IT'S ABOUT TIME…

INTERTEMPORAL DECISION MAKING AND THE BRAIN

INAUGURAL DISSERTATION

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Abbreviations

ADHD	Attention deficit hyperactivity disorder
AUC	Area under the curve
BIS	Barratt impulsiveness scale
BOLD activity	Blood-oxygen-level dependent activity
DBS	Deep brain stimulation
DUT	Discounted Utility Theory
fMRI	Functional magnetic resonance imaging
FNPA task	Face-name paired-associates task
GP	Globus pallidus
- **GPi**	Globus pallidus interna
- **GPe**	Globus pallidus externa
ICDs	Impulse control disorders
IPS	Intraparietal sulcus
LED	Levodopa equivalent dose
MTL	Medial temporal lobe
NAc	Nucleus accumbens
PD	Parkinson's disease
OFC	Orbitofrontal cortex
- **mOFC**	Medial orbitofrontal cortex
PFC	Prefrontal cortex
- **lPFC**	Lateral prefrontal cortex
- **vmPFC**	Ventromedial prefrontal cortex
- **dmPFC**	Dorsomedial prefrontal cortex
pPC	Posterior parietal cortex
QDQ	Quick delay questionnaire
SN	Substantia nigra
- **SNr**	Substantia nigra pars reticulata
- **SNc**	Substantia nigra pars compacta
SOGS	South Oaks gambling screen
STN	Subthalamic nucleus
UPDRS	Unified Parkinson's disease rating scale
VS	Ventral striatum

Abstract *English*

Intertemporal decision making, where tradeoffs are made between differently timed rewards, is a well studied topic. The way we make intertemporal choices can have far reaching consequences on individual level, but also for society's economic well being. Intertemporal choice behavior is affected by many demographic, psychological, and physiological factors. It is therefore important to investigate the effects of specific relevant factors that make up the context in which these decisions are made, to gain insight in the underlying behavioral and neuronal mechanisms and to be able to predict intertemporal choice behavior. We investigated three specific choice contexts:

The world is ageing, and the (intertemporal) choices made by older adults have more impact on society. Different intertemporal choice behavior is observed in distinct age groups, but the effect of older age on choice behavior is relatively unclear. In one study (*Chapter 2*) we investigated the potentially mediating role of episodic memory performance on intertemporal choice behavior in older adults. We found that autobiographical memory performance and gender interact in determining older people's choice behavior.

Intertemporal choice behavior is not only affected by trait factors, such as age, but also by diseases and specific treatments. In a second study (*Chapter 3*) we investigated the effect of subthalamic deep brain stimulation (STN-DBS), a common treatment of Parkinson's disease, on intertemporal choice in Parkinson patients. We found no evidence of DBS treatment affecting choice behavior. This finding contributes to the notion that STN-DBS is a safe treatment option for Parkinson's disease when it comes to cognitive side effects.

We further asked a more fundamental question to investigate which currency we actually maximize when we make intertemporal decisions (*Chapter 4*): do we maximize 'economic utility' in the form of a *discounted value*, as often suggested by (behavioral) economists, or do we maximize reward rate, as suggested by behavioral ecologists? We asked students to make a series of intertemporal choices with experienced delays, and found that we actually seem to maximize reward rate. Rate maximization may have led to the often observed *'immediacy effects*', which could explain why hyperbolic-like discounting models often describe intertemporal choice behavior so well.

Abstract *German*

Bei Intertemporalen Entscheidungen, bei denen zwischen Belohnungen zu verschiedenen Zeitpunkten gewählt wird, handelt es sich um ein umfassend erforschtes Thema. Die Art und Weise, wie wir intertemporale Entscheidungen treffen kann weitreichende Folgen auf persönlicher Ebene haben, aber auch auf das wirtschaftliche Wohlergehen der Gesellschaft. Intertemporale Entscheidungen werden durch zahlreiche demografische, psychologische und physiologische Faktoren beeinflusst. Daher ist es von großer Bedeutung, die Effekte der relevanten Faktoren zu untersuchen, um die zugrundeliegenden verhaltensbezogenen und neuronalen Mechanismen zu isolieren und so intertemporale Entscheidungen vorhersagen zu können. Wir haben drei spezifische Entscheidungsbereiche untersucht:

Die Welt altert und somit haben die Entscheidungen, die von älteren Erwachsenen getroffen werden, einen größeren Einfluss auf die Gesellschaft. In verschiedenen Altersgruppen kann unterschiedliches intertemporales Entscheidungsverhalten beobachtet werden. Welchen Effekt aber ein höheres Alter auf das Entscheidungsverhalten ausübt ist noch relativ unklar. In einer Studie (*Kapitel 2*) haben wir die potentiell modulierende Rolle des episodischen Gedächtnis bei intertemporalen Entscheidungen von älteren Erwachsenen untersucht. Wir konnten zeigen, dass sich sowohl das autobiografische Gedächtnis als auch das Geschlecht auf intertemporale Entscheidungen von älteren Erwachsenen auswirken.

Intertemporale Entscheidungen werden nicht nur durch Eigenschaften wie das Alter beeinflusst, sondern auch durch Erkrankungen. Auch die spezifische

Behandlung dieser Erkrankungen haben einen Einfluss auf intertemporales Entscheidungsverhalten. In einer zweiten Studie (*Kapitel 3*) haben wir den Effekt der tiefen Hirnstimulation des Nucleus subthalamicus, eine Behandlunsgsweise der Parkinsonerkankung, auf intertemporale Entscheidungen von Parkinson-Patienten untersucht. Es konnte nicht festgestellt werden, dass die tiefe Hirnstimulation das Entscheidungsverhalten beeinflusst hat. Dies bestätigt die Ansicht, dass die tiefe Hirnstimulation eine sichere Behandlunsgsmöglichkeit von Parkinsonpatienten im Hinblick auf kognitive Nebenwirkungen ist.

Letztlich widmeten wir uns noch der Grundlagenforschung um herauszufinden, welche Variable wir bei intertemporalen Entscheidungen zu maximieren versuchen. Maximieren wir den „wirtschaftlichen Nutzen“ in Form einer Diskontierungsvariable, so wie es von (Verhaltens-) Ökonomen angenommen wird? Oder maximieren wir die Verstärkerrate, so wie es von Verhaltensökologen angenommen wird? Dazu trafen Studenten eine Reihe intertemporaler Entscheidungen mit verschiedenen zeitlichen Verzögerungen. Wir haben herausgefunden, dass eher die Verstärkerrate maximiert wird. Die Maximierung der Verstärkerrate könnte zu dem häufiger beobachteten „*immediacy effect*“ geführt haben. Dieser Effekt könnte wiederum erklären, warum intertemporales Entscheidungsverhalten sehr gut durch hyperbolische Diskontierungsmodelle beschrieben werden kann.

1. General introduction

"All we have to decide is what to do with the time that is given us."

- J.R.R. Tolkien

On an average day we make countless choices. When the alarm clock sounds, do we snooze, or do we get out of bed immediately? What shall we have for breakfast? Most of these choices do not have far-reaching consequences. But some do. For instance, moving to a different residence, switching career path or making important financial decisions are all choices that will impact our future in a dramatic fashion and will influence our long-term personal and financial well-being.

On one hand, several aspects of our society encourage long-term and profitable outcomes. For example, we benefit from a long and elaborate education by obtaining well-paid jobs that will ensure we can live the life we want. Consequently, we put part of our salary into a pension-fund so we can have a fair amount of money to spend when we are retired. Another example of long-term decision making nowadays increasingly emphasized is a choice for a healthy lifestyle. Every day, we are confronted with the choice between, for example, a healthy salad and a delicious, but fatty, chicken burger. While choosing the burger would be more delicious and thus more rewarding on short-term, the salad would be in favor of our long-term health and interest.

At the same time, many companies try to sell their wares by emphasizing the immediate benefits of their products, thereby biasing our decisions in favor of immediate gratification. This could cause less optimal long-term outcomes (e.g.

buying that new car now while it is on sale, which leaves no money for potential emergency situations, like a malfunctioning computer). Companies regularly use our sensitivity for immediate rewards by offering delayed payment options or by putting unhealthy but delicious snacks right next to the cashier.

These decisions, in which a trade-off needs to be made between smaller but sooner, and larger but later available rewards are called *intertemporal decisions*, and are the focus of my dissertation.

"Genius is nothing but a great capacity for patience"

- Georges-Louis Leclerc Buffon

When making decisions, your level of patience (i.e. choosing the long-term, more beneficial outcome) and impulsivity (its opposite) are influenced by many factors, such as age, income and type of reinforcement. These factors, known and yet to be discovered, are the cause of a large variation in choice behavior within and between individuals. Research is still being conducted to identify these factors, and how they together determine our intertemporal choice behavior in real life. This research is of crucial importance, given that understanding all the factors involved would allow one to identify which populations might be at risk of - and which situations could result in - the development of financial or health problems (e.g. pathological gambling or other *impulse control disorders*) due to excessive *impulsive choice* behavior. Another powerful approach to inter-temporal decision making, which emerged in last decades of research, is to investigate the neural signals involved in such decisions. Indeed, while determining behavioral factors influencing inter-temporal decision making would

allow the implementation of societal programs in risky populations to promote patience and limit impulsivity, the identification of neural mechanisms involved in such choices would enable de development of pharmacological targets and focal psychopharmacological therapies for individuals with deficits in inter-temporal choice.

The research presented in this dissertation focused on specific open questions regarding intertemporal choice behavior. Therefore, this introduction is structured as a review of the most relevant aspects as background information for the presented research. First, I provide a theoretical framework as well as an overview of how intertemporal choice behavior is generally measured. Subsequently I present specific factors associated with intertemporal choice behavior, followed by the neural correlates of intertemporal decision making. I end the introduction with a short overview of the studies that form the body of this dissertation.

1.1 Intertemporal choice behavior

Over the years many different tasks have been designed to investigate intertemporal decision making in laboratory conditions. In this section I will provide an overview of the most common way intertemporal choice behavior is measured in studies with human participants, and what we learned from these studies about the factors influencing intertemporal decision making in healthy persons, as well as in disorders involving *impulsive behavior*.

1.1.1 Delay discounting

We generally prefer receiving €10 today over receiving €10 in one week. It seems as if the delayed €10 are worth less. In other words, a delay reduces the

subjective value of the €10 obtained in a week compared to its subjective value when available immediately. This phenomenon, typically referred to as '*delay discounting*', describes the subjective devaluation of a reward when its receipt is delayed. This term stems from the idea that all our intertemporal choice behavior can be described by a *discount rate* (Samuelson, 1937), which reflects how steeply a reward loses its subjective value when its receipt is delayed. *Discount rates* can be determined by the choice patterns a person makes. This is explained in more detail in *box 1.1*. Note that *delay discounting* is one way to describe intertemporal choice behavior (see *Chapter 4* for more information on an alternative model: rate maximization), and by describing choice behavior in terms of discounting several assumptions are made. See *box 1.2* for those assumptions.

Discounting Models

There are several models that describe how delayed rewards are discounted, i.e. how a particular reward loses its value when delayed. One of the first *delay discounting* models is a normative (descriptive) model from the economic literature, the *Discounted Utility Model (DUT)* (Samuelson, 1937). The DUT predicts that a rational decision maker should make intertemporal decisions following an exponential discounting curve (see *figure 1.1*). Exponential discounting is a form of constant discounting where each additional delay causes the value of a reward to decrease at a fixed rate. However, early empirical research with human participants (e.g. Thaler, 1981; Benzion *et al.*, 1989; Green *et al.*, 1997; Madden *et al.*, 1999) has shown that a change of one unit delay (e.g. one day) from no delay yields a larger relative decrease in subjective value compared to a change from, e.g. delay 10 to delay 11 (also a difference of one

BOX 1.1 Measuring discount rates

Researchers have come up with clever ways to measure how aversive a one-week delay is to a given person. Typically, this is done by increasing the magnitude of the (delayed) reward, until the negative effect of the delay is compensated by the positive effect of the increased reward magnitude. For example, a person is given the choice between a reward of €10 received immediately and €15 to be received in one week. Due to this delay, it seems as if the value of the €15 reward is reduced, or discounted, in comparison to the subjective value of €15 received immediately. If this discounted value is lower than the subjective value of €10 received now, the person would choose to the immediate reward of €10. If the immediate €10 reward would then be decreased, e.g. to €5, its new subjective value may be lower than the subjective value of receiving €15 in one week, and as a result this person would show a preference for the delayed reward over the immediate reward.

Given a specific delayed reward, the amount of the smaller, but sooner available option at which a person is indifferent between the two options (also called the indifference value or *indifference point*), is generally taken as an indication of how aversive the delay is to this person, i.e. how strongly a person discounts the delayed reward. For example, the person above may be indifferent between €7.50 now and €15 in a week (i.e. given the same choice several times, she would choose each option with equal probability). The *indifference point* would then be 7.50. Usually several *indifference points* estimated for different reward sizes and delays are used to fit specific discounting models to choice behavior (see *Discounting models*), which give a more general indication of how strongly a person discounts delayed rewards, and can, for example, be used to investigate whether there are significant differences between population samples. The *indifference point* of a delayed reward can be obtained in several different ways. One can simply ask participants the monetary equivalent (available immediately) of a certain delayed reward, or the monetary equivalent of an immediate reward at a specific point in the future (Thaler, 1981; Malkoc & Zauberman, 2006).

A more elaborate, and less cognitively demanding approach (Hardisty *et al.*, 2013) is to present a series of binary choices, using a range of reward amounts and delays. The monetary amounts and delays can be systematically and parametrically increased or decreased to identify the *indifference points*, which in turn are used to fit a discounting model. Since such behavioral designs take considerably more time, shorter versions have been developed. The Delay Discount Questionnaire, developed by Madden *et al.* (1997), is a computerized task that uses an adjusting amount procedure to determine indifference points: the monetary amount of the immediate

[BOX 1.1 Continued]
option in a subsequent trial is adjusted based on the choice in the current trial, which ultimately reduces the number of trials required to find the indifference point. The disadvantage of this procedure is that one wrong answer (e.g. due to a momentary lack of attention) can have a profound influence on the estimated indifference point.

Kirby and colleagues (Kirby *et al.*, 1999) created a 27-item questionnaire, in which each item consists of a binary choice between a smaller, sooner and a larger, later reward, that directly results in a discounting measure based on the hyperbolic model (see *Discounting Models*). Here, the items/binary choices are determined such that indifference between the two options reflect a specific hyperbolic discounting parameter value. The specific choice profile of one person would therefore lead to an approximation of the discount rate of a person. However, although this questionnaire is very short, the estimated *k-values* have limited accuracy.

More recently computational approaches become increasingly popular, in which several components of choice can be implemented in a model, such as the stochastic nature of choice behavior, the translation of reward magnitude into a subjective value, in addition to the temporal discount rate. This approach does not require a specific task structure, as long as trial number and parameter values (i.e. rewards and delays) vary sufficiently for reliable estimates of the model parameters (e.g. the discount rate).

day). This means that the *discount rate* is not constant, but is relatively high at first and decreases with a decreasing rate as the delay increases (*figure 1.1*).

The observation that initial delays yield higher *discount rates* is also called the '*immediacy effect*' (Thaler, 1981) and is well described by a hyperbolic function (*figure 1.1*; Mazur, 1984):

$$SV = 1 / (1+k*D) \qquad (1.1)$$

In this equation *SV* is the subjective value, *D* is the delay and *k* is the parameter that determines the overall steepness of the curve. The hyperbolic model shows

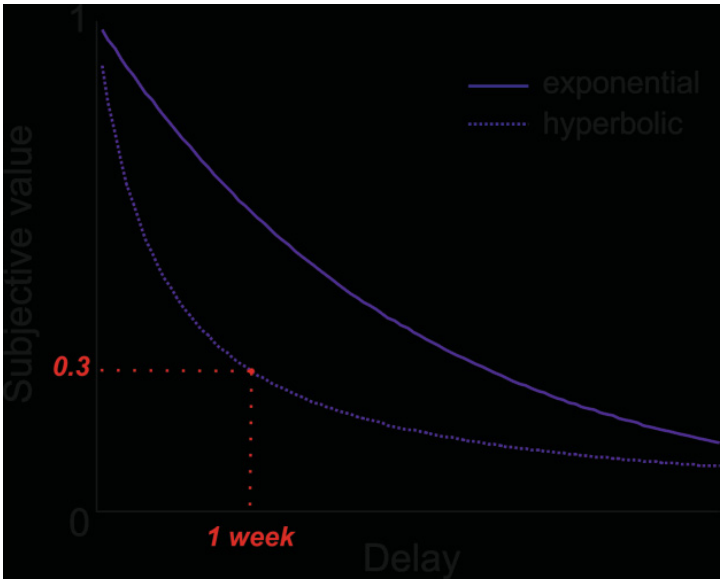

Figure 1.1 *A delay discounting curve according to the exponential and the hyperbolic model (equation 1.1). The hyperbolic model is characterized by a steep initial decline in subjective value, whereas the exponential model reflects less sensitivity to initial delays. The red dot on the hyperbolic discount curve indicates an indifference point: the value of the delayed reward (1 week delay) equals 0.3 times the value of the delayed reward when obtained without a delay.*

an initial steeper decline of subjective value than the exponential model (see *figure 1.1*) and defines the *discount rate* (i.e. the loss in value at a particular point in time) to be non-constant, but depending on the delay:

$$r(D) = -k / (1+k*D)^2 \qquad (1.2)$$

In this equation *r* is the *discount rate* at delay *D*, which depends on the parameter *k* as well as on the delay *D*. The parameter *k*, which is often used as measure of *discount rate*, therefore does not represent the *discount rate* itself (as the rate itself changes at each point on the curve), but rather reflects the average *discount rate* of the curve. In many studies, the hyperbolic discounting model showed a better fit to the data than the exponential model (Ainslie & Haendel, 1983;

Frederick *et al.*, 2002; Green & Myerson, 2004; Soman *et al.*, 2005). We thus seem to be particularly sensitive to any initial delay in reward reception.

Hyperbolic discounting can also explain the so called '*common difference effect*' (Prelec & Loewenstein, 1991): this effect reflects a preference reversal caused by an increase of the delay to both rewards by the same *front-end delay* (see also *Chapter 4*). Several studies found that when participants preferred the smaller reward at delay 0 over the larger reward at delay +2, they would reverse their preference if the delay to both rewards was increased equally, e.g. resulting in a delay of +10 for the small reward and +12 for the large reward (Green *et al.*, 1981; Thaler, 1981; Green *et al.*, 1994b; Kirby & Herrnstein, 1995; see Kalenscher & Pennartz, 2008). This effect possibly explains why one decides to get up early the next morning so one can be more productive (longer-term reward), but when the alarm sounds, one switches preference and decides to snooze (short-term reward). These so called *preference reversals* cannot be explained by models assuming constant discounting, such as the DUT, but are predicted by the hyperbolic discounting model.

Another famous model that can account for the initial steep decline in value is Laibson's (1997) quasi-hyperbolic model (see *figure 1.2*). This model separates the initial (from delay 0 to delay +1) steep decline in value, which is described as being linear, from further increases in delay, for which the decline in value follows an exponential curve. By having a separate parameter for these two parts of the model (β and δ, respectively), one could dissociate effects of specific factors or manipulations on each of these parameters separately, and thus more precisely check for effects on '*present-bias*' (β) and/or 'patience' (δ).

This model is in line with the dual process hypothesis stating that a 'hot' (affective, present-biased) and a 'cold' (contemplative, patient) process interact and compete during intertemporal decision making (Metcalfe & Mischel, 1999;

McClure *et al.*, 2004a; McClure *et al.*, 2007). However, several more recent findings were inconsistent with this hypothesis (Kable & Glimcher, 2007; 2010), see next section for more details.

These models are commonly used to describe intertemporal choice behavior and help us determine whether specific factors systematically influence our discounting behavior. Individuals differ in their level of discounting, and these differences are reflected by the parameter *k* in the hyperbolic model (see *figure 1.2*).

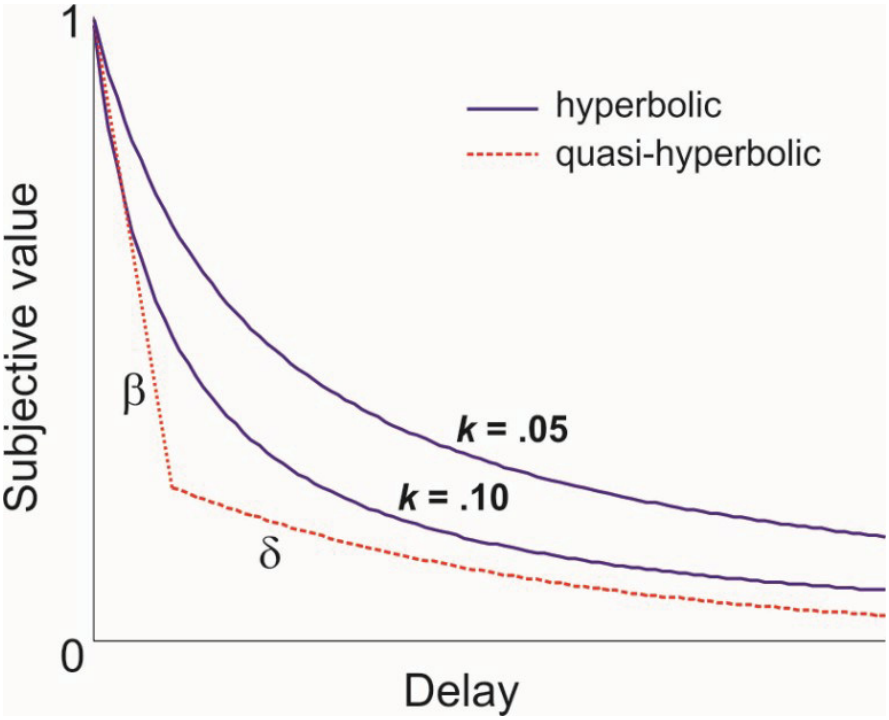

Figure 1.2 *The hyperbolic and quasi-hyperbolic model. Two hyperbolic curves are shown in blue/solid line, with k-values of .05 and .10. The red/dotted curve shows a quasi-hyperbolic curve, with an initial linear decline, reflected by parameter β, and the subsequent exponential decline, reflected by parameter δ.*

Higher values of *k* indicate steeper discounting and thus reflect more overall impatience. Individual *k*-values obtained using monetary rewards have been found to be relatively stable over time intervals up to 6 years (Simpson & Vuchinich, 2000; Audrain-McGovern *et al.*, 2009; Kirby, 2009; Jimura *et al.*, 2011).

Even though models provide insight into the most likely way we discount rewards, fitting models to the *indifference values* (see *box 1.1*) discards variation not in accordance with the model, but which may be systematic nonetheless. One model might fit better than the other, but both models may, in a specific situation, fit poorly to the data. Model-free measures are free of any assumptions, and can be used to complement model-based findings. When all participants are given the same set of choices, one could simply use the number of choice situations in which the participant chose the smaller, sooner reward as model-free measure of impatience. Another model-free measure is the calculation of the area under the curve (AUC; Myerson *et al.*, 2001), connecting the *indifference points* to create the discount curve.

1.1.2 What influences delay discounting?

In the following subsections, I shortly summarize the effects of (the most relevant) demographics and psychological factors on *delay discounting*.

Demographics

In addition to the specific time and reward properties used, many studies indicate that several demographic factors are related to discounting behavior.

One demographic linked to discount rates is age (Green *et al.*, 1994c; Green *et al.*, 1999b; Warner & Pleeter, 2001; Deakin *et al.*, 2004; Denburg *et al.*, 2006; Agarwal *et al.*, 2009; Reimers *et al.*, 2009; Whelan & McHugh, 2009; Samanez-Larkin *et al.*, 2010; Tanaka *et al.*, 2010; Lockenhoff *et al.*, 2011; Worthy *et al.*,

2011). Next to age, a person's income is found to be negatively correlated with discount rates (Lawrance, 1991; Green *et al.*, 1996; Warner & Pleeter, 2001; Harrison *et al.*, 2002; de Wit *et al.*, 2007; Reimers *et al.*, 2009; Tanaka *et al.*, 2010). Whether a higher income results in less discounting or vice versa is yet unclear.

Although several studies have reported gender effects on discounting (Kirby & Marakovic, 1996; Reynolds *et al.*, 2006; Reimers *et al.*, 2009), they are far from conclusive due to opposing findings. Additionally, Harrison *et al.* (2002) found no effect of gender on discounting. However, gender effects are occasionally reported in specific populations, e.g. in children with a specific type of attention deficit hyperactivity disorder (ADHD) (Rosch & Mostofsky, 2016) in alcohol-dependent African Americans (Myerson *et al.*, 2015), or in older adults in relationship with memory performance (Seinstra *et al.*, 2015)(see *Chapter 2*).

Psychological factors

Intertemporal decision making has always been linked with decision making under risk (see Kalenscher, 2007). For example, when deciding whether to spend a monthly fee into a retirement fund, in exchange for a decent monthly fee to be received after a certain age, there is a temporal as well as a risk factor involved. You choose between more money to spend each month, or a higher sum to spend when you have reached retirement age. However, there is always the risk that something happens in the meantime, either to you or to the retirement fund, that makes the investment uncertain. The reason a person prefers an immediate outcome over a delayed one might simply be due to the associated risk of not receiving the long-term reward. A person choosing the smaller, but sooner option may therefore not (just) be impatient, but (also) risk-averse (Hayden & Platt, 2007; Kalenscher, 2007).

BOX 1.2 Assumptions of delay discounting

Delay discounting is based on the idea that we generate an overall subjective value of a reward by integrating magnitude and delay information, but this might not be the case. One could instead focus on the differences in delay and reward (the attributes) of two options separately, and for example decide to choose the largest reward when the delay difference is negligible, but switch preference when the delay difference crosses a personal threshold. Such a choice rule, or heuristic, would seem advantageous because it involves less effort than computing a subjective value for each choice option every time. When a person always translates the relevant attributes of a choice option, e.g. delay or risk and reward magnitude, into one subjective value for each option, one would predict what is called '*transitivity of preference*'. A person is transitive when, if he/she prefers option A over B and option B over C, he/she therefore also prefers A over C, i.e. there is a logical order in which the choice options can be categorized from best to worst.

However, violations of transitivity have been reported (Tversky, 1969; Roelofsma & Read, 2000; Kalenscher *et al.*, 2010), and theories have been developed that accommodate these violations. For example, the additive difference model (Tversky, 1969) assumes that one compares and weighs specific attributes separately when making decisions, much like in the heuristic mentioned above. The comparison process inherently makes context dependent choices (i.e. dependent on which other options are available).

Important to note is that when decisions are indeed based on comparing and weighing attributes separately, this can still lead to transitive choice patterns, depending on the particular choice context and the weighing of the attributes. If, for example, a person is extremely sensitive to delays and therefore puts a high weight on any delay differences, regardless of reward magnitude differences, this person would always choose the option with the shortest delay, resulting in perfectly transitive choice patterns. Therefore, transitive choice patterns cannot rule out context dependent choice processes.

Regardless of the underlying mental process (comparing attributes between options or generating an overall subjective value per option), many studies show that the obtained indifference points in behavioral tasks are well described by a hyperbolic function (Ainslie & Haendel, 1983; Frederick *et al.*, 2002; Green & Myerson, 2004; Soman *et al.*, 2005). However, it is important to note that intransitivity reflects context dependent choice behavior, and thus implies that the decisions one makes in the specific choice context (i.e. the set of options available) of one task, might not reflect absolute preferences for the specific rewards used, and thus the choices one makes in a different choice context.

Indeed, risky rewards seem to be discounted like delayed rewards. Similar to *delay discounting*, researchers have found preference reversals in risky decisions, indicating non-constant discounting of probability: when a smaller reward with a high probability of receiving it is preferred over a slightly less probable but larger reward, preferences may reverse when the probabilities of obtaining a larger, less probable and a smaller, more probable reward are increased proportionally (Rachlin *et al.*, 1987). Furthermore, similar to delay discounting, a hyperbolic discounting function seems to describe discounting of probabilistic rewards well (Ostaszewski *et al.*, 1998; Green *et al.*, 1999a), and more accurately than an exponential function (Rachlin *et al.*, 1991). This suggests a common underlying process (Rachlin *et al.*, 1986; Stevenson, 1986; Prelec & Loewenstein, 1991; Rachlin *et al.*, 1994; Green & Myerson, 1996; 2004).

However, specific (contextual) factors (e.g. culture, inflation) influence probability discounting differently than delay discounting, which seems to indicate that, even though behavior looks similar for risky and temporal decisions, underlying processes might be different (Ostaszewski, 1997; Ostaszewski *et al.*, 1998; Du *et al.*, 2002; see Green & Myerson, 2004). For example, the *magnitude effect* seems to be reversed with probability discounting: larger probabilistic rewards are discounted more steeply than smaller probabilistic rewards, whereas larger delayed rewards are discounted less steeply than smaller delayed rewards (Christensen *et al.*, 1998; Green *et al.*, 1999a; Du *et al.*, 2002; Myerson *et al.*, 2003; see Green & Myerson, 2004).

Regardless of whether the processes underlying probability and delay discounting are similar or different, the apparent link between time and probability requires controlling for risk tendencies when investigating temporal discounting behavior. For example, Alessi and Petry (2003) found that scores on the South Oaks Gambling Screen (SOGS; Lesieur & Blume, 1987), a measure used

to identify pathological gambling, significantly correlated with discount rate. Furthermore, positive correlations between temporal and probability discounting have been found in several studies (Mitchell, 1999; Richards *et al.*, 1999; Myerson *et al.*, 2003; Reynolds *et al.*, 2004b), indicating that a larger tendency to be patient (i.e. to choose the larger, more delayed reward) is related with a larger tendency to take risks. However, a study with gamblers (Holt *et al.*, 2003) showed that, even though they discounted probabilistic rewards less steeply than non-gamblers, there was no difference in delay discounting between the two groups, indicating that the level of probability discounting does not always affect delay discounting. In addition, Olson *et al.* (2007) found that while delay discounting decreased with age, this was not the case for probability discounting. These results are inconsistent with the idea of a common mechanism. However, it is likely that the extent to which the level of probability discounting affects delay discounting mainly depends on the perceived risk associated with choosing the delayed rewards (e.g. Green & Myerson, 1996). A research laboratory might in general be seen as fairly reliable, which could lead to an underestimation of the discounting steepness in real life choice situations.

Another important psychological factor influencing choice behavior is cognitive functioning (Frederick, 2005). A recent study by Lee *et al.* (2012) showed that 12-18 year old adolescents with lower delay discount rates (i.e. more patient choice behavior) achieved higher grades, which was mediated by academic motivation. Similar results were found with psychology students discounting money and credits (Silva & Gross, 2004) and Chilean high-school students (Benjamin *et al.*, 2013). In a meta-analysis of 24 studies, Shamosh and Gray (2008) found a negative correlation of intelligence and delay discounting, thus indicating that higher intelligence is associated with more patient choice behavior.

In addition to intelligence, the ability to exhibit *self-control* is often related to intertemporal choice behavior. *Self-control* can be defined as the quality that allows you to forego immediate gratification in favor of more optimal outcomes later. Although this might seem similar to showing a preference for delayed rewards, the ability to maintain the commitment to go for delayed outcomes while tempted by immediately available rewards has shown to be due to a distinct, though related, process (Reynolds & Schiffbauer, 2005; Mischel, 2007). In a famous test to assess *self-control* in children, the "marshmallow task" (Mischel & Ebbesen, 1970), children received one marshmallow, but were told that they will receive a second marshmallow if they refrained from eating the first marshmallow until the experimenter returned. Better performance on the marshmallow task at 4 years of age has been linked to lower body mass 30 years later (Schlam *et al.*, 2013), smaller likelihood of developing substance abuse (Ayduk *et al.*, 2000), as well as better school performance (Shoda *et al.*, 1990) and better performing children seemed to cope better with frustration and stress (Mischel *et al.*, 1989). Although *self-control* has also been associated with intelligence, early childhood levels of self-control are predictive of health, wealth and crime measures later in life even after controlling for intelligence levels (Moffitt *et al.*, 2011). Similarly, it has recently been shown that the predictive power of the marshmallow task is indeed primarily derived from its assessment of *self-control*, even though task performance may be affected by other factors, such as intelligence (Duckworth *et al.*, 2013).

Interestingly, waiting times in the marshmallow task were significantly affected by manipulation of the certainty of the receipt of the second marshmallow, by means of a reliable or unreliable experimenter (Kidd *et al.*, 2013), indicating that even in very young children, the estimated probability of obtaining the delayed reward influences intertemporal choice behavior.

Lastly, the ability to imagine future events (i.e. episodic future thinking) is related with lower discount rates (Peters & Buchel, 2010b; Benoit *et al.*, 2011; Lebreton *et al.*, 2013; Lin & Epstein, 2014). This supports the hypothesis that the subjective value of the larger, more delayed reward is affected by the ability to imagine its receipt (see also *Chapter 2*). Recently, Kwan *et al.* (2015) showed that cueing future events to decrease discounting does not have to depend on purely episodic future thinking. Amnesic patients with impaired episodic prospection were also able to use the cues to decrease their discounting behavior, suggesting that a more abstract representation of the future could be sufficient to affect delay discounting.

Thus, intertemporal decision making in healthy populations depends on several factors, such as individual risk-seeking tendencies, self-control, and intelligence levels, and several demographic factors also modulate discount rates. It is therefore important to control for demographic factors when investigating impulsive decision making in populations with disorders and pathologies, and to keep in mind that differences found in delay discounting behavior can be due to differences in cognitive functioning.

1.1.3 Intertemporal choice, impulsivity and disorders

So far I have discussed studies involving only healthy human populations. However, many studies have found aberrant intertemporal decision making in different types of disorders and pathologies (e.g. Bickel *et al.*, 2012).

In the literature, when one shows a general preference for immediate gratification over long-term more rewarding outcomes, this is also referred to as *impulsive choice behavior*, a specific subtype of *impulsivity*. Ainslie (1975) already suggested that studying hyperbolic discounting would be useful for understanding *impulsive behavior*, in particular when studying disorders associated with aberrant

impulse control. "*Impulsivity*" is a very broad and heterogeneous concept, encompassing several different types of behavior (Barratt, 1985; Evenden, 1999; Winstanley *et al.*, 2004; Dalley *et al.*, 2011; Bari & Robbins, 2013). In general, *impulsivity* can be defined as the tendency to respond prematurely and without foresight (Robinson *et al.*, 2009), and is related to several behavioral disorders, such as *impulse control disorders* (*ICDs*), ADHD, as well as substance-related disorders (e.g. Bickel *et al.*, 1999; Kirby *et al.*, 1999; Fillmore & Rush, 2002; Alessi & Petry, 2003; Billieux *et al.*, 2010; Li *et al.*, 2010; Paloyelis *et al.*, 2010; Bednarski *et al.*, 2012; Luo *et al.*, 2013; Hu *et al.*, 2015).

Often a dissociation is made between *impulsive action*, indicating poor response inhibition and action without foresight, and *impulsive choice*, which refers to delay aversion and/or the sensitivity to delay of gratification (Evenden, 1999; Winstanley *et al.*, 2004; Dalley *et al.*, 2011; Bari & Robbins, 2013; Wang *et al.*, 2016). Impulsive action has also been called motor impulsivity (Barratt, 1985) and is related to the more emotionally laden impulsiveness facet 'urgency' identified by Whiteside and Lynam (2001). *Impulsive choice* includes what is termed 'non-planning', or 'cognitive impulsivity' (Barratt, 1985; Patton *et al.*, 1995) and is also described as a 'lack of premeditation' (Whiteside & Lynam, 2001). It is therefore important to note that *impulsive choice* behavior can be either due to poorly considering future events or a strong aversion of delays. Additional types of impulsivity that have been identified are attention impulsivity (Patton *et al.*, 1995), lack of perseverance and sensation seeking impulsiveness (Whiteside & Lynam, 2001).

The main distinction of *impulsive action* and *impulsive choice* is important, as both are, often differentially, related to *ICDs*, such as pathological gambling (Petry, 2001; Alessi & Petry, 2003; Lawrence *et al.*, 2009), binge eating (Nasser *et al.*, 2004; Fischer & Smith, 2008), compulsive buying (Billieux *et al.*, 2008) and also

ADHD (Barkley, 1999; Paloyelis *et al.*, 2010; Wilson *et al.*, 2011). These different types of impulsivity seem to have distinct (but sometimes overlapping) neural substrates (Evenden, 1999; Winstanley *et al.*, 2006; Dalley *et al.*, 2008; Eagle *et al.*, 2008; Paterson *et al.*, 2012; D'Amour-Horvat & Leyton, 2014; Wang *et al.*, 2016; Zeeb *et al.*, 2016) and behavior on tasks measuring impulsive action and choice is often not correlated (Solanto *et al.*, 2001; Broos *et al.*, 2012; Weafer & de Wit, 2014; Wang *et al.*, 2016).

Impulsive choice behavior is generally measured with a delay discounting task. Recently, Bickel *et al.* (2012) reviewed the literature indicating that smoking (Audrain-McGovern *et al.*, 2009), and chronic use of cocaine (e.g. Coffey *et al.*, 2003), methamphetamine (Hoffman *et al.*, 2006), heroin (e.g. Madden *et al.*, 1997) and alcohol (Dom *et al.*, 2006) are all associated with higher discount rates. In a longitudinal study, Audrain-McGovern *et al.* (2009) found that delay discount rates predicted entry into smoking and smoking rates in adolescents, indicating a causal effect of increased discount rates on smoking behavior. In addition, behavioral disorders, such as pathological gambling (e.g. Dixon *et al.*, 2003), overeating (e.g. Weller *et al.*, 2008) and poor health behaviors (such as using safety measures) (Daugherty & Brase, 2010) were also related with higher discount rates. These findings were considered evidence for abnormal delay discounting, and thus impulsive choice behavior, as trans-disease process (Bickel *et al.*, 2012).

1.2 The neural correlates of intertemporal choice

So far I have covered what is known about intertemporal choice behavior and several important mediating variables. Understanding how and why these variables influence choice behavior requires knowledge on how the brain makes decisions and which brain areas and networks are involved. For example,

discounting behavior in 9-23 year old participants was related to white matter integrity in bilateral frontal and temporal clusters, of which some, but not all, were accounted for by adding the factor age (Olson *et al.*, 2009), indicating that age differences in delay discounting may be due to specific white matter differences between individuals. In this section I provide a limited overview of what is known about brain areas and network processes linked to intertemporal choice.

Intertemporal decision making is one type of what is called *value-based decision making* (choices based on the subjective valuation of outcomes), which has been the focus of the recently fast developing field called *neuroeconomics*. How exactly do we value specific goods upon which we base our decisions? Which brain areas are involved in this decision process? Time is only one of the many variables (or attributes) that can play a role in value-based decisions. Other important variables can be the taste, risk or specific social situations. However, it is likely that the general decision process occurring in the brain is relatively similar for any value-based decision, and therefore this section focuses mainly on value-based decision making in general.

In recent years, (computational) network models have become increasingly popular as a tool to uncover the role of specific brain areas in value-based decision making and shed light on the exact mechanisms of the transformation of value into choice. To bridge the gap between valuation of the available options, choosing one of the options and the subsequent motor response, value signals need to be compared in a competitive manner, and the winning signal coupled to the appropriate action. For binary decisions, *accumulator models,* developed to explain perceptual decisions (i.e. choices based on perceptual evidence), have been found to be applicable to value-based decisions as well (Cavanagh *et al.*, 2011; Hare *et al.*, 2011; Gluth *et al.*, 2012; 2013; Rodriguez *et al.*, 2015). These

models explain binary decisions as a competitive process between evidence gathered (accumulated) over time for each option (*figure 1.3*).

1.2.1 The valuation of rewards and delays

To make the correct decision, one requires a representation of the value of each option under consideration. Several areas are found to represent subjective value signals, of which the prefrontal cortex (Watanabe, 1996), more specifically the ventromedial prefrontal cortex (vmPFC) in humans (McClure *et al.*, 2004b; Kable & Glimcher, 2007; 2009), the orbitofrontal cortex (OFC) in humans (McClure *et al.*, 2004a; McClure *et al.*, 2004b) as well as animals (Schultz *et al.*, 2000), and the posterior cingulate cortex (PCC) (Kable & Glimcher, 2007), areas in the parietal cortex (Dorris & Glimcher, 2004; Sugrue *et al.*, 2004) the amygdala (Roesch *et al.*, 2010), and the ventral striatum (VS) (Kawagoe *et al.*, 1998; McClure *et al.*, 2004a; Kable & Glimcher, 2007; Rangel & Hare, 2010; Levy & Glimcher, 2012) are thought to play a key role in predicting reward value. Separate groups of neurons in the animal OFC have been shown to represent different types of rewards, as well as different aspects of rewards (Roesch & Bryden, 2011), such as its modality, quality and quantity.

Integration of reward related costs into the value signals give rise to the so called *decision value* (Chib *et al.*, 2009; Peters & Buchel, 2010b), which is termed *discounted value* in case of intertemporal decision making. Activity in the vmPFC has been associated with *decision values* during value-based decision making (Kable & Glimcher, 2007; Hare *et al.*, 2008; Peters & Buchel, 2009; Kable & Glimcher, 2010; Peters & Buchel, 2010b; Rangel & Hare, 2010; Wallis & Kennerley, 2010; Padoa-Schioppa, 2011; Liu *et al.*, 2012). Functional magnetic resonance imaging (fMRI) blood-oxygen-level dependent (BOLD) activity in humans is correlated with *discounted value* during intertemporal choice in the human

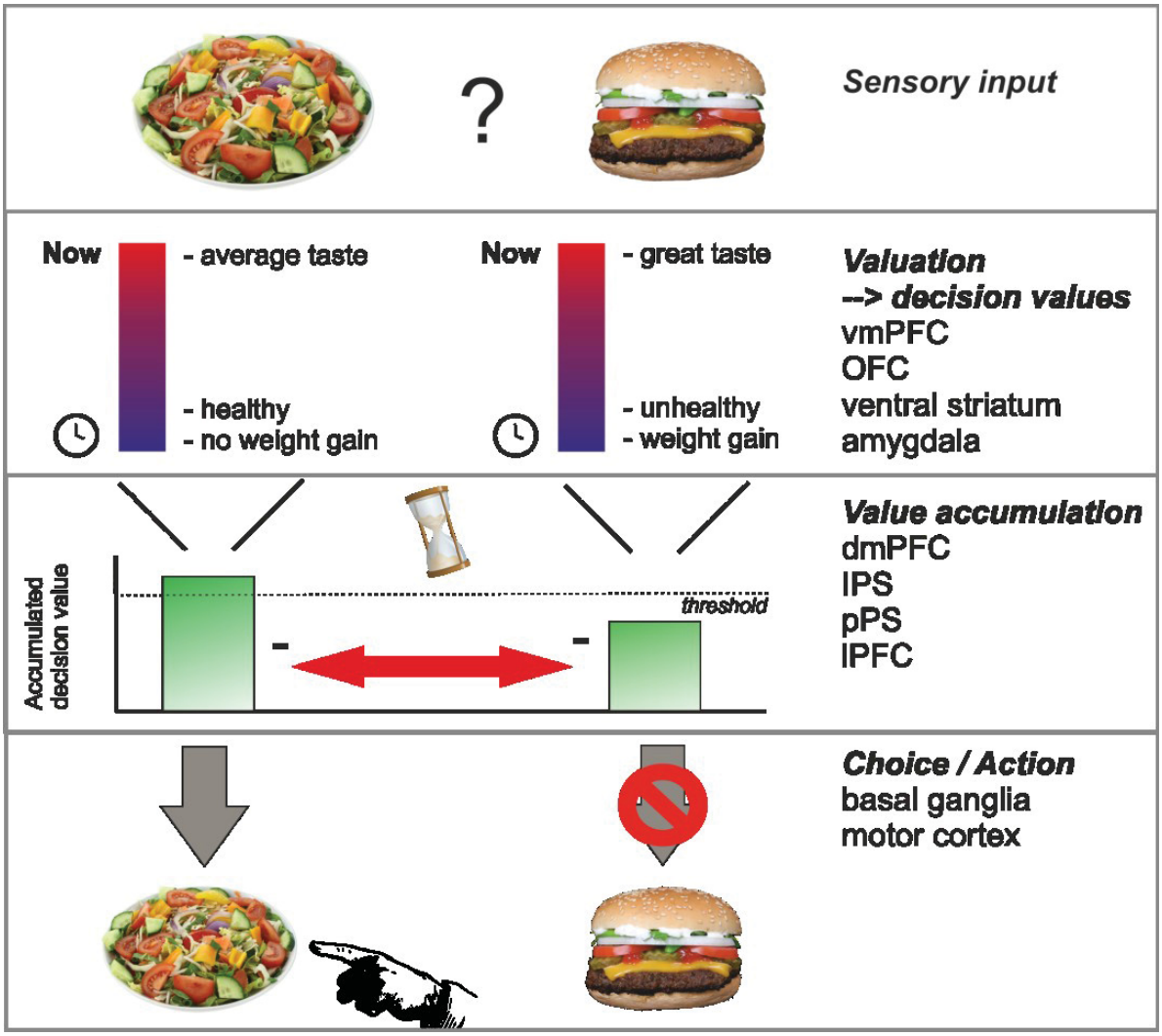

Figure 1.3 *Simplified schematic overview of a value-based choice between a salad and a burger, based on the accumulator model. Both options have short and long-term advantages and/or disadvantages that are evaluated. Value signals of each option are accumulated in specific brain areas and compete via mutual inhibition, which leads to the choice of the most valued option. This may occur when a specific threshold is reached. The brain areas mainly (but not exclusively) found to be involved in the specific steps of the process are listed on the right. Images available under a creative commons license. For image references, see reference Images (Figure 1.3).*

ventral striatum, PCC, mOFC and vmPFC (Kable & Glimcher, 2007; Peters & Buchel, 2009; Kable & Glimcher, 2010; Peters & Buchel, 2010b; Liu *et al.*, 2012)

and these areas were found to be sensitive to changes in both magnitude and delay (Ballard & Knutson, 2009; Pine *et al.*, 2009).

One line of research suggested that two separate brain systems involved in decision making are the cause of our hyperbolic choice behavior, which are the 'hot', more emotionally engaged system and the 'cold', more deliberate system already mentioned above (McClure *et al.*, 2004a). If both systems discount rewards in an exponential fashion, the combination of the two systems would result in hyperbolic discount behavior (Laibson, 1997; McClure *et al.*, 2004a). However, Kable and Glimcher (2007) found that activity in areas thought to belong to the 'hot' system reflected subjective value changes and not immediacy per se, and did not reflect more impatient valuation than was observed behaviorally. Others have replicated this finding (Peters & Buchel, 2009; 2010b), and Sellitto *et al.* (2010) found that lesions of a 'hot' area, the medial orbitofrontal cortex (mOFC), did not result in the expected decrease in discounting, but instead was found to increase discounting, indicating that at least on the level of whole brain areas, the dual system hypothesis did not hold, though investigation of subareas or subsets of neural networks may show a different picture (Tanaka *et al.*, 2004).

Furthermore, valuation during intertemporal decision making seems to be modulated when future outcomes are imagined, which is linked with activity in the hippocampus (Lebreton *et al.*, 2013). More specifically, Benoit *et al.* (2011) found that imagining future rewards resulted in greater reward sensitivity and less discounting, which was associated with increased coupling of the hippocampus with the medial rostral PFC. More information on memory and delay discounting can be found in *Chapter 2*.

However, it is important to note that the encoding of (subjective) value seems more broadly distributed across the brain and at the same time more narrowly

distributed within specific regions than is indicated by average bold signals from specific regions (Vickery *et al.*, 2011), making it essential for further research to focus on single unit activity in combination with network processes. This is where research using animal models prove particularly useful as they enable the use of techniques with high spatial resolution, such as electrophysiology or optogenetics (Kalenscher & van Wingerden, 2011).

1.2.2 Evidence/value accumulation

Decision value signals seem to accumulate over time in specific areas. Accumulation areas do not only integrate value information of the options over time, but also compare the *decision values* in the process (Busemeyer & Townsend, 1993; Usher & McClelland, 2001; Wang, 2002). In the literature, several areas have been identified as accumulation and comparison areas during value-based decision making; the dorsomedial PFC (dmPFC) and the intraparietal sulcus (IPS) (Hare *et al.*, 2011), as well as the posterior parietal cortex (pPC) and lateral PFC (lPFC) in intertemporal choice specifically (Rodriguez *et al.*, 2015).

Importantly, the vmPFC has been found to be interacting with these frontoparietal areas during simple value-based decision making between juices of different quality and quantity (Hare *et al.*, 2011) and intertemporal decision making (Rodriguez *et al.*, 2015). In a paradigm with single stimuli representing specific monetary costs and benefits that were either accepted or rejected, the difference in costs and benefits were reflected in the vmPFC, while the IPS was found to accumulate this difference between costs and benefits (Basten *et al.*, 2010). Furthermore, Hare *et al.* (2011) found that activity in the dmPFC and IPS was coupled to activity in the motor cortex in a choice-dependent manner, thereby indicating that these two areas are optimal candidates for evidence accumulation. Similarly, Rodriguez *et al.* (2015) found that the dmFC, pPC and lPFC showed functional connectivity with the motor cortex during intertemporal

choice. The interaction between mPFC and lPFC has been considered critical for the exhibition of self-control (Hare *et al.*, 2009; Baumgartner *et al.*, 2011) and several studies have shown that activity in the VS as well as the connectivity between the VS and the lPFC are related to the individual level of impulsive decision making (Hariri *et al.*, 2006; Peper *et al.*, 2013; van den Bos *et al.*, 2014).

1.2.3 Choice selection and modulation

Value accumulation eventually leads to the selection of one of the choice options under consideration, followed by subsequent action to obtain the reward. The basal ganglia are thought to play an important role in this final step (Bogacz & Gurney, 2007). The general role of the basal ganglia has mostly been described as a selective gate for the execution of motor programs, with dynamic interaction of selective disinhibition of appropriate motor commands via the direct pathway and inhibition via the indirect and hyperdirect pathways (e.g. Redgrave *et al.*, 1999; Nambu *et al.*, 2002; Frank, 2006) (see *figure 1.4*). Signals from the cortex that activate striatal neurons of the direct pathway disinhibit the thalamus and thus motor output via the substantia nigra pars reticulata (SNr) and globus pallidus interna (GPi). Activating striatal neurons that are part of the indirect pathway strengthen inhibition of the thalamus (and thus motor output) by inhibiting the globus pallidus externa (GPe), which in turn disinhibits the subthalamic nucleus (STN). The STN subsequently activates the SNr and GPi, thereby strengthening their inhibitory effect on the thalamus. The hyperdirect pathway consists of direct excitatory input from widespread areas of the cortex to the STN (Maurice *et al.*, 1998; 1999; Brunenberg *et al.*, 2012; Lambert *et al.*, 2012).

The STN has been considered important for cognitive control, for example during response inhibition (Baunez *et al.*, 2001; Aron & Poldrack, 2006; Frank, 2006). Not only motor areas are found to be projecting to the STN (Parent & Hazrati, 1995b; Brunenberg *et al.*, 2012), but also areas involved in valuation of

choice options, such as the medial/orbital cortex in rats (Maurice *et al.*, 1998), monkeys (Haynes & Haber, 2013) as well as humans (Brunenberg *et al.*, 2012). In addition, evidence from rats shows that the STN not only receives projections from the cortex, it also projects to the cortical areas it receives input from, with the more rostral part of the STN bi-directionally linked to motor areas and medial and caudal regions of the STN receiving from and projecting to the medial prefrontal cortex (Degos *et al.*, 2008). In recent years STN functioning has been linked to cognitive functions such as attention, motivation, impulsive action and choice and decision making (see Baunez & Lardeux, 2011; Weintraub & Zaghloul, 2013).

When options under consideration have a similar subjective value, reaction times have been found to increase, buying more time for comparison. The connection of the prefrontal cortex with the basal ganglia via the STN (the hyperdirect pathway) is thought to be important for setting the altering decision times when choice options are similar (Nambu *et al.*, 2002; Frank, 2006; Cavanagh *et al.*, 2011; Zaghloul *et al.*, 2012). Cavanagh *et al.* (2011) found that local field activity in the STN is similarly modulated as EEG measures of mPFC activity when comparing high-conflict (i.e. choices with similar reward probabilities) with low-conflict choices, suggesting that communication between the mPFC and STN is important for decision threshold modulation. Similarly, on single cell level, Zaghloul et al. (2012) found that spiking activity was positively correlated with degree of decision conflict.

When focusing on impulsive choice behavior, two areas of the basal ganglia, the STN and nucleus accumbens (NAc), both sub-sections of the VS, seem to have opposing roles. Whereas lesions of the NAc seem to increase impulsive choice on

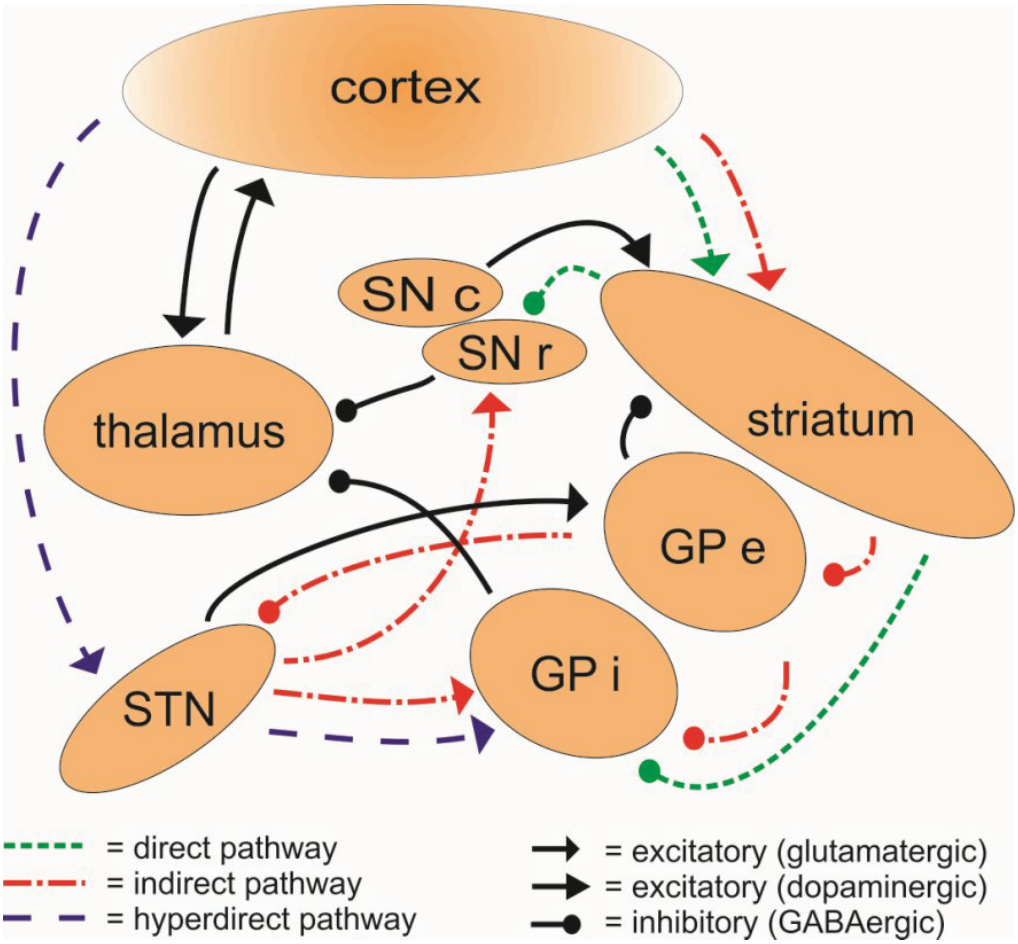

Figure 1.4 *Overview of the basal ganglia pathways. For the thalamus to send signals to the cortex (e.g. to initiate movement), inhibitory signals from the SNr and GPi need to be suppressed. This can be achieved by direct inhibition of SNr/GPi via the striatum (direct pathway). Increased activity of the SNr/GPi suppresses thalamic output and can be achieved by decreased inhibition of SNr/GPi via the GPe (indirect pathway) or increased activation via the STN (hyperdirect pathway).*

an intertemporal choice task (Cardinal *et al.*, 2001; Bezzina *et al.*, 2007; Bezzina *et al.*, 2008; Araujo *et al.*, 2009), lesions of the STN seem to reduce impulsive choice (Winstanley *et al.*, 2005; Uslaner & Robinson, 2006). This decrease in temporal discounting found after STN lesions might only be a transient effect (Uslaner & Robinson, 2006; Bezzina *et al.*, 2009) and thus only a side effect of the lesion.

However, it is also possible that the observed effects of STN lesions on intertemporal choice slowly evaporate due to compensatory processes that develop after the lesions. If this is the case, the decreased discounting initially found might indicate that normal STN functioning biases choice towards immediate rewards. The fact that STN lesions always seem to decrease discounting indeed suggests a more directional role of the STN in discounting behavior.

STN lesions have been shown to increase the incentive motivation to work for rewards (Baunez *et al.*, 2002). If delay sensitivity does not change, STN lesions would only change delay discount behavior when it alters the relative value of the involved rewards. Bezzina *et al.* (2009) used an intertemporal choice paradigm that dissociates between the effects on reward and delay sensitivity and reported that STN lesions increased reward sensitivity, whereas the sensitivity to delays did not change. However, the parameter that was interpreted as reflecting delay sensitivity did not only depend on delay sensitivity itself, but also on reward sensitivity. The fact that they found a difference in the reward sensitivity thus seems to suggest that there must also be a difference in delay sensitivity in order for their delay sensitivity parameter to be similar between conditions. Therefore, their results may possibly indicate a significant decrease of impulsive choice after STN lesions when these estimates are corrected for the difference in reward sensitivity. When the STN normally puts a hold on incentive motivation to work or wait for rewards, this might be how the STN mediates a bias toward immediate rewards.

Thus, although the hyperdirect pathway, including the STN, seems to be involved in setting the decision threshold, it is less clear to what extent and how exactly the STN is involved in intertemporal decision making. See *Chapter 3* for more on this subject.

1.3 Thesis outline

Intertemporal decision making is a popular and well-studied topic, and the literature presented above does not cover all of what is known at this moment, although it is clear that many state and trait factors together determine choice behavior. The experiments presented in the following chapters cover rather specific states and/or traits in which intertemporal choices are made, with the aim of answering several important open questions.

First of all, the literature is not consistent regarding the effect of old-age on intertemporal choice, and we therefore investigated whether a second factor that declines with old-age, i.e. episodic memory, moderated intertemporal choice behavior (see *Chapter 2*). Since our society is ageing, it becomes increasingly important to understand how older adults make (financial) decisions. We found a rather unexpected interaction between delay discounting, gender, and autobiographical memory.

Next to individual differences in intertemporal choice behavior, researchers have found differences in discounting behavior between healthy persons and individuals with a specific addiction, *impulse control disorder* or several other diseases/disorders. Aside from the disorders themselves, specific treatments affecting brain functioning can cause changes in choice behavior. In a clinical study we investigated the effects of deep brain stimulation of the STN, which is a commonly used treatment for Parkinson's disease (PD), on intertemporal choice behavior of Parkinson patients (see *Chapter 3*). PD is a progressive neurodegenerative disease mostly known for its motor symptoms due to the loss of dopaminergic neurons. Every year about 50.000 individuals in America are diagnosed with PD (NINDS, 2014), and treatment consists of symptom reduction with medication and increasingly with deep brain stimulation (DBS) of the internal globus pallidus or STN. As altered intertemporal decision making can have

profound impact on social and financial well-being, it is important to find out whether such a treatment affects these decisions. In addition, clinical studies could shed light on the brain areas and networks involved in intertemporal choice behavior, in this case the STN.

So far, we have approached intertemporal decision making mostly from an economic perspective, with a hyperbolic discounting model to describe choice behavior. In the third experiment presented here (*Chapter 4*), we asked whether humans actually maximize a discounted value or, alternatively, reward rate on a sequential and experiential intertemporal choice task. Reward rate, or more generally, energy intake has been considered the currency maximized by animals in foraging contexts (Pyke *et al.*, 1977). Interestingly, maximizing reward rate can result in choice patterns that also led to the adoption of hyperbolic discounting models, such as preference reversals.

So, this is how I have been spending my time during the last four years; in the hope that my efforts now yield valuable results in and for the future. And of course for the PhD title as my personal long-term reward.

2. Gender-specific differences in the relationship between autobiographical memory and intertemporal choice in older adults

"Time moves in one direction, memory in another."

- William Gibson

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2.1 Abstract

As the population of older adults grows, their economic choices will have increasing impact on society. Research on the effects of aging on intertemporal decisions shows inconsistent, often opposing results, indicating that yet unexplored factors might play an essential role in guiding one's choices. Recent studies suggest that episodic future thinking, which is based on the same neural network involved in episodic memory functions, leads to reductions in discounting of future rewards. As episodic memory functioning declines with normal aging, but to greatly variable degrees, individual differences in delay discounting might be due to individual differences in the vitality of this memory system in older adults. We investigated this hypothesis, using a sample of healthy older adults who completed an intertemporal choice task as well as two episodic memory tasks. We found no clear evidence for a relationship between episodic memory performance and delay discounting in older adults. However, when additionally considering gender differences, we found an interaction effect of gender and autobiographical memory on delay discounting: while men with higher memory scores showed less delay discounting, women with higher memory scores tended to discount the future more. We speculate that this gender effect might stem from the gender-specific use of different modal representation formats (i.e. temporal or visual) during assessment of intertemporal choice options.

2.2 Introduction

You are retired. Would you now finally spend your money on small pleasures right now, or rather save for that new car you always dreamed of having? Throughout our lives we make countless choices of this kind where the outcomes become available over time, for example when we decide to refrain from eating the tasty hamburger to go for the healthy salad instead. As these intertemporal decisions can have far reaching consequences, it is important to understand how our preferences develop over time and which factors influence our choice behavior.

Intertemporal decision making is usually assessed using monetary incentives available at specific points in the future. Because a delay has a negative effect on the subjective value of a reward, amounts available in the future are worth less (i.e. are discounted) compared to when they are received now. It is commonly found that the value of a monetary amount (or other goods) is discounted in a hyperbolic fashion (Mazur, 1984; see Kalenscher & Pennartz, 2008), with initial steep discounting of reward values with short delays to reward consumption, and flatter discounting with longer delays. The initial steep decline in the discount function is often related to the characteristic '*present-bias*' which relates to the tendency to reverse preferences in favor of immediate gratification at the expense of meeting long-term goals. The general steepness of the discount function can be used as an index of subjective '(im)patience', i.e., the general sensitivity to delays.

Our time preferences change with age (Deakin *et al.*, 2004; Denburg *et al.*, 2006; Agarwal *et al.*, 2009; Samanez-Larkin *et al.*, 2010; Worthy *et al.*, 2011). Studies on the effects of age on discounting often find increased discounting in children and adolescents, with decreasing discount rates in adulthood (Green *et al.*, 1994c; Reimers *et al.*, 2009; Whelan & McHugh, 2009; Lockenhoff *et al.*,

2011). The change in discounting across childhood and adolescence presumably reflects the maturation process of prefrontal areas important for executive control. With regard to older aged groups, evidence is inconsistent: while some studies found no difference in discount rates between older and younger adults (Green *et al.*, 1996; Chao *et al.*, 2009; Whelan & McHugh, 2009), other studies suggest increasing discount rates with age (Harrison *et al.*, 2002; Read & Read, 2004), yet others found decreasing discount rates (Green *et al.*, 1994c; Reimers *et al.*, 2009; Jimura *et al.*, 2011; Lockenhoff *et al.*, 2011; Eppinger *et al.*, 2012). Moreover, the findings seem to depend on the type of reward (primary or secondary) as well (Jimura *et al.*, 2011). For very old adults, it can be argued that the shortened life expectancy renders the preference for long term outcomes more risky because they may not live to experience the realization of the future outcome (Sozou & Seymour, 2003). On the other hand, a lifetime of decision making might increase the ability to delay gratification because the older adults have learned the value of patience through experience (Logue *et al.*, 1984; Green *et al.*, 1994c; Samanez-Larkin *et al.*, 2011; Eppinger *et al.*, 2012).

However, a third possibility to explain the inconsistency in the results on old age and discounting is the great variability in age-related decline of decision-relevant mental and neural functionality: older age comes with neuronal changes in areas involved in reward processing and decision making (Raz *et al.*, 1997; Marschner *et al.*, 2005; Raz *et al.*, 2005; Backman *et al.*, 2006; Weiler *et al.*, 2008; see Brown & Ridderinkhof, 2009; Mell *et al.*, 2009; see Mohr *et al.*, 2010; Samanez-Larkin *et al.*, 2010). It is therefore possible that changes in discounting in older individuals depend on the (variable) degree in cognitive decline associated with older age (Boyle *et al.*, 2012). One mental function that declines with age is episodic thinking (Salthouse, 2009; Lundervold *et al.*, 2014). Interestingly, several studies have linked episodic future thinking, i.e., mental time travel, or imagining

possible future outcomes, to delay discounting behavior (Peters & Buchel, 2010a; Benoit *et al.*, 2011; Lebreton *et al.*, 2013; Lin & Epstein, 2014). The core finding of these studies is that episodic future thinking goes along with decreased delay discounting (Peters & Buchel, 2010a; Lebreton *et al.*, 2013; Lin & Epstein, 2014), supporting the hypothesis that the better one is able to imagine the future outcome, the higher the subjective valuation of that future outcome will be.

These and other studies indicated that imagining future events activates the same core neural network that is involved in episodic memory functioning (see Schacter & Addis, 2007a; Suddendorf & Corballis, 2007), supporting the theory that the episodic memory system is used to create images of future events in the mind's eye (Johnson *et al.*, 2007; Schacter & Addis, 2007c; b; 2009). It has been suggested that to assess whether a delayed reward is the most preferable option, one needs to have a representation of future states of oneself to determine how valuable that reward will be, and use this representation to maintain motivation for overcoming short-term temptations (Boyer, 2008; Rick & Loewenstein, 2008; Lebreton *et al.*, 2013). This assessment could depend on recalling similar rewards obtained in the past.

Thus, because episodic future simulation and episodic memory draw on similar neural systems, and because delay discounting might depend on recalling rewards from the past, it is tempting to speculate that episodic memory performance affects discounting behavior. However, behavioral studies linking delay discounting with episodic simulation focused on the episodic projection of *future*, not the recall of *past* events. In addition, memory recall processes that bias decisions do not necessarily need to be conscious or effortful (Wimmer & Shohamy, 2012). It is therefore unclear whether more general memory processes or episodic memory mechanisms in particular play a significant role in

determining discounting levels in situations where episodic future thinking is not explicitly prompted in the choice task.

Not only future rewarding events, but also immediate rewards could trigger memory processes that do not necessarily have to be episodic. High integrity of the memory network, including the hippocampus, would in that case not necessarily lead to a decrease in discounting. On the other hand, unconscious preferences for more profitable delayed rewards, potentially due to a general bias towards long-term thinking in our society**,** could render (unconscious) memory retrieval mechanisms an important factor for biasing choice towards delayed rewards. This would be in line with findings of Kwan *et al.* (2013), who found that in persons with hippocampal amnesia, future-orientated decision making was relatively intact, whereas they were unable to imagine detailed future events. A more recent study found that, even though persons with hippocampal amnesia show similar discounting as healthy controls, when prompted to imagine spending future rewards amnesic patients did not show decreased discounting, whereas healthy controls did (Palombo *et al.*, 2014). This is in line with the idea that episodic future thinking is one of the factors that influences intertemporal decision making, but shows that engagement of the hippocampal network is not a necessary requirement for discounting.

The current study could shed more light on whether episodic memory retrieval processes influence intertemporal decision making without explicitly triggering future simulation. Evidence for the importance of episodic memory, i.e. the storage and retrieval of *past* episodes, for delay discounting is elusive. In order to test this idea, it would be desirable to have a population sample with a substantial degree of variability in episodic memory performance. As mentioned, this is the case in older subjects: several studies have shown that episodic memory functioning declines with age (Salthouse, 2009; Lundervold *et al.*, 2014), but the

extent of decline differs strongly between individuals (Ronnlund *et al.*, 2005; Nyberg *et al.*, 2012). We therefore aimed to investigate the relationship between episodic memory functioning and discount behavior in older aged individuals. We hypothesize that age-related variability in episodic memory performance may be an important mediating variable on discounting behavior that could explain some of the discrepancies found in the literature.

Our study was designed to investigate the relationship between episodic memory performance and delay discounting in a group of older adults. We expected that episodic memory performance correlated with decreased discounting when memory performance was higher. Overall, our results do not support our hypothesis. However, we additionally explored the role of gender, as several studies have shown gender effects in episodic memory tasks (Herlitz *et al.*, 1997; Kramer *et al.*, 1997; Oberg *et al.*, 2002; see Herlitz & Rehnman, 2008) and found an interaction effects of gender and autobiographical memory on discounting.

2.3 Methods

2.3.1 Participants

Sixty-two older adults (33 female) between 60 and 89 years (M = 72.60, SD = 6.47) were recruited from an internal database of the Institute of Experimental Psychology at Heinrich-Heine-University Düsseldorf. Of this sample, all participants denied to suffer from any neurological or psychiatric disease or to have been taking psychiatric medication at any time in their life. None of the participants used drugs or exceeded the limits of low-risk alcohol use (> 20 g alcohol per day for women; > 40 g alcohol per day for men). Of the three smokers in the sample, all smoked less than 20 cigarettes a day. All participants were German native speakers and scored at least 25 points (M = 28.37, SD = 1.54) in the

Mini-Mental State Examination (MMSE; Folstein *et al.*, 1975). With the exception of two, all participants were retired.

Results of four participants were excluded from analyses due to incorrectly answering catch trials in the intertemporal choice task (see below). The results reported below are therefore based on a sample of 58 adults (30 female) between 60 and 89 years (M = 72.57, SD = 6.39). See *table 2.1* for further demographic information. Participants received a general allowance of 5 Euro immediately after participation. Additionally, participants were paid according to their choice in the intertemporal choice task between 10 Euro tomorrow and 20 Euro in 9 months. All payments were made by checks and given directly (allowance) or sent to participant's home address either 1 day or 9 months after the date of participation. Checks could be cashed at any bank of choice.

Table 2.1 *Descriptive variables of the complete sample and the gender subgroups.*

		Age	IQ	Income(year)
Complete sample	Mean (SE)	72.6 (0.8)	16.1 (0.6)	22,882 (1,976)
Males	Mean (SE)	73.8 (1.1)	16.8 (0.8)	29,409 (2,879)
Females	Mean (SE)	71.5 (1.3)	15.4 (0.9)	15,833 (1,890)
Statistics (m/f)	t or U	1.369	385[a]	3.942
	p	.176	.584	.000**

Means (s.e.m.) of age, IQ score and yearly income. The t or U scores with their p-values are reported for the statistical comparison of age, IQ and income between the male and female subgroups.

[a] *Mann-Whitney U test was used instead of t-test due to violation of normality assumption.*

* $p < 0.05$

** $p < 0.01$

The study was approved by the ethics committee of the Department of Experimental Psychology at the University of Düsseldorf. Participants were informed about the course of the study, their right to quit the study at any moment for any reason as well as the payment procedure, and all provided written informed consent prior to data collection.

2.3.2 Materials

Intertemporal choice task. Temporal discounting was assessed by a computer-based intertemporal choice task implemented using the MATLAB Toolbox Cogent 2000 (developed by the Cogent 2000 team at the FIL and the ICN). The task consisted of 6 randomized blocks of trials with financial offers that differed in the delays to the smaller, sooner and larger, later reward. In four blocks the delay to the sooner option was *tomorrow*, while the delay to the later option was 3, 6, 9 or 12 months. In the remaining two blocks the sooner option was delayed for 6 months, while the later option was delayed for 9 (block 5) or 12 months (block 6). The delay of the soonest reward was set to *tomorrow* instead of *today* to prevent potential effects of transaction costs on decisions; the expectation of receiving cash payment directly instead by check might bias choices towards immediate rewards. Within each block the later option was fixed at 20 Euro, whereas the sooner option varied between 0 and 20 Euro in steps of 2.50 Euro. Each of the immediate reward values was presented twice within each block, yielding 18 trials per block and 108 trials in total.

Trials in which the immediate reward was either 0 or 20 Euro functioned as *catch* trials, as the preference within these trials should logically be the delayed (e.g., €0 now versus €20 in six months), or immediate reward (e.g., €20 now versus €20 in six months), respectively. Within each trial one option was shown on the left side of the screen (53 cm x 30 cm), while the other was shown on the right

side. The side-allocation of smaller-sooner or larger-later rewards was randomized across trials. Choices were indicated by pressing either the ‘x’ or ‘m’ key on a standard keyboard, corresponding to the left or right option shown. The relevant keys were color-coded. Participants received detailed oral and visual instructions before the task was started. It was emphasized that there were no right or wrong answers and their personal preference should guide their decisions. Before the start of each new block the subsequent delays were shown. Participants were told that one of the trials would be randomly picked and their choice paid out by means of checks after the corresponding delay. The final screen of the task displayed their earnings.

Episodic memory performance. Episodic memory can be defined as the conscious recollection of past personal events linked to a particular temporal and spatial context (e.g. Tulving, 2001). In the literature, episodic memory is often decomposed into several sub-functions: associative memory, autobiographical memory for personal events, and autobiographical memory for personal facts and dates. Associative memory is the ability to learn and remember the relationship between unrelated items and is known to rely strongly on the hippocampus (Eichenbaum, 2000; Davachi & Wagner, 2002; Suzuki, 2007), autobiographical memory refers to the 'meaningful reconstruction of one's own past' (Fink *et al.*, 1996). Although autobiographical memory for facts and dates shares the personal component with episodic memory, as well as neural correlates in specific operationalizations (see Renoult *et al.*, 2012), it has also been related to semantic memory, and termed 'personal semantics' (Renoult *et al.*, 2012). We assessed memory performance using independent standard tests for associative and autobiographical memory, as explained in the following paragraphs**.**

Associative memory task. Associative memory performance was measured with a face-name paired-associates (FNPA) task, in which new face-name

associations need to be stored in memory and subsequently remembered. This task was implemented using the online survey tool Unipark (QuestBack GmbH, Hürth, Germany). It consisted of 4 blocks, each with 10 encoding, 3 subsequent distraction and 10 retrieval trials. The encoding trials consisted of 10 face-name pairs successively presented for 4 seconds each, followed by a fixation dot for 1 second (see *figure 2.1*). Participants were instructed to memorize the name belonging to each face. The face-name pairs were only shown once in random order and were not repeated across blocks. To prevent rehearsal, the encoding trials were followed by the distraction trials, which consisted of mathematical equations presented with a solution that was either correct or false. In each trial participants had to indicate by a mouse click whether the proposed solution was correct or false. In the following retrieval block ten face-name pairs were presented in randomized order, consisting of the same names and faces as shown during the previous encoding trials. However, only half of the trials showed the correct face-name combinations from the first round, the other half contained incorrect face-name combinations. In each trial participants had to indicate with a mouse click whether the face-name pair was *correct* or *false.* Blocks were intermitted by a short break of 10 seconds. Before starting the experiment participants received detailed instructions and performed a test trial to practice handling the mouse and to make sure that they had understood the instructions. In addition, block-specific instructions were shown at the beginning of each block.

The 40 face stimuli used in this task were taken from the FACES database (Ebner *et al.*, 2010) and were unknown to the participants. The stimuli included 14 young (19-28 years), 12 middle-aged (39-54 years) and 14 older (69-80 years) faces with an equal number of male and female faces from each age group and within each block. The fictional names were taken from public lists of popular

German forenames and were carefully chosen and assigned to the faces so that they were not suggestive of the person's age.

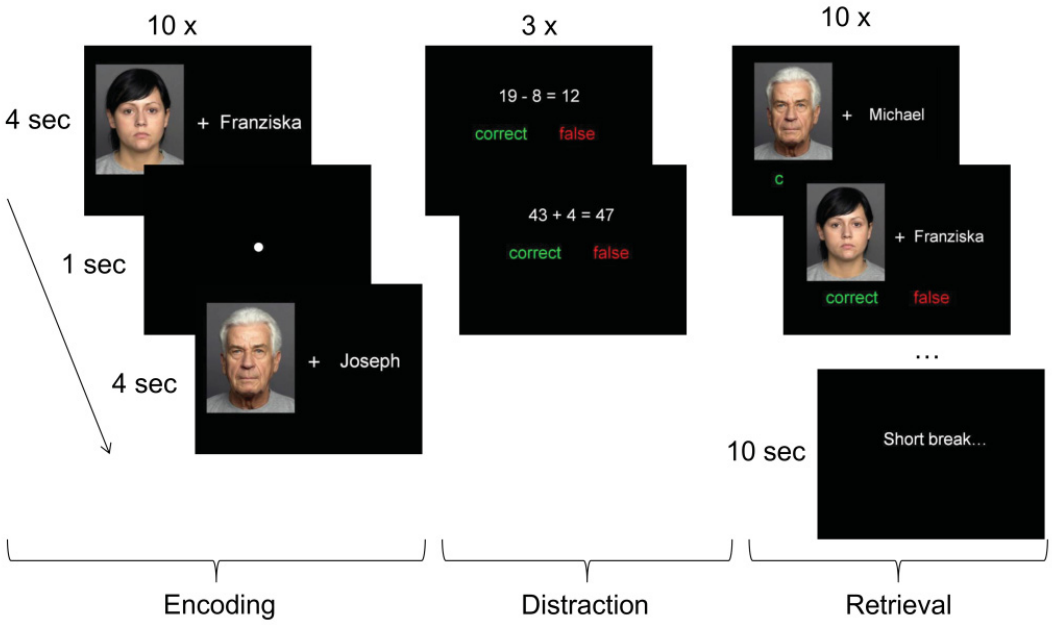

Figure 2.1 Schematic overview of the Face-Name Paired-Associates (FNPA) task. *Participants went through four blocks, consisting of encoding, distraction and retrieval trials. At the beginning of each block participants were required to memorize ten face-name pairs. These were followed by three distraction trials, in which participants had to indicate whether the shown equation was correct or false. Each block ended with ten retrieval trials, in which participants indicated whether the shown face-name pair was correct or false. The faces shown in the figure are from two exemplary persons of the FACES database (Ebner et al., 2010).*

Autobiographical memory task. The participants' ability to remember episodes from their past was tested using Module C of the *Inventar zur Gedächtnisdiagnostik* (IGD; Baller *et al.*, 2006) which is a German memory inventory. While Modules A and B measure memory retention and semantic memory, Module C was specifically designed to capture autobiographical

memory. Module C again is divided into two sub modules, C1 and C2. While C1 measures memory performance and memory quality for personal events, C2 captures memory performance and quality for dates and facts related to oneself and one's personal environment.

Sub-module C1 required participants to describe several personal events that occurred before the age of 6, between the age of 7 and 16, from the age of 17 until one year ago and within the last 12 months. The described events must be concrete (i.e. restricted in time and location). For example, having been at college was not counted as an event, whereas the first party at college was. Participants were instructed only to recall events they really *remembered* and not just *knew* from photos, movies or narratives. To ensure that the recalled events fulfilled the requirements and avoid biases due to differences in writing speed, sub module C1 was implemented as interview. A time limit was set to 4 minutes, in which the participants had the chance to describe a maximum of 5 events per life episode. The interviewer was instructed not to prompt or give any hints to facilitate recall, and wrote down the recalled events in note form. Before continuing to the next episode, participants rated one of the recalled events on its *vividness*, *specificity* and *emotionality*, each on a 4-point scale. The to-be-rated event was specified in the test.

Submodule C2 contained 64 items about 11 different general life-related topics (i.e. work, transportation, education). For each item participants had to indicate by ticking 'yes' or 'no' whether they were able to remember a certain date or fact like, for instance, their partner's or child's date of birth, previous home addresses or how they used to travel to school or work. If participants answered 'yes' they additionally had to rate how confident they were about the specific memory. Questions about topics that did not apply to the participant (e.g. questions about

children with childless subjects) were skipped. There was no time restriction for this part of the IGD.

Although Baller *et al.* (2006) evaluate the content validity of Module C to be sufficient, it should nevertheless be admitted that the participants' descriptions, answers and ratings could not be verified and were therefore interpreted with caution.

General level of intelligence. To control for potential confounding effects of general intelligence, the 10-Minutes-Test (Musch *et al.*, 2009) was used as a short measure of fluid as well as crystallized intelligence. The test includes 32 items that require mathematical and deductive reasoning or general knowledge and vocabulary. The total test score corresponds to the sum of all items that were solved correctly within 10 minutes. This relatively short implementation time allows for a fast, yet valid and reliable estimate of general intelligence. Beside its objective administration and interpretation, the test was shown to have a high loading on Spearman's g factor with r = .57 (Ostapczuk, 2006). First validation studies also found a high internal consistency of Cronbach's $\alpha >$ .80 and significant correlations with several other cognitive measures (Musch *et al.*, 2009; Ostapczuk *et al.*, 2011). To date the 10-Minutes-Test has only been standardized for pupils and students. However, due to the lack of alternative short intelligence screening methods and the possibility that a long test session might overstrain the cognitive capacity of older participants, the 10-Minutes-Test was considered to be suitable for our purposes.

Dementia. Participants were screened for dementia or severe cognitive impairment using the mini-mental state examination (MMSE). This interview assesses global cognitive abilities like orientation, attention and memory as well as numerical and language skills. Participants with scores lower than 13 out of 30,

which indicate global cognitive disorders, were excluded from participation. All screened participants had a score above 13.

Post-test questionnaire. General demographic information (education, job status, income and lifestyle habits) was obtained with a post-test questionnaire.

2.3.3 Procedure

The experiment took place in a laboratory at Heinrich-Heine-University Düsseldorf. Participants were tested individually in one 90 minute session. Participants were given verbal and written information on the procedure of the experiment before giving informed written consent. All participants were screened for dementia before performing the tasks. The order of tasks was determined depending on their importance and degree of difficulty, with the most demanding tasks set at the beginning. Thus, participants started with the intertemporal choice task, followed by the FNPA task, the 10-Minutes-Test, and finally the IGD task. In the end, participants filled out the post-test questionnaire and received their general show-up fee of 5 Euro. In addition, they were given a signed receipt stating that the remaining amount earned in the intertemporal choice task, to be received at the specified date, would be sent in the form of a check by post.

2.3.4 Data analysis

Delay discounting. All mathematical procedures to determine the participants' discount rates were performed using the MATLAB (The MathWorks, Inc.). First of all, we identified, for each of the six blocks, the individual indifference points (IPs; the amount for the smaller, sooner reward that renders the smaller, sooner reward equally valuable as the larger, later reward) using logistic regression. For

further analysis, all IPs were converted into proportions of the late reward of 20 Euro.

We fitted two different models to the estimated IPs of blocks 1 to 4. First, we fitted the standard hyperbolic model (Chung & Herrnstein, 1967; Ainslie, 1975; Mazur, 1984):

$$SV_T = A / (1 + kT) \quad (2.1)$$

where *SV* is the subjective value of the reward, *A* is the monetary amount of the reward and *T* is the delay in months. The amount was set to *A* = 1 as the values were expressed as proportions of the later reward. Larger *k*-values indicate a greater impact of delay on value and therefore steeper discounting.

In addition, Laibson's (1997) quasi-hyperbolic β-δ model was fitted to the indifference point to obtain measures of present-bias and patience:

$$SV_{T=0} = 1$$
$$SV_{T>0} = \beta \times \delta^T \quad (2.2)$$

SV_t is the subjective value of a reward at time *T*. This equation models the often found initial rapid decline in subjective value with small delays (present-bias) separately, represented by the parameter β (with $0 \leq \beta \leq 1$). The inverse of β can be interpreted as the extra weight added to immediacy, thus smaller β-values can be construed as stronger present-bias. In our analysis, T=0 corresponds to 'tomorrow', as this was the soonest option available in our task. We opted to define tomorrow, and not today, as the soonest option to control for potential transaction costs, and assumed that tomorrow would be part of the extended present (Haushofer *et al.*, 2013).The discount function's discount rate is log(1/δ).

Thus, the parameter δ (with $0 \leq \delta \leq 1$) can be interpreted as a measure of patience with higher δ-values indicating higher patience.

The hyperbolic and quasi-hyperbolic models were fit to the first four indifference points, which were implemented as proportions of the delayed reward (e.g. an indifference point of 10 Euro would yield a proportion of .5 relative to an immediately available 20 Euro reward) for each participant individually, using a least-squares algorithm implemented in MATLAB R2013a (The MathWorks, Inc.). The fitting parameters *k*, β and δ were allowed to vary freely. *Figure 2.2* shows the average indifference points of the whole sample as well as their hyperbolic and quasi-hyperbolic fits. Goodness of fit analyses using the Akaike Information Criterion (AIC), which takes into account the number of parameters, showed that the data was better described by Laibson's quasi-hyperbolic model (M = -27.8) than the standard hyperbolic model (M = -11.5).

We furthermore conducted additional analyses with several model-free parameters, which yielded similar results (see supporting information, Appendix A).

Associative and autobiographical memory performance. The four retrieval blocks of the FNPA task contained 20 correctly and 20 falsely paired face-name pairs. Correct face-name pairs that were recognized as such were counted as hits (FNPA-Hits), whereas face-name pairs that were actually false but judged as correct were counted as false alarms (FNPA-FA). Overall associative memory performance (FNPA-PF) was calculated by subtracting false alarms from hits (FNPA-PF = FNPA-Hits – FNPA-FA).

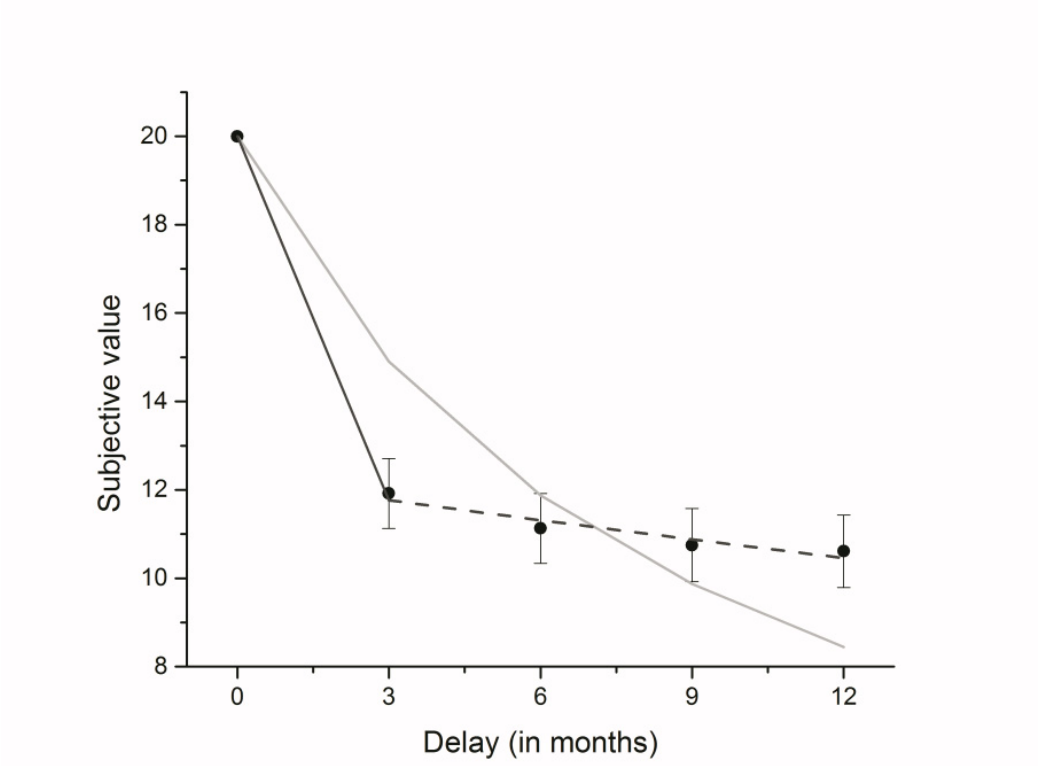

Figure 2.2 Illustrative hyperbolic and quasi-hyperbolic model fit to the average choice data of the whole sample. *The indifference points at 3, 6, 9 and 12 months and one day, averaged across participants, were used to fit the hyperbolic model (light gray line) and the quasi-hyperbolic model (dark gray and dashed line). Errorbars show the standard error of the mean (s.e.m.). The steepness of the hyperbolic function is reflected by parameter k. The dark grey line of the quasi-hyperbolic model represents present-bias and is reflected by parameter β, whereas further decline in value (dashed line) is reflected by 'patience' parameter δ.*

Module C of the IGD was analyzed according to the standard procedure suggested in the test manual (Baller *et al.*, 2006). The overall score of sub module C1 (IGD-C1) consists of the total number of events recalled proportional to the maximum of 20 recalled events, added to the sum of the quality rating scores from all four episodes proportional to the maximum rating score of 36. The score of sub module C2 (IGD-C2) is the proportion of all items answered with *yes*

relative to the total number of answered items added to the proportion of quality rating scores from all answered areas.

Statistical analyses. Statistical analyses reported below were performed using the software package IBM SPSS Statistics 20. The main analysis consisted of OLS regressions using the discounting parameters as dependent variables and the memory scores and mediator/moderator variables age, IQ and income as predictors. We used three models. In the first model,

$$\textit{Discounting parameter} = b_0 + b_1*\textit{FNPA-PF} + b_2*\textit{IGD-C1} + b_3*\textit{IGD-C2} \qquad (2.4)$$

we check for the effects of the memory scores on the discounting parameters. In the second model the mediator/moderator variables and gender were added:

$$\textit{Discounting parameter} = b_0 + b_1*\textit{FNPA-PF} + b_2*\textit{IGD-C1} + b_3*\textit{IGD-C2} + b_4*\textit{Gender} + b_5*\textit{age} + b_6*\textit{IQ} + b_7*\textit{income} \qquad (2.5)$$

In the third model, three interaction terms of gender and memory performance were added:

$$\textit{Discounting parameter} = b_0 + b_1*\textit{FNPA-PF} + b_2*\textit{IGD-C1} + b_3*\textit{IGD-C2} + b_4*\textit{Gender} + b_5*\textit{age} + b_6*\textit{IQ} + b_7*\textit{income} + b_8*(\textit{FNPA-PF}*\textit{Gender}) + b_9*(\textit{IGD-C1}*\textit{Gender}) + b_{10}*(\textit{IGD-C2}*\textit{Gender}) \qquad (2.6)$$

Missing data (see results) was replaced using the Expectation-Maximization procedure (Dempster *et al.*, 1977) to ensure inclusion of all participants in the regression analyses.

In addition, several correlation analyses were performed (see supplemental material, appendix A). Where necessary, the significance level α was adjusted using the Holm-Bonferroni method to control the familywise error rate.

2.4 Results

We excluded participants from further analysis when more than half of the *catch trials* in the intertemporal choice task were answered incorrectly. We assumed that this indicated insufficient attention or understanding of the task. Four participants met this criterion and were therefore excluded from further analyses, rendering the overall sample size at $n = 58$. However, the main results reported in the following sections did not change when these participants were included. Furthermore, *income* data was missing in 6 participants.

Since we also found gender effects (see below), results are presented for the complete sample as well as the male ($n = 28$) and female ($n = 30$) subsamples. *Table 2.1* summarizes the descriptive variables *age*, *IQ* and *income* for the complete, male and female group. The gender subgroups only differed in their income, with the women subgroup earning significantly less than men, $t(56) = 3.942, p < .001$. In addition, *table 2.2* shows the averages and standard deviations for the memory task scores and the discount parameter values, for the complete group as well as the gender subgroups. As predicted, women scored higher than men on the episodic memory tasks, but there was no significant gender difference in discount behavior. Correlations of the different episodic memory scores for men and women are summarized in *table S2 (Appendix A)*.

Since we expected our participant sample to show variable memory scores that would reflect the level of cognitive decline related to healthy aging, we checked for correlations between the memory scores *FNPA-PF*, *IGD-C1* and *IGD-C2* and *age*, as well as *IQ* and *income*. Results are shown in *table 2.3*. Only the

FNPA-PF scores showed a close-to-significant negative correlation with *age*, $r = -.308$, $p = .018 > \alpha = .017$, $r^2 = .09$, suggesting that older participants have lower scores on the FNPA task.

Table 2.2 *Intertemporal choice and episodic memory scores of the complete sample and the gender subgroups.*

		FNPA-PF	IGD-C1	IGD-C2	k	β	δ
Complete sample	Mean (SE)	0.45 (0.03)	1.68 (0.03)	1.72 (0.03)	0.36 (0.08)	0.65 (0.04)	0.98 (0.00)
Males	Mean (SE)	0.33 (0.04)	1.62 (0.05)	1.66 (0.04)	0.29 (0.09)	0.67 (0.05)	0.98 (0.01)
Females	Mean (SE)	0.57 (0.04)	1.74 (0.03)	1.77 (0.03)	0.43 (0.12)	0.62 (0.05)	0.97 (0.01)
Statistics (m/f)	t or U	-4.322	-2.126	-2.130	-.784[b]	.716	416[a]
	p	.000**	.038*	.038*	.437	.477	.950

Means (s.e.m.) of the episodic memory scores and the discount parameters for the complete sample as well as the gender subgroups. The t or U scores, as well as the p-values are reported for the comparison of the task scores between the male and female subgroups.

[a] *Mann-Whitney U test was used instead of t-test due to violation of normality assumption.*

[b] *Ln(k) was used to test difference between male and female subgroups.*

* $p < 0.05$ ** $p < 0.01$

Table 2.3 *Correlations of memory scores with age, IQ and income within the complete sample.*

	Age	IQ	Income
Associative memory			
FNPA-PF	-.308 (.018)	.248 (.061)	-.243 (.082) [a]
Autobiographical memory			
IGD-C1	-.062 (.644)	-.061 (.649)	-.019 (.893) [a]
IGD-C2	-.201 (.130) [a]	.190 (.154) [a]	-.141 (.318) [a]

Correlation coefficients and p-values (in brackets) of the correlations of episodic memory scores and mediator/moderator variables, using the complete sample.

All p-values are two-tailed.

[a] *Spearman's Rho was used due to violation of normality assumption.*

** p < 0.017*

Regression analyses. Separate regression analyses with the discounting parameters *ln(k),* β and δ as dependent variables and memory scores (*FNPA-PF*, *IGD-C1* and *IGD-C2*) as predictors show no significant contribution of any memory score on the model-based discounting values on group level, *ln(k): F(3,54) = .153, p = .928,* R^2 *= .008;* β*: F(3,54) = .067, p = .977,* R^2 *= .004;* δ*: F(3,54) = .272, p = .846,* R^2 *= .015* (*table 2.4*). Thus, our results did not support the hypothesis that a better functioning episodic memory system is associated with reduced discounting.

The second regression model showed no significant contribution of *gender*, *age* or *IQ* on discounting parameters *ln(k),* β and δ, whereas the variable *income* significantly predicted *ln(k)* (*beta = -.427*, *p = .005*) and β (*beta = .326*, *p = .009*) (*table 2.4*). A higher income was related to lower values of *k* and thus less discounting. This was reflected by a similar significant effect of *income* on the *number of impulsive choices (NImp)* (see *table S1, Appendix A*). Similarly, a higher income was associated with higher values of β, indicating a lower present-bias.

Table 2.4 *Relationship of memory scores, moderator variables and gender x memory interactions with discounting parameters.*

	Ln(k)			β			δ		
Model	*(1)*	*(2)*	*(3)*	*(1)*	*(2)*	*(3)*	*(1)*	*(2)*	*(3)*
FNPA-PF	-.087 (.545)	-.140 (.348)	.098 (.828)	.023 (.872)	.025 (.883)	-.253 (.575)	.106 (.459)	.211 (.241)	.349 (.499)
IGD-C1	.045 (.755)	.042 (.758)	-.218 (.601)	-.047 (.741)	-.039 (.786)	-.074 (.860)	-.033 (.818)	-.028 (.855)	.934 (.055)
IGD-C2	.033 (.822)	.032 (.819)	-1.032 (.015)*	.045 (.762)	.029 (.842)	1.389 (.002)**	-.087 (.555)	-.056 (.719)	-.249 (.600)
Gender		-.026 (.882)	-.054 (.741)		.038 (.833)	.088 (.596)		-.126 (.508)	-.170 (.370)
Age		.119 (.387)	.122 (.354)		-.151 (.289)	-.146 (.271)		.018 (.902)	-.015 (.922)
Income		-.427 (.005)*	-.382 (.009)**		.326 (.036)*	.298 (.041)*		.082 (.611)	.008 (.962)
IQ		.000 (.999)	-.109 (.913)		.059 (.691)	.105 (.455)		-.106 (.498)	-.182 (.255)
Gender*FNPA-PF			-.248 (.576)			.267 (.550)			-.082 (.872)
Gender*IGD-C1			.358 (.383)			-.069 (.866)			-.977 (.038)*
Gender*IGD-C2			1.129 (.007)**			-3.538 (.001)**			.138 (.764)
F Statistic (df)	*.153 (3,54)*	*1.741 (7,50)*	*2.374 (10,47)*	*.067 (3,54)*	*1.158 (7,50)*	*2.285 (10,47)*	*.272 (3,54)*	*.292 (7,50)*	*.673 (.10,47)*
R^2	*.008*	*.196*	*.579*	*.004*	*.139*	*.327*	*.015*	*.039*	*.125*
Adjusted R^2	*-.047*	*.083*	*.194*	*-.052*	*.019*	*.184*	*-.040*	*-.095*	*-.061*
p-value	*.928*	*.121*	*.023**	*.977*	*.344*	*.028**	*.846*	*.954*	*.743*

Each column represents one OLS regression. Dependent variables are shown in the column titles. Each row represents one predictor variable or statistics of the regression model. Cells show regression coefficients (beta) and p-values in brackets or model statistics.

* $p < .05$

** $p < .01$

To further explore a potential effect of gender, interaction terms were calculated by multiplying centered memory scores with gender. The addition of the three interaction terms (*gender* x *FNPA-PF*, *gender* x *IGD-C1* and *gender* x *IGD-C2*) in the third regression model revealed several interaction effects (*table 2.4*).

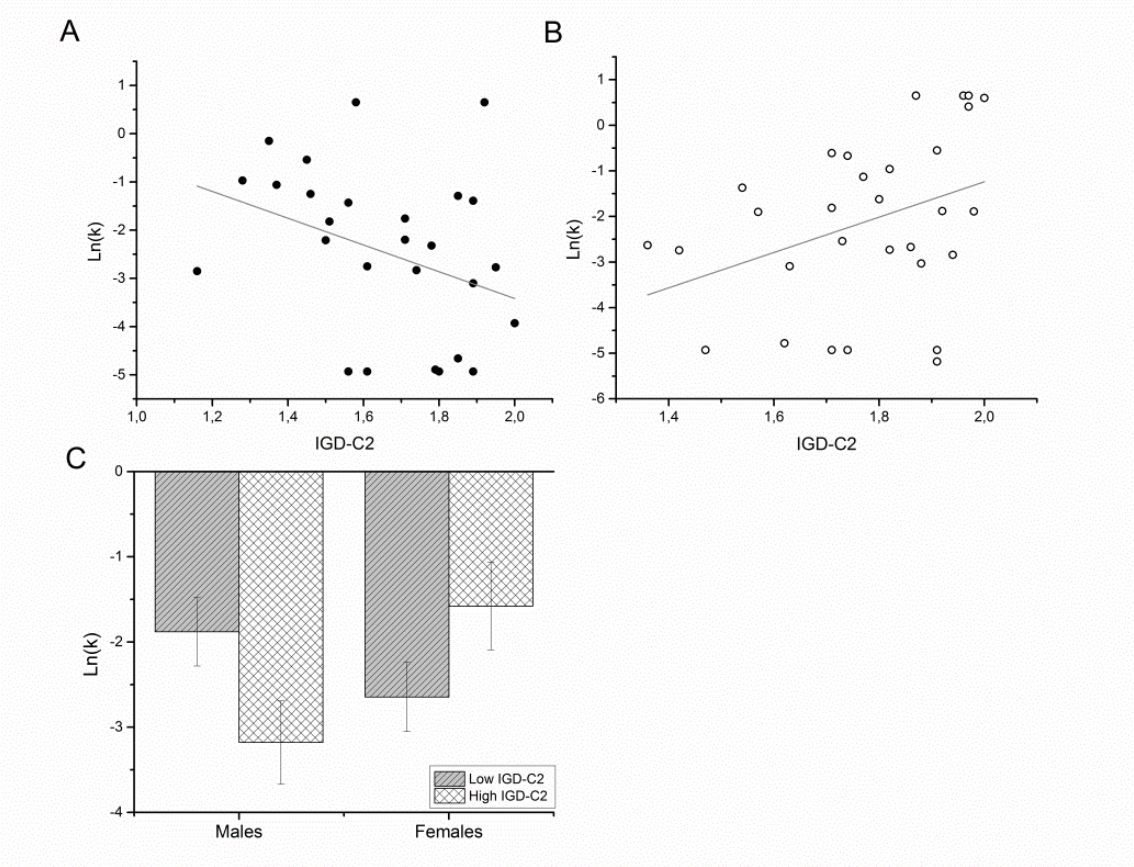

Figure 2.3 Interaction effects of gender and IGD-C2 scores on ln(k). *(A) Scatterplot with regression line of the IGD-C2 and ln(k) scores in the male subsample. (B) Scatterplot with regression line of the IGD-C2 and ln(k) scores in the female subsample. (C) To further illustrate the gender-dependent differences in the relationship between memory performance and discounting, we performed a median split to categorize participants according to their IGD-C2 performance (high- vs. low performers). Individual bars show mean ln(k) values for subgroups with high and low IGD-C2 scores. Error bars show the standard error of the mean (s.e.m.).*

The interaction between *gender* and *IGD-C2* scores significantly predicted discount parameters *ln(k)* (*beta = 1.129*, *p = .007*) as well as β (*beta = -3.538*, *p =.001*) (*table 2.4*), indicating that in males, a higher scores for autobiographical fact and date recall went along with less discounting, whereas in females higher

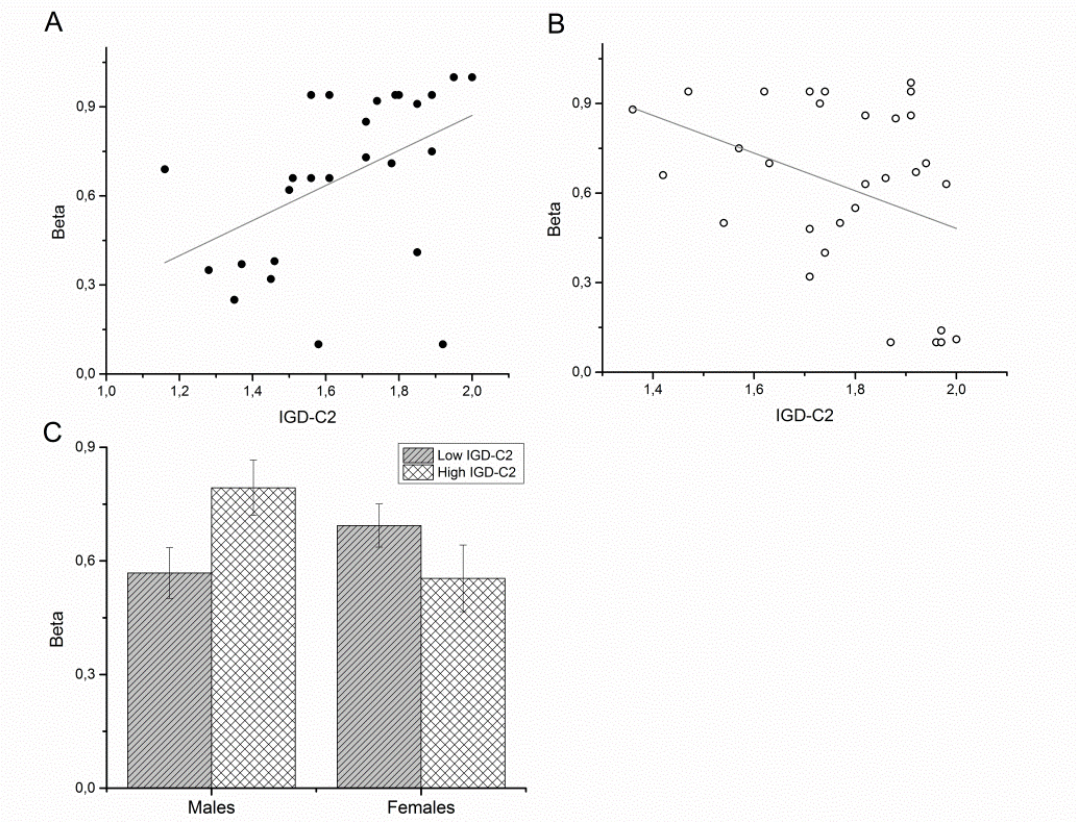

Figure 2.4 Interaction effects of gender and IGD-C2 scores on parameter β. *(A) Scatterplot with regression line of the IGD-C2 and β scores in the male subsample. (B) Scatterplot with regression line of the IGD-C2 and β scores in the female subsample. (C) To further illustrate the gender-dependent differences in the relationship between memory performance and discounting, we performed a median split to categorize participants according to their IGD-C2 performance (high- vs. low performers). Individual bars show mean β values for subgroups with high and low IGD-C2 scores. Error bars show the standard error of the mean (s.e.m.).*

recall scores went along with more discounting (see *figure 2.3* and *figure 2.4*). The increase in R^2 was significant compared to the second regression model for both *ln(k)*, $F(3,47) = 3.292$, $p = .029$, and β, $F(3,47) = 4.371$, $p = .009$, as dependent variable. As gender is a binary variable, there was a high correlation between the

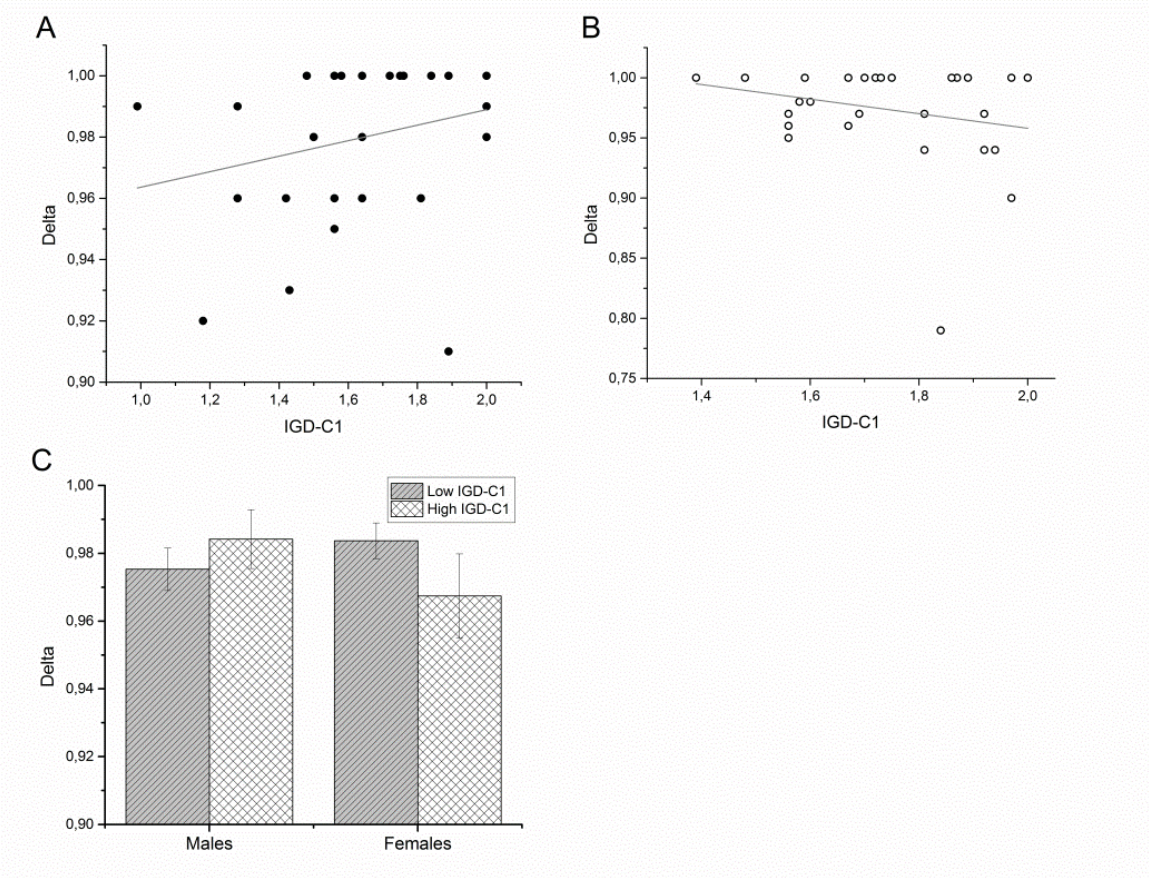

Figure 2.5 Interaction effects of gender and IGD-C1 scores on parameter δ. *(A) Scatterplot with regression line of the IGD-C1 and δ scores in the male subsample. (B) Scatterplot with regression line of the IGD-C1 and δ scores in the female subsample. (C) To further illustrate the gender-dependent differences in the relationship between memory performance and discounting, we performed a median split to categorize participants according to their IGD-C1 performance (high- vs. low performers). Individual bars show mean δ values for subgroups with high and low IGD-C1 scores. Error bars show the standard error of the mean (s.e.m.).*

interaction terms and the corresponding memory terms. Therefore, the significant effects of the memory measures in regression model 3 should be ignored.

Further, a similar significant interaction was found for *IGD-C1* scores and the discounting parameter *δ* (*beta = -.977*, *p = .038*) (*table 2.4*), indicating that better

recall of autobiographical events went along with more patience in males, whereas in females better autobiographical memory predicted more impatience (see *figure 2.5*). However, the model itself as well as the increase in R^2 was not significant, $F(3,47) = 1.540, p = .217.$

2.5 Discussion

The aim of this experiment was to investigate the relationship between episodic memory and delay discounting in older adults. We hypothesized that episodic memory performance correlated with intertemporal choice behavior. Overall, we found no evidence for a relationship between episodic memory scores and time discounting. However, when considering gender differences, we found several interactions of gender and memory scores on discounting. First of all, we found that higher memory scores for autobiographical facts and dates, but not associative memory performance or memory for personal events, were related to a decreased level of discounting in men, as indicated by lower values of the hyperbolic discounting parameter *k* and higher values of present-bias parameter β. By contrast, in women, we found the opposite pattern; higher autobiographical memory scores for facts and dates were related to higher levels of discounting, as indicated by higher values of *k* and lower values of β. Furthermore, a similar interaction was found for gender and recall of autobiographical events on the discounting parameter δ, representing patience. Whereas men with better autobiographical event recall showed more patience, women with better autobiographical event recall showed less patience. These findings were not due to a general difference in discounting behavior between men and women.

Our hypothesis that episodic memory functioning and time discounting may be related was based on the finding that the core network involved in episodic

memory functioning is also responsible for episodic future thinking, which has been related to lower rates of discounting (Peters & Buchel, 2010a; Lebreton *et al.*, 2013; Lin & Epstein, 2014), e.g. through episodic tagging techniques. Here, we focused on memory retrieval of past episodes and events instead of eliciting future thinking. The question remains whether participants still use future simulation during intertemporal choice when not explicitly elicited.

If future rewards are indeed imagined when not being explicitly triggered during temporal discounting, one explanation of our findings could be that imagining future outcomes might depend on recall of past personal facts, rather than events, to form a new 'image' of the future. Although we do not find a general effect of autobiographical memory on discounting, we do find interaction effects of gender with autobiographical memory recall on discounting, with recall of events linked to patience, and recall of facts and dates linked to present-bias as well as the overall level of discounting.

Present-bias can be characterized using Laibson's quasi-hyperbolic model (Laibson, 1997) as the drop in subjective value between obtaining the monetary reward now and obtaining it in the nearest possible future. In contrast, the level of patience (reflected by parameter δ) gives an indication of how further delays affect the subjective value of the reward. Present-bias can be seen as a measure of intertemporal inconsistency, as a stronger present-bias indicates a larger deviation from constant time discounting (e.g. a linear or exponential decrease in value of a reward with time), due to a disproportionally strong focus on the present. That personal semantics might have a particular effect on present-bias makes sense with regard to the semantic content of any imagined future event, which would be similar regardless of the specific delay associated with it. As the parameter δ indicates further decline of value with increasing delays, this parameter is sensitive to the temporal context, which is an important aspect of a

particular event and thus of episodic memory. It therefore makes sense that this parameter is related to recall of autobiographical events.

Previous literature has shown not only a dissociation between memory for autobiographical events and autobiographical facts and dates on behavioral level (Levine *et al.*, 2002; Piolino *et al.*, 2002), but also in underlying brain mechanisms (Maguire *et al.*, 2000; Maguire & Frith, 2003). Just as retrieval of general facts and events, the retrieval of autobiographical facts is less dependent on the connectivity between the parahippocampal gyrus and hippocampus than the recall of autobiographical events (Maguire *et al.*, 2000). Hence, recall mechanisms for autobiographical facts might have more in common with recall of general facts and events, which is less hippocampus-dependent, and less with recall of specific autobiographical events. For example, the recall of the means of transportation during one's first job does not require recall of a specific time and space. Indeed, the memory of autobiographical facts and dates is also termed 'personal semantics' (Renoult *et al.*, 2012). The specificity of the relationship between recall of autobiographical facts and dates and present-bias might therefore depend more on general memory retrieval mechanisms, and less on mechanisms specific for retrieval of highly context-dependent memories, such as autobiographical events.

That other (i.e. semantic or unconscious) long-term memory mechanisms could play a role is also supported by the absence of a relationship between associative memory performance and discounting. It is thought that with healthy aging, primarily the formation of new memories is affected, whereas older episodic memories are relatively preserved (Rybash & Monaghan, 1999; Schroots *et al.*, 2004). The autobiographical memory task used here probably depends less on hippocampal functioning and more on neocortical integrity, as memory retrieval of items stored long ago in general seems to depend more on the latter

(Squire, 1992; see Piefke & Fink, 2005), whereas the associative memory task used here assessed both the formation and recall of newly formed face-name associations, which might rely most on hippocampal areas affected early with aging. In line with this view, we found a close-to-significant negative correlation between associative memory (FNPA) scores and age, but not between autobiographical memory scores and age. Why would older-aged men and women with better recall of autobiographical facts and dates/events show such opposing patterns regarding their present-bias/patience? It is possible that men differ from women regarding their "cognitive style" by which they make economic decisions. In a fMRI study by Piefke *et al.* (2005), three brain areas were found to exhibit differential responses in men and women during autobiographical memory retrieval; whereas the parahippocampal region was more active in men, the right dorsolateral prefrontal cortex (dlPFC) as well as the right insular cortex showed increased activity in women compared to men. More recently, Young *et al.* (2013) replicated the finding that women showed increased activity in the right dlPFC during autobiographical memory recall. Since there were no gender differences in behavioral performance, these findings likely support the "cognitive style hypothesis", which states that men and women differ in the way they encode, rehearse and process emotional experiences, and exhibit differential response strategies during laboratory memory tasks (Seidlitz & Diener, 1998; see Piefke & Fink, 2005; Young *et al.*, 2013).

The prefrontal cortex (PFC) is one of the areas found to be important for episodic memory retrieval, and PFC functioning is related to recalling the temporal context of memories (Cabeza *et al.*, 1997; Kopelman *et al.*, 1997; Henson *et al.*, 1999; Cabeza *et al.*, 2000; Suzuki *et al.*, 2002). An fMRI study by Suzuki *et al.* (2002) indicated that the right dlPFC is predominantly engaged in recall of the temporal order of separate events, whereas the left dlPFC showed

more engagement in recall of the temporal order within a specific event. It was therefore argued that the increased activity in the right dlPFC in women compared to men might reflect that women relied more strongly on the temporal context of autobiographical memories when recalling these events (Piefke & Fink, 2005). If this is indeed the case, it is possible that women are differentially sensitive to temporal information when it comes to imagining future rewards. This might explain why women with better recall for *past* autobiographical facts/events showed more sensitivity for the delays to *future* outcomes in our task, and as a result showed increased discounting.

The parahippocampal region has been shown to be involved in spatial learning, navigation and spatial context memory (Maguire *et al.*, 1996; Tsukiura *et al.*, 2002; Malkova & Mishkin, 2003). In men, the increased activity found in this area during episodic memory tasks compared to women (Piefke *et al.*, 2005) could therefore point towards an increased role of spatial context, not only during recall of autobiographical events, but also when imagining future rewards. A general larger emphasis on spatial context processing in men, in combination with increased dependence of autobiographical memory recall performance on spatial context processing, could potentially explain why men, but not women, with better memory scores showed less discounting. It thus seems that men and women differ in their cognitive styles and strategies when performing episodic memory tasks (Piefke & Fink, 2005; St Jacques *et al.*, 2011; Young *et al.*, 2013), and arguably this difference might generalize to performance on other tasks requiring putatively similar cognitive strategies, such as future episodic simulation during delay discounting.

It is possible that this gender difference only occurs in older-aged individuals. One of the aims of this study was to investigate whether individual differences in episodic memory functioning and age-related decline could potentially explain the

large variability in the effects of aging on time discounting. Although gender effects are not consistently found in time discounting, memory decline could give rise to differential choice preferences in males and females, which can bias the overall picture towards more or less discounting in older adults compared to younger groups. However, more research is necessary to shed light on this issue.

Recent studies (Palombo *et al.*, 2014; Kwan *et al.*, 2015), in which patients with medial temporal lobe (MTL) lesions that showed impaired episodic future thinking completed an intertemporal choice task, indicated that processes involving the MTL are not essential for discounting, as these amnesic patients had similar discounting rates as control participants (Kwan *et al.*, 2013; Palombo *et al.*, 2014; Kwan *et al.*, 2015). However, when amnesic patients were cued to imagine future events during the intertemporal choice task, they did not show decreased levels of discounting, whereas a healthy control group did show the decreased levels of discounting shown in previous studies (Palombo *et al.*, 2014). Therefore, processes involving the MTL, such as episodic future thinking, may only play a role as moderators on intertemporal decision making (Palombo *et al.*, 2014; Kwan *et al.*, 2015) and might therefore not necessarily be invoked by default.

Interestingly, when amnesic patients were asked to imagine personal future situations (Kwan *et al.*, 2015), instead of more general future events (Palombo *et al.*, 2014), they also show the attenuating effect of episodic future thinking on discounting, suggesting that different 'types' of future thinking depend more or less on MTL functioning. A study with patients with semantic dementia shows that episodic future thinking is critically dependent on semantic memory, as these patients showed relatively intact episodic memory for recent past events, but impaired episodic future thinking (Irish *et al.*, 2012). Kwan *et al.* (2015) suggest this role of semantic memory could have been the cause of the differential effects of their study compared to the results found by Palombo *et al.* (2014); the

personal cues might have triggered semantic future thinking instead of episodic future thinking (Kwan *et al.*, 2015), yielding similar reductions in discounting. This would be in line with our finding that memory for autobiographical facts and dates (i.e. personal semantics) is related to discounting.

Several additional measures were found to differ between the gender groups. In line with previous findings, we found that women scored higher on episodic memory tasks than men (Herlitz *et al.*, 1997; Kramer *et al.*, 1997; Herlitz & Rehnman, 2008; Lundervold *et al.*, 2014). Whether this is due to differences in verbal production/visuospatial processing (Herlitz & Rehnman, 2008) or possibly a difference in the richness of detail encoding between men and women (Seidlitz & Diener, 1998) remains unclear, although our results showed that this gender effect is not limited to autobiographical events, as also associative memory performance showed a gender effect. In contrast, our results revealed no gender-difference in discounting, present-bias or patience in older subjects. Second, men and women differed in their income. This is potentially important as income is found to be related to time discounting (Harrison *et al.*, 2002; Eisenhauer & Ventura, 2006; Anderson & Gugerty, 2009; Reimers *et al.*, 2009). However, our results did not change when including income as additional variable in our partial correlation analyses, suggesting that income affected discounting independent of episodic memory.

In summary, we found no clear evidence for a general relationship between episodic memory and delay discounting in older-aged adults. However, we found a gender difference in this relationship: whereas men with better memory for autobiographical facts and dates/events showed less present-bias/more patience, women with better autobiographical memory were more present-biased/impatient. The finding that older-aged men and women with better autobiographical recall discount less, or more respectively, could be explained by

assuming gender-differences in “cognitive styles” when making intertemporal decisions. As these interaction effects were not predicted, further behavioral studies should confirm these findings. Whether this interaction of gender and temporal discounting in older adults depends on neocortical integrity, in particular of the right dlPFC, hippocampus, or entirely different networks, requires verification using additional methods, such as fMRI.

3. STN-DBS in PD patients and intertemporal choice

"Don't judge my choices without understanding my reasons"

- unknown

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3.1 Abstract

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is a widely used treatment for the motor symptoms of Parkinson's disease (PD). DBS or pharmacological treatment is believed to modulate the tendency to, or reverse, impulse control disorders. Several brain areas involved in impulsivity and reward valuation, such as the prefrontal cortex and striatum, are linked to the STN, and activity in these areas might be affected by STN-DBS. To investigate the effect of STN-DBS on one type of impulsive decision making – delay discounting (i.e. the devaluation of reward with increasing delay to its receipt) - we tested 40 human PD patients receiving STN-DBS treatment and medication for at least 3 months. Patients were pseudo-randomly assigned to one of four groups to test the effects of DBS on/off states as well as medication on/off states on delay discounting. The delay discounting task consisted of a series of choices between a smaller, sooner or a larger, later monetary reward. Despite considerable DBS-effects on motor performance, patients receiving STN-DBS did not choose more or less impulsively compared to the off-DBS group, also when controlling for risk attitude. Although null results have to be interpreted with caution, our findings are of significance to other researchers studying the effects of PD treatment on impulsive decision-making, and they are of clinical relevance for determining the therapeutic benefits of using STN-DBS.

3.2 Significance Statement

To improve the quality of life of patients suffering from Parkinson's disease, it is important to uncover the cognitive side effects of deep brain stimulation of subthalamic nucleus. In this study, we show no effect of deep brain stimulation on altered impulsive decision making, measured with a financial delay-discounting paradigm. Our study adds an important piece of information on the cognitive side

effects of deep brain stimulation, although further studies are needed to verify our results.

3.3 Introduction

Parkinson's disease (PD) is characterized by a cell loss in substantia nigra and ventral tegmental area, leading to a reduced level of the neurotransmitter dopamine and abnormal functionality of the basal ganglia. The progressive loss of dopamine results in impaired motor functioning, such as bradykinesia, muscle rigor and/or resting tremor, as well as in characteristic non-motor symptoms, including depression and memory deficits. Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is a widely used treatment for the motor symptoms of PD. STN-DBS is usually applied when conventional medication starts to become increasingly ineffective (Deuschl *et al.*, 2006). Although STN-DBS has major benefits in reducing motor symptoms (Deuschl *et al.*, 2006; Wichmann & DeLong, 2006), side-effects of STN-DBS on cognition are often less clear (e.g. Demetriades *et al.*, 2011).

Several studies indicate that DBS affects neural activity in surrounding areas, thereby altering the activity of a whole network of brain structures (Chang *et al.*, 2007; Li *et al.*, 2007; McCracken & Grace, 2007; Montgomery & Gale, 2007; Li *et al.*, 2012). Since the STN is connected to a number of basal ganglia nuclei as well as cortical areas, STN-DBS can have widespread effects that are not just limited to motor behavior. Not only motor areas are found to be projecting to the STN , but also brain areas involved in valuation of choice options, such as the medial/orbital cortex in rats (Maurice *et al.*, 1998) and monkeys (Haynes & Haber, 2013) via the so-called hyperdirect pathway (Nambu *et al.*, 2002), which links the cortex with the basal ganglia via the STN. In addition, the STN can be subdivided into several functional zones that can, according to their structural connectivity, be identified as motor, associative and limbic regions (Lambert *et al.*, 2012), which are part of

cortico-basal ganglia-thalamo-cortical loops involved in emotion, movement and cognition (Parent & Hazrati, 1995a; b).

Patients have often undergone a long period of dopaminergic medical treatment before DBS is considered as therapy of choice. Dopaminergic treatment usually consists of the intake of levodopa (L-dopa), a dopamine precursor, and/or dopamine agonists. PD patients can develop an increased tendency for impulse control disorders (ICDs), which include pathological gambling, compulsive shopping, hypersexuality and hyperphagia (Weintraub, 2008). These ICDs are associated with dopaminergic treatment, in particular with the use of dopamine agonists (Voon & Fox, 2007; Voon *et al.*, 2011a; Voon *et al.*, 2011b; Raja & Bentivoglio, 2012) as well as L-dopa treatment (Zurowski & O'Brien, 2015).

How STN-DBS affects impulsive behavior is unclear, with reports of both increases in severity or even new development of ICDs (Halbig *et al.*, 2009; Lim *et al.*, 2009; Broen *et al.*, 2011; Moum *et al.*, 2012) as well as attenuation or disappearance of ICD symptoms after the start of STN-DBS treatment (Witjas *et al.*, 2005; Ardouin *et al.*, 2006; Bandini *et al.*, 2007; Lim *et al.*, 2009; Broen *et al.*, 2011). As the dopaminergic medication intake can usually be decreased after onset of STN-DBS treatment, the reduction in ICD severity might be due to a decrease in the medication dosage, but other factors, such as electrode placement, stimulation parameters or patient history may underlie changes in ICD severity, too (e.g. Zurowski & O'Brien, 2015). Several brain areas connected with the STN are involved in impulsive behavior, including the orbitofrontal cortex and the nucleus accumbens (Cardinal *et al.*, 2001; Kheramin *et al.*, 2002; Kalenscher & Pennartz, 2008). Stimulation of the STN can therefore affect impulsive choice in two ways: either by directly altering STN functioning, and/or via indirect moderation of activity in connected areas known to be involved in impulsive decision making.

Since (case study) reports concerning the effects of therapeutic STN-DBS on ICDs are ambiguous, it is important to uncover exactly how STN-DBS affects impulsive behavior, and in particular impulsive choice. The study presented here focuses on delay discounting (i.e. the devaluation of a reward when its receipt is delayed to a future point in time), which can be seen as a measure of impulsive economic decision-making, and is often used to assess impulsive decision making (e.g. Bickel et al., 2012). Although delay discounting captures only one of the many facets of ICDs, reduced delay sensitivity lies at the heart of most concepts of impulsive choice. To dissociate the putative effects of STN-DBS from the effects of dopaminergic medication on delay discounting, we employed a 2 x 2 design for DBS (on/off) and medication state (L-dopa on/off).

3.4 Methods

3.4.1 Participants

Fifty-four patients with bilaterally implanted stimulation electrodes in the STN were recruited for a screening session at the University clinic (Center for Movement Disorders and Neuromodulation, Department of Neurology & Institute of Clinical Neuroscience and Medical Psychology) in Düsseldorf, with the aim of identifying patients with no current severe depression (Beck Depression Inventory, BDI, < 20) and no indication of dementia (Mattis Dementia Rating Scale, MDRS, > 130) and inconspicuous performance in a range of other cognitive and mnemonic tests (see below) for inclusion in the experiment. Forty patients (16 female) aged between 42 and 78 (M = 62.7, SD = 7.4) met the inclusion criteria. Further inclusion criteria were bilateral DBS of the STN for a period of at least three months and no pre-implant history of major depression.

DBS treatment consisted of bilateral 130Hz stimulation, except for two patients who received 174Hz stimulation in the right hemisphere and 130Hz

stimulation in the left hemisphere, two patients who received bilateral 150Hz stimulation and one patient who received unilateral (right) 130Hz stimulation. Stimulation intensity was either fixed on voltage (N = 26) or amperage (N = 14), with voltages ranging between 1.2 and 4.0 Volt and amperage ranging between 1.1 mA and 3.4 mA. Pulse width was set at 60µs, with the exception of three patients receiving 62µs pulses and one patient receiving 65µs pulses. One patient received 60µs in the left and 90µs in the right hemisphere. The average time since DBS implantation was 30.0 months (SD = 23.7), with a minimum of 3 months and a maximum of 85 months. All but one patient received dopamine replacement therapy, with an L-dopa equivalent dose (LED) ranging from 120 to 1975 (*M* = 675, *SD* = 390). All participants were recruited within a time period of 16 months, during their periodical inpatient visit that lasted at least two nights. The year of diagnosis ranged from 1989 until 2012. All participants were instructed in detail about the experimental procedure as well as the payment procedure before they provided written informed consent. The study was approved by the local ethics committee of the Medical Faculty of the Heinrich-Heine University in Düsseldorf, Germany.

3.4.2 Materials

During screening, patients performed a range of tests designed to measure mood as well as cognitive and mnemonic traits (Mattis Dementia rating scale (MDRS), Beck Depression Inventory (BDI-II), Quick Delay Questionnaire (QDQ), Baratt Impulsiveness Scale (BIS), South Oaks Gambling Screen (SOGS), Ardouin Behavior Scale (ABS), see below), along with a delay discounting task (intertemporal choice task, ICT), risk attitude measurements (Holt-Laury task) and motor skills (Unified Parkinson's Disease Rating Scale, UPDRS) during testing sessions. We used the following tests:

Mattis Dementia Rating Scale (MDRS). The MDRS was used to test for cognitive deficits (Mattis, 1988). This test is commonly used in clinical settings for older patients and can detect dementia disorders such as Alzheimer disease. It is subdivided into five categories: attention, verbal and motor initiation and preservation, construction, conceptualization and memory (Lucas et al., 1998). Patients with scores <130 (out of 144) points were excluded from further testing (cf. Schmidt et al. 1994).

Beck Depression Inventory II (BDI-II). The German version of the BDI-II (Beck et al., 1996) was used to assess depressive symptoms reported for the past two weeks. It consists of 21 items, and each item is ranked from 0 to 3. Exclusion criterion was a count of 20 points or higher, which is indicative of severe depression.

Quick Delay Questionnaire (QDQ). The QDQ was administered to assess subjective delay aversion and delay discounting (Clare et al., 2010). The subjects have to rate five items on delay aversion and five items on delay discounting on a 5-point-Likert scale. This questionnaire was added to obtain a baseline self-reported measure of delay discounting / delay aversion.

Barratt Impulsiveness Scale (BIS). The BIS is often used as a measure of impulsivity, and its short German version (BIS-15; Spinella, 2007) has been used in the current study. Fifteen items assess either non-planning, motor or attention impulsivity (Spinella, 2007). Each item is rated on a 4-point-Likert scale. This questionnaire was added to obtain a baseline self-reported measure of impulsiveness.

South Oaks Gambling Screen (SOGS). The SOGS (Lesieur and Blume, 1987) consists of 20 items and is commonly used to screen for pathological gambling. In this test, a score of 5 or higher is considered as probable pathological gambling.

This questionnaire was added to identify and control for problem gambling, or gambling tendencies, respectively.

Ardouin Behavior Scale (ABS). This scale was designed to detect changes in mood and behavior in PD patients (Ardouin et al., 2009). This semi-structured interview entails 18 items and is rated in five points, from 0 to 4 from absent to severe. The ABS was used to identify potential addictive tendencies (regarding food or medication intake) that might hint at an impulse control disorder (ICD).

Unified Parkinson's Disease Rating Scale (MDS-UPDRS). Part III of the MDS-UPDRS was used to assess the severity of motor impairment, as well as the efficacy of the different treatment states. Patients had to perform specific movements and were rated from 0 to 4 on each of 18 items covering tremor, rigidity, posture, agility and general movement (Goetz *et al.*, 2008). The MDS-UPDRS-III was used to assess differences in motor symptoms between the respective on/off states during sessions.

Intertemporal Choice task (ICT). The ICT used in this study is a common and well-validated task to elicit time preferences and measure delay discounting (e.g. Kirby & Marakovic, 1996; Hardisty *et al.*, 2013). The task consisted of a series of binary choices between a smaller sooner, and a larger later monetary reward. Choice items were arranged in 6 blocks with 11 trials each, with an instruction screen after each block to provide the opportunity to take a short break. Within each block, the amount of the smaller, sooner option varied over trials while the larger, later option remained constant across trials within a given block. The delays used within each block were specified in the instruction screen before each block. In three blocks, the larger, later reward was fixed at €20, with the smaller, sooner option ranging from 0-20 in steps of €2, presented in randomized order. In the other three blocks the larger, later reward was fixed at €30, with the smaller, sooner option ranging from 0-30 in steps of €3, presented in randomized order.

The smaller, sooner option was always immediate. For each of the two large reward amounts, the delay was either 3, 6 or 9 months, and the order was randomized across blocks. The options were presented simultaneously on the left and right side of the screen and the side of presentation of each choice option was randomized (*figure 3.1a*). Participants pressed the 'E' key to choose the left option and the 'I' key to choose the right option. There was no time limit for each choice. The trials with either €0 'now' or €20/€30 'now' were considered *catch* trials, as the choices in these trials indicate whether the participant paid attention or chose rationally. The task was programmed and conducted using the Matlab (Mathworks, Inc.) toolbox *Cogent*. One out of the 66 trials was randomly chosen for payment after task performance. Participants received the amount they had selected with the corresponding delay. Both immediate and delayed payment was done by a cheque that was given either right after the session (immediate payment) or was sent by mail (delayed payment).

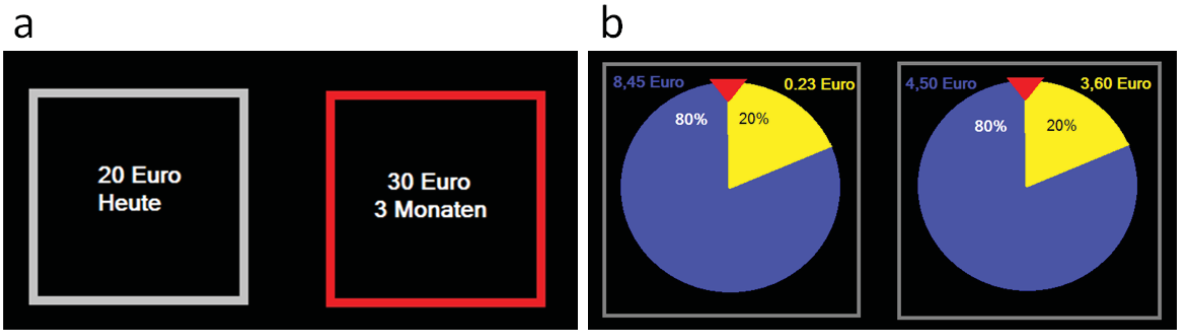

Figure 3.1 *Screenshot of tasks.* ***a:*** *Intertemporal choice task. Participants chose between a smaller reward now or a larger reward later by pressing the 'E' or 'I' key. When the choice was made, the chosen option was highlighted by a red frame.* ***b:*** *Holt-Laury task: participants chose one of two gambles, one considered risky and one considered safer. Lotteries were depicted as wheels of fortune.*

Holt-Laury task. The Holt-Laury task (Holt & Laury, 2002) is a short, thoroughly validated 10 trial task to measure risk attitude (see Filippin & Crosetto, 2014). Here, we elicited risk attitude as a control variable as time preference measures may potentially be confounded with risk preference. In each trial, participants chose between two lotteries. In one of the lotteries, the payout was either €8.45 or €0.23 with variable probability (riskier lottery), in the other lottery the payout was either €4.50 or €3.60 with the same variable probability (safer lottery). The probability of winning the large reward of each lottery varied from 10% to 100% in steps of 10% across trials in randomized order. Correspondingly, the probability of winning the small reward was 100%-p(large reward). The probabilities of large and small rewards were identical for both lotteries in a given trial (see *figure 3.1b*). After task performance, the computer randomly picked one trial and played the lottery that was chosen. The outcome was paid by cheque at the end of the session.

3.4.3 Procedure

PD patients were recruited and tested during their regular visit to the clinic, which lasted at least two nights. After patients were informed about the procedure of our experiment and provided written informed consent, they underwent the screening session in the afternoon on the day of their arrival, or one day after, at the clinic. The screening session involved the mood-, memory- and cognition-tests outlined above and lasted approximately one hour. During screening, patients were always in their most optimal treatment state (i.e. on-stimulation and on-medication).

To test the effect of DBS and L-dopa on delay discounting, we employed a between-subject 2x2 design with the factors medication (medication on vs. off) and STN-DBS (on vs. off). Forty patients were randomly assigned to one of the

four treatment groups (10 patients per group). The testing procedures were as follows:

A regular visit included a ~16 hour period in which patients refrained from taking medication either the first or the second night of their stay, starting at about 8 pm. If the test session took place in the on-medication state, patients received 1,5x their regular dose of L-dopa (but never more than the maximum dosage of 200 mg), and/or other medication (dopamine agonists, see *table 3.4*), on the morning of the test session, one hour before start of the session, to ensure a robust on-state during the whole procedure. Off-medication testing was always done in the morning after spending a night without medication.

A test session (see *figure 3.2* for an overview) took place between 9:00 am and noon and was conducted by two experimenters, of which only one knew the current DBS state of the patient (passive experimenter), and the other exclusively interacted with and guided the patient through the session (active experimenter). The test sessions started with switching the DBS state of the patient. To ensure double-blindness regarding the DBS state, the stimulator was either turned off or left on by a nurse or doctor who was informed by the passive experimenter, without informing the patient what was done. The patient was aware that the stimulator would be either turned off or remain on and was informed beforehand about the necessity of the double-blind procedure. At least 50 minutes after the switch, the MDS-UPDRS-III was conducted, followed by the delay discounting task (intertemporal choice task, ICT) and subsequently the Holt-Laury risk attitude task. Each patient received oral instructions before each task, and was asked control questions to ensure they understood the tasks. The MDS-UPDRS-III, ICT and Holt-Laury tasks were completed in about 30 to 40 minutes. Several trials in the tasks were randomly selected for payout (see above). The patient received feedback about the trials chosen for payment immediately after completing the

two tasks and was paid accordingly by means of a cheque. Directly after, the patient was asked about his/her strategy during the choice tasks and was informed about the goal of the experiment. Thirty minutes after changing the stimulation state, a second motor assessment using the MDS-UPDRS-III was conducted as a within-subjects control of DBS-state. A within-subjects repetition of the ICT and Holt-Laury task was not conducted because both tasks were not deemed suitable for repeated-measures within the short timeframe of one or two mornings.

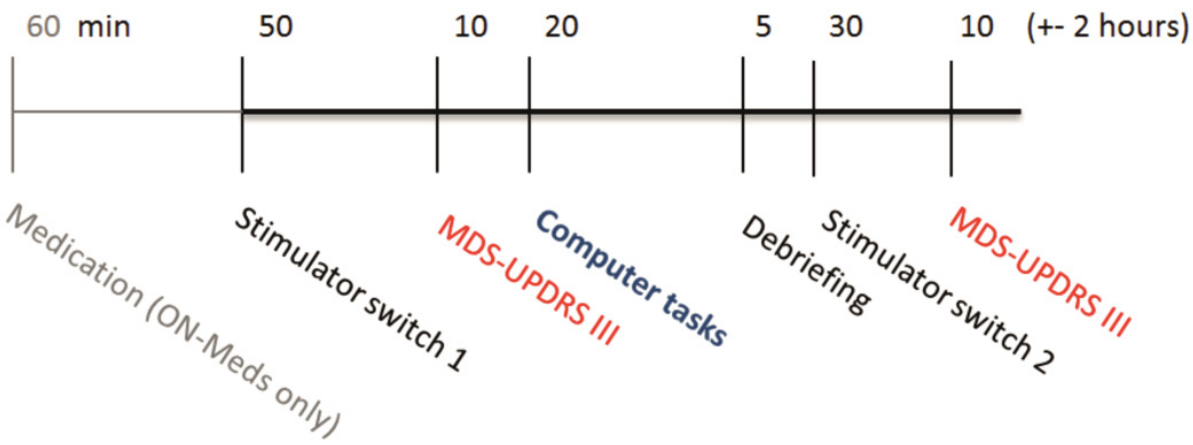

Figure 3.2 *Schematic overview of a session. If patients were tested in the on-medication condition, they received medication (1,5x their regular L-dopa dose) 60 min before DBS was switched off or left on. Patients in the off-medication condition had not ingested dopaminergic medication since the previous evening. At the end of a session, a second MDS-UPDRS III was conducted in the opposite DBS state to confirm DBS effects within-subjects.*

3.4.4 Data analysis

We used a 2 x 2 between subjects factorial design with medication (on vs. off) and DBS state (on vs. off) as independent factors and choice parameters (see below) as dependent variable. To estimate discounting parameters in the ICT, we used two different, well established models: the hyperbolic discounting model (Mazur, 1984) and Laibson's (1997) quasi-hyperbolic discounting model (see below). In addition, we also used the total amount of choices of the smaller, sooner option as a model-free measure of discounting (yielding a value between 0 and 66), as well as a model-free measure of present-bias (i.e., the overweighting of immediate outcomes, see below for details). For the Holt-Laury task, we used the switching point, i.e. the probability at which the participant was indifferent between the two gambles (*HL-IPs*). This measure was obtained using logistic regression. A higher switching point indicated more risk aversion.

Fitting of discounting models. All mathematical procedures to determine the participants' discount parameters were performed using MATLAB (The MathWorks, Inc.). We first identified the individual indifference points (IPs; the magnitude of the smaller, sooner reward that renders it equally valuable to the larger, later reward) for each of the six blocks, using logistic regression. This resulted in three values between 0 and 20 for the three blocks with €20 as maximum reward, and three values between 0 and 30 for the three blocks with €30 as maximum reward.

We first fitted the standard hyperbolic model separately to the IPs of blocks 1 to 3 and blocks 4 to 6, using the following equation (Mazur, 1984):

$$SV_T = A / (1 + kT) \quad (3.1)$$

where *SV* is the subjective value of the reward at delay *T* (in months), *A* is the monetary amount of the reward and *k* is the hyperbolic discount parameter describing the steepness of the discount function. The amount was set to *A* = 1 as the values were expressed as proportions of the later reward. Larger *k*-values indicate a greater impact of delay on value and therefore steeper discounting. The resulting *k*-values for the €20 and €30 blocks were subsequently log-transformed and averaged to obtain one *k*-value per individual (note that the correlation between the two *k*-values for the €20 and €30 blocks was very high, $r = .96$, $p < .000$).

Further, Laibson's quasi-hyperbolic β-δ model was separately fitted to the indifference points of blocks 1-3 and 4-6 to obtain measures of present-bias and patience:

$$SV_{T=0} = 1$$
$$SV_{T>0} = \beta \times \delta^{T} \quad (3.3)$$

SV_t is the subjective value of a reward at time *T*. This equation models the often observed initial rapid decline in subjective value with small delays (present-bias) separately, represented by the parameter β (with $0 \leq \beta \leq 1$). The inverse of β can be interpreted as the extra weight added to immediacy, thus smaller β-values can be construed as stronger present-bias. The discount function's discount rate is $\log(1/\delta)$. Thus, the parameter δ (with $0 \leq \delta \leq 1$) can be interpreted as a measure of patience with higher δ-values indicating higher patience. The resulting β and δ parameters for the €20 and €30 blocks were subsequently averaged to obtain one β an δ value for each participant (note that there was a strong correlation between the β values of the €20 and €30 blocks, $r = .83$, $p < .000$, as well as the δ values, $r = .59$, $p < .000$).

The model fits were performed for each participant individually, using a least-squares algorithm implemented in MATLAB R2013a (The MathWorks, Inc.). The fitting parameters k, β and δ were allowed to vary freely. We calculated the Akaike Information Criterion (AIC) for each model per participant to check the goodness of fit of each model. We then averaged the scores across all participants, resulting in one average AIC value for the hyperbolic model and another AIC value for Laibson's quasi-hyperbolic model. These AIC scores showed that, in general, the data were better described by the quasi-hyperbolic model (M = -17.5) than the standard hyperbolic model (M = -10.1). However, when comparing individual AIC values, the quasi-hyperbolic model had higher AIC values compared to the hyperbolic model in 10 participants, indicating a better fit of the hyperbolic model in these participants.

To obtain an additional, model-free measure of present-bias, we used the following formula:

Present-bias = (Large reward – 3 months IP) / (6 months IP – 9 months IP).

To obtain an overall measure, we averaged the model-free present-bias measure for the €20 and €30 blocks (*PB*). A higher score indicated more present-bias.

Statistical analysis. Statistical analyses reported below were performed using the software package IBM SPSS Statistics 20. We mainly used standard ANOVAs and ANCOVAs to investigate the main effects of DBS and medication state, as well as their interaction on the dependent variables as described above. When necessary, we selected Gabriel's pairwise comparisons test as post-hoc test, which is robust against differences in group sample size. Furthermore, we used Bayesian statistics (Wagenmakers, 2007; Masson, 2011) to calculate the evidence in favor of the null-hypothesis.

3.5 Results

3.5.1 Subject demographics and trait variables

Data of eight participants were excluded as they chose the dominated alternative on more than six of the twelve catch trials in the ICT (that is, they selected €0 now over €20/€30 later; or they selected €20/€30 later over the same reward now, see above). In addition, two of these participants scored 5 points or higher on the SOGS, indicating potential pathological gambling behavior. Our results do not change when these subjects are included in our analysis, except when explicitly mentioned below. *Table 3.1* shows the general descriptive statistics of the remaining 32 patients. The DBS-on group consisted of 18 participants, of which 8 were tested in the on-medication state. The DBS-off group consisted of 14 participants, of which 7 were tested in the on-medication state. There was no significant difference in any of the demographic parameters between DBS and medication groups, except age, $F(3,28) = 3.00, p = .047, \eta^2 = .24$ (*table 3.1*).

Table 3.1 shows the descriptive statistics of the screening tasks and questionnaires. A one-way ANOVA showed a significant difference between the groups in the self-reported impulsiveness (BIS-total), $F(3,28) = 4.34, p = .012, \eta^2 = .317$. However, Gabriel post-hoc tests showed no significant differences between groups, *group 1 vs. 2: mean difference = -6.54, p = .157; group 1 vs. 3: mean difference = -6.75, p = .084; group 1 vs. 4: mean difference = .75, p > .999; group 2 vs. 3: mean difference = -.21, p >.999; group 2 vs. 4: mean difference = 7.50, p = .107; group 3 vs. 4: mean difference = 7.50, p = .055*. Nevertheless, we included BIS-total scores as a covariate in all subsequent analyses to account for potential group differences in impulsiveness. Note that all participants filled out the questionnaires in their optimal (on-medication, on-stimulation) state, so this

difference in BIS-total scores reflects a trait difference between groups, not the effect of DBS on impulsiveness.

3.5.2 Differential treatment effects on motor scores, but not delay discounting

As expected, UPDRS-III scores were significantly different between DBS/medication states, *F(3,28) = 11.96, p < .001,* η^2 *= .56* (*figure 3.3*). Post-hoc tests revealed a significant difference between DBS states, *group 1 vs. 2: .002;*

Table 3.1 *Demographic, screening and questionnaire results per DBS/Med state.*

	State (MED / DBS)				**Statistics**	
	1) On / On (N = 8)	**2) On / Off (N = 7)**	**3) Off / On (N = 10)**	**4) Off / Off (N = 7)**	***F* (*p*-value)**	**Post hoc (Gabriel)**
Age	66.5 (1.4)	57.1 (1.4)	63.5 (2.6)	64.7 (2.9)	*3.00 (.047)**	*1 vs. 2: p = .045**
Year diagnosis	2001 (2.3)	2001 (2.0)	2000 (2.2)	2000 (2.0)	*0.09 (.963)*	
Months on DBS	30 (8.6)	20 (5.1)	30 (8,6)	39 (10.0)	*0.75 (.534)*	
Levodopa equivalent dose (LED)	594 (209.4)	671 (118.0)	623 (120.3)	642 (125.0)	*0.04 (.988)*	
MDRS	139 (1.2)	138 (1.6)	138 (1.1)	138 (1.3)	*0.19 (.902)*	
BDI	6.1 (1.4)	8.4 (1.5)	7.9 (1.2)	7.0 (1.0)	*0.60 (.620)*	
BIS Total	25.8 (1.7)	32.3 (1.9)	32.5 (1.7)	25.0 (2.5)	*4.34 (.012)**	*3 vs. 4: p = .055*
BIS-NonPlanning	9.3 (1.0)	11.9 (0.5)	11.5 (1.2)	8.1 (1.1)	*2.74 (.062)*	
BIS-Motor	8.9 (1.1)	10.0 (1.3)	11.1 (0.6)	8.4 (0.8)	*1.66 (.197)*	
BIS-Attention	7.6 (0.9)	10.4 (1.0)	9.9 (0.6)	8.4 (0.8)	*2.54 (.076)*	
QDQ Total	22.9 (2.5)	24.9 (2.0)	26.0 (1.8)	20.3 (2.1)	*1.40 (.264)*	
QDQ-Discounting	11.1 (1.4)	12.0 (1.1)	12.5 (1.0)	10.6 (1.5)	*0.48 (.698)*	
QDQ-Aversion	11.8 (1.3)	12.9 (1.5)	13.5 (1.6)	9.7 (1.3)	*1.30 (.294)*	

* $p < .05$

3 vs. 4: p = <.001, whereas no significant difference was observed between medication states, *group 1 vs. 3: p = .993; group 2 vs. 4: p = .990*. This is likely due to relatively high inter-individual differences in motor scores obscuring the relatively small but often beneficial effect of medication treatment within subjects. Comparing the UPDRS-III scores within patients (DBS on vs. off only)

Table 3.2 *Delay discounting parameters and risk measure per DBS/Med state.*

	DBS				**Med**				**Inter-action**	
	On	**Off**	**ANOVA**	**ANCOVA[c]**	**On**	**Off**	**ANOVA**	**ANCOVA[c]**	**ANOVA**	**ANCOVA[c]**
Ln(k)	-1.67 (.38)	-2.17 (.34)	*0.90 (.352)*	*0.23 (.636)*	-1.90 (.33)	-1.88 (.429)	*0.003 (.972)*	*0.09 (.767)*	*.18 (.677)*	*.13 (.725)*
NImp	33.2 (3.8)	27.1 (3.6)	*1.31 (.262)*	*0.41 (.526)*	31.6 (4.2)	29.5 (3.5)	*0.17 (.684)*	*.46 (.502)*	*.053 (.820)*	*.24 (.625)*
β[a]	.70 (.08-1.0)	.78 (.35-.98)	*.95 (.338)*	*0.82 (.374)[b]*	.62 (.08-.97)	.80 (.14-1.0)	*1.25 (.274)*	*1.55 (.223)[b]*	*.09 (.765)*	*.00 (.999)[b]*
δ[a]	.97 (.83-1.0)	.98 (.78-1.0)	*.44 (.511)*	*0.002 (.967)[b]*	.99 (.83-1.0)	.97 (.78-1.0)	*1.19 (.285)*	*1.21 (.282)[b]*	*1.09 (.306)*	*1.66 (.208)[b]*
PB	9.19 (1.60)	7.00 (1.34)	*1.20 (.283)*	*1.00 (.325)*	9.48 (1.86)	7.13 (1.19)	*1.14 (.295)*	*1.10 (.303)*	*.31 (.580)*	*.003 (.956)*
HL-IPs	41.5 (7.5)	46.5 (11.4)	*0.22 (.641)*	-	49.3 (8.6)	38.7 (9.5)	*1.24 (.375)*	-	*5.29 (.029)**	-

a. *Due to violation of normality, median and range is shown instead of mean and standard error. The rank transform procedure was used to test for main effects and interactions.*

b. *A non-parametric equivalent of ANCOVA as discussed in (Quade, 1967) was used. Here the resulting F-statistic and p-value are shown.*

c. *Age and BIS-Total scores were added as covariates.*

** p < .05*

also showed a significant improvement of motor symptoms with stimulation, *time*DBS interaction: F(1,31) = 138.84, p < .001, η^2 = .82*. Overall, this indicates that, DBS significantly improved motor symptoms in our sample, while medication did not.

Table 3.2 shows the discounting parameters *k*, β, δ, the number of impulsive choices (*NImp*), the model-free measure of present-bias (*PB*) as well as the indifference points of the Holt-Laury task (*HL-IP*) within each group. We used a two-way ANOVA to test for the effects of DBS and medication on discounting and risk parameters, as well as their interaction. We found no significant main or interaction effects of DBS or medication on any of the discounting parameters (see *table 3.2*).

Figure 3.4 A and *B* show the discounting curves for each medication/DBS state for €20 and €30 blocks, respectively. *Figure 3.4 C* and *D* show the median fits of the hyperbolic and quasi-hyperbolic model, respectively, as well as the 25 and 75 percentile border, for each DBS state. *Figure 3.5* shows the total number of impulsive choices for each medication/DBS state. When adding age and the BIS-total score as covariates in an additional analysis of covariance, main and interaction effects of DBS and medication states on any of the discounting parameters remained non-significant, *DBS state: ln(k): F(1,28) = .23, p = .636, η^2 = .009; NImp: F(1,28) = .41, p = .526, η^2 = .018; β: F(1,28) = .819, p = .37, η^2 = .029; δ: F(1,28) = .002, p = .967, η^2 = <.001; PB: F(1,28) = 1.00, p = .325, η^2 = .037 (table 3.2).*

To calculate the probability that the null-hypothesis (no effect of DBS on delay discounting) is true given our data ($p(H_0|D)$), we used a Bayesian approach developed by (Wagenmakers, 2007) and also described in detail in a tutorial by (Masson, 2011). We used the Bayesian information criterion (BIC) to calculate the posterior probability $p(H0|D)$, with the assumption that the null and alternative

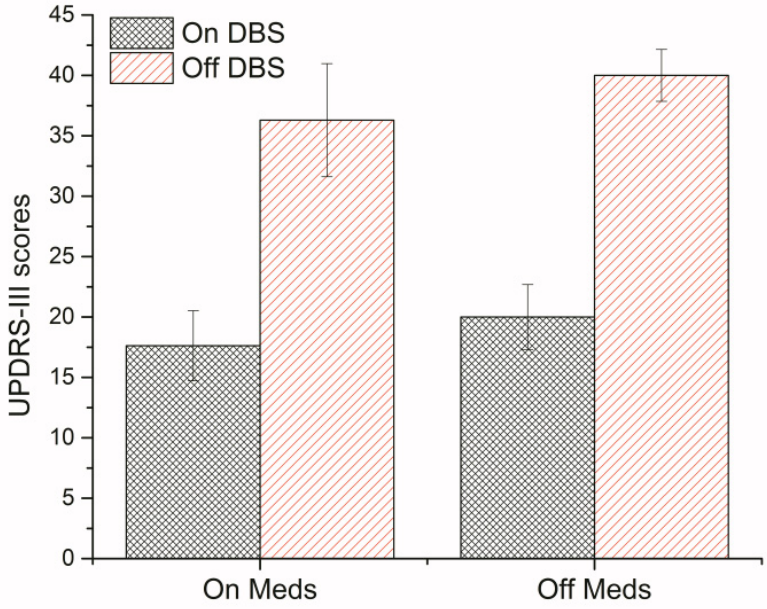

Figure 3.3 *MDS-UPDRS-III scores for each DBS and medication state. Higher scores indicate greater motor impairments. Error bars show standard errors.*

hypotheses are equally likely. The results are presented in *table 3.3*. We found $p(H_0|D)$ ranging between .73 and .81, indicating positive evidence in favor of the null-hypothesis, as suggested by Raftery (1995).

Some patients were treated with dopamine agonists instead, or in addition to, L-dopa. As dopamine agonists are associated with impulsive behavior (Zurowski & O'Brien, 2015), we checked for differences between the DBS groups in the LED when considering only patients who receive dopamine agonists (LED-agonists; see *table 3.4*). In each of the DBS groups, five patients used dopamine agonists, with no significant difference in LED-agonist levels between groups, *U = 110.50, p = .561*, *r = .13*.

The Holt-Laury task was added as a control for the fact that impulsive behavior sometimes correlates with altered risk preferences (Kalenscher & Pennartz, 2008).

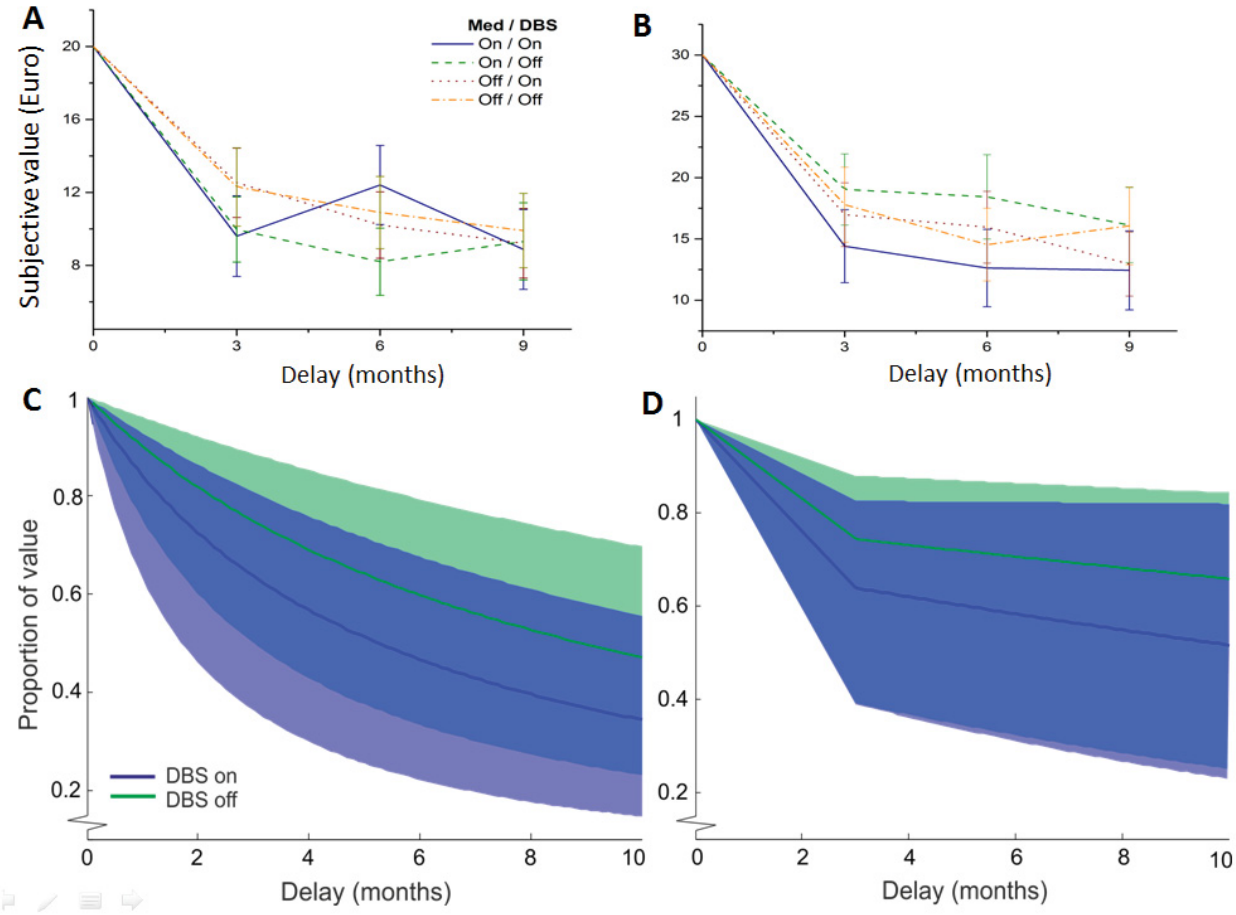

Figure 3.4 A,B: *Discounting curves per medication/DBS state subgroup for €20 (A) and €30 (B), based on the indifference point at 3, 6 and 9 months. Error bars show standard errors.* ***C:*** *Plots of the hyperbolic model in the on- and off- DBS state, based on the median k-value. Shaded areas show the 25% and 75% percentile range.* ***D:*** *Plots of the quasi-hyperbolic model in the on- and off- DBS state based on the median* β *and* δ *values. The initial linear decline represents 'present-bias' and is determined by the* β *parameter, whereas the subsequent exponential curve represent 'patience' and is determined by the* δ *parameter. Shaded areas show the 25% and 75% percentile range.*

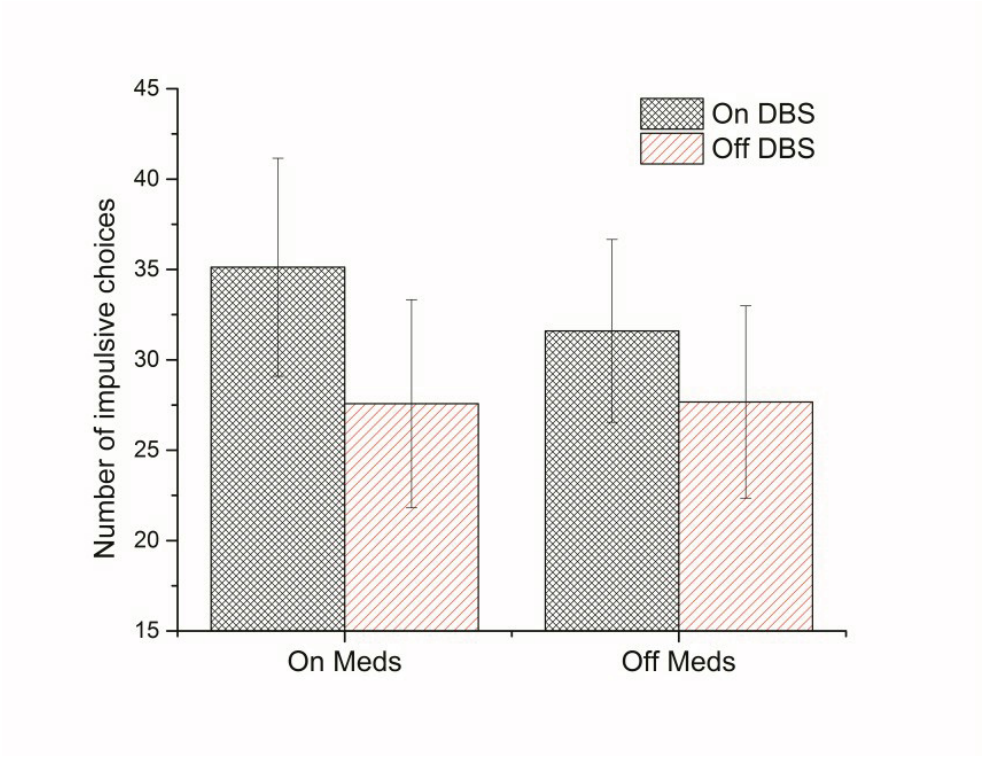

Figure 3.5 *The total number of impulsive choices (smaller, sooner reward) for each DBS and medication state. Error bars show standard deviations.*

There were no significant main effects of DBS or medication on Holt-Laury scores, DBS state: $F(1,28) = .22$, $p = .641$, $\eta 2 = .01$; medication: $F(1,28) = 1.24$, $p = .275$, $\eta 2 = .04$, suggesting no effect of DBS and/or medication on risk attitude. Note, though, that we found a significant interaction effect of DBS and medication state on HL-IPs, $F(1,28) = 5.29$, $p = .029$, $\eta 2 = .16$. However, when using the complete sample of 40 patients, the interaction effect of DBS and medication state on HL-IPs failed to reach significance, $F(1,39) = 1.00$, $p = .325$, $\eta 2 = .027$. Note that a relatively large number of patients showed an inconsistent choice pattern (i.e. switching more than once between the risky and safe gamble), with 47,5% making at least one error (one more switch) and 30% having at least 2 errors, compared to the numbers mentioned in the original paper on the Holt-Laury task (Holt & Laury, 2002), where only 13,2% of the participants made at least one error.

Table 3.3 *Bayesian posterior probabilities for the hypothesis that there is an effect (H_1), or for the hypothesis that there is no effect (H_0), of DBS on discounting measures, given our data.*

	NImp	***Ln(k)***	β	δ
$p(H_0\|D)$	.731	.774	.765	.813
$p(H_1\|D)$	.269	.226	.235	.187

Table 3.4 *Number of participants receiving dopamine agonists, and the levodopa equivalent dose (LED-Agonists) of the dopamine agonists used, per DBS group.*

	N	***LED-Agonists***	***Average LED-Agonists***
DBS on	5	595	119,0
DBS off	5	837	167,4

3.6 Discussion

In this study, we aimed to investigate the effect of STN-DBS on impulsive decision-making, using a delay discounting paradigm. We found evidence for effect of neither STN-DBS, nor of medication, on delay discounting behavior - a commonly used measure of impulsive choice. Although we found a significant interaction of DBS and medication state on risk aversion, this effect did not hold when all participants were included in the analysis. In addition, due to the relatively large number of errors the participants made in this task, we refrain from further interpreting this finding.

Our findings are in line with a study by (Torta *et al.*, 2012) who investigated the effects of STN-DBS on delay aversion. Twenty-one PD patients with STN-DBS turned on and off (patients were off medication) performed the Cambridge Gambling Task, which measured both risk-behavior and delay aversion, and filled out questionnaires assessing self-reported delay aversion, delay discounting and impulsivity. The authors found no effects of stimulation on delay aversion or task behavior, although patients self-reported a higher feeling of impulsivity in the off-stimulation state. Thus, while increased levels of delay discounting have been

associated with several impulse control disorders, such as substance abuse, attention deficit hyperactivity disorder (ADHD) as well as pathological gambling and overeating (Bickel *et al.*, 2012) – behaviors often shown by PD patients in response to their treatment – there is no evidence so far that STN-DBS alters delay discounting.

Although the development of ICDs is often attributed to side-effects of dopaminergic medication (Voon & Fox, 2007; Voon *et al.*, 2011a; Voon *et al.*, 2011b; Poletti *et al.*, 2013) several studies point toward a potential role of STN-DBS on the development of ICDs in PD patients (Halbig *et al.*, 2009; Lim *et al.*, 2009; Moum *et al.*, 2012). However, it has been argued that development of ICDs after STN-DBS onset may be an indirect consequence of disease history and treatment as they may result from long-term alterations of fronto-limbic structures, which are presumed involved in ICDs (see Brewer & Potenza, 2008), due to disease progress and chronic medication (e.g. Moum *et al.*, 2012). Because ICDs themselves are considered chronic disorders, a short change in DBS state, as applied here, after several months of chronic stimulation might not be sufficient to uncover potential long-term effects leading to the development of ICDs. This would be in line with findings pointing at an increase in cognitive impulsivity reported by both patients and relatives three months after STN-DBS onset compared to a baseline taken before STN-DBS onset (Pham *et al.*, 2015), but contradicts the above-mentioned self-reported increase in impulsivity in a short-term off-state compared to scores in the DBS-on state (Torta *et al.*, 2012). Although motor effects of STN-DBS are often visible within minutes, cognitive effects of STN-DBS on impulsive decision making might not be visible on short-term. For example, as reward learning seems to be affected by STN-DBS, perhaps experiences with rewards after STN-DBS onset influence subsequent choice behavior that could lead to development of ICDs in a subgroup of patients. Future

studies need to monitor long-term changes in delay discounting in particular, and impulsivity in general, after STN-DBS treatment onset.

Impulsivity itself is considered a multifaceted construct (Evenden, 1999; Kalenscher *et al.*, 2006), with one subtype being defined as impulsive action (the inability to inhibit a prepotent response) and another subtype as impulsive choice (preferring a smaller, more immediate reward over a larger, more delayed reward) (Winstanley *et al.*, 2004; Kalenscher & Pennartz, 2008; Robinson *et al.*, 2009). Motor impulsivity is commonly assessed with reaction time tasks, in which motor responses need to be inhibited either before ('waiting') or during ('stopping') execution, whereas choice impulsivity is often assessed with an intertemporal choice task, in which participants make repetitive choices between a smaller-sooner and larger-later (often monetary) reward. Several studies have dissociated the cognitive and neural bases of these two types of impulsivity (Winstanley *et al.*, 2004; Van den Bergh *et al.*, 2006; Broos *et al.*, 2012). So far, studies have uncovered effects of STN-DBS on motor impulsivity (Witt *et al.*, 2004; Frank *et al.*, 2007; Aleksandrova *et al.*, 2013), which is in line with literature supporting the involvement of the STN in controlling the threshold for responding in situations with high conflict, i.e. when two choice options are relatively similar in value (Baunez & Robbins, 1997; Baunez *et al.*, 2001; Desbonnet *et al.*, 2004; Frank, 2006; Cavanagh *et al.*, 2011). With regard to reward processing and decision making, STN-DBS seems to mainly influence reward learning (Serranova *et al.*, 2011; van Wouwe *et al.*, 2011) and the evaluation of losses (Rogers *et al.*, 2011), but, to the best of our knowledge, there is no evidence so far of an effect of STN-DBS on risky decision making (Brandt *et al.*, 2015).

One concern with our study is the small sample size, and, by consequence, the low statistical power. We cannot reject the possibility that we missed a small effect of STN-DBS on delay discounting because we lacked the statistical power to

detect it. However, our Bayesian analysis showed positive evidence in favor of the null hypothesis. This suggests that the effect size is either very small or non-existent. Therefore, we can conclude with some confidence that, if there were a short-term effect of STN-DBS on delay discounting, it would be miniscule and probably negligible.

Note that we started off with a small pilot experiment to check if our task was suitable for repeated-measures, as this would greatly increase power. However, we found that patients often made stereotypical, repetitive choices on subsequent repetitions of the task, which was supported by anecdotal remarks about their choice behavior and strategy (e.g. they would ask why they had to do the same task again; or they specifically commented on the fact that they would remember their choices in the previous task, and aimed to copy their own choices). For this reason, we opted against using a repeated-measures design.

Additionally, we would like to note that, although highly undesirable, underpowered statistics are frequently unavoidable in studies with clinical populations; due to the difficulty of finding a sufficient number of patients meeting the inclusion criteria, patient samples in medical studies are often smaller than desired. Nevertheless, despite the admittedly low power, we believe that our results are of significance to other scientists studying the effects of PD treatment on impulsive decision-making. To prevent the so-called 'file drawer effect', i.e. publication biases because potentially informative studies ending up not being published due to non-significant findings (Sterling *et al.*, 1995; Hopewell *et al.*, 2009; Song *et al.*, 2009), we would like to make our findings accessible to researchers interested in similar research problems.

In conclusion, we failed to demonstrate a significant effect of STN-DBS on delay discounting. Although absence of evidence is not evidence of absence, calling for interpretative caution, this could potentially imply that STN-DBS effects

on delay discounting do not exist. From a clinical perspective, this study provides evidence for a lack of negative cognitive side-effects of STN-DBS in the form of altered intertemporal decision-making. Even if a small effect of STN-DBS on delay discounting existed, a risk of slightly altered decision making likely does not weigh up to the benefits of STN-DBS on motor functioning. Our findings therefore underscore the clinical safety of DBS-STN as therapeutic treatment.

4. Rate maximization and hyperbolic discounting in human experiential intertemporal decision making

"Perhaps our greatest distinction as a species is our capacity, unique among animals, to make counter-evolutionary choices."

- Jared Diamond

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4.1 Abstract

Decisions between differently timed outcomes are a well-studied topic in as diverse academic disciplines as economics, psychology and behavioral ecology. In behavioral economics and psychology, it is often assumed that such intertemporal choices are based on the hyperbolic devaluation of reward values as a function of their delays ('delay discounting'). By contrast, in behavioral ecology, intertemporal choices are assumed to reflect optimization principles, that is, the maximization of energy or reward rate. Thus far it is unclear which currency, discounted value or reward rate, is maximized during intertemporal choice. Here we investigated whether humans (N = 81) maximize reward rate or discounted value when making intertemporal decisions. We found that, compared to hyperbolic discounting, rate maximization better approximated the choices made in a range of different intertemporal choice design conditions. Notably, rate maximization rules provided better fits to the choice data than hyperbolic discounting models in natural, foraging settings as well as binary choice frames. Interestingly, in contrast to previous findings, rate maximization was universally observed in all choice frames, and not confined to foraging settings. We speculate that evolution may have favored reward rate maximization over utility maximization, and that rate maximization may be a universal principle that has shaped intertemporal decision making in general and across a wide range of choice problems.

4.2 Introduction

In our life we make countless decisions between delayed consequences. These intertemporal decisions shape important aspects of our life, such as our education, housing, diet, and financial well-being. Intertemporal decision making is well studied in both humans and non-human animals (Kalenscher & Pennartz, 2008) by as diverse disciplines as economics, psychology and behavioral ecology. Although trying to explain the same phenomenon – intertemporal choice – approaches in the different academic disciplines came up with distinct and remarkably different accounts.

For example, inspired by evolution theory, optimal foraging theory in behavioral ecology (Stephens & Krebs, 1986) prescribes that a Darwinian-fitness-maximizing animal should maximize energy intake over time when foraging for food (Pyke *et al.*, 1977). However, much like humans, animals typically overweight short-term outcomes or underweight long-term outcomes and, by consequence, make impulsive decisions that fail to maximize long-term energy rate (Mcdiarmid & Rilling, 1965; Kalenscher *et al.*, 2005). To reconcile these findings with the assumption in optimal foraging theory that evolution should have shaped optimal intertemporal decision making, Stephens and colleagues (Stephens & Anderson, 2001; Stephens *et al.*, 2004) argued that short-sighted, present-biased decisions *can* result in energy rate maximization, but only in natural foraging contexts to which animals' decision systems are adapted to. They maintained that natural foraging contexts are characterized by sequential background-foreground problems (Stephens, 2008) in which one alternative is the background to all other alternatives. For instance, a flying bird spotting a potential food source has to decide whether to put its background activity (flying) on hold to exploit the potential food source (foreground), or whether to continue the exploration of the environment to find a potentially richer/safer source later.

However, in most studies, intertemporal decisions in animals or humans are typically *not* probed with sequential choice problems, but with binary, mutually exclusive choice tasks (so-called *self-control tasks*: "choose either A or B") to which they are supposedly *not* adapted to. By consequence, humans, as well as animals, have been shown to fail to maximize energy rate in self-control tasks (Kalenscher & Pennartz, 2008). One possible reason why animals perform poorly is because they may disregard post-reward delays, i.e., delays between reward delivery and the onset of the next decision, such as inter-trial intervals (Pearson *et al.*, 2010). Post-reward delays matter for energy-rate maximization in self-control tasks, as a change in post-reward delay may result in a different option having the highest long-term energy rate.

Why do animals fail to maximize long-term energy rate in self-control tasks, although they *are* thought to maximize it in sequential choice tasks, so-called *patch-designs*, that are intended to model natural foraging contexts, and thus are supposed to have higher ecological validity? One answer is that long-term energy maximization is achieved because short-sighted decision rules that consider only the delay to the next reward, maximizing short-term rate (STR), automatically also lead to long-term rate (LTR) maximization in patch designs (Stephens & Anderson, 2001). Organisms may thus have evolved to implement short-sighted rules because they lead to LTR maximization in sequential choice contexts, even though they result in poor performance on binary self-control problems. This was indeed shown in animals (Stephens & Anderson, 2001; Stephens & McLinn, 2003) and more recently also in humans (Carter *et al.*, 2015).

Next to the ecological approach, intertemporal decision making is also extensively discussed in the economics and psychology literature because the myopic, short-sighted choice patterns of humans (and animals) are not only a problem for optimal foraging theory, but also represent violations of the

efficiency assumptions of utility maximization in economics (Kalenscher & Pennartz, 2008). In behavioral economics and psychology, intertemporal choice behavior in *self-control* paradigms is often expressed as delay discounting (Samuelson, 1937; Kalenscher & Pennartz, 2008) according to which the subjective value of a delayed reward decreases with increasing delay. Delay discounting is best described by hyperbolic discounting models, which reflect a decrease in the subjective value of a reward with a non-constant decay rate, characterized by a steep decline in subjective value at initial delays, and flatter decline at longer delays (Mazur, 1984; Green & Myerson, 1996; Kalenscher & Pennartz, 2008).

The hyperbolic discounting and energy rate maximization hypotheses differ in one important aspect: because of the non-constant discount rate in hyperbolic discounting, different units of time have unequal weight on decreasing the subjective value of the reward. By contrast, rate maximization suggests equal weighting of every time unit because animals are supposed to calculate the average (rate) value per time, based on the considered time interval and reward magnitude.

To date, it is unclear whether rate maximization or hyperbolic discounting explains intertemporal choices best, if they are mutually exclusive or complementary accounts, and if they are task- and species-dependent. Here we address the question whether humans maximize reward rate or rather adopt hyperbolic discounting when performing an experiential intertemporal choice task. We asked human participants to make binary and sequential intertemporal choices between smaller/sooner and larger/later monetary rewards, with immediately experienced delays. We adopted a repeated-measures design with two design conditions (self-control versus patch). The task enabled us to obtain individual discount rates and rate maximization scores for each design condition

and thus to uncover whether humans rather deploy rate maximization or hyperbolic discounting, with its inherent short-sightedness.

4.3 Methods

4.3.1 Participants

We recruited 93 participants (60 female) at the Heinrich-Heine University Düsseldorf. Exclusion criteria were psychiatric or psychological disorders, lack of German language proficiency, smoking more than five cigarettes per day, drinking more than one bottle of wine or 1,5 liter beer a day on average, and consumption of recreational illicit drugs more than two times a month. These criteria were chosen to avoid drug-related effects on intertemporal decision making (Bickel *et al.*, 2012). Participants were between 18 and 45 years old (M = 23.2, SD = 5.2) and were enrolled in various study programs (language studies: 22; psychology: 13; (business) economics: 9; history: 8; computer science: 6; law: 6; media and culture: 6; biology: 5; other studies (n<5): 20). Participants received a monetary reimbursement consisting of a show up fee of 3€ and their earnings during one part of the experiment (see below), which could lead up to a total amount of 17€. Payment was received in the form of a personal cheque at the end of a session. This study was approved by the local ethical committee of the Psychology department at the Heinrich-Heine University, Düsseldorf.

4.3.2 Materials

General task procedure. Participants performed four variants of an intertemporal choice task in which they could choose between a smaller/sooner (SS) monetary reward, and a larger/later (LL) reward. The nature of the task was experiential, i.e., delays and rewards were real and experienced by the

participants. In a within-subject design, we manipulated task design (sequential "patch" condition versus binary "self-control" condition, see below and *figure 4.1*).

Each design condition consisted of six separate blocks of trials that varied in delay to the smaller/sooner reward as well as the delay to the larger/later reward (see *table 4.1*; in our task, the delay indicates the time between the decision and the onset of the reward screen, informing the participant about the reward magnitude see below). Each of the six blocks was presented in the self-control as well as the patch design (see below and *figure 4.1*). The three blocks with the same delay to the small reward (i.e. either 3s or 9s) within a task design were presented together in a cluster (to maintain some structure in the task for participants; note that the blocks in one cluster differed in delay to the larger/later reward only). Within each cluster the blocks were presented in pseudorandom fashion. Participants thus completed two clusters of three blocks in the self-control design, and two clusters of three blocks in the patch-design. After each cluster participants had a short, approximately one-minute break while the next cluster was started. The clusters were presented pseudo-randomly as well.

Participants made one decision per trial; the number of trials per block was variable; trials in a block were repeated until the block duration elapsed. Block duration was fixed and determined such that participants could choose the option with the longest delay at least seven times in each block, including a decision time of 5s per trial.

Self-control design. In the self-control design condition (see *figure 4.1*), participants made binary, binding choices between smaller/sooner and larger/later rewards. The smaller/sooner reward consisted of 5 cents and was delayed by either 3s, or 9s. The larger/later reward consisted of 10 cents, with a

delay of 5, 10, or 15s (with smaller/sooner delay of 3s), or 11, 21, or 31s (with smaller/sooner delay of 9s). The delay of the larger/later option was varied across

Table 4.1 *Task parameters per block. Blocks and parameters were identical in the self-control and patch designs.*

Block	R_{SS}	R_{LL}	D_{SS}	D_{LL}	ITI[a]	rr_{SS}[b]	rr_{LL}	ΔLTR[c]	Block duration
1	5 Cent	10 Cent	3s	5s	5s	0.63	1.00	20.0	119s
2	5 Cent	10 Cent	3s	10s	5s	0.63	0.67	5.30	154s
3	5 Cent	10 Cent	3s	15s	5s	0.63	0.25	-2.70	189s
4	5 Cent	10 Cent	9s	11s	5s	0.36	0.63	14.60	161s
5	5 Cent	10 Cent	9s	21s	5s	0.36	0.38	2.70	231s
6	5 Cent	10 Cent	9s	31s	5s	0.36	0.28	-3.00	301s

a. ITI = intertrial interval;
b. rr = reward rate;
c. long-term rate (LTR) difference between the SS and LL option. A positive value indicates a higher LTR for the LL option.

three blocks of trials in a given condition in a pseudo-random fashion so that each block yielded a new pair of options; delay/reward option pairs were kept constant across trials within a block. Trial duration was not fixed, the number of trials per block was variable and depended on block duration.

Participants were not instructed about delay and reward magnitudes, but had to learn them by experience. A trial started with the inter-trial interval (ITI), indicated by a white cross at the center of the screen, which was fixed at 5s. The ITI was followed by the choice screen, on which two differently colored circles were presented on each side of the screen. The different delay/reward combinations were associated with unique circle-colors. Participants indicated their choice on a standard keyboard by pressing the ‘x’ key for the left option, and the ‘m’ key for the right option. Key-side assignment was also indicated on the screen below the circles for participants’ convenience. Participants had unlimited time to make their decisions, but after three seconds they were prompted by the message ‘please make a choice’, blinking red below the circles on the screen.

After participants selected one of the colored circles, a dynamic progress bar indicated the delay length until reward presentation. After the delay, information about the reward magnitude was shown at the center of the screen for two seconds, and the cumulated earnings across past trials were additionally shown below the reward information. Following reward presentation, the next trial started immediately. Trials were repeated within a block until the block duration expired. When the block time was up in the middle of a trial, this trial was finished before the next block started.

Patch-design. The two clusters with a patch design were economically identical to the self-control condition in terms of delays, rewards, trial and block structure, screen composition, information format, as well as participant instructions. The only difference to the self-control condition was the sequential nature of the decision structure: while, in the self-control condition, participants made binding binary choices between the smaller/sooner and larger/later rewards, in the patch condition they chose whether to stay in a 'reward patch' for a fixed delay to obtain a large reward, or 'leave the patch' and start a new trial after having obtained a small reward (see *figure 4.1*). Sequential choice was implemented as follows: each trial started with the ITI (5s), followed by a delay of 3s (delays were indicated by dynamic progress bars as in the self-control condition) or 9s. Subsequently, a reward screen (two seconds) indicated that the participant had earned 5 cents (the smaller/sooner reward magnitude), after which the choice screen was presented. Participants indicated their choice on a standard keyboard by pressing the 'x' key for the left option, and the 'm' key for the right option. A choice of the smaller/sooner option resulted in the start of the next trial (i.e. was followed by the ITI of the next trial) and a choice of the larger/later option resulted in a further delay of 2, 7 or 12s in the short smaller/sooner delay blocks, or a further delay of 2, 12, or 32s in the 9s smaller/sooner delay blocks. Following

the end of the delay, a further screen indicated that participants earned another 5 cents (thus, resulting in a sum of 5+5=10 cents in this trial, equivalent to the magnitude of a larger/later reward), and the next trial started. Again, the order of delay conditions was pseudo-randomized across blocks.

As mentioned, block duration, trial setup and general design features were identical in the patch- and the self-control conditions. Also, as before, participants

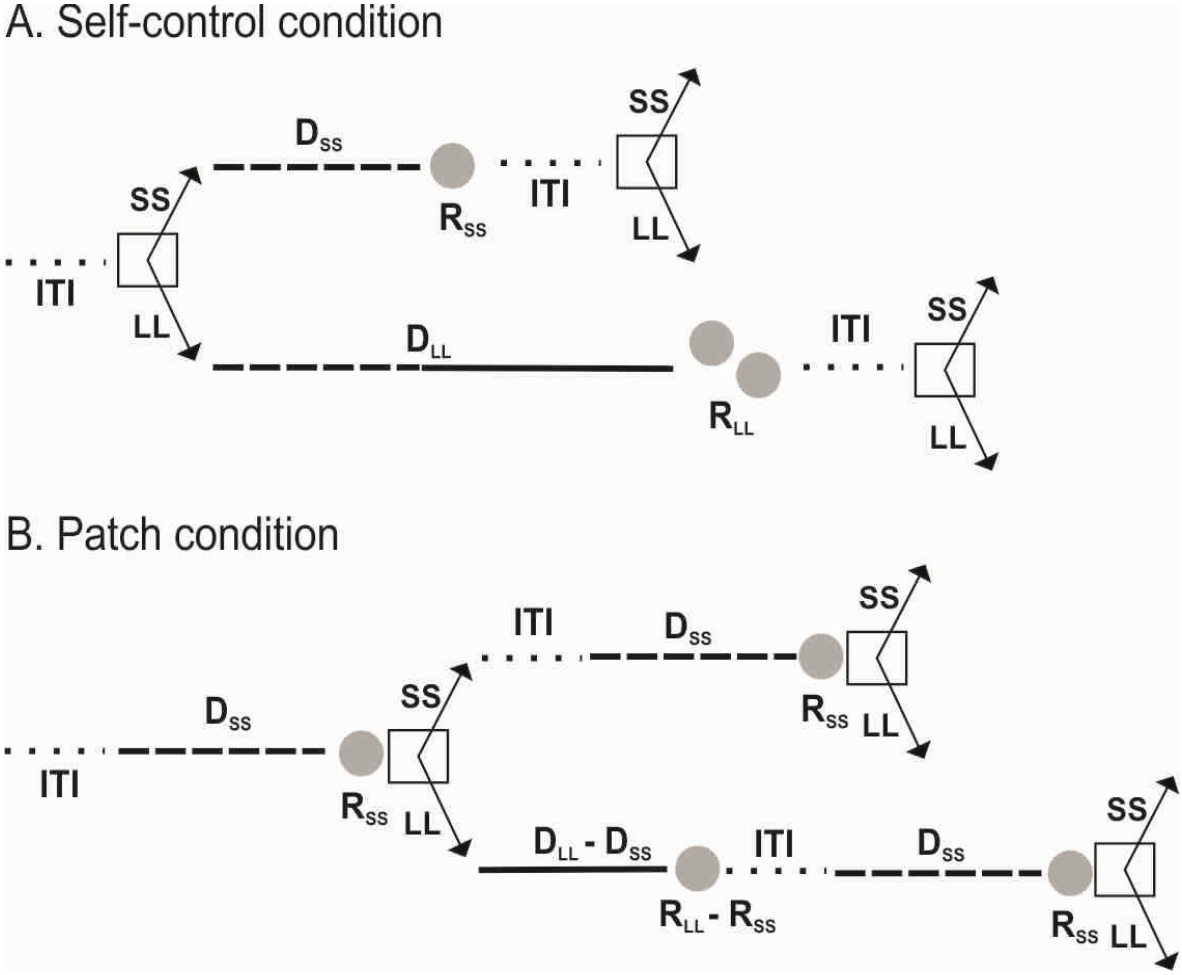

Figure 4.1 *Task structure in the self-control (A) and patch (B) condition. Choices were made between a smaller, sooner (SS) and a larger, later (LL) option. One grey circle indicates a reward of 5 cents. ITI: inter-trial interval; D = delay; R = reward.*

were not instructed about the outcome parameters, but had to learn them through experience. Note that, in the patch condition, the pre-choice delays (3 or 9s) and default rewards (5 cent in all conditions) were identical to the smaller/sooner rewards in the self-control condition (see above and *figure 4.1*), and the sum of pre- and post-choice delays in the patch condition (5, 10 and 15s for blocks 1-3 and 11, 21 and 31s for blocks 4-6) as well as the sum of rewards (10 cents) matched the larger/later parameters in the self-control condition.

All conditions were fully incentive-compatible and accumulated earnings were paid out to the participants after experiment completion. The task was programmed in Matlab (Mathworks, Inc.) using the Cogent Graphics toolbox developed by John Romaya at the LON at the Wellcome Department of Imaging Neuroscience.

Offline delay discounting task. To obtain an offline measure of the participants' hyperbolic discount rates, we used a task design similar to the one described by Kirby *et al.* (1999). This enabled us to compare participant's hyperbolic discount rates in a task structure commonly used to measure hyperbolic discounting with the hyperbolic discount rates in the general task described above. This task estimated the individual discount rates *k* by assuming a hyperbolic discount function underlying choice behavior. The task consisted of 27 choices between hypothetical rewards. In each trial, participants were offered the choice between a smaller reward available now and a larger but delayed reward. The smaller rewards ranged between 11 and 80 Euro, and the larger rewards between 25 and 85 Euro. The delays ranged between 7 and 186 days. Combinations of reward amounts and delays were such that indifference between the options would yield one of nine distinct discount rate k_{Kirby}, i.e. there were nine sets of three trials yielding the same *k*-value, one with a relatively small, medium and large delayed reward. Trials were presented in a specific order. One

option was presented on the left of the screen, while the alternative option was presented on the right side of the screen. Participants had to press ‘x’ or ‘m’ to choose the left or the right option, respectively. Participants had unlimited time to make their decisions. At the start of the task participants were asked to make the choices in accordance with their personal preference, and that there were no right or wrong answers. Participants were informed beforehand that this task would not be reimbursed.

Post-test questionnaire. This questionnaire consisted of questions about demographics (age, income, marital status, nationality, profession, field of study), questions regarding current physical state (known diseases, psychiatric treatment, smoking behavior, alcohol use) as well as questions regarding the decision tasks: we asked whether participants had problems focusing on the task (yes/no), how easy it was to understand the tasks (5-point Likert scale), which strategy participants used when making their choices (open question), whether they calculated the total duration of choice options (yes/no), to what extent they tried to obtain the highest possible reward (5-point Likert scale), whether they always chose the same color, independent of the outcome (always, often, sometimes or never), whether their choices reflected their personal preferences (yes/no) and whether we could trust their answers (yes/no).

Additional measures. We additionally measured self-reported impulsivity using the Quick Delay Questionnaire (QDQ) and the Barratt Impulsiveness Scale(BIS) as well as time perception using a time production task. For procedure and results, see supplemental materials.

4.3.3 Procedure

Upon arrival, participants were asked to read and sign an informed consent form and the procedure of the session. The number of participants tested at the

same time ranged from one to four. Each participant was seated in his/her own cubicle that ensured privacy throughout the session. Identical laptops were used to ensure similar processing speed. No other participants nor the experimenter could see the laptop screens during task performance. Before staring the tasks, participants received written instructions. The instructions stressed, among others, that, although the four tasks (i.e. conditions) may look similar, they were independent of each other. In addition, participants were told that each task had a fixed duration, independent of the choices that were made, and that their earnings depended on their choices. After written and verbal instructions and an opportunity for questions and answers, participants performed the four task conditions in random order. After each task condition, participants saw the monetary amount they had earned in that particular condition and were prompted to ask the experimenter to start the next task. The main task was followed by Kirby's discounting task, before which the participant received short oral instructions that were also repeated on screen before the task started. This was followed by the time production task, and QDQ and BIS questionnaires (see supplemental materials). Finally, the participants filled out the post-test questionnaire. Participants then received a show-up fee of €3,- plus their earnings from the main task in the form of a personal cheque that they could cash at any bank. If requested, participants were informed about the aim of the study.

4.3.4 Analysis

Rate maximization scores. The choice alternatives in each trial differed in their long-term reward rate (here: the cumulative reward amount per block; *note that larger, later rewards do not always yield higher reward rates, depending on the task parameters, choices of smaller, sooner rewards may produce more optimal outcomes,* see *table 4.1 for details*). To estimate to what extent individuals

maximize long-term reward rate we calculated LTR scores, which reflect the proportion of choices of the alternative with the highest reward rate, averaged across all six blocks in each design condition, resulting in two rate scores per individual. We used a softmax rule to approximate the probability of choosing the alternative with the highest reward rate:

$$p_j = 1 / (1+ e^{-\mu*(C)}) \quad (4.1)$$

in which p is the proportion of choices for alternative with the highest reward rate in block j, μ is a temperature parameter indicating the sensitivity to differences in reward rates, and C is the currency to be maximized, here reflecting the difference in reward rates. Goodness of fit was estimated using the Akaike Information Criterion (AIC).

Hyperbolic discounting. To estimate hyperbolic discounting, we used the same softmax decision rule in eq. 1 to estimate hyperbolic discount rates k from the proportion of choices for the larger/later reward p_{LL}, which were calculated based on the first seven trials in each block (we restricted our analysis to the first seven trials because the number of trials per block was variable, but all subjects performed at least seven trials per block).

For hyperbolic discounting, the currency C in eq. 1 was given by v_{LL} -v_{SS}, where v_{LL} and v_{SS} were the subjective, discounted values of the larger/later reward in block j, or smaller/sooner reward, respectively, obtained from Mazur's hyperbolic model (Mazur, 1984):

$$v_i = \frac{R_i}{1+k(D_i)} \quad (4.2)$$

where v_i indicates the subjective, time-discounted reward value of reward *i* with reward magnitude *R*, and delay *D*. *k* is an individual discount factor determining the steepness of the discount function.

We used all six blocks of each design (self-control and patch) to estimate the individual discount parameter *k.* We computed a single *k*-value per participant, pooling across trials from both design conditions. Additionally, separate *k*-values were estimated for each design condition, resulting in two different model fits for each individual. Reward magnitude *R* and delay *D* in *equation (4.2)* was adjusted for each design (see *figure 4.1*). Again, goodness of fit was estimated using the Akaike Information Criterion (AIC).

Model comparisons and data analysis. All parameter estimations were performed using least squares methods in MATLAB R2011a (Mathworks, inc). When estimates in raw form as well as their log transformations violated the normality assumption, non-parametric tests were performed.

Predictions. *Table 4.2* shows the predicted choice preferences per block for the rate maximization and hyperbolic discounting model. The predictions of the hyperbolic model depend on the individual discount parameter *k estimates*.

4.4 Results

4.4.1 Task and trial completion

Thirteen participants were excluded because they indicated, in the post-experiment debriefing questionnaires, having based their choice on the option with their favorite color (N = 5), to be unmotivated or unwilling to maximize their payoff (N = 2), to deliberately choose against their preference (N = 5), or they indicated that their given answers were not to be trusted (N = 1). Together this resulted in a final sample of 81 participants (mean age= 23.2, SD = 5.0). On

Table 4.2 *Predicted preference for the smaller/sooner (SS) or larger/later (LL) reward per block per decision model.*

Block	*Maximizing LTR: Both designs*	*Discounting: Self-control design*	*Discounting: Patch design*
1	LL	LL	LL
2	LL	$k < .25$: LL $k > .25$: SS	LL
3	SS	$k < .12$: LL $k > .12$: SS	SS
4	LL	LL	LL
5	LL	$k < .35$: LL $k > .35$: SS	LL
6	SS	$k < .09$: LL $k > .09$: SS	SS

Predictions for LTR maximization were based on the calculation of reward rates using the total delay (pre-reward delay + ITI) and reward of each option. Predictions with regard to delay discounting were based on the discounted value of the options, which were calculated using Mazur's hyperbolic function (Mazur, 1984). Only pre-reward delays were included when calculating the discounted value for k-values ranging from 0.0 to 1.0.

average, participants completed 11 trials in the first, 13 trials in the second and 17 trials in the third block in each task design (note that the more often the smaller/sooner reward was chosen, the more trials could be completed within the fixed time). There were no notable differences in number of trials completed between the four conditions. All participants completed at least seven trials in each block, except for one participant who completed only one trial in the second block of the patch condition (this block was excluded from further analysis). Therefore, for each participant, the first seven trials per block were used in subsequent analyses.

4.4.2 Manipulation check: sensitivity to parameter manipulations

As a manipulation check, we tested whether participants were sensitive to the delay differences across blocks. To this end, we compared *the proportion of large reward choices* (p_{LL}) between blocks with similar smaller/sooner reward delay within each design condition (*figure 4.2*). There was a significant difference in p_{LL} across blocks within each smaller/sooner delay (3s and 9s) and design (self-control and patch) condition*: Friedman's Chi-square test for multiple repeated measures, all* $\chi^2 > 11.00$*, all p<.003.*

Also within each smaller/sooner delay and task design, participants were sensitive to the changes in delay to the large reward: Wilcoxon pair-wise comparisons showed significant differences in p_{LL} between consecutive blocks with similar smaller/sooner delays, *, all Z < -3.5, all p < .001, with the exception of patch-condition (3s), block 2 vs. 3: Z = -1.09, p = .274.* These results suggest that participants were sensitive to reward delays and magnitudes.

4.4.3 Choice behavior

Choice proportions. Choice proportions were mostly similar between design conditions: block-wise comparisons (Wilcoxon) of p_{LL} choices between self-control and patch conditions revealed no significant effect of design, *all Z > -1.13, all p > .257*. except in blocks 1 and 2, *block 1: Z = -2.60, p = .009, r = .20; block 2: Z = -2.71, p = .007, r = .21.* In blocks 1 and 2, the proportion of large reward choices was higher in the self-control than patch design.

Rate maximization. The LTR-scores indicate to what extent participants' choices produced long-term reward maximization. The median scores were .64 ($LTR_{self\text{-}conrol}$) and .60 (LTR_{patch}) (see *table 4.3*). A comparison of LTR-scores showed significantly higher scores in the self-control than patch condition, Z = -2.08, p = .038, r = .16, indicating that participants selected the choice alternative with the higher LTR score more often in the self-control than the patch condition.

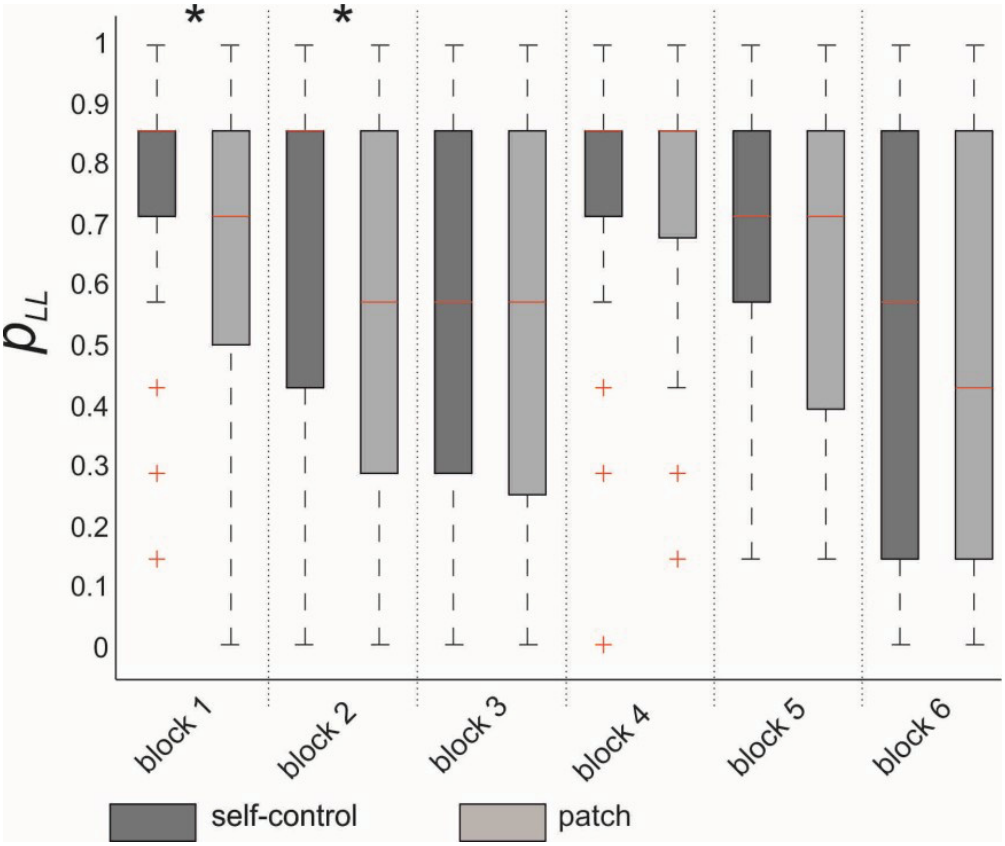

Figure 4.2 *Boxplots of the proportion of choices for the large reward (p_{LL}) in each blocks per condition.*

Accordingly, LTR-scores in the self-control and patch condition were not significantly correlated, r_s = .16, p = .156 (*table 4.4*), indicating that participants did not maximize long-term reward rate to the same extent across design conditions. These results suggest that, unlike in previous animal (Stephens & Anderson, 2001) and human experiments (Carter *et al.*, 2015), optimal decision-making was not restricted to a sequential patch design.

Hyperbolic discounting. *Table 4.4* shows the Spearman correlations of the estimated *k*-values with the rate maximization scores and total earnings between designs. Whereas LTR scores were positively correlated with *k*-values in the self-control condition, r_s = .23, p = .036, this was not the case in the patch condition, r_s =- .03, p = .790. This indicates that, although higher discount parameters *k* went

Table 4.3 *Summary of parameters for each decision model.*

	LTR scores[a]	***k[a]***	***AIC[a] reward rate (LTR)***	***AIC[a] hyperbolic discounting***
Self-control	.64 (.40-83)	.10 (.00-1.00)	21.78 (19.59 - 22.38)	22.62 (17.98-24.22)
Patch	.60 (.43-.90)	1.00 (.00-1.00)	21.95 (16.14 - 22.38)	23.75 (18.03-24.38)

a. median and range is shown due to violation of normality

along with higher LTR maximization in the self-control condition , implying that more impulsivity (the higher k, the stronger discounting) correlated with better long-term rate maximization, LTR maximizing scores in the patch condition were unrelated to discounting.

Table 4.4 additionally shows the Spearman correlations of *k*-values of the main task with *k*-values of Kirby's offline (binary) discounting task. The estimated *k*-values from Kirby's discounting task were positively correlated with the *k*-values in the self-control condition, r_s = .23, p = .041, but not with the *k*-values in the patch condition, r_s = -.07, p = .568. These results make sense considering the self-control design of Kirby's task and the fact that Kirby's task does not facilitate long-term considerations since the task structure lacks post-reward delays.

Earnings. The earnings within each design condition provide an indication of economic success. A Wilcoxon Signed Ranks test showed that earnings in the self-control condition (*Mdn* = 6.70, *range* = 5.50-7.20) were significantly higher compared to the earnings in the patch-condition (*Mdn* = 6.13, *range* = 5.15-6.65), Z = -7.65, p < .001, r = .60. Earnings were furthermore significantly correlated with LTR measures in both designs, but not with the hyperbolic discount parameter *k* (see *table 4.4*), suggesting that optimal choice behavior was rather reflected by long-term reward rate maximization than the hyperbolic discount rate.

Table 4.4 *Spearman correlations of hyperbolic discount rates with rate maximization scores and earnings.*

	Main task			***Kirby***	***Earnings***	
	$LTR_{self\text{-}control}$	LTR_{patch}	$k_{self\text{-}control}$	k_{Kirby}	*Self-control*	*Patch*
$k_{self\text{-}control}$	.23 (.036)*	.09 (.447)	-	.23 (.041)*	-.08 (.477)	.14 (.206)
k_{patch}	-.13 (.252)	.03 (.790)	-.30 (.007)**	-.07 (.568)	-.07 (.559)	-.15 (.182)
$LTR_{self\text{-}control}$	-	.16 (.156)	.23 (.036)*	-.01 (.962)	.36 (.001)**	.28 (.012)*
LTR_{patch}	.16 (.156)	-	.09 (.447)	-.22 (.045)*	.30 (.008) **	.64 (<.001)**

** p < .05*
*** p < .01*

4.4.4 Overall model comparison

To test whether the rate maximization model or the hyperbolic discounting model provided a better fit to overall choice behavior, data of both designs were pooled to compare AIC values of the rate and hyperbolic discounting model. A Wilcoxon Signed Ranks test indicated that AIC values were significantly lower for the LTR model (*Mdn* = 26.00, *range* = 23.21-26.54) compared to the hyperbolic discounting model (*Mdn* = 27.37, *range* = 20.58-28.54), $Z = -4.79$, $p < .001$, $r = .38$. Overall, the long-term rate maximizing model thus better represents the data than the hyperbolic discounting model.

4.4.5 Comparisons of model fits per condition

Table 4.3 shows the median and ranges of parameter *k*, as well as the AIC values for hyperbolic discounting and reward rate maximization in the self-control and patch conditions. There was no difference in AIC values between designs regarding LTR scores, $Z = -1.63$, $p = .104$, indicating that the rate maximization model did equally well in both designs.

Furthermore, in both designs the rate maximization model provided a significantly better fit than the hyperbolic discounting model: in both design conditions, AIC values for long-term rate maximization were significantly lower

than AIC values for the hyperbolic discounting model, *self-control:* Z = -3.43, p = .001, r = .27; *patch-design*: Z = -7.82, p < .001, r = .61.

4.5 Discussion

We examined whether participants maximize reward rate or hyperbolically discounted reward value in an experiential intertemporal decision making task. To this end we compared the goodness-of-fits of a rate maximization and a hyperbolic discounting model, using choice behavior in the 'classical' binary-choice self-control design as well as the putatively more ecologically valid patch design. Long-term rate (LTR) maximization scores were higher in the self-control condition compared to the patch-condition. When comparing rate maximization and hyperbolic discounting choice models, the LTR maximization model provided a better fit to the data than the hyperbolic discounting model in both the self-control and patch designs.

Hyperbolic discounting has become an important tool in describing intertemporal choice behavior (Frederick *et al.*, 2002; Peters & Buchel, 2011), in describing its neural correlates (Kable & Glimcher, 2007; Kalenscher & Pennartz, 2008), and in the assessment of aberrant intertemporal choice behavior in various disorders (Bickel *et al.*, 2012). However, our results show that human's intertemporal choices resemble LTR maximization more than hyperbolic discounting. Stephens *et al.* (2004) already indicated that delay discounting may not be required to explain impulsiveness in animals, suggesting that short-sighted rules (i.e. taking only pre-reward delays into account) explained choice behavior sufficiently well in a foreground-background choice context (i.e. a patch-design) and may be the cause of the high levels of impulsivity observed in self-control contexts.

This idea is in stark contrast to literally hundreds of studies referring to hyperbolic discounting in humans and animals to account for intertemporal choice behavior (Kalenscher & Pennartz, 2008). Why is hyperbolic discounting, which is often considered an irrational deviation from time-constant exponential discounting (Kalenscher & Pennartz, 2008) so widely assumed in intertemporal choice experiments? We suggest that one possible reason for its pervasiveness is that individuals may implement a decision rule that happens to produce choices that superficially appear to follow a hyperbolic discount function, but in reality maximizes reward rate. We will elaborate on this in the following.

They key point is that the so-called 'preference reversals' that have led to the adoption of hyperbolic discounting models over exponential discounting models, and which seems to suggest an irrational form of impulsivity, are in fact also predicted when maximizing reward rate. To explain this, we need to take a step back to normative economic theory, which states that rational decision makers discount delayed rewards in a constant, exponential fashion, which implies stable choice preferences over time (Samuelson, 1937). Time-consistent preferences can be epitomized by the stationarity axiom: when a subject prefers reward A at time t1 over reward B at time t2, she should also prefer reward A at t1+T over reward B at t2+T, that is, when a common interval T, i.e., a *front-end delay*, is added to both delays. For instance, if a decision maker prefers €10 today over €20 in six months, she should also prefer the €10-option if both alternatives were shifted into the future by one year (€10 in one year versus €20 in one year and six months).

When humans or non-human animals make intertemporal decisions between smaller/sooner and larger/later rewards, they often reverse their preference when front-end delays are added or subtracted from a choice set (Green *et al.*, 1994a; Kirby & Herrnstein, 1995). For example, even though an individual may prefer €10 now over €20 in six months, she may prefer 20€ in 1.5 years over €10

in one year. Preference reversals suggest that individuals attach disproportionally large weights to short-term outcomes (Thaler, 1981; Benzion *et al.*, 1989). This 'present-bias' (also known as common difference effects or immediacy effects) can be better described by a hyperbolic than an exponential discount function (Mazur, 1984; Mazur, 1987; Kalenscher & Pennartz, 2008). Present-bias and immediacy effects are ubiquitous, yet they are anomalies in choice because they cause violations of the stationarity axiom and, thus, go along with time-inconsistent preferences. By consequence, from a normative economic perspective, they ultimately result in the tendency to act against one's own future interest.

The pervasiveness of present bias, time-inconsistent preferences and preference reversals is perplexing for economists, psychologists and behavioral ecologists alike: what is the adaptive value of a choice pattern that so obviously creates non-optimal results? One possible answer to this puzzle is, hence, that natural selection has favored a decision rule that produces time-inconsistent preferences, and thus resembles hyperbolic discounting, because an individual implementing such a decision rule maximizes a different currency than economic utility.

Long-term energy rate maximization could be this currency. Consider the following example. An animal chooses between option A: 2 food-items in 2 seconds (rate: 1 item/s) and B: 4 items in 8 seconds (rate: 0.5 items/s). The rate maximization principle would prescribe choosing option A because of its higher energy rate. If both outcomes were then shifted in time by 10s, the alternatives would now yield A': 2 food-items in 10+2 seconds (rate: 0.17 items/s) and B': 4 items in 10+8 seconds (rate: 0.22 items/s). Discounted utility theory in economics prescribes that a rational agent should meet the stationarity axiom and choose option A' since she preferred option A before. However, option B' yields a higher

energy rate, therefore optimal foraging theory would predict a preference reversal, thus preference for B' over A'. Hence, rate maximization could only be achieved by a decision rule allowing for time-inconsistent preference reversals.

To understand why this example is not merely a special case, but illustrates a systematic, general requisite for preference reversals, one has to realize that energy rate does not drop at a constant rate with increasing delays, but in a hyperbolic fashion (see *figure 4.3*). By consequence, an optimal decision rule

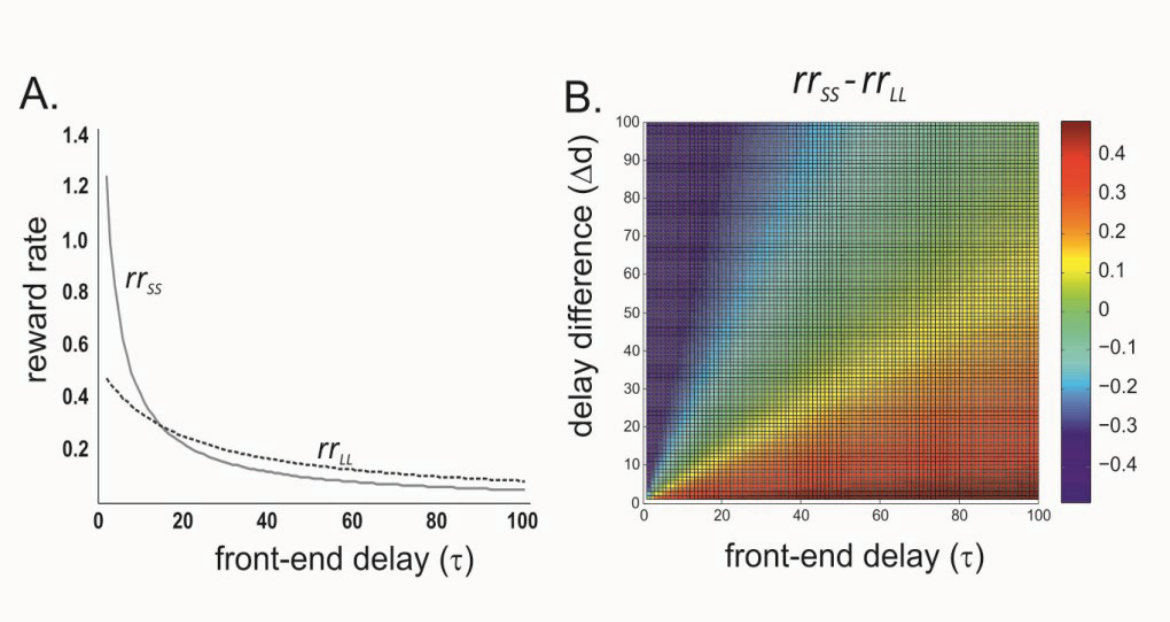

Figure 4.3 A. *Development of reward rates (rr) of a smaller, sooner and a larger, later reward with increasing front-end delay, for $rr_{SS} > rr_{LL}$ at τ=0. Reward rate decreases hyperbolically across front-end delays. Given the hyperbolic nature of the asymptotes, rr_{SS} and rr_{LL} cross over, implying optimal choice of smaller, sooner rewards left of the cross-over point, and larger, later rewards right of the cross-over point.* ***B.*** *Heat plot indicating the difference in reward rate (rr_{SS} - rr_{LL}) at a range of delay differences and front-end delays, when the large to small reward ratio is .5. The heat plot indicates that the rate difference (in color) is determined by a linear relationship between front-end delay τ and delay difference Δd. For any delay difference Δd there is a front-end delay τ at which the rate difference rr_{SS} - rr_{LL} is 0.*

should allow for preference reversals in order to maximize energy rate in any choice situation with variably delayed outcomes. Or, in other words, to make optimal choices, a forager would have to do the very thing that economists stigmatize as irrational: show time-inconsistent preference reversals; were we the time-constant discounters prescribed by economic theory, we would systematically fail to maximize energy rate when front-end delays were added to a binary choice set.

Hence, preference reversals – the hallmark of hyperbolic discounting – are adaptive. But our results showed that rate maximization, and *not* hyperbolic discounting, described our participants' choice data best. How can we reconcile this seeming logical inconsistency? We argue that, because of the hyperbolic decay of energy rate over time, a decision maker maximizing energy rate will, most of the time, appear as if she was showing hyperbolic discounting although the real currency maximized is reward rate instead of discounted value. The true nature of the currency maximized may surface only in special cases, such as the current design with its particular parameters. Hyperbolic discounting, thus, still has high descriptive and heuristic value, but it is possible that choices are not the over revelation of a covert, internally represented hyperbolic discount function, but reflect rate maximization efforts instead.

Our results are in seemingly partial disagreement with previous findings. Notably, in contrast to earlier results (Stephens & Anderson, 2001; Carter *et al.*, 2015), we could not replicate a patch effect as participants maximized LTR more often in the self-control than the patch design, also reflected by higher earnings in the self-control condition compared to the patch condition.

Carter et al. (2015) suggested that different cognitive mechanisms may underlie choices in the patch and self-control conditions, which could have led to the patch-effect. However, our results suggest otherwise: in both design

conditions, the LTR maximization model provides the best fit with the data. Furthermore, the estimated hyperbolic discount rates (represented by parameter *k*) in both design conditions were positively correlated, and discount rates in the self-control condition also correlated with discount rates in the often used hypothetical discounting task (Kirby's discounting task). This hints at similar, possibly identical cognitive mechanisms in all three intertemporal choice contexts.

Why did we find evidence in favor of a single cognitive mechanism underlying choices in the patch and the self-control design, while Carter et al. (2015) suggested different mechanisms? The main difference between the studies is that we, in contrast to Carter et al. (2015), used a full within-subject design: while, in our experiment, all participants experienced all task manipulations, Carter and colleagues randomly assigned participants to the different ITI-, short- and long-delay conditions. Intertemporal choice patterns are known to be strongly modulated by the range of delays and reward magnitudes used in a given task (Read, 2001). Hence, the most parsimonious explanation for the discrepancy in results is that the inference of the cognitive mechanism underlying a revealed choice pattern depends on whether the data pool comprises observations from individuals who observe the full set of parameter manipulations, or only subsets of it. Future studies need to directly compare results from within-subject and between-subject designs.

In summary, we found evidence in favor of a long-term reward rate maximization over a hyperbolic discounting account of human intertemporal choice behavior in an experiential choice task. We argue that natural selection may have favored the evolution of a decision rule supporting long-term energy rate maximization that allows preference reversals over timed outcomes because time-constant discounting would result in a systematic violation of optimization principles. Crucially, while the time-inconsistent preference pattern produced by

the underlying decision rule seemingly resembles hyperbolic discounting, our data support the idea that the currency maximized in intertemporal choice is *not* discounted value, but long-term energy rate. It is perhaps noteworthy that, in contrast to previous literature, we did not find an improvement in long-term rate maximization by implementing a 'patch' design, which could be due to differences in levels of impulsiveness between our sample and samples in previous studies. Further studies should focus on how reward rate maximization may be expressed in different intertemporal choice task designs as well as in different species. For example, a study design that allows for discounters with specific discount rates to reveal a patch-effect could explain why our results differ from the results of Carter *et al.* (2015).

5. General discussion

"Nothing in the world is worth having or worth doing unless it means effort, pain, difficulty…"

- Theodore Roosevelt

In this discussion I will shortly summarize the results and conclusions of each of the studies presented in the previous three chapters, followed by a discussion of the used task and choice context, the contributions to the neuroscience of intertemporal choice and lastly, a summary of the final conclusions.

5.1 Summary of main results

In *Chapter 2* we investigated the relationship between episodic memory performance and delay discounting in older adults. Factors such as a variable episodic memory performance (and hence impaired episodic future thinking) may have caused the conflicting results reported in the literature regarding the relationship of age and delay discounting in older aged adults. We did not find the expected positive correlation of episodic memory and more patient decision making, but we found a rather interesting gender effect. In men, higher memory scores for autobiographical facts and dates were related to lower delay discounting rates, whereas in women higher autobiographical memory score were related to higher discounting rates. This gender interaction regarding autobiographical facts and dates was linked to the general discounting rate (k) as well as present-bias (β), and a similar gender-interaction was found for autobiographical events and patience (δ). Speculatively, this result might have been due to gender differences in cognitive strategies during the delay

discounting task, with men and women being less and more sensitive to the temporal information presented in the discounting task, respectively, when they also performed high on autobiographical memory recall. Our findings also support the idea that semantic memory (or semantic future thinking) may play an important role in delay discounting (Kwan *et al.*, 2015).

In *Chapter 3* we investigated whether DBS of the STN in patients with Parkinson's disease would affect intertemporal decision making. We tested 40 patients either on- or off-DBS, but found no difference in intertemporal choice behavior between conditions. It thus seems that STN-DBS does not affect impulsive choice behavior in PD patients. However, we cannot completely exclude the potential existence of small effects of STN-DBS on delay discounting, and further studies should investigate the effects of chronic stimulation on impulsive decision making.

In *Chapter 4* we asked whether humans maximize reward rate or economic utility (discounted value) when making decisions on an experiential intertemporal choice task. The rate maximization model provided a better fit to the choice data of 81 young adults than the hyperbolic discounting model, suggesting we maximize reward rate. Further studies should investigate whether this is true in different choice contexts, e.g. with different paradigms and population samples.

5.2 Task and choice context

5.2.1 From discounting in the lab to real-life intertemporal choice

The three studies presented in this dissertation are rather different in terms of research question and target population, but with a common theme: intertemporal decision making. In the first two studies we chose to use a 'classical' delay discounting task, with two mutually exclusive choice options presented simultaneously and delays in the range of months, to obtain discounting measures

of the participants. As mentioned in the introduction, this way of measuring intertemporal choice behavior has proven sensitive to specific manipulations, states and traits, as well as specific disorders. However, it is important to note that the outcomes also partially depend on the specific way in which intertemporal choices are presented in the task.

Choice context and framing effects

Money is often used as reinforcer in discounting experiments. However, the discount rate of money is not always indicative of how we make intertemporal choices involving other types of rewards, such as food or cigarettes (Odum & Rainaud, 2003; Mitchell, 2004; Odum *et al.*, 2006). Several studies show that discount rates for monetary rewards and liquid rewards differ, with liquid rewards being discounted more steeply than monetary rewards (Jimura *et al.*, 2009; Jimura *et al.*, 2011). Furthermore, Jimura *et al.* (2009) found that discount rates of liquid rewards and monetary rewards were not correlated within individuals. These studies show that discount rates are stable over time, but domain specific. A person discounting steeply in one domain, might not do so in another. This also counts for gains vs. loss discounting (the sign effect; Thaler, 1981), with discount rates being higher for gains.

Furthermore, a *magnitude effect* on discounting has been reported in several studies (Thaler, 1981; Benzion *et al.*, 1989; Raineri & Rachlin, 1993; Green *et al.*, 1994b; Myerson & Green, 1995; Kirby & Marakovic, 1996; Green *et al.*, 1997; Kirby, 1997; Johnson & Bickel, 2002), with larger monetary amounts being discounted less than smaller amounts. A similar magnitude effect has been observed for other commodities, such as health or career options (Raineri & Rachlin, 1993; Chapman & Elstein, 1995; Chapman, 1996; Baker *et al.*, 2003; Schoenfelder & Hantula, 2003).

With regard to the temporal aspect, one could use various different time ranges, from seconds or minutes to days, months, or even years. Studies using calendar dates instead of a more neutral indication (e.g. 'in three months') found less steep discounting as a result (Read *et al.*, 2005; LeBoeuf, 2006). In many studies delays are hypothetical and not experienced before the next choice is made. However, experiencing delays might change subsequent choices due to feedback mechanisms. Several studies have used contingent procedures in which participants experienced the delays and the subsequent reward delivery (Lane *et al.*, 2003; Smits *et al.*, 2013). Lane *et al.* (2003) found no difference in *k*-values and *AUC* values between a hypothetical and contingent procedure, although some participants showed no discounting at all in the contingent procedure.

Payment procedures may also affect choice behavior. To incentivize participants when delays are not directly experienced and rewards not directly obtained, one of their choices is often randomly selected and reimbursed after the selected delay. This would provide participants with the motivation to choose in accordance with their true preference in each trial, although several studies have shown that discount rates were similar for real and hypothetical reinforcers (Johnson & Bickel, 2002; Baker *et al.*, 2003; Madden *et al.*, 2003; Madden *et al.*, 2004; Johnson *et al.*, 2007; Bickel *et al.*, 2009).

Often when intertemporal choices are presented to us, we do not explicitly consider the consequences of each option now and in the future and ignore *opportunity costs* (Read *et al.*, 2013; Zhao *et al.*, 2015). The *opportunity cost* of a choice is the value of the option foregone and occurs when choice options are mutually exclusive. For example, a smaller sum obtained now could be more valuable than the delayed alternative if interest rates are high enough. Similarly, advertisements for specific products make us consider the immediate benefits of these products. When we decide to buy such a product, we may not consciously

consider the consequence of that choice at a later point in time (i.e. less or no money later for something else we would like to buy). One study investigated this 'effect of hidden zeros' by presenting each choice option as a sequence, e.g. $5 today and $0 in 26 days versus $0 today and $6.20 in 26 days (Magen *et al.*, 2008). This resulted in a significant reduction in impulsive choices compared to the condition in which the same options were presented without the zeros. We might not always be able to imagine the long-term consequences of choosing a smaller, sooner reward or have an explicit long-term goal in mind, but this study on the *hidden-zero effect* illustrates that this might influence our choice behavior in a beneficial way.

Thus, discount rates are dependent on the specific framing of the task, i.e. the type of reinforcement, magnitude, scale and implicit/explicit information provided.

Discounting (hypothetical) monetary sums and real-life decision making

To what extent does choice behavior on a classical delay discounting task, used in the studies presented in *Chapter 2* and *3*, reflect our intertemporal decision making in real life? Fisher (1930) proposed that, from an economic perspective, when credit and investment opportunities are available, individuals should discount monetary rewards at the market interest rate. One might prefer a smaller monetary amount now over a larger sum later because, with interest, this amount obtained now would be worth as much as (or more than) the larger, more delayed option. However, discounting rates have been found to be several times higher than the market interest rate (Frederick *et al.*, 2002; Soman *et al.*, 2005), indicating that individuals more often choose smaller sooner options, even though they would be worth less in the future than the foregone larger, later reward. These relatively high discounting rates found could not be due to experimental

settings, as field studies investigating consumer choice of specific products with different prices and long-term costs also found discounting rates far exceeding market interest rates (see Frederick *et al.*, 2002).

Another study investigating the real-life choice 60.000 U.S. military servicemen had to make, showed that most participants preferred receiving one lump-sum payment now over a yearly sum that would yield 17.5% more, while the interest rate was only 7% (Warner & Pleeter, 2001). Furthermore, high discounting rates were also observed for high-stakes real monetary choices made by rural villagers in Vietnam (Tanaka *et al.*, 2010) as well as Bolivian villagers (Kirby *et al.*, 2002). Thus, relatively high discounting rates are not only observed in delay discounting paradigms in the laboratory, but also in real-life decision making, at least when monetary outcomes are involved. In addition, the hyperbolic or quasi-hyperbolic form of discounting, observed with experimental (delay discounting) paradigms, is also compatible with real-life behavior, e.g. consumption patterns (Bernheim *et al.*, 2001) and savings behavior (Laibson, 1997; Bernheim & Rangel, 2007).

On individual level, Chabris *et al.* (2008) found that discount rates as measured with Kirby's discounting task (Kirby *et al.*, 1999) correlated weakly with field behaviors including smoking, exercise, nutrition and wealth, although an aggregate index of these field behaviors showed a stronger correlation with individual discounting levels. However, individual discount rates were found to be the most important variable - among factors such as age, education and cognitive ability - to influence these field behaviors (Chabris *et al.*, 2008).

These findings indicate that, at least in similar choice contexts (e.g. involving monetary reinforcement), performance on the often used delay discounting paradigms likely reflects real-life intertemporal choice behavior.

5.2.2 Intertemporal choice, impulsivity and self-control

Can we generalize our findings to all real-life intertemporal choice behavior? Different measures of intertemporal choice do not always correlate with each other (e.g. Lane *et al.*, 2003). We have seen in *Chapter 4* that discount rates of Kirby's discounting task were positively related with discount rates in the self-control condition of the experiential choice task. However, these discount rates did not correlate with self-reported measures or impulsiveness (Kirby's *k* and *BIS* total scores: r_s = .16, p = .177) or delay aversion/discounting (Kirby's *k* and *QDQ-delay aversion* scores: r_s = .01, p = .918; Kirby's *k* and *QDQ-delay discounting* scores: r_s = .19, p = .099). Correlations of discount rates and self-reported impulsivity measures reported in the literature are usually limited to subscales and are inconsistent (Reynolds *et al.*, 2004a; de Wit *et al.*, 2007). Correlations likely also depend on the task structure and context. Behavior on a delay discounting task may therefore only partly reflect impulsive choice behavior.

In *Chapter 4* the term 'self-control' was linked to the binary, non-sequential task design with two mutually exclusive rewards (e.g. the classical delay discounting task). As mentioned in the introduction, the concept *self-control* is often used to indicate refraining from taking an *immediately available* reward in favor of a long-term more profitable reward. A *self-control* task in which participants need to refrain from responding to tempting immediately available rewards to obtain a larger reward (generally referred to as a delay-of-gratification paradigm), like the marshmallow task, might therefore yield a different impulsivity level than the classical delay discounting task. For example, one can imagine that for a person who wants to lose weight, choosing between a chocolate pie now or the loss of a few kilograms in a week would be more difficult if that delicious pie is already placed in front of him/her. In such situations the magnitude and delay of the larger, later reward is unclear, which is also the case in delay-of-gratification

tasks. Such a task is therefore more realistic with regard to some specific real-life intertemporal choice situations. A delay-of-gratification task likely requires more cognitive control than the classical discounting task and thus related brain areas may be differentially engaged in these tasks (Reynolds & Schiffbauer, 2005; Casey *et al.*, 2011).

In real-life we might experience a binary choice situation more often when making financial decisions and more often encounter temptations with primary reinforcers, such as food or clothes. As mentioned above, different reward types or domains also yield non-correlating discounting rates. Indeed, monetary and food rewards have been shown to differentially activate reward related brain areas, such as the medial and lateral OFC, vmPFC and parietal cortex (Simon *et al.*, 2015). We can therefore not simply generalize impulsive choice levels measured with monetary reinforcement using a classical delay discounting task to real life decision making involving different intertemporal choice context and types of rewards.

The classical delay discounting paradigm used in *Chapter 2* and *3* also does not include experiencing the delays before subsequent choices are made. In *Chapter 2* we saw that memory for autobiographical facts and dates was related to discounting behavior. In the study presented in *Chapter 3* we investigated the effect of STN-DBS in Parkinson patients on delay discounting using monetary rewards. Most Parkinson patients receiving DBS can be considered 'older-adults' (the average age of PD diagnosis is 60 years) for which it has been hypothesized that their discounting pattern has become less impatient due to experience (e.g. Green *et al.*, 1994b; Samanez-Larkin *et al.*, 2011). This may have been one of the reasons why we did not find an effect of stimulation on discounting, as the patients might have used their lifetime experience to make their choices, which would depend more on memory processes rather than the current DBS-state (i.e.

either on- or off-DBS) of the patient. Memory impairments have also been found after STN-DBS onset (see Moberg *et al.*, 2007), however, differences in memory performance might not be visible after a short period off- stimulation.

A paradigm in which task performance is less dependent on memory and more on the current DBS-state of the patient (e.g. when delays are experienced, or with direct reward feedback or consumption) might reveal very specific effects of STN-DBS on impulsive decision making. Furthermore, a delay-of-gratification task may uncover issues with *self-control* or willpower, which could underlie the impulsivity issues after DBS-onset, such as ICD development or worsening (e.g. Broen *et al.*, 2011). As impulsive decision making comprises several facets that might be separately affected (e.g. delay sensitivity, reward sensitivity, self-control or risk assessment), it is important to use several distinct tasks before general conclusions can be drawn about the effect of a specific treatment or state on intertemporal choice behavior in general.

For example, one could use the multiplicative hyperbolic model developed by Ho *et al.* (1999) to distinguish between delay and reward sensitivity, using a model that combines the hyperbolic delay discounting function (equation 1.1) with a hyperbolic function that translates the objective reward magnitude into a subjective reward magnitude or quantity, depending on magnitude discounting parameter *Q*. This requires a specific design in which both variations of reward magnitude and delay are sufficiently implemented to be able to obtain a reliable *Q* as well as *k* (i.e. by obtaining the discount functions for a sufficient amount of reward magnitudes). Alternatively, one can use the Cambridge Gamble Tasks (CGT; Rogers *et al.*, 1999), which combines waiting for a good bet with a certain risk factor of having made the correct choice, and can thus be used to measure both delay aversion and risk-taking. Thus, the use of different types of impulsive choice measures (hypothetical and experiential, with different types of rewards,

and different choice structures) should be used to get a clear picture of which aspect(s) playing a role in intertemporal decision making is/are affected.

5.2.3 Timing effects on discounting behavior

Not only the specific task, but also the timing of the experiment influences intertemporal choice behavior. In the case of STN-DBS as treatment of Parkinson's disease, the timing of testing may be relevant for observing potential changes in impulsive choice behavior. Several studies on the development of ICDs after DBS onset mention that the disorders appeared after a few months and were transient, resolving within a year (Smeding *et al.*, 2007; Lim *et al.*, 2009), although not in all cases the ICDs resolve within a year (e.g. Halbig *et al.*, 2009). Changes in the brain occurring within several months after DBS onset might lead to aberrant impulsive choice behavior or self-control, which may (or may not) be compensated by other structures/processes later. Investigating choice behavior in specific time periods after DBS onset (e.g. within the first month, after three months and after a year) could therefore reveal differential patterns in choice behavior that may be very informative with regard to the development of cognitive/impulsive side effects of STN-DBS. The stimulation duration differences in our patient sample could thus be another potential reason for the lack of an effect in our study.

Timing may not only be relevant in studies of specific treatment effects on delay discounting, but could be a general factor influencing intertemporal choice on a daily basis. It has been argued that self-control required to pursue a long-term goal relies on a limited cognitive resource that, when used, is depleted over time (Muraven & Baumeister, 2000). However, more recent studies show that self-control exhibition does not necessarily depend on a limited resource, but rather motivational and attention processes (Inzlicht & Schmeichel, 2012; Inzlicht *et al.*, 2014). Regardless of the underlying mechanism, behavior reflecting self-

control has thus been found to decline over time, which could lead to more self-controlled intertemporal choice behavior in the morning compared to the evening.

5.3 Contributions to the neuroscience of intertemporal decision making

The memory study presented in *Chapter 2* has provided insight into the role of the hippocampus in intertemporal choice. Our results, together with Palombo *et al.* (2014)'s study with amnesic patients, indicate that when episodic future thinking is not triggered, there seems to be no relationship between episodic memory functioning and delay discounting. This further indicates that the mOFC, whose functional connectivity with the hippocampus was found to be related to influences of prospection on intertemporal choice (Peters & Buchel, 2010a), is not only involved in episodic prospection when making intertemporal decisions (Peters, 2011), but has a more general role in valuation processes.

The fact that semantic memory does not decline with age as much as episodic memory suggests that the found interaction of gender, personal semantics and delay discounting may be age-independent. Whether semantic memory is generally triggered when making intertemporal choice requires further study, although several areas linked to the autobiographical network are also known to be involved in intertemporal choice, such as the mPFC and the cingulate cortex (Kalenscher & Pennartz, 2008; Schmaal *et al.*, 2012). A recent study by Compere *et al.* (2016) shows differential brain activity in the dorsal anterior cingulate cortex (dACC), the inferior parietal gyrus and the precentral gyrus in men and women when recalling semantic autobiographical memories, but not when recalling episodic autobiographical memories, although the authors found no difference in

behavior and brain activity was not linked to individual performances. This finding supports the idea of differential cognitive processes being engaged by men and women with regard to semantic autobiographical memories, which could also be involved in intertemporal choice.

While we found that the semantic memory network may influence the valuation during intertemporal choice, it remains less clear what is the exact function of the STN in valuation and choice processes. Recent evidence confirms the role of the STN in high conflict situations (Zavala *et al.*, 2016) and impulsive action (Pote *et al.*, 2016). Direct electrophysiological evidence was provided of threshold mediation by the STN during a perceptual decision task (Herz *et al.*, 2016), which was found to be dependent on the level of cautiousness, and possibly mediated by communication between the STN and mPFC. Whereas this study implicates low frequency field potentials (2-8 Hz) in the STN in decision threshold mediation, Zenon *et al.* (2016) found that STN low frequency oscillations (1-10 Hz) in a task involving reward-effort weighing actually reflected subjective cost-benefit comparisons predictive of participants' subsequent decisions. Both electrophysiology studies were performed with Parkinson patients. An fMRI study with healthy individuals performing a sequential gambling task found the STN to be one of the structures involved in computing the trade-off between reward and risk (Meder *et al.*, 2016). These recent findings seem to confirm the involvement of the STN in both motor impulsivity and value-based decision making.

Interestingly, the tasks used in the latter studies had a clear self-control context, such as deciding to continue or stop in the sequential gambling task used by Meder *et al.* (2016), or whether or not to withhold a response in the effort task used by Zenon *et al.* (2016), in which consequences of the choices were immediately experienced during the task. Together with our no-results involving a

delay discounting paradigm, these findings indicate that involvement of the STN in value-based decision making - and thus intertemporal choice - may depend on the specific circumstances in which the decisions are made, in particular when the required response is closely related to a conflicting choice situation, when response inhibition plays a role, and possibly also when response time is limited.

5.4 Conclusions

The research presented in this thesis are an important step toward understanding how intertemporal decisions are made in specific relevant contexts.

- Not episodic memory in general, but semantic (autobiographical) memory may be an important factor determining intertemporal choice behavior.
- Gender may interact with factors such as memory performance to determine choice behavior.
- STN-DBS treatment for Parkinson's disease does not seem to affect intertemporal choice behavior.
- The STN is likely not directly involved in the valuation of choice options when making intertemporal decisions.
- Our intertemporal choice behavior may be fundamentally shaped by efforts to maximize reward rate, which may have resulted in the choice patterns well described with hyperbolic discounting models.

Glossary

accumulator (area) - a brain area involved in the integration of value signals over time and the comparison of accumulated value signals for subsequent choice (*p. 19*)

common difference effect - the switch of preference from the smaller, sooner to the larger later reward, observed when a certain delay is added to both options (see *front-end delay*) (*p. 8*)

decision value - the resulting *subjective value* of an option when benefits and costs are integrated (*p.20*)

delay discounting - reduction of the *subjective value* of a reward due to its delayed delivery (*p. 4*)

discount rate - the steepness with which a reward loses its value when the time until delivery increases. On a discounting curve this is the negative slope at a certain delay. When one refers to the *k-value* as discount rate, the average discount rate (across the curve) is implied (*p. 4*)

discounted value - the resulting *subjective value* of a rewarding choice option when delay and reward value are integrated (*p. 20*)

front-end delay - the delay that a sooner reward and a later reward have in common (i.e. the delay to the choice option with the shortest delay in a choice set) (*p. 8*)

hidden-zero effect - the reduction in discount rate observed when the otherwise not mentioned (immediate and delayed) consequences of each option are made explicit, described by Magen *et al.* (2008) (*p. 124*)

immediacy effect - a relatively steeper decline in subjective value of a reward when that reward is not available immediately but delayed by relatively short time periods (i.e. relatively high *discount rates* observed at shorter delays) compared to a more shallow decline in subjective value (i.e. smaller *discount rates*) when delay increases further (see also present-bias). This indicates that a high value is placed on the immediate availability of rewards (*p. 6*)

impulse control disorder (ICD) - a disorder characterized by *impulsive behavior* that is harmful to the person or others, such as pathological gambling or compulsive shopping (*p. 2*)

impulsive action / motor impulsivity - premature responding to an internal or external cue, and the opposite of response inhibition, which refers to the ability to prevent or stop a (prepotent) response (*p. 17*)

impulsive behavior / impulsivity - a multifaceted construct that encompasses all behavior that is premature and seemingly without forethought. It includes *impulsive action* and *impulsive choice*, but several more types of impulsivity have been identified (Evenden, 1999) (*p.16*)

impulsive choice - choosing in favor of more immediate gratification at the cost of potential larger benefits in the future due to a lack of premeditation or delay aversion (*p. 16*)

indifference point / indifference value - the delay (or reward) at which the discounted value of a reward equals the (discounted) value of another reward.

Indifference points are frequently used to plot discount curves and acquire discount rates (*p. 10*)

k-value/parameter - the parameter of Mazur (1984)'s hyperbolic discount function that reflects the average discount rate and is often used to compare individual and population discount rates (*p. 7*)

magnitude effect - the finding that larger sums of monetary rewards are discounted less steeply than smaller sums when their delivery is delayed (*p.13*)

opportunity cost - the value of the option foregone when options are mutually exclusive (*p. 123*)

present-bias - the relatively high value that is placed on immediate rewards, resulting in a steeper decline in subjective value of a reward when that reward is not available immediately but delayed by short time periods, compared to its decline in value after larger delays (see also *immediacy-effect*) (*p. 8*)

self-control - the ability to resist immediate gratification when confronted with an immediate reward in favor of long-term more optimal outcome / goal (*p. 15*)

subjective value - the value one attached to a specific reward, which is based on personal preferences (*p. 4*)

transitivity of preference - the independent valuation of options such that they can be ordered from most to least preferred, which does not depend on the other options available (*p. 12*)

value-based decision making - decisions based on personal preferences and not on perceptual or otherwise deterministic criteria (*p. 19*)

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Appendix A - Supplemental information Chapter 2

S1 Text

Methods

In addition to the intertemporal choice models mentioned in the main text, we used additional models to characterize our participants' choices. To obtain a model free measure of discounting, the total number of choices for the smaller, sooner reward (not including the catch trials) made by each participant within one session was counted as the *number of impulsive choices (NImp)*.

Choice data of blocks 5 and 6 were used to calculate model-free measures of present-bias. Individual IPs of block 5 (*6 months vs. 9 months*) were divided by the IPs of block 1 (*tomorrow vs. 3 months*) and referred to as Present-Bias 3 months (PB-3). Similarly, the IPs of block 6 (*6 months vs. 12 months*) were divided by the IPs of block 2 (*tomorrow vs. 6 months*) and referred to as Present-Bias 6 months (PB-6). As the relative delay difference between the two rewards is the same in blocks 1 and 5 as well as in blocks 2 and 6, their ratios, PB-3 and PB-6, provide a measure of how much temporal proximity itself is valued.

Results

Regression. *Table S1* shows the results of regression analyses using the three model-free discounting measures. Again three different models were analyzed. In line with the results regarding hyperbolic discounting parameter *k*, there was no significant effect of any of the memory scores on the overall discounting measure *NImp*, whereas the predictors *income* as well as the interaction between *gender* and *IGD-C2* were significant in further models.

In addition, results of the regression analyses with *PB-3* as dependent variable reflected findings with regard to present-bias parameter β. Although there was no

significant contribution of *income*, we again observed a significant contribution of the interaction term *gender*IGD-C2* on *PB-3*. No measure significantly predicted *PB-6*.

Table S1. *Relationship of memory scores, moderator variables and gender x memory interactions on model-free discounting measures.*

	NImp			**PB-3**			**PB-6**		
Model	*(1)*	*(2)*	*(3)*	*(1)*	*(2)*	*(3)*	*(1)*	*(2)*	*(3)*
FNPA-PF	-.065 (.652)	-.090 (.578)	.183 (.678)	.080 (.575)	.040 (.822)	-.304 (.538)	-.142 (.308)	-.278 (.107)	.068 (.891)
IGD-C1	.390 (.698)	.043 (.758)	-.300 (.467)	-.028 (.844)	-.013 (.931)	-.336 (.464)	.180 (.200)	.174 (.229)	-.365 (.431)
IGD-C2	.030 (.840)	.035 (.804)	-1.007 (.016)	.026 (.862)	.011 (.944)	-.888 (.055)	.136 (.343)	.095 (.518)	-.209 (.647)
Gender		.008 (.963)	.015 (.926)		-.097 (.610)	-.111 (.544)		.093 (.611)	.101 (.581)
Age		.191 (.163)	.195 (.136)		-.131 (.379)	-.094 (.517)		-.161 (.263)	-.162 (.270)
Income		-.390 (.010)*	-.338 (.019)*		-.232 (.151)	-.176 (.263)		-.181 (.244)	-.132 (.404)
IQ		-.034 (.808)	-.043 (.753)		-.013 (.931)	-.016 (.914)		.044 (.768)	.072 (.640)
Gender*FNPA-PF			-.292 (.503)			.359 (.462)			-.395 (.423)
Gender*IGD-C1			.443 (.275)			.400 (.377)			.597 (.193)
Gender*IGD-C2			1.112 (.007)**			.973 (.031)*			.347 (.437)
F Statistic (df)	*.121 (3,54)*	*1.908(7, 50)*	*2.589 (10,47)*	*.143(3,54)*	*.441 (7,50)*	*1.156 (10,47)*	*1.249 (3,54)*	*1.049 (7,50)*	*1.048 (10,47)*
R^2	*.007*	*.211*	*.355*	*.008*	*.058*	*.197*	*.065*	*.128*	*.182*
Adjusted R^2	*-.048*	*.100*	*.218*	*-.047*	*-.074*	*.027*	*.013*	*.006*	*.008*
p-value	*.947*	*.088*	*.014**	*.934*	*.872*	*.343*	*.301*	*.410*	*.420*

Each column represents one OLS regression. Dependent variables are shown in the column titles. Each row represents one predictor variable or statistics of the regression model. Cells show regression coefficients (beta) and p-values in brackets or model statistics.

** p < .05*

*** p < .01*

Table S2. *Correlations of the different episodic memory tasks.*

		IGD-C1	IGD-C2
FNPA-Performance	**All participants**	.160 (.231)	.324 (.013)*
	Males	.013 (.948)	.216 (.269)
	Females	.132 (.488)	.157 (.409)
IGD-C2	**All participants**	.186 (.162)	
	Males	.387 (.042)	
	Females	-.009 (.964)	

Correlation coefficients and p-values (in brackets) are reported.
All p-values are two-tailed.
** $p < .025$*

Correlations. *Table S2* shows correlations between scores of the different memory tasks. A significant positive correlation was found between FNPA-PF scores and IGD-C2 scores on group level, $r = .324$, $p = .013 < \alpha = .025$, $r^2 = 0.10$, which is somewhat surprising considering the more semantic nature of the IGD-C2 task, but does suggest a relationship between these measures. Additionally, a correlation was found between IGD-C1 and IGD-C2 scores for men, $r = .387$, $p = .042 > \alpha = .025$, $r^2 = 0.15$, however, this correlation was not significant after correction for multiple comparisons.

Appendix B - Supplemental information Chapter 4

S1 Text.

Methods

Time production. To measure personal perception of time, we additionally tested subjects in a short time production task. Participants had to press the space key for 5, 10, 20 and 30 seconds. At the beginning of each trial, participants were instructed about the to-be-estimated time interval and then saw a grey square in the middle of the screen. Once the grey square turned green, they were to press the space bar for the duration indicated on screen. Participants were not informed about the time elapsed and had to internally produce the time interval duration. While the space bar was held, the square turned yellow and remained yellow until the space bar was released. Once they let go of the space bar, the square turned grey again and a new trial started. No feedback regarding their timing was given at any time during the task.

Barratt Impulsiveness Scale (BIS). We used the short German version of the BIS (BIS-15) (Spinella, 2007) as a self-reported baseline measure of impulsivity. Fifteen items assess either non-planning (BIS-NP), motor (BIS-M) or attention (BIS-A) impulsivity (Spinella, 2007). Each item is rated on a 4-point-Likert scale.

Quick Delay Questionnaire (QDQ). The QDQ was administered to assess baseline self-reported subjective delay aversion and delay discounting (Clare *et al.*, 2010). The subjects have to rate five items on delay aversion (QDQ-DA) and five items on delay discounting (QDQ-DD) on a 5-point-Likert scale.

Results

Impulsivity questionnaires. *Table S1* shows Spearman correlations of the k-values and LTR-scores per design condition with the scores on the QDQ and BIS.

Self-reported impulsivity did not correlate with any of the LTR/discounting measures, *all* $r_s < .12$, *all* $p > .309$. Regarding the QDQ, only in the patch design we found a significant negative correlation of k-values and LTR-scores with QDQ scores, in particular with the delay-discounting subscores. Why lower k scores, and thus relatively lower discounting in the patch task resulted in higher self-reported delay discounting is unclear, although the k-estimates of the patch task may have little predictive power with regard to (self-reported) impulsiveness, due to its design (k-values do not have predictive power with regard to the optimal choice pattern, see *table S2*). In addition, higher self-reported delay aversion, was found to be negatively correlated with LTR scores in the patch-condition, indicating that higher levels of self-reported delay aversion were related to lower LTR scores in the patch design.

Time production. *Table S2* shows Spearman correlations of time production scores of each interval with the k-values and LTR-scores. There were no significant correlations found, *all* $r_s < .16$, *all* $p > .093$, indicating that LTR scores or k-values were not related to differences in subjective time estimation between participants.

Table S1. *Correlations of LTR and hyperbolic discounting measures with self-reported impulsiveness measures.*

	Questionnaires			
	QDQ-total	*QDQ-Delay discounting*	*QDQ-Delay aversion*	*BIS-total*
$k_{\text{self-control}}$	-.04 (.742)	.00 (.997)	-.06 (.626)	-.06 (.584)
k_{patch}	-.30 (.008)**	-.34 (.003)**	-.20 (.088)	-.02 (.889)
$LTR_{self\text{-}control}$	-.03 (.816)	.02 (.837)	-.10 (.403)	-.01 (.932)
LTR_{patch}	-.24 (.037)*	-.16 (.157)	-.26 (.025)*	-.12 (.309)

** p < .05*

*** p < .01*

Table S2. *Correlations of LTR and hyperbolic discounting measures with time production measures.*

	Time production			
	5 s	*10s*	*20s*	*30s*
$k_{self\text{-}control}$	.04 (.752)	.01 (.954)	.02 (.894)	.09 (.426)
k_{patch}	-.05 (.670)	.14 (.250)	.16 (.175)	.12 (.309)
$LTR_{self\text{-}control}$	-.14 (.243)	-.14 (.220)	-.07 (.558)	-.06 (.614)
LTR_{patch}	.07 (.559)	.11 (.354)	.20 (.093)	.05 (.659)

Publications

2017 **Seinstra M**, Kalenscher T (*submitted*). Rate maximization and hyperbolic discounting in human experiential decision making. *Submitted to Behavioral Ecology*.

2016 **Seinstra M**, Wojtecki L, Storzer L, Schnitzler A, Kalenscher T (2016). No effect of subthalamic deep brain stimulation on intertemporal decision making in Parkinson patients. eNeuro: DOI: 10.1523/ENEURO.0019-16.2016

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Chapter Contributions

Chapter 2

Author contributions

Conceived and designed the experiments: K. Grzymek, T. Kalenscher. Performed the experiments: K. Grzymek, M. Seinstra. Analyzed the data: M. Seinstra. Contributed reagents/materials/analysis tools: M. Seinstra, T. Kalenscher. Wrote the paper: M. Seinstra, K. Grzymek, T. Kalenscher.

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Chapter 3

Author contributions

Conceived and designed the experiments: L. Wojtecki, T. Kalenscher, M. Seinstra, A. Schnitzler. Performed the experiments: L. Storzer, M. Seinstra. Analyzed the data: M. Seinstra. Contributed materials/analysis tools: L. Wojtecki, T. Kalenscher, M. Seinstra. Wrote the paper: M. Seinstra, T. Kalenscher.

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Chapter 4

Author contributions

Conceived and designed the experiments: M. Seinstra, T. Kalenscher. Performed the experiments: M. Seinstra. Analyzed the data: M. Seinstra. Contributed materials/analysis tools: T. Kalenscher, M. Seinstra. Wrote the paper: M. Seinstra, T. Kalenscher.

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"There are only two mistakes one can make along the road to truth; not going all the way, and not starting."

- Buddha

When I came to Düsseldorf I was returning to work with an 'old' friend, my promotor Prof. Dr. Tobias Kalenscher, whom I had met during my bachelor internship in Amsterdam. During that internship I discovered how very interesting research could be and I subsequently chose to do a research master. We stayed in touch and after receiving my master's degree I was very excited to become PhD student in your brand new lab in Düsseldorf, to start (or actually continue) studying intertemporal choice. Thank you, Tobias, for this opportunity, and for all the advice and in particular the support you have given me during these four years. You always knew how to get the best out of my work and with your friendly leadership you kept me motivated when things were tougher than expected.

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Maayke Seinstra

(on the first day I started writing)

Eidesstattliche Erklärung

Hiermit erkläre ich an Eides statt,

- dass ich die vorgelegte Dissertation selbständig und ohne unzulässige fremde Hilfe angefertigt und verfasst habe, dass alle Hilfsmittel und sonstigen Hilfen angegeben und dass alle Stellen, die ich wörtlich oder dem Sinne nach aus anderen Veröffentlichungen entnommen habe, kenntlich gemacht worden sind;

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