer, M. (2008). Normal aging affects decisions under ambiguity, but not decisions under risk. *Neuropsychology, 22*(5), 645-657.

Zhang, L., Ravipati, A., Joseph, J., & Roth, G. S. (1995). Aging-related changes in rat striatal D2 receptor mRNA-containing neurons: a quantitative nonradioactive in situ hybridization study. *J Neurosci, 15*(3 Pt 1), 1735-1740.

Appendix

Relationship between Mean-Variance Model and Expected Utility Theory

In certain conditions the *MVM* and the *EUT* become equivalent. For instance, if the utility function is quadratic,

$$u(x) = ax^2 + bx + c$$

the expected utility can be written in the form of the *MVM*

$$EU(X) = u(\mu) + a \cdot \sigma^2,$$

where μ and σ^2 are the expected value and variance of the gamble X.

In general, utility functions can always be approximated by means of a Taylor series expansion

$$u(x) \cong u(\mu) + u'(\mu)(x - \mu) + \frac{1}{2}u''(x - \mu)^2,$$

where u´and u´´denote the first and the second derivative of u. Taking the expected value of the utility results in

$$EU(X) = u(\mu) + \frac{1}{2}u''(\mu) \cdot \sigma^2,$$

which has the form of a *MVM*. As such valuations from *EUT* can be always approximated by the *MVM*.

Project I

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Behavioral/Systems/Cognitive

Neural Processing of Risk

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In our everyday life, we often have to make decisions with risky consequences, such as choosing a restaurant for dinner or choosing a form of retirement saving. To date, however, little is known about how the brain processes risk. Recent conceptualizations of risky decision making highlight that it is generally associated with emotions but do not specify how emotions are implicated in risk processing. Moreover, little is known about risk processing in non-choice situations and how potential losses influence risk processing. Here we used quantitative meta-analyses of functional magnetic resonance imaging experiments on risk processing in the brain to investigate (1) how risk processing is influenced by emotions, (2) how it differs between choice and non-choice situations, and (3) how it changes when losses are possible. By showing that, over a range of experiments and paradigms, risk is consistently represented in the anterior insula, a brain region known to process aversive emotions such as anxiety, disappointment, or regret, we provide evidence that risk processing is influenced by emotions. Furthermore, our results show risk-related activity in the dorsolateral prefrontal cortex and the parietal cortex in choice situations but not in situations in which no choice is involved or a choice has already been made. The anterior insula was predominantly active in the presence of potential losses, indicating that potential losses modulate risk processing.

Introduction

Many decisions in our everyday life, such as choosing a restaurant for dinner or choosing a form of retirement saving, can be described as decisions under risk. Decision sciences such as psychology and economics usually define risk as the uncertainty about which of several possible outcomes will occur, whereby the probability of each possible outcome is known (Knight, 1921). In contrast, ambiguity describes a form of uncertainty in which probabilities and/or possible outcomes are unknown.

Traditional models of risky decision making implicitly assume that the characteristics of a choice option (e.g., magnitude of possible outcomes) are cognitively evaluated. In the framework of expected utility theory, people's willingness to take risk depends on the concavity of the utility function. In prospect theory, it additionally depends on the shape of the probability weighting function (for review, see Bossaerts et al., 2009; Fox and Poldrack, 2009).

Recent approaches, however, highlighted the role of emotions in decision making. Based on psychological and neuroscientific research, theories such as the affect heuristic (Slovic et al., 2004), the risk-as-feelings hypothesis (Loewenstein et al., 2001), and the somatic marker hypothesis (Damasio et al., 1991) propose that emotions interact with a cognitive evaluation of the choice problem to guide behavior. To date, however, it remains unclear how risk processing is influenced by emotions.

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Traditional models of risky decision making further often assume that risk is a context-independent function of the variability of possible outcomes (e.g., variance) (Markowitz, 1952). Research on the perception of risk, however, indicates that risk perception is neither context independent nor a pure measure of outcome variability (Weber et al., 2002). One can distinguish risk processing during or before choice (decision risk) and risk processing after or without a choice (anticipation risk), with the crucial difference that risk information is likely used to guide choices in the context of decision risk but not in the context of anticipation risk. Furthermore, individuals' judgments of perceived risk are more sensitive to downside variability and losses than to upside variability, indicating that risk might be processed differently if losses are possible (Weber et al., 1992).

Thus, three main questions regarding risk processing remain unresolved, namely (1) how risk processing is generally influenced by emotions, (2) whether the neural processing of risk is context dependent, differing between decision making and pure outcome anticipation, and (3) whether risk is processed differently in the brain when individuals are faced with potential losses.

Because single studies use specific tasks, their ability to answer such general questions is limited. In contrast, quantitative meta-analyses provide unbiased, objective measures of brain functioning and provide a useful approach to address such questions. Here, we performed quantitative voxelwise meta-analyses on neural representations of risk using the activation likelihood estimation method (ALE) (Turkeltaub et al., 2002; Laird et al., 2005). Importantly, ALE also allows a comparison of different task conditions (e.g., decision and anticipation) that were not contrasted in the same study.

Materials and Methods

Study selection. To identify studies investigating the neural processing of risk, we performed a literature search in two databases, namely Web of

Science and Medline. Both databases were searched with the following logic conjunction of keywords: ("risk" OR "uncertainty") AND ("decision making" OR "choice" OR "anticipation") AND ("fMRI" OR "neuroimaging"). The search (performed on November 1, 2009) identified 285 hits. We further identified recent review papers about risky decision making that explicitly discuss the issue of risk processing in the brain (Knutson and Bossaerts, 2007; Platt and Huettel, 2008; Rangel et al., 2008; Rushworth and Behrens, 2008; Mohr et al., 2010b). All studies found through the database search and those that were cited by one of these review papers underwent the study selection process. The full selection process included a reading of introduction and methods part of each article by at least one of the three authors, followed by application of the following inclusion criteria: (1) functional magnetic resonance imaging (fMRI) study involving healthy young adult human participants; (2) imaging data acquired over the whole brain; (3) availability of peak activation coordinates from group activation maps; (4) outcomes of the task are at least partly uncertain; (5) available information for participants regarding outcome probabilities; and (6) outcomes of the task are independent of the behavior of others.

The inclusion criteria were chosen to ensure that our results could be generalized to the population of young healthy adult humans. Several studies on cognitive aging showed that cognitive changes across the adult lifespan are paralleled by structural and functional changes in the brain (Cabeza et al., 2005; Mohr et al., 2010b). Furthermore, older adults often show activations that are qualitatively different from those of young adults (Park et al., 2004). Therefore we included only studies that investigated risk processing in young healthy adults (criterion 1).

Driven by specific functional hypotheses, some neuroimaging studies do not acquire images of the whole brain but only of parts of the brain, allowing a higher image resolution. These images, however, impede the detection of nonhypothesized activations in brain regions that were not scanned. That is why criterion 2 excludes studies that did not scan the whole brain.

Because the ALE approach is based on activation foci (see below), we only included studies that report peak activation coordinates of group activation maps (criterion 3).

Because risk is usually contrasted with ambiguity—a form of uncertainty in which probabilities are unknown—we included only studies in which outcomes are uncertain (criterion 4) and probabilities are known, learned, or could be estimated (criterion 5). We further limited the included studies/analyses to those in which outcomes are independent of the behavior of others (criterion 6), because these might be confounded with other effects of, e.g., trust or reciprocity.

Because of non-independence considerations, we set an additional inclusion criterion on the level of analyses. If two risk analyses (e.g., contrast and correlation) were performed on the same dataset (and same time window), we included only the more specific risk analysis (correlation) because it reflects risk processing likely better than the less specific analysis (contrast).

Thirty studies met the inclusion criteria (Table 1) (supplemental Table S1, available online on www.jneurosci.org), representing 232 risk-related foci. Fifteen studies (101 foci) compared conditions, whereas 15 studies (131 foci) correlated risk with brain activity. Twenty-one studies (172 foci) investigated decision risk, and 10 studies (60 foci) investigated anticipation risk (one study investigated both). We further categorized studies according to potential outcomes. Eleven studies (101 foci) investigated risk in the context of only gains, whereas in 11 (92 foci) studies gains and losses were possible outcomes. For two studies (28 foci), the categorization was ambiguous because they investigated objective gains but included an obvious reference point that could lead to the perception of some positive outcomes as losses (with regard to the reference point). The tasks of six studies (39 foci) did not include monetary gains or losses (e.g., only right/wrong as outcomes).

ALE meta-analysis. In contrast to meta-analyses in behavioral sciences that aim to estimate the true effect size for an effect, fMRI meta-analyses aim to identify networks of brain regions implicated in certain cognitive processes (Turkeltaub et al., 2002). The focal question of fMRI meta-analyses is thus about the location of brain activity associated with specific cognitive processes rather than about the effect size of the relationship. Because of this difference in research questions, new meta-analytic techniques were developed, which are adapted to the format of fMRI results. Specifically, whereas the key results of behavioral studies are test statistics (p, t, or z score) and effect sizes, test statistics in fMRI studies usually have meaning only together with information about the location of the effect, often given by the voxel with the highest test statistic. One frequently used meta-analytic technique that exploits this location information is ALE.

Table 1. Included risk studies

	No. of risk-related foci	Context		Analysis		Domain		
		DR	AR	Corr	Contr	G	G + L	O
Volz et al. (2004)	5	x		x		x		
Volz et al. (2003)	7	x		x		x		
Preuschoff et al. (2006)	22		x	x			x	
Paulus et al. (2003)	5	x			x		x	
Paulus et al. (2001)	10	x			x	x		
Preuschoff et al. (2008)	16		x	x			x	
Critchley et al. (2001)	4		x	x			x	
Kuhnen and Knutson (2005)	2		x	x			x	
Matthews et al. (2004)	4	x			x		x	
Tobler et al. (2006)	1		x		x	x		
Huettel et al. (2005)	10	x		x				x
Hsu et al. (2005)	12	x			x			x
Dreher et al. (2006)	4		x		x		x	
Huettel (2006)	15	x		x		x		
Grinband et al. (2006)	8	x		x				x
Behrens et al. (2007)	1		x	x		x		
Rolls et al. (2008)	1		x	x		x		
Yoshida and Ishii (2006)	3	x		x				x
Smith et al. (2009)	2	x			x	x		
Weber and Huettel (2008)	16	x			x			x
Bach et al. (2009)	2		x		x			x
Blackwood et al. (2004)	6	x			x			x
Elliott et al. (1999)	12	x			x			x
Engelmann and Tamir (2009)	32	x (25)[a]	x (7)[a]	x		x		
Labudda et al. (2008)	6	x			x		x	
Lee et al. (2008)	3	x			x		x	
van Leijenhorst et al. (2006)	16	x			x	x		
Xue et al. (2009)	3	x		x			x	
Christopoulos et al. (2009)	2	x			x	x		
Mohr et al. (2010a)	2	x		x			x	
Number of foci	232	172	60	131	101	101	92	67

DR, Decision risk; AR, anticipation risk; Corr, correlation; Contr, contrast; G, gains; G + L, gains and losses; O, other.
[a]Engelmann and Tamir (2009) investigated risk in both contexts.

ALE is a quantitative meta-analysis technique that compares activation likelihoods calculated from observed activation foci with a null distribution of randomly generated activation likelihoods. In ALE, peak activation coordinates from a number of studies investigating similar effects are pooled (Chein et al., 2002; Turkeltaub et al., 2002; Laird et al., 2005). These coordinates are generally published relative to Talairach or Montreal Neurological Institute (MNI) space and therefore need to be spatially renormalized to a single template.

The resulting coordinates are used to generate "activation likelihoods" for each voxel in the brain. For each focus, ALE scores each voxel as a function of its distance from that focus using a three-dimensional Gaussian probability density function centered at the coordinates of the focus. As a result, ALE gets vectors of values for each voxel representing probabilities to belong to specific foci. These values are assumed to be independent (the existence of one focus does not give information about whether another focus will occur) and are combined with the addition rule for log-probabilities, yielding so-called ALE statistics. The ALE statistic represents the probability of a certain voxel to belong to any of the included foci.

To test for significance, the ALE statistic in each voxel is compared with a null distribution, generated via repeatedly calculating ALE statistics from randomly placed activation foci (same number as included in the study). This null distribution is then used to estimate the threshold

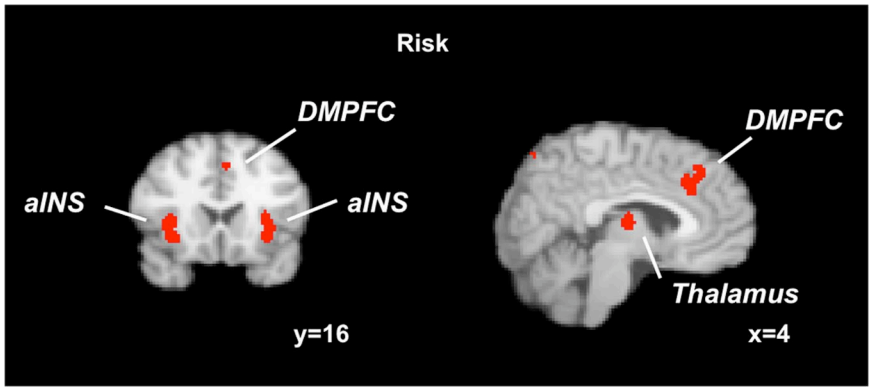

Figure 1. Neural representations of risk. Results from an ALE meta-analysis on risk independent of the context (decision risk or anticipation risk) and the domain (gains + losses or only gains in which risk was investigated). Activated clusters included bilateral aINS, DMPFC, and thalamus (FDR of <0.05; cluster size of >200 mm^3).

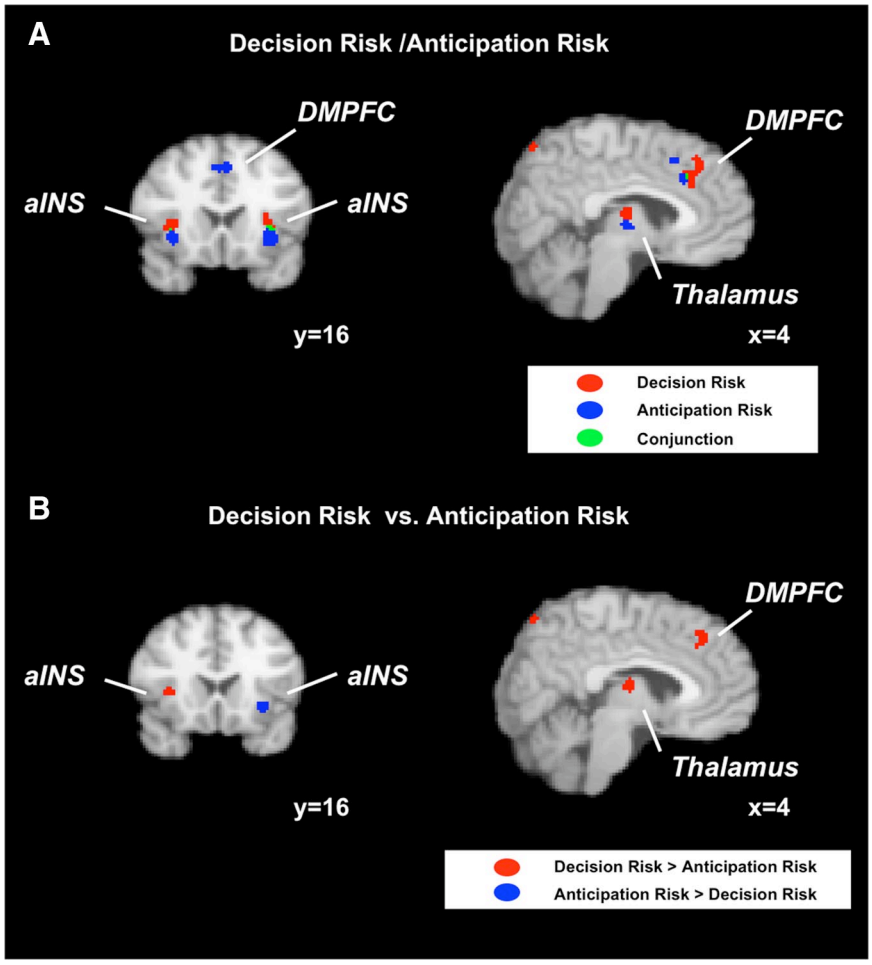

Figure 2. Neural representations of decision risk and anticipation risk. ***A***, Risk activated bilateral aINS and DMPFC in both a meta-analysis on decision risk and a meta-analysis on anticipation risk (although there is in all cases only a small overlap). Right DLPFC and right parietal cortex (both not displayed) were solely activated by decision risk. ***B***, Right aINS, right DLPFC (not displayed), DMPFC, and right parietal cortex (not displayed) were more likely to be activated by decision risk compared with anticipation risk in a meta-analysis on the contrast between the two contexts in which risk was investigated. Left aINS, in contrast, was more likely to be activated by anticipation risk.

resulting for a given false discovery rate (FDR). Finally, a cluster threshold (minimum spatial extent of significant clusters) can be applied.

The ALE meta-analysis can also be used to contrast two independent meta-analyses. In this case, the ALE statistic in each voxel is calculated as the difference in ALE values between the two meta-analyses. Whereas ALE values can only be positive in a single ALE meta-analysis, they can be negative as well in a contrast of ALE meta-analyses. The null distribution is calculated accordingly via calculating the differences between ALE statistics of randomly generated foci (again, same number of foci as included in the respective studies). Additional steps of the analysis equal the procedure used for a single ALE meta-analysis described above.

The ALE procedure was recently improved in that activation foci are now smoothed only in gray matter and in that group statistics are calculated as random effects, so that results can now be generalized beyond the studies in the sample (Eickhoff, 2009). Because this approach does not yet allow contrasting two sets of foci, we applied the standard approach in this study. Still, we report the results of each single meta-analysis using the new approach in the supplemental data (available at www.jneurosci.org as supplemental material) and show that they do not differ qualitatively from the results obtained with the standard approach. Actually, most clusters of significant foci were larger using the new approach (see supplemental data, available at www.jneurosci.org as supplemental material).

Application of the ALE meta-analysis. We first transformed MNI coordinates into Talairach space using the icbm2tal (Lancaster et al., 2007) transformation implemented in the GingerALE toolbox (http://brainmap.org; Research Imaging Center of the University of Texas Health Science Center, San Antonio, Texas). Second, we calculated different ALE meta-analyses with GingerALE. The ALE statistics in each of these meta-analyses is calculated by modeling each equally weighted activation peak using a three-dimensional Gaussian probability density function with a full-width half-maximum that is calculated as the average smoothing kernel of the included studies weighted with the number of foci for each study. To test for significance, we generated null distributions from 10,000 permutations for each meta-analysis.

The first meta-analysis included all risk-related foci (risk analysis), independent of the context. Additionally, we divided risk-related foci in two groups according to their context (decision risk vs anticipation risk) and conducted separate meta-analyses for each group of foci (decision risk analysis and anticipation risk analysis). A contrast of these two meta-analyses identified regions that are more active in one context than in the other context (decision risk vs anticipation risk analysis). Similarly, we divided risk-related foci into two different groups according to the presence of losses (gains only and gains + losses, respectively). A third group of foci that represented neither gains nor gains + losses (but, e.g., right vs wrong or pain) was omitted from these analyses. To identify the effect of losses on risk processing, we contrasted the gains foci with the gains + losses foci (gains + losses vs gains only analysis). One has to note, however, that the two comparisons of groups of foci (decision risk vs anticipation risk and gains + losses vs gains, respectively) were not independent

(Table 1). Most foci from the gains group were investigated during decision making (and vice versa), whereas most foci from the gains + losses group also belong to the set of foci for anticipation risk.

Results

In the risk analysis, we included all risk-related foci from all studies (232 foci) independent of the specific context (decision context vs anticipation context) and domain (gains + losses vs gains). We found representations of risk in bilateral anterior insula (aINS), thalamus, dorsomedial prefrontal cortex (DMPFC), right dorsolateral prefrontal cortex (DLPFC), right parietal cortex, left precentral gyrus, and occipital cortex (supplemental Table S2, available at www.jneurosci.org as supplemental material) (Fig. 1).

To analyze the differences in representation of decision risk and anticipation risk, we conducted separate meta-analyses of studies involving these types of risk. The goal was to identify common neural substrates by using a conjunction analysis and to identify dissociations by contrasting the results of the meta-analyses. Both decision risk and anticipation risk activated bilateral aINS, DMPFC, and thalamus (supplemental Table S3, S4, available at www.jneurosci.org as supplemental material) (Fig. 2*A*). Significant clusters of the two contexts showed, however, only small overlap in these regions or did not overlap at all (thalamus).

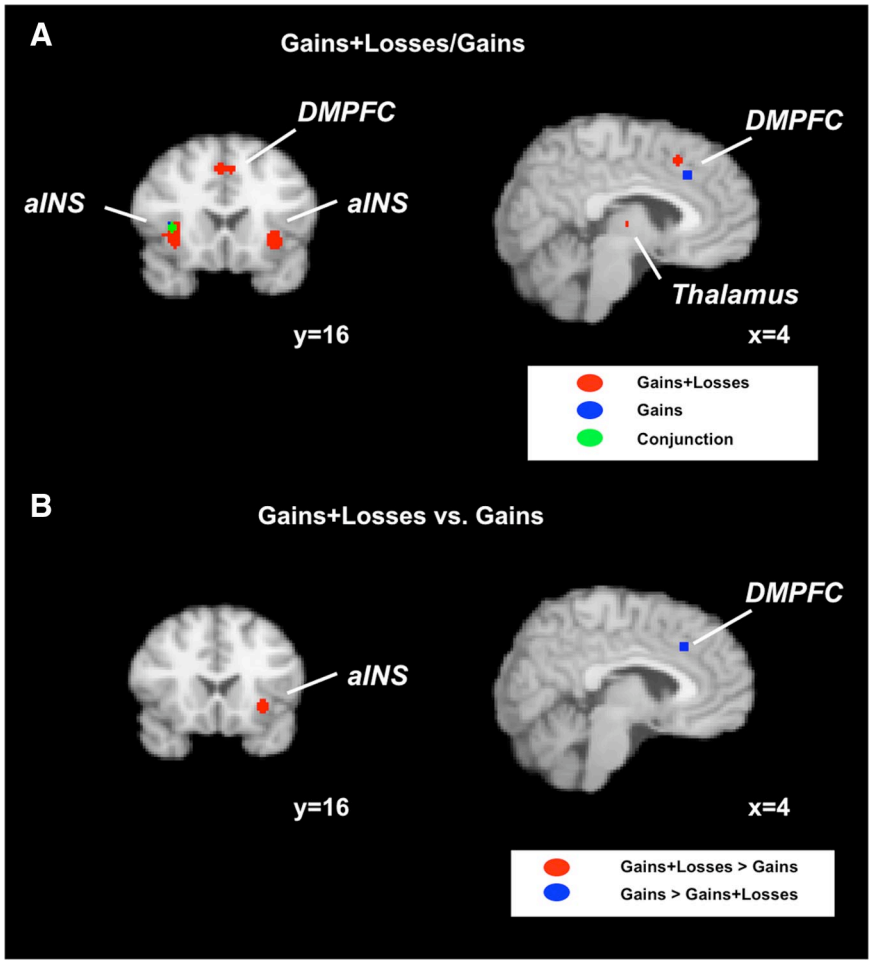

Figure 3. Domain-specific neural representations of risk. ***A***, Risk investigated in tasks that included both the gain and the loss domain activated bilateral aINS, DMPFC, and thalamus. In contrast, risk representations investigated only in the gain domain only include right aINS and DMPFC. ***B***, Left aINS was more likely to be activated if both gains and losses were possible outcomes, whereas DMPFC was more likely to be activated if only gains were possible.

To investigate activations associated only with decision or anticipation risk, respectively, we conducted an ALE meta-analysis on the contrast between decision risk and anticipation risk (decision risk vs anticipation risk analysis). Right aINS, DMPFC, DLPFC, parietal cortex, striatum, and occipital cortex were significantly more likely to be activated by decision risk, whereas left aINS and left superior temporal gyrus (STG) showed significantly higher ALE values for anticipation risk (supplemental Table S5, available at www.jneurosci.org as supplemental material) (Fig. 2*B*).

Because tasks that investigated neural representations of risk sometimes only included gains as possible outcomes and others also included losses, we formed two groups of foci according to this criterion. The goal of these analyses was to investigate whether risk is processed differently if subjects could lose money. Here we again conducted separate meta-analyses for the two groups of foci to identify common neural substrates and contrasted the results of the meta-analyses to identify significant differences. We found risk-related activations in both analyses in right aINS, DMPFC, and thalamus (supplemental Tables S6, S7, available at www.jneurosci.org as supplemental material) (Fig. 3*A*). Only the cluster in right aINS, however, showed an overlap between the two analyses. When contrasting the two sets of foci, we found that left aINS, left STG, and left precentral gyrus were more likely to be activated when losses were possible, whereas DMPFC, DLPFC, right parietal cortex, thalamus, and occipital cortex were more likely to be activated if only gains were possible (supplemental Table S8, available at www.jneurosci.org as supplemental material) (Fig. 3*B*).

Discussion

In our everyday life, we often have to make decisions with risky consequences. In fact, the outcome of a specific action is rarely certain. That is why risk has become an important concept in decision sciences. In the present study, we investigated three main questions regarding risk processing, namely (1) how risk processing is influenced by emotions, (2) whether the neural processing of risk is context-dependent, differing between decision making and pure outcome anticipation, and (3) whether risk is processed differently in the brain when individuals are faced with potential losses.

To answer these questions, we conducted quantitative coordinate-based meta-analyses on studies investigating neural representations of risk. By using the ALE approach (Laird et al., 2005), we can base our argumentation not only on a single study or a qualitative view on several studies but on a quantitative integration of 30 studies investigating risk. Although the ALE approach does not take the cluster size and significance-level (p, t, or z score) of an activated cluster into account, it offers the opportunity to locate an effect precisely, which is especially impor-

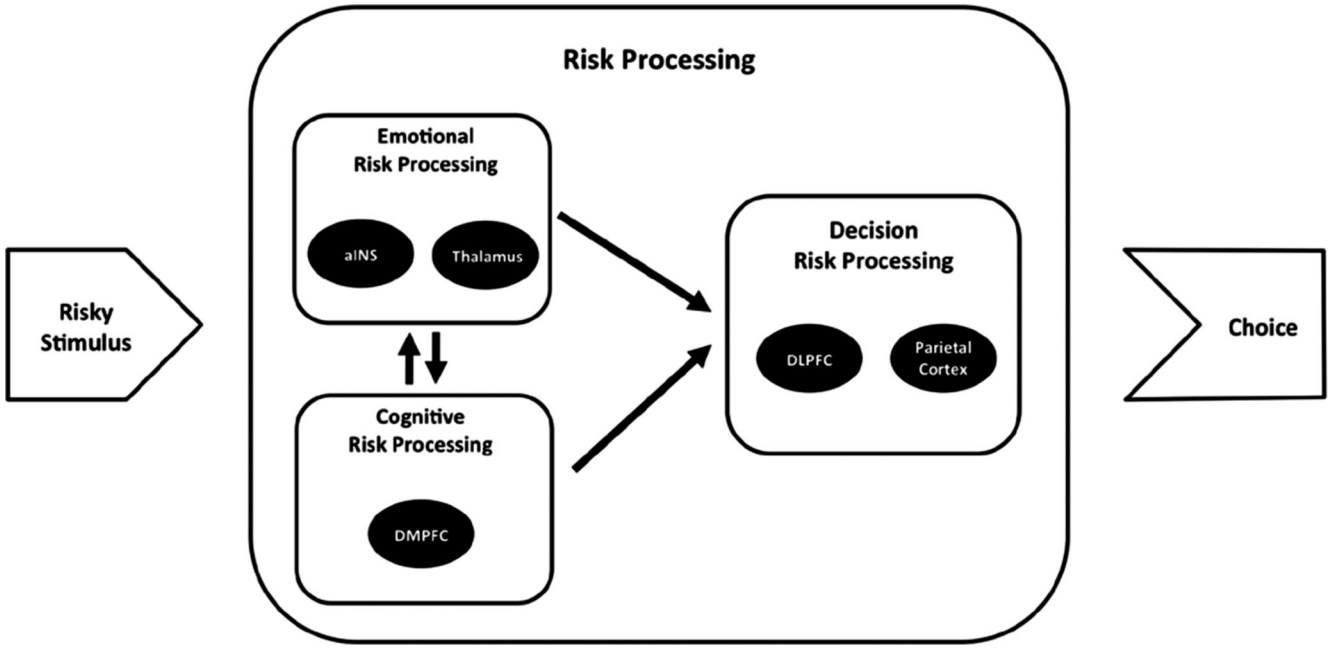

Figure 4. A potential mechanism of risky decision making. A risky stimulus such as a gamble with uncertain outcomes or a choice menu with different financial investments is initially evaluated on an emotional level. Activity in the aINS thereby serves as an estimate for the potential of the risky stimulus to result in an unwanted outcome, whereas the thalamus reflects important aspects of potential outcomes (e.g., their variability). At the cognitive level, the risky stimulus is processed in the DMPFC. Both parts of risk processing (emotional and cognitive) inform the actual decision process performed in DLPFC and parietal cortex. In situations, in which no decision has to be made, such as in the bingo game, the process concludes after emotional and cognitive risk processing.

tant in the context of large brain regions that likely consist of subregions serving different functions (e.g., medial prefrontal cortex) (Venkatraman et al., 2009a). Note that an alternative approach for fMRI meta-analyses could summarize studies based on effect sizes (and their SEs). This approach would have the advantage that small effects that remained undetected in single studies could be discovered as being significant. To our knowledge, however, no fMRI meta-analysis based on effect sizes has been published to date. One reason for this is that fMRI meta-analyses are only feasible, when whole brain maps of these statistics are available. When effect sizes are reported only for significant activations (as is currently the standard), effect sizes for all other areas remain unknown, and there is currently no method to estimate them with any confidence (Costafreda, 2009). Hence, the current reporting format of fMRI studies does not allow performing (effect-size based) meta-analyses that could detect weak but stable effects that were not published because of a publication bias for results with strong effects (that is inherent to fMRI studies with often small sample sizes). Note, however, that our identification of the thalamus as an important part of the risk processing network shows that coordinate-based meta-analyses allow identifying task-relevant brain regions that are activated in many studies and yet have remained unnoticed before.

We identified a network including bilateral aINS, dorsomedial thalamus, posterior thalamus, DMPFC, right DLPFC, and right parietal cortex for processing risk. The aINS was active for both decision risk and anticipation risk but predominantly when individuals were faced with potential losses. The aINS is regarded as a key brain region in emotion processing and arousal (Quartz, 2009) but also in the mapping of internal bodily states (Critchley, 2005; Craig, 2009). Several studies related activity in the aINS especially to aversive emotions such as fear, sadness, disgust, or anxiety (for review, see Phan et al., 2002; Paulus and Stein, 2006). Thus, our results clearly support the hypothesis that aversive emotions are implicated in risk processing independent of the context but predominantly (not solely) when individuals are faced with potential losses.

Standing alone, this conclusion is based on reverse inference (Poldrack, 2006) and needs to be qualified because the aINS is also active in a variety of tasks not explicitly related to emotions (Yang et al., 2010). Still, additional evidence comes from behavioral research on the influence of emotions on decision making. Several studies demonstrated that incidental emotions (i.e., emotions not related to the decision problem) significantly influence judgment and decision making. Risk judgments, for example, change when individuals perceive fear or anger (Lerner and Keltner, 2000).

The thalamus is one of the most ignored brain regions in functional neuroimaging. Although most of the studies included in our meta-analyses found risk representations in the thalamus, none of the studies discussed them. We found representations of risk in posterior and dorsomedial thalamus. The posterior thalamus was found to be active in the processing of emotions such as regret (Chandrasekhar et al., 2008) and showed stronger activity for losses compared with gains (Xu et al., 2009). Furthermore, the posterior thalamus is connected to the parietal cortex, which we also found to be active in risk processing. The dorsomedial thalamus is part of the striatal loop and reflects information about reward magnitudes (Glimcher and Lau, 2005). Interestingly, activity in the dorsomedial thalamus covaries with the magnitude of the smaller of two possible rewards (Minamimoto et al., 2009). The dorsomedial thalamus is also connected with the prefrontal cortex, a region that is consistently implicated in risk processing. Thus, both parts of the thalamus likely process important aspects of the risky stimulus and relay them to other brain regions of the risk processing network.

The DMPFC was active during decision risk and anticipation risk as well as in both domains (gains + losses and gains). It was, however, more likely to be active during decision risk compared with anticipation risk. Activity in the DMPFC was found in a

variety of different tasks related to the cognitive processing of stimuli. These studies included investigations of response conflict, error monitoring, decision making, as well as strategy selection (for review, see Ridderinkhof et al., 2004; Venkatraman et al., 2009b). As recently reported, some of these functions can be attributed to subregions of the DMPFC (Venkatraman et al., 2009a). The cluster that we identified overlaps with the subregions for decision control and strategy control in the study by Venkatraman et al. (2009a). Because taking risks can be seen as acting against the dominant strategy of avoiding risks in risk-averse individuals, our findings are consistent with those previous findings about neural representations of strategy control.

We further found that both the right DLPFC and parietal cortex were active for decision risk but not for anticipation risk. Both brain regions were usually observed in the context of decision making (for review, see Heekeren et al., 2008). In the context of reward-based decision making, activity in the right DLPFC is related to valuing choice options (Camus et al., 2009; Mohr et al., 2010a). These results indicate that DLPFC and parietal cortex do not play a general role in risk processing but a specific role in risk processing during decision making.

In summary, our finding of insula activity supports the hypothesis that emotions are implicated in risk processing. The differential activation patterns for decision risk versus anticipation risk and for the gain versus gain + loss domain suggest that risk processing on the neural level is context dependent and specifically influenced by potential losses (note, however, that context and domain are not fully independent in the fMRI studies we found).

Based on the results of our meta-analyses, we propose the following account of a risk-processing mechanism (Fig. 4): when individuals observe a risky stimulus such as a gamble with uncertain outcomes or an investment option, two parallel and reciprocal risk processes are induced, an emotional and a cognitive risk process. On the emotional level, activity in the aINS initially serves as a fast and rough estimate for the potential of the stimulus to result in an unwanted outcome (e.g., a loss). At the same time, this signal prepares the organism to take action to avoid the unwanted outcome. Activity in the thalamus could thereby reflect an anticipation of regret in response to possible outcomes of the risky stimulus. The DMPFC evaluates the risk of the stimulus on a cognitive level, for instance, computing the variance of outcomes or the probability of a loss, thereby using the information from the aINS and the thalamus as a first estimate for the riskiness of the stimulus. During this process, information is repeatedly exchanged between DMPFC on the one hand and aINS and thalamus on the other hand, updating the emotional response to the stimulus, which in turn informs the cognitive processing of risk. If a decision has to be made, parietal cortex and DLPFC integrate the risk information with other aspects of the stimulus (e.g., expected reward) and form the final decision. If no decision has to be made, like in the bingo game, the process stops after risk processing on the emotional and the cognitive level. The mechanism proposed here is compatible with the general approach of the risk-as-feelings hypothesis (Loewenstein et al., 2001). Note that the temporal sequence of risk processing we propose cannot be derived from our meta-analysis or fMRI data in general. EEG and/or magnetoencephalographic experiments could shed light on the temporal sequence of cortical risk processing. Moreover, the suggested mechanism is based on results of experiments that investigated risk processing in the presence of only gains or both gains and losses. No study has so far investigated risk processing specifically in the loss domain. Future research should target this obvious lack of research and complete the picture of risk processing for the loss domain.

References

Bach DR, Seymour B, Dolan RJ (2009) Neural activity associated with the passive prediction of ambiguity and risk for aversive events. J Neurosci 29:1648–1656.

Behrens TE, Woolrich MW, Walton ME, Rushworth MF (2007) Learning the value of information in an uncertain world. Nat Neurosci 10:1214–1221.

Blackwood N, Ffytche D, Simmons A, Bentall R, Murray R, Howard R (2004) The cerebellum and decision making under uncertainty. Brain Res Cogn Brain Res 20:46–53.

Bossaerts P, Preuschoff K, Hsu M (2009) The neurobiological foundations of valuation in human decision making under uncertainty. In: Neuroeconomics. Decision making and the brain (Glimcher PW, Camerer CF, Fehr E, Poldrack RA, eds), pp 353–366. London: Elsevier.

Cabeza R, Nyberg L, Park DC, eds (2005) Cognitive neuroscience of aging. New York: Oxford UP.

Camus M, Halelamien N, Plassmann H, Shimojo S, O'Doherty J, Camerer C, Rangel A (2009) Repetitive transcranial magnetic stimulation over the right dorsolateral prefrontal cortex decreases valuations during food choices. Eur J Neurosci 30:1980–1988.

Chandrasekhar PV, Capra CM, Moore S, Noussair C, Berns GS (2008) Neurobiological regret and rejoice functions for aversive outcomes. Neuroimage 39:1472–1484.

Chein JM, Fissell K, Jacobs S, Fiez JA (2002) Functional heterogeneity within Broca's area during verbal working memory. Physiol Behav 77:635–639.

Christopoulos GI, Tobler PN, Bossaerts P, Dolan RJ, Schultz W (2009) Neural correlates of value, risk, and risk aversion contributing to decision making under risk. J Neurosci 29:12574–12583.

Costafreda SG (2009) Pooling FMRI data: meta-analysis, mega-analysis and multi-center studies. Front Neuroinformatics 3:33.

Craig AD (2009) How do you feel–now? The anterior insula and human awareness. Nat Rev Neurosci 10:59–70.

Critchley HD (2005) Neural mechanisms of autonomic, affective, and cognitive integration. J Comp Neurol 493:154–166.

Critchley HD, Mathias CJ, Dolan RJ (2001) Neural activity in the human brain relating to uncertainty and arousal during anticipation. Neuron 29:537–545.

Damasio AR, Tranel D, Damasio H (1991) Somatic markers and guidance of behaviour:theory and preliminary testing. In: Frontal lobe function and dysfunction (Levin HS, Eisenberg HM, Benton AL, eds). New York: Oxford UP.

Dreher JC, Kohn P, Berman KF (2006) Neural coding of distinct statistical properties of reward information in humans. Cereb Cortex 16:561–573.

Eickhoff SB, Laird AR, Grefkes C, Wang LE, Ziles K, Fox PT (2009) Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: a random-effects approach based on empirical estimates of spatial uncertainty. Hum Brain Mapp 30:2907–2926.

Elliott R, Rees G, Dolan RJ (1999) Ventromedial prefrontal cortex mediates guessing. Neuropsychologia 37:403–411.

Engelmann JB, Tamir D (2009) Individual differences in risk preference predict neural responses during financial decision-making. Brain Res 1290:28–51.

Fox PT, Poldrack RA (2009) Prospect theory and the brain. In: Neuroeconomics. Decision making and the brain (Glimcher PW, Camerer CF, Fehr E, Poldrack RA, eds), pp 145–173. London: Elsevier.

Glimcher PW, Lau B (2005) Rethinking the thalamus. Nat Neurosci 8:983–984.

Grinband J, Hirsch J, Ferrera VP (2006) A neural representation of categorization uncertainty in the human brain. Neuron 49:757–763.

Heekeren HR, Marrett S, Ungerleider LG (2008) The neural systems that mediate human perceptual decision making. Nat Rev Neurosci 9:467–479.

Hsu M, Bhatt M, Adolphs R, Tranel D, Camerer CF (2005) Neural systems responding to degrees of uncertainty in human decision-making. Science 310:1680–1683.

Huettel SA (2006) Behavioral, but not reward, risk modulates activation of prefrontal, parietal, and insular cortices. Cogn Affect Behav Neurosci 6:141–151.

Huettel SA, Song AW, McCarthy G (2005) Decisions under uncertainty: probabilistic context influences activation of prefrontal and parietal cortices. J Neurosci 25:3304–3311.

Knight FH (1921) Risk, uncertainty and profit. Boston: Houghton Mifflin.

Knutson B, Bossaerts P (2007) Neural antecedents of financial decisions. J Neurosci 27:8174–8177.

Kuhnen CM, Knutson B (2005) The neural basis of financial risk taking. Neuron 47:763–770.

Labudda K, Woermann FG, Mertens M, Pohlmann-Eden B, Markowitsch HJ, Brand M (2008) Neural correlates of decision making with explicit information about probabilities and incentives in elderly healthy subjects. Exp Brain Res 187:641–650.

Laird AR, Fox PM, Price CJ, Glahn DC, Uecker AM, Lancaster JL, Turkeltaub PE, Kochunov P, Fox PT (2005) ALE meta-analysis: controlling the false discovery rate and performing statistical contrasts. Hum Brain Mapp 25:155–164.

Lancaster JL, Tordesillas-Gutiérrez D, Martinez M, Salinas F, Evans A, Zilles K, Mazziotta JC, Fox PT (2007) Bias between MNI and Talairach coordinates analyzed using the ICBM-152 brain template. Hum Brain Mapp 28:1194–1205.

Lee TM, Leung AW, Fox PT, Gao JH, Chan CC (2008) Age-related differences in neural activities during risk taking as revealed by functional MRI. Soc Cogn Affect Neurosci 3:7–15.

Lerner JS, Keltner D (2000) Beyond valence: toward a model of emotion-specific influences on judgement and choice. Cogn Emot 14:473–493.

Loewenstein GF, Weber EU, Hsee CK, Welch N (2001) Risk as feelings. Psychol Bull 127:267–286.

Markowitz H (1952) Portfolio selection. J Finance 7:77–91.

Matthews SC, Simmons AN, Lane SD, Paulus MP (2004) Selective activation of the nucleus accumbens during risk-taking decision making. Neuroreport 15:2123–2127.

Minamimoto T, Hori Y, Kimura M (2009) Roles of the thalamic CM-PF complex-basal ganglia circuit in externally driven rebias of action. Brain Res Bull 78:75–79.

Mohr PN, Biele G, Krugel LK, Li SC, Heekeren HR (2010a) Neural foundations of risk-return trade-off in investment decisions. Neuroimage 49:2556–2563.

Mohr PN, Li SC, Heekeren HR (2010b) Neuroeconomics and aging: neuromodulation of economic decision making in old age. Neurosci Biobehav Rev 34:678–688.

Park DC, Polk TA, Park R, Minear M, Savage A, Smith MR (2004) Aging reduces neural specialization in ventral visual cortex. Proc Natl Acad Sci U S A 101:13091–13095.

Paulus MP, Stein MB (2006) An insular view of anxiety. Biol Psychiatry 60:383–387.

Paulus MP, Hozack N, Zauscher B, McDowell JE, Frank L, Brown GG, Braff DL (2001) Prefrontal, parietal, and temporal cortex networks underlie decision-making in the presence of uncertainty. Neuroimage 13:91–100.

Paulus MP, Rogalsky C, Simmons A, Feinstein JS, Stein MB (2003) Increased activation in the right insula during risk-taking decision making is related to harm avoidance and neuroticism. Neuroimage 19:1439–1448.

Phan KL, Wager T, Taylor SF, Liberzon I (2002) Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. Neuroimage 16:331–348.

Platt ML, Huettel SA (2008) Risky business: the neuroeconomics of decision making under uncertainty. Nat Neurosci 11:398–403.

Poldrack RA (2006) Can cognitive processes be inferred from neuroimaging data? Trends Cogn Sci 10:59–63.

Preuschoff K, Bossaerts P, Quartz SR (2006) Neural differentiation of expected reward and risk in human subcortical structures. Neuron 51:381–390.

Preuschoff K, Quartz SR, Bossaerts P (2008) Human insula activation reflects risk prediction errors as well as risk. J Neurosci 28:2745–2752.

Quartz SR (2009) Reason, emotion and decision-making: risk and reward computation with feeling. Trends Cogn Sci 13:209–215.

Rangel A, Camerer C, Montague PR (2008) A framework for studying the neurobiology of value-based decision making. Nat Rev Neurosci 9:545–556.

Ridderinkhof KR, Ullsperger M, Crone EA, Nieuwenhuis S (2004) The role of the medial frontal cortex in cognitive control. Science 306:443–447.

Rolls ET, McCabe C, Redoute J (2008) Expected value, reward outcome, and temporal difference error representations in a probabilistic decision task. Cereb Cortex 18:652–663.

Rushworth MF, Behrens TE (2008) Choice, uncertainty and value in prefrontal and cingulate cortex. Nat Neurosci 11:389–397.

Slovic P, Finucane ML, Peters E, MacGregor DG (2004) Risk as analysis and risk as feelings: some thoughts about affect, reason, risk, and rationality. Risk Anal 24:311–322.

Smith BW, Mitchell DG, Hardin MG, Jazbec S, Fridberg D, Blair RJ, Ernst M (2009) Neural substrates of reward magnitude, probability, and risk during a wheel of fortune decision-making task. Neuroimage 44:600–609.

Tobler PN, O'doherty JP, Dolan RJ, Schultz W (2006) Human neural learning depends on reward prediction errors in the blocking paradigm. J Neurophysiol 95:301–310.

Turkeltaub PE, Eden GF, Jones KM, Zeffiro TA (2002) Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. Neuroimage 16:765–780.

van Leijenhorst L, Crone EA, Bunge SA (2006) Neural correlates of developmental differences in risk estimation and feedback processing. Neuropsychologia 44:2158–2170.

Venkatraman V, Rosati AG, Taren AA, Huettel SA (2009a) Resolving response, decision, and strategic control: evidence for a functional topography in dorsomedial prefrontal cortex. J Neurosci 29:13158–13164.

Venkatraman V, Payne JW, Bettman JR, Luce MF, Huettel SA (2009b) Separate neural mechanisms underlie choices and strategic preferences in risky decision making. Neuron 62:593–602.

Volz KG, Schubotz RI, von Cramon DY (2003) Predicting events of varying probability: uncertainty investigated by fMRI. Neuroimage 19:271–280.

Volz KG, Schubotz RI, von Cramon DY (2004) Why am I unsure? Internal and external attributions of uncertainty dissociated by fMRI. Neuroimage 21:848–857.

Weber BJ, Huettel SA (2008) The neural substrates of probabilistic and intertemporal decision making. Brain Res 1234:104–115.

Weber EU, Anderson CJ, Birnbaum MH (1992) A theory of perceived risk and attractiveness. Organ Behav Hum Decis Process 52:492–523.

Weber EU, Blais AR, Betz NE (2002) A domain-specific risk-attitude scale: Measuring risk perceptions and risk behaviors. J Behav Decis Mak 15:263–290.

Xu L, Liang ZY, Wang K, Li S, Jiang T (2009) Neural mechanism of intertemporal choice: from discounting future gains to future losses. Brain Res 1261:65–74.

Xue G, Lu Z, Levin IP, Weller JA, Li X, Bechara A (2009) Functional dissociations of risk and reward processing in the medial prefrontal cortex. Cereb Cortex 19:1019–1027.

Yang J, Weng X, Zang Y, Xu M, Xu X (2010) Sustained activity within the default mode network during an implicit memory task. Cortex 46:354–366.

Yoshida W, Ishii S (2006) Resolution of uncertainty in prefrontal cortex. Neuron 50:781–789.

Project II

Mohr, P. N. C., Biele, G., Krugel, L. K., Li, S. C., & Heekeren, H. R. (2010). Neural foundations of risk-return trade-off in investment decisions. *Neuroimage, 49*(3), 2556-2563, DOI: 10.1016/j.neuroimage.200910.060.

Project III

Mohr, P. N., Li, S. C., & Heekeren, H. R. (2010). Neuroeconomics and aging: neuromodulation of economic decision making in old age. *Neurosci Biobehav Rev, 34*(5), 678-688, DOI: 10.1016/j.neubiorev.2009.05.010.