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Delay Discounting of Aversive Consequences:
A Potential Cognitive Pathomechanism in Alcohol Use Disorder

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Abbreviations

AUD – Alcohol Use Disorder

AUDIT – Alcohol Use Disorders Identification Test

CBT – Cognitive Behavioral Therapy

DRD – Delayed Reward Discounting

DSM-5 – Diagnostic and Statistical Manual of Mental Disorders, 5th edition

DLD – Delayed Loss Discounting

ICD - International Classification of Diseases

RDoC – Research Domain Criteria

SUD – Substance Use Disorder

1 Submitted Research Articles

Study 1: Pinger, M., Thome, J., Halli, P., Sommer, W. H., Koppe, G., & Kirsch, P. (2022). Comparing Discounting of Potentially Real Rewards and Losses by Means of Functional Magnetic Resonance Imaging. *Frontiers in Systems Neuroscience*, *16:867202*. https://doi.org/10.3389/fnsys.2022.867202

Individual Contributions: Collaboration on Study Design, Data Collection, Data Analysis, Manuscript Writing (First Draft and Finalizing)

Study 2: Thome, J., Pinger, M., Halli, P., Durstewitz, D., Sommer, W. H., Kirsch, P., & Koppe, G. (2022). A Model Guided Approach to Evoke Homogeneous Behavior During Temporal Reward and Loss Discounting. *Frontiers in Psychiatry*, *13:846119*. https://www.frontiersin.org/articles/10.3389/fpsyt.2022.846119

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Study 3: Pinger, M., Skirke, M., Thome, J., Wommer, W.H., Koppe, G., Kirsch, P. (under review). The association between reward and loss discounting, alcohol use and socioeconomic status. Submitted to: *Alcohol, Clinical and Experimental Research.*

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2 Introduction

Intertemporal decision-making is a task that we encounter on a daily basis. We constantly weigh options: Should I invest my money in long-term funds or indulge in immediate purchases? Should I eat a quick chocolate bar or wait for a nutritious lunch? Should I buy this TV now or wait for a discount?

These examples demonstrate a pattern whereby a smaller-sooner reward is weighed against long-term benefits of a delayed option. Intuitively, both the options' relative value and the delay influence our decision-making. For example, if given the choice between winning 10€ now or 15€ in a month, one might prefer the larger-later option. However, if given the choice between 10€ now and 15€ in two years, one might suddenly choose 10€ now. Then again, if both options are delayed by one more year, i.e. 10€ in one year or 15€ in three years, the decision might revert to the larger-later option. *Delay Discounting* is a theoretical account used to describe and quantify behavior in these intertemporal decision-making situations. It assumes that motivational values of future outcomes decrease as a function of delay and objective value, and that the slope of this devaluation can be modelled and compared between individuals (Odum, 2011a). Steeper discounting (i.e. preference for immediate rewards) has been linked to a number of mental disorders, including addiction (Amlung et al., 2017, 2019), and to alterations in fronto-striatal brain networks (Owens et al., 2019). Therefore, Delay Discounting has emerged as a promising candidate pathomechanism and behavioral marker of addiction which may inform development of specialized treatments (Bickel et al., 2014).

Conversely, research on Delay Discounting of aversive rather than rewarding outcomes is relatively lacking, although continued consumption despite delayed aversive consequences (e.g. health, financial well-being) is a hallmark symptom of addiction (American Psychiatric Association, 2013). This dissertation project therefore aimed at investigating to which extent aversive consequences are subject to discounting, and whether aversion discounting is a relevant cognitive mechanism involved in pathological decision-making leading to addiction.

3 Theoretical Background

3.1 Alcohol Use Disorder

Substance Use Disorder (SUD) is a chronic relapsing disorder characterized by loss of control, craving, tolerance, withdrawal symptoms, and substance intake despite negative consequences such as social, financial or health losses (American Psychiatric Association, 2013). A number of substance classes such as alcohol, opioids, cannabinoids, stimulants and benzodiazepines have the potential to induce SUD. In 2016, the global 12-month prevalence of *Alcohol Use Disorder (AUD)* was estimated at 283 million adults or 5.1% of the adult population, and up to 8.8% of the European population (World Health Organization, 2018). Prevalence rates vary substantially depending on the classification system used. The most common systems are the International Classification of Diseases (ICD) and the Diagnostic and Statistical Manual of Mental Disorders (DSM), with multiple versions in use either currently or until recently. Whereas ICD-10 (World Health Organization, 2004), ICD-11 (World Health Organization, 2019) and DSM-IV (American Psychiatric Association & American Psychiatric Association, 2009) distinguish between *alcohol dependence* and *harmful alcohol use* or *abuse*, the dimensional AUD diagnosis in DSM-5 (American Psychiatric Association, 2013) aims at encompassing heterogeneous disorders from harmful use to severe dependence (Saunders et al., 2019). Concordance rates between the new DSM-5 AUD diagnosis with alcohol dependence (ICD-10, ICD-11, DSM-IV) were found to be only moderate (Degenhardt et al., 2019; Lago et al., 2016). In addition, the utilization of both DSM-5 and ICD-11 criteria results in elevated prevalence rates attributable to the expanded definitions of AUD (Saunders et al., 2019). For instance, a recent longitudinal cohort study on Swedish women found lifetime prevalence rates of AUD and alcohol dependence varying from 4.0% (ICD-10) to 10.6% (ICD-11) and 14.3% (DSM-5) (Lundin et al., 2021).

Around 4-5% of worldwide mortality is attributable to alcohol use alone (Rehm et al., 2009; World Health Organization, 2018). In Europe, AUD ranges at the second place (first place for men) behind depression for burden of disease due to mental disorders (Wittchen et al., 2011). Individuals with AUD face a relative mortality risk of 3.38 to 4.57, with disproportionally higher mortality in young individuals and women (Roerecke & Rehm, 2013). In addition to AUD, the 2023 World Drug Report estimated a 45% increase in prevalence of SUD (excluding alcohol and tobacco) over the last 10 years, with a current estimation of 39.5 million individuals suffering from SUD worldwide (United Nations Office on Drugs and Crime, 2023). Given the higher prevalence of AUD compared to other SUD, the present work focused on AUD. Note that the more general term *addiction* includes SUD and behavioral addictions such as pathological gambling (American Psychiatric Association, 2013) which have been shown to share underlying circuits and psychopathology (Grant et al., 2006; Karim & Chaudhri, 2012). Definitions and

diagnostic criteria of behavioral addictions are still evolving (Grant & Chamberlain, 2016). In the present work, the term addiction is used with reference to SUD including AUD.

Treatment rates for AUD are low and stagnating at 17.3% worldwide (Mekonen et al., 2021). In a large European study, 17.7% of diagnosed AUD patients in primary health care reported "receiving professional help" (Manthey et al., 2016). Severe stigmatization of AUD as a character weakness rather than a mental disorder makes it difficult for patients to seek help (Schomerus et al., 2011), and even within professional healthcare, treatment was found to be impeded by negative attitudes of healthcare professionals towards SUD patients (van Boekel et al., 2013). Even among those seeking treatment, attrition rates are estimated at 80% in the United States (Loveland & Driscoll, 2014).

Treatment options include pharmacotherapy and psychotherapy. Cognitive behavioral therapy (CBT) integrating addiction-specific components such as Motivational Interviewing or Cue Exposure Therapy has demonstrated small but robust effect sizes (Kiyak et al., 2023; Riper et al., 2014). Similarly, effect sizes of pharmacotherapy were shown to be robust but rather small (Bahji et al., 2022; Swift & Aston, 2015). Taken together, the combination of high prevalence, substantial disease burden and limited treatment success, it becomes evident that better understanding of addiction mechanisms and treatment interventions is urgently required.

3.2 Theories of Addiction

Many psychological and neurobiological models try to explain the onset and continuation of SUD. In the DSM-5, SUD is predominantly regarded as a brain disorder: "All drugs that are taken in excess have in common direct activation of the brain reward system, which is involved in the reinforcement of behaviors and the production of memories." (American Psychiatric Association, 2013, p. 481). A commonality of all substances with addictive potential is their direct effect on dopamine release in the brain's reward system, and a similar underlying psychopathology is assumed for all SUD (Koob & Volkow, 2016; Volkow et al., 2019). Put simply, these substances act as potent artificial reinforcers, posing a threat to the regulation of neural systems underlying reward-driven behavior. Although it has been argued that not all substances of addiction directly trigger dopamine release in the brain (Nutt et al., 2015), Volkow et al. (2019) illustrated that even cannabinoids and opiates stimulate dopamine release via indirect pathways. Some critics have argued that the brain disease model reduces complex socio-economic processes to "deterministic" biological circuits, thus reinforcing stigmatization (Hammer et al., 2013; Hogarth, 2020, 2022). While this debate is somewhat heated and out of the scope of this work, it should be noted that addiction-related alterations in the brain's reward system are well established (Heilig et al., 2021). Importantly, there is not just one brain disease model, but several theoretical approaches which will be briefly summarized in the next sections.

Habit theories are based on classical and operant conditioning (Everitt & Robbins, 2005). Initially, drug intake is perceived as purposeful, driven by specific goals. As individuals discover the rewarding outcomes of drug use within certain contexts (such as alleviating social anxiety), this behavior becomes reinforced through operant conditioning. At this stage, the individual consciously selects drug use as a means to attain desired goals. Over time, prolonged drug use triggers classical conditioning, linking contextual cues (e.g., social situations) with drug consumption. In the long run, drug use becomes progressively compulsive, ignorant towards negative outcomes, and can be involuntarily triggered by conditioned cues. In other words, addiction can be understood as a shift from goal-directed to automatic behavior.

Conceptually related to Habit theory, the *Incentive Sensitization* theory posits a shift between pleasure-oriented ("liking") and compulsive ("wanting") drug use in the course of addiction (Berridge & Robinson, 2016). Unlike habit theory, which construes addiction as learned automatic behavior, incentive sensitization theory focuses on motivational changes underlying addiction. Its central assumption is that repeated drug exposure leads to conditioned hypersensitivity to drug-related cues, strongly enhancing their incentive value. Rather than triggering an automatic behavioral response, drug cues are thought to elicit a strong motivational state known as "wanting". Wanting is characterized as an intense feeling of craving which is hard to resist. Over time, drug use becomes a means of satisfying this motivation state even if the primary drug effect has long diminished due to tolerance (Bickel et al., 2018)

Whereas Habit and Incentive Senitization theory are derivatives of behavioral learning theories, the *Reward Deficiency Syndrome* model stems from genetic research. It proposes blunted activity in the midbrain dopamine system as a consequence of genetic variation in dopamine receptor genes, resulting in anhedonia or understimulation (Blum et al., 1996). Consequently, individuals seek out dopamine-inducing activities such as substance use as a compensatory mechanism. Clinical evidence includes prolonged amotivation in individuals with remitted stimulant dependency, and blunted ventral striatal activity during the anticipation of non-drug rewards in SUD patients (Leventhal et al., 2008; Luijten et al., 2017). More recently, a multitude of potential gene variations related to dopamine and other neurotransmitters were identified, and effect sizes were found to be minimal (Berggren et al., 2006; Blum et al., 2022). In addition, the proposed generalized hypoactivity of the reward system has been challenged both on a theoretical and empirical level (Becker et al., 2017; Leyton, 2014). Therefore, the authors of the Reward Deficiency model now suggest genetic variations as one of many risk factors (Blum et al., 2022).

Lastly, dual-system approaches such as the *Competing Neurobehavioral Systems Theory* have their origins in decision-making and behavioral economic research. They posit that decision-making is driven by two competing systems, an "impulsive", limbic and paralimbic reward system, and a "rational", executive frontoparietal control system (Bickel et al., 2018; McClure et al., 2004). A dysregulation of this

system towards the impulsive system – either as a consequence of drug use or as a predisposing factor – is thought to cause an excessive bias towards immediate rewards such as drug use. Behavioral evidence for this account stems from stronger Delay Discounting, i.e. increased preference for immediate rewards, in populations with SUD (Amlung et al., 2017). Neuroimaging studies further identified an association between excessive discounting with a combination of increased striatal response towards immediate rewards and a decreased frontoparietal regulation (McClure et al., 2004). Continued consumption despite negative consequence is therefore seen as a consequence of an hyperactive impulse system favoring immediate rewards.

Although the previous section only described a handful of theories, comparable points of reference across all theories become clear - the role of reward processes in explaining continued consumption despite negative consequences. Recent commentaries emphasize the commonalities between these theories (Epstein, 2020; Heilig et al., 2021). Later, this dissertation will aim to embed Delay Discounting as a possible pathomechanism, crossing multiple of the aforementioned theories.

3.3 Delay Discounting

Delay Discounting is defined as a devaluation of future events as a function of the time delay until their occurrence (Madden & Johnson, 2010). *Delayed Reward Discounting (DRD)* in particular is a prominent candidate pathomechanism of addiction. Due to the relative ease of measuring DRD, its dimensional nature and consistent associations with transdiagnostic psychopathology (Amlung et al., 2019; Levitt et al., 2022), DRD was suggested as a paradigm for the Research Domain Criteria (RDoC) matrix (Lempert et al., 2019). After hundreds of studies, Bickel et al. (2014, p. 518) claimed that DRD "*1) identifies individuals who are drugdependent, 2) identifies those at risk of developing drug dependence, 3) acts as a gauge of addiction severity, 4) correlates with all stages of addiction development, 5) changes with effective treatment, and 6) may be related to the biological and genetic processes that underlie addiction*.". The following sections will provide an overview over DRD and the current state of evidence regarding these claims. Thereafter, the putative pathomechanism of Delayed Loss Discounting (DLD) will be introduced.

3.3.1 Delayed Reward Discounting

Intertemporal decision-making has inspired a plethora of behavioral research since the middle of the 20th century. At the center has always been the question of why people seem to behave rationally in some situations, choosing an objectively larger reward, while in other situations, they exhibit a tendency towards seemingly irrational behavior, preferring an objectively smaller reward simply because it is closer

in the future. As an example, humans often prefer a smaller-sooner monetary win (e.g. 10€ now) over a larger-later win (e.g. 15€ in a year) (Loewenstein, 1988; Rachlin et al., 1991).

In 1871, the influential economist William Jevons suggested decaying utilities of remote events to explain the observation that "a future feeling is always less influential than a present one" (Jevons, 2013, p. 72). Another economist, Paul A. Samuelson, brought forward the influential Discounted Utility model, whereby intertemporal decisions can be mathematically described as comparisons between discounted values:

$$U = \beta^t u(x) \qquad (Eq. 1)$$

where U is the time-discounted utility, u is the undiscounted utility of the option x which is discounted by an amount-dependent free parameter β scaled by time t. This exponential discount function assumes a "rational" constant value ratio between smaller-sooner and larger-later options as they progress in time. Importantly, this model was not developed on empirical data, but reflected theoretical assumptions in rational choice situations (Samuelson, 1937).

Discounting functions were first introduced to behavioral data by animal researchers. Mowrer and Ullman (1945) suggested an extension of Thorndike's Law of Effect (Thorndike, 1898) whereby immediate consequences, both rewarding and punishing, exert stronger influence on operant conditioning than delayed ones. Thereafter, a variety of conditioning experiments in animals modeled the temporal decline of reward effectiveness using exponential functions (Ainslie, 1975). Strotz (1955) was the first economist to point out *myopic preference changes* which signify an "irrational" shift from larger-later choices towards smaller-sooner choices in the presence of immediate rewards. He theorized about concave, hyperbola-like discount functions, leading to a steeper decline of utility in the near future and a bias towards immediacy.

Ainslie and Herrnstein (1981) integrated economic and behavioral lines of research and demonstrated preference reversals in pigeons matching with hyperbolic discounting. Mazur (1987), and shortly after, Rodriguez and Logue (1988) empirically established the hyperbolic function against other discount functions using titrating procedures in pigeons. Rachlin et al. (1991) applied the same principle to a monetary decision-making task in humans and confirmed the hyperbolic function, modeling how the subjective value of rewards is systematically devalued (discounted) as a function of the delay:

$$SV = \frac{V}{1 + \kappa D} \qquad (Eq. 2)$$

where SV is the subjective (discounted) value, V is the objective value, κ is a free discounting parameter and D is the delay expressed in days. The discounting parameter κ reflects the steepness of the discounting curve and therefore the individual degree of short-term preference. By that time, multiple lines of work had found considerable inter-individual differences in discounting rates (Frederick et al., 2002;

Thaler, 1981), and time preference appeared to be linked to personality traits, career success and psychopathology, among others (Ainslie, 1975; Mischel, 1974). In the following, a number of derivatives of the original hyperbolic function have been suggested to account for more individual variance. Myerson and Green (Myerson & Green, 1995) demonstrated a better model fit using a general hyperbola (also known as hyperboloid model) with an additional exponent:

$$SV = \frac{V}{(1 + \kappa D)^s} \qquad (Eq. 3)$$

Where s is a non-linear scaling factor of time and amount. If s < 1, the discounting curve flattens as the delay increases, indicating less discounting of outcomes in the far future. This hyperboloid model is the mathematical equivalent to exponential discounting with a logarithmic decrease of time perception following the Weber-Fechner law (Takahashi et al., 2008).

Rachlin (2006) suggested to only raise the delay to the s exponent rather than the entire denominator:

$$SV = \frac{V}{1 + \kappa D^s} \qquad (Eq. 4)$$

This equates to hyperbolic discounting of time scaled by Steven's power law (Vincent & Stewart, 2020). Hyperboloid models (s < 1) have since been established as providing a better fit to human data, whereas simple hyperbolic models (s = 1) are sufficient to model behavior of most animals, with the possible exception of non-human primates (Vanderveldt et al., 2016). Importantly, hyperboloid models allow disentangling between effects of discounting and time perception, whereas hyperbolic models either assume objective time perception or ignore subjective time perception, effectively leading to model misspecification (Vincent & Stewart, 2020).

3.3.2 Measuring DRD

A variety of tasks and analysis methods have been developed to assess DRD rates (for a comprehensive review, see Madden & Johnson, 2010). All procedures are based on two forced-choice intertemporal choice tasks where participants have to decide between a smaller-sooner win (e.g. 5€ now) or a larger-later win (e.g. 10€ in a year). The majority of tasks use monetary outcomes, but alternative rewards such as health, drug and food rewards are also available (Chapman, 1996; Giordano et al., 2002; Odum et al., 2002). Outcomes can be hypothetical, real or potentially real (random trials are selected and paid out), but since high correlations have been found between all options, hypothetical outcomes prevail (Bickel et al., 2009; Madden & Johnson, 2010). However, note that some of the most frequently cited studies supporting equal behavior during real and hypothetical outcomes reported extremely small sample

sizes (Johnson & Bickel, 2002) or excluded behavioral data from longer hypothetical delays (Bickel et al., 2009).

Intertemporal choice tasks can be either delivered in form of a questionnaire (Kirby, 2009) or a computerized tasks which is most common. Presented amounts and delays, and therefore number of trials, can either be fixed (Rachlin et al., 1991) or delivered in an adjusting procedure. The most basic adjusting procedure is an amount-titrating task where the amount of the immediate option is increased by 50% if the participant chooses the delayed option, or vice versa (Du et al., 2002). This is continued for a fixed number of trials or until the preference changes, which marks the indifference point, i.e. the amount ratio where the participant is indifferent between two options. The adjusting procedure is then repeated for a series of delays. Other tasks, predominantly in animal research, adjust for delays while keeping rewards constant (Mazur, 1987). More sophisticated techniques estimate individualized discounting models on a trial-by-trial basis using Bayesian methods and adapt amounts based on predicted choice probabilities (Ahn et al., 2020; Pooseh et al., 2018).

Based on these tasks, three main indicators of DRD rates can be calculated. In fixed procedures, it is possible to obtain the atheoretical percentage of larger-later or sooner-smaller choices. Procedures which obtain indifference points for a series of delays allow for using Area Under the Curve (AUC) which quantifies DRD rates without assuming a specific discounting model (Odum, 2011a). The last and most popular measure of DRD rates is to fit models (such as the hyperbolic model) to the data and derive individual discounting parameters such as κ and s (see Eq. 1, Eq. 2).

3.3.3 Delay Discounting as a Construct

Historically, DRD tasks were developed as a means to understand impulsive behavior such as "irrational" economic spending and substance use despite negative consequences. Over the years, the construct of impulsivity has been separated into many facets which have proven to be mutually independent (Stahl et al., 2014). The ambiguous term *impulsivity* therefore offers little discriminatory power and should not be equated with DRD. Ainslie (1975, p. 463) already commented that the term impulsivity can be used to describe both a systematic preference for smaller-sooner rewards and "behavior that is simply unpremeditated". A recent study revealed risk aversion as a confounding factor in DRD, as individuals with greater risk aversion tended to favor immediate rewards (Lopez-Guzman et al., 2018). This underscores the role of other, "non-impulsive" factors contributing to DRD rates. To accommodate the popularity of the term, DRD is often interpreted as a facet of "choice impulsivity", involving a lack of anticipation of the future, as opposed to "action impulsivity", which is related to habit formation and lack of inhibition (Hamilton et al., 2015; Robbins et al., 2012).

In the light of moderate to high long-term and measurement-independent reliability of DRD rates, Odum (2011a, 2011b) suggested to conceptualize DRD as a trait variable in itself rather than a facet of an overarching construct. Kirby (2009) reported a retest-reliability of .71 over one year for his Monetary Choice Questionnaire. Prospective cohort studies have found relatively stable DRD rates over time, even spanning from adolescence to adulthood (Audrain-McGovern et al., 2009).

However, the validity and reliability of DRD rates have also been questioned. Popular short-form adjusting amount procedures have shown only moderate correlations with long-form procedures, which by themselves are not completely reliable (Bailey et al., 2021). Key concerns also arise from the suggested modeling procedures: nonsystematic and unexpected intertemporal choice behavior is common across intertemporal choice tasks. A meta-analysis estimated the rate of nonsystematic behavior in DRD tasks at 18% (Smith et al., 2018). Critically, handling of these data is not consistently reported in studies, and an influential paper cited 511 times recommended to remove these cases as outliers (Johnson & Bickel, 2008). Lastly, discounting rates between different domains, e.g. health and money, were shown to be unrelated, which casts doubt on the external validity of monetary discounting (Chapman, 1996; Chapman & Elstein, 1995).

Loewenstein and Prelec (1991) extensively studied effects of psychological context factors of Delay Discounting. They found significantly reduced DRD rates in sequential decision-making tasks and demonstrated verbal framing effects; for example, the same monetary loss is discounted more if it is formulated as a (weaker) discount (Loewenstein & Prelec, 1992). Since then, more state-dependent cognitive biases have been identified (Lempert & Phelps, 2016). Even order of task presentation was found to influence discounting behavior. Participants who started with a reward discounting task discounted both rewards and losses more steeply than participants who started with a loss discounting task (Murphy et al., 2001). Other context factors include cortisol levels, which have been associated with gain/loss-tradeoffs in decision-making (Honk et al., 2003), stress, which increases preference for immediate rewards (Fields et al., 2014), and hunger (Skrynka & Vincent, 2019). Hormonal influences on DRD rates are implicated by changing DRD rates over the course of the female cycle, with stronger DRD during fertile phases and in women taking hormonal contraception (Vincent et al., 2023). In conclusion, while Delay Discounting is often understood as a trait of decision-making, it is significantly influenced by various state factors.

3.3.4 Neurobiology of Delayed Reward Discounting

Decision-making during DRD tasks has been found to be associated with activation in widespread brain regions. Different analytic strategies have led to two major theoretical approaches of understanding neural processing during DRD. Dual systems approaches such as the Competing Neurobehavioral Systems Theory described earlier assume separate brain networks underlying impulsive (short-term) and rational

(long-term) decision-making, which are typically tested using "smaller-sooner vs. larger-later choices" contrasts (Bickel et al., 2014; McClure et al., 2004; van den Bos & McClure, 2013). In contrast, single system approaches assume a unitary valuation and decision-making system and often parametrically modulate brain activity during decision-making using model-based subjective values of presented options (Kable & Glimcher, 2007; Peters & Büchel, 2009). These approaches are not necessarily mutually exclusive and have yielded similar activated brain regions during DRD tasks (Scheres et al., 2013; Schüller et al., 2019). Prominent networks during intertemporal decision-making include the valuation network (ventral striatum and ventromedial prefrontal cortex) and the executive control network (prefrontal and parietal cortex regions), but also regions associated with salience such as anterior cingulate cortex and insula (de Water et al., 2017; Frost & McNaughton, 2017; Kable & Glimcher, 2009; Scheres et al., 2013; Schüller et al., 2019). Steeper DRD (in both healthy and addicted populations) has been consistently associated with weaker activation in prefrontal control areas and stronger activation in striatal valuation areas during decision-making (Frost & McNaughton, 2017; Owens et al., 2019). However, a recent meta-analysis compared analysis strategies in fMRI studies of DRD and found no reliable activation pattern related to the popular contrast of "smaller-sooner vs. larger-later choices", instead only finding robust task activation during "task > baseline" contrasts and parametric modulations with reward value (Souther et al., 2022). Similar to the behavioral domain, methodological differences in DRD tasks and analysis strategies may limit the external validity of individual findings and impede the comparison between studies.

3.3.5 DRD and Addiction

Steeper Delay Discounting in addiction is a well-established finding and is thought to reflect the devaluation of long-term alternative rewards compared to the immediate reward of drug use (Verharen et al., 2020). Within this framing, a relapse is conceptualized as an "impulsive" decision in favor of a short-term reward (e.g. alcohol) instead of the long-term reward of abstinence (e.g. health) (Robbins et al., 2012). A large body of studies has demonstrated that individuals with SUD appear to discount rewards more steeply, i.e. have a stronger preference for short-term rewards. A meta-analysis found an omnibus correlation of r = .14 between DRD rates and substance-related problems, with comparable effect sizes between substances, including alcohol (Amlung et al., 2017). This finding extends to behavioral addiction, again with comparable effect sizes (Weinsztok et al., 2021). Smaller and more inconsistent effects (average r = .08) were found for cannabis use disorder (Strickland et al., 2021). Regarding obesity, Veillard and Vincent (2022) conducted both a correlative meta-analysis and an own experimental study on 381 participants and found a small effect (r = .15) between DRD rates and BMI in the meta-analysis, but not in the experiment. Using Bayesian estimation, they demonstrated extreme levels of study-level

heterogeneity contributing to potentially spurious effects. A general observation is that comparisons between patients and healthy controls yield stronger effects than continuous associations (MacKillop et al., 2011). Strikingly, a large study in 1388 community adults found no association between DRD rates and scores in the Alcohol Use Disorder Identification Test (AUDIT), though association with other substances and disorders were found (Levitt et al., 2022). Fewer studies investigated DRD of non-monetary commodities like health or drug rewards and provided evidence for similar associations with addiction (Giordano et al., 2002; Odum et al., 2002).

In addition to cross-sectional associations, many studies investigated longitudinal effects of DRD rates on consumption trajectories and treatment outcomes, and vice versa. In a sample of 30 smokers, Krishnan-Sarin et al. (2007) found that baseline DRD rates were higher in participants who did not reach abstinence within a 4-week cessation program compared to those who reached abstinence (d = 0.73). Sheffer et al. (2014) found DRD to be a robust predictor (β = .37) of relapse hazard in a sample of 131 smokers undergoing a CBT smoking cessation and nicotine replacement program. The effect of DRD was found to remain robust when dependence severity, perceived stress and therapy adherence were controlled for. A larger (N = 947) prospective cohort study spanning 6 years found a much smaller yet significant prediction (β = .08) of smoking levels by baseline DRD rates (Audrain-McGovern et al., 2009). A longitudinal cohort study following 2220 adolescents from age 14 to 22 found a similar effect size between baseline DRD and cumulative alcohol consumption (r = .09). Conversely, no effect of alcohol consumption on DRD was found, suggesting steeper DRD as a trait-like risk factor rather than a consequence of alcohol use (Fröhner et al., 2022). Similarly, baseline DRD was found to be associated to smoking during a nicotine patch treatment, but the treatment was not found to influence DRD rates (Dallery & Raiff, 2007). Nevertheless, not all studies report significant longitudinal effects of DRD on substance use. For example, the reverse pattern of the two studies above was found in two opioid-dependent samples undergoing burprenophine and contingency management treatment. DRD rates were found to decrease over the course of all treatments, but no association with treatment outcomes was present (Landes et al., 2012). In a sample of 198 adolescent social drinkers, baseline DRD was associated with baseline alcohol use, but not predictive of 12-month drinking trajectories (Bernhardt et al., 2017). Two studies did not find a predictive effect of DRD rates on any outcome measure in heavy-drinking college students undergoing treatment (Dennhardt et al., 2015; Murphy et al., 2012). Exum et al. (2023) conducted a systematic review and found that only 47% of studies reported significant associations between DRD at baseline and treatment outcomes. They highlighted that only a few studies include dimensional outcome measures, and among those that do, significant effects of DRD are not often found. Another important insight came from a treatment study in marijuana-dependent patients where the association between DRD

and treatment outcome diminished when socio-economic and demographic factors were controlled for (Stanger et al., 2012).

3.3.6 Delayed Aversion Discounting

If reward discounting uniquely combines consistent behavioral and neural effects in addiction research, much less attention has been given to temporal discounting of aversive events. This is surprising given the very nature of addiction according to clinical criteria: continued consumption despite negative consequences (American Psychiatric Association, 2013). Explanations of this symptom include the aforementioned learning theories (e.g. automatic behavior ignoring negative consequences), socio-economic context, drug use as self-punishments and denial (Hogarth, 2020; Pickard & Ahmed, 2016). However, much like the benefits of abstinence, most downsides of drug use occur at a delay. Conversely, the negative effect of abstinence is immediate (e.g. withdrawal, craving), just like the positive effect of drug use. Steep aversion discounting, i.e. devaluation of delayed aversive consequences, would result in a preference for larger but delayed aversive consequences. Therefore, if aversive events are subject to temporal discounting, a relationship between aversion discounting and addiction could be assumed, even more so as neural processing of both rewards and punishment are altered in addiction (Luijten et al., 2017; Patel et al., 2013). As aversion discounting is almost exclusively operationalized using the same monetary choice tasks as DRD (using losses instead of rewards), the term *Delayed Loss Discounting (DLD)* will subsequently be used.

Thaler (1981) initiated the comparison between DRD and DLD using monetary decision tasks. The author found that losses were devalued less steeply, a phenomenon termed the sign-effect. This effect was replicated by subsequent studies (Estle et al., 2006; Loewenstein & Prelec, 1991, 1992), including those involving SUD populations (Johnson et al., 2015). Chapman (1996) extended the aversion discounting and the sign-effect to health discounting, further noting that monetary losses are as much discounted as health losses, a finding later replicated for pain (Harris, 2012) and drug availability (Johnson et al., 2015).

The sign effect does not appear to be limited to quantitative differences in discounting steepness. One group conducted two online studies using an intertemporal choice questionnaire with 428 participants and reported that only about 60% of participants discount losses as expected, compared to 90% in the DRD task. 20-25% of participants did not discount losses at all (i.e. never chose the larger-later loss), 15-23% discounted losses in a opposite way, i.e. preferring immediate losses with increasing delays (Myerson et al., 2017; Yeh et al., 2020). Almost the same numbers were found by a different group (Gonçalves & Silva, 2015). Importantly, there were no difference in age, gender and SES regarding these subgroups (Yeh et al., 2020)

Different explanations have emerged to explain the sign effect. Based on a comparison of model parameters in a q-exponential discounting model (a more generalized hyperboloid model), Han and Takahashi (2012) suggested that differences in time perception, rather than outcome valuation, underlie the sign effect, but without providing a cognitive or mechanistic explanation. Loewenstein (1987) emphasized the role of *dread*, i.e. aversiveness of anticipating future losses, leading to reduced discounting. Qualitative evidence for this was provided by Furrebøe (2020) who asked participants which strategies they used. She found that most participants decided based on both temporal and monetary information in the DRD task, but focused on only one dimension in DLD (either delay *or* amount). Notably, this was especially pronounced in non-discounters, who almost exclusively reported aiming to minimize dread by immediately paying losses. The author noted that paying immediate losses is not merely a smaller-sooner aversive event; it involves the positive contingency of alleviating dread. Delay-independent aversion against waiting was also found to explain additional variance in DLD but not DRD when added as a third parameter to a hyperboloid discounting model (Gonçalves & Silva, 2015).

Whereas the concept of dread focuses on the temporal aspect of anticipating future events, *loss aversion* is defined as a tendency to place greater weight on losses compared to equivalent rewards (Kahneman & Tversky, 1979). Significant inter-individual differences and moderators have been found for loss aversion (Blake et al., 2021; Mrkva et al., 2020). Chapman (1996) incorporated a loss aversion term into utility functions and was able to eliminate the sign effect in monetary discounting. However, this effect was not replicated for health discounting.

Another common finding is the lack of magnitude effects in DLD. In DRD, discounting is most pronounced with small rewards and decreases as reward magnitude increases. In DLD, small losses are discounted at the same rate as high losses (Green et al., 2014; Mitchell & Wilson, 2010; Yeh et al., 2020). These findings provide evidence for DLD as a qualitatively separate process than DRD.

Apart from the sign effect, many studies investigated within-subject correlations between DLD and DRD, yielding very inconclusive findings (Frederick et al., 2002). Murphy et al. (2001) found a moderate correlation of $r = .57$ between DLD and DRD discounting parameters. Halfman et al. (2013) reported correlation coefficients between $r = .44$ and $r = .55$ between DRD and DLD depending on age group. Mitchell and Wilson (2010) found significant correlations between $r = .39$ and $r = .51$ depending on outcome magnitudes. Chapman (1996) reported lower correlations (average $r = .29$) between DRD and DLD for both monetary and health discounting. In contrast, recent studies with relatively large sample sizes observed no significant correlations between DLD and DRD (Gonçalves & Silva, 2015; Myerson et al., 2017; Yeh et al., 2020). Myerson et al. (2017) identified sub-group interactions whereby only those participants with expected (positive) DLD showed a moderate correlation of $r = .35$ between DRD and DLD. However, this was not replicated in another study by the same group (Yeh et al., 2020). The use of

different comparison parameters (behavioural frequencies, discounting parameters, discounting factors, area-under-the-curve) and discounting functions complicates the interpretation of these unclear findings.

Only few studies have compared neural correlates of DRD and DLD. Bickel et al. (2009) found no significant BOLD response differences. However, Xu et al. (2009) noted increased BOLD activity in the dorsolateral PFC, posterior cingulate, insula, thalamus, and striatum during DLD. Using dynamic causal modeling, Zhang et al. (2018) identified distinct networks for gains and losses, with dorsolateral PFC implicated in loss valuation and medial cortical regions in gain valuation.

Conceptual evidence whether DRD and DLD may be more than different polarities of the same process comes from studies investigating the anticipation of monetary rewards and losses. Monetary incentive delay (MID) tasks require participants to anticipate rewards, losses and null trials based on conditioned cues. A few seconds later, a reaction time task is prompted by another cue (e.g. a flash) and participants have to react as quickly as possible to a obtain the reward/avoid the loss (Kirsch et al., 2003; Knutson et al., 2001). Three meta-analyses analyzed neural correlates of MID tasks involving losses. Oldham et al. (2018) found a common activation for both reward and loss anticipation within striatum, insula, amygdala and thalamus, and motor areas. Differences between reward and loss were only found using a more liberate threshold of $p < .005$, yielding stronger activation in the ventral striatum, the supplementary motor area and the occipital lobe during reward anticipation, and stronger activation in the caudate and media-dorsal thalamus during loss anticipation. The meta-analysis by Dugré et al. (2018) only analyzed loss MID tasks and did not provide a comparison with reward tasks, but noted subtle differences to activation patterns seen in prior reward MID meta-analyses, including activity in the median cingulate and ventro-lateral prefrontal regions. The latter finding received support by a meta-analysis conducted on only whole-brain studies that directly compared reward and loss MID task and found more activation in the inferior frontal gyrus during loss anticipation. Taken together, the findings on MID tasks suggest a largely valence-independent salience network. The activation of salience network nodes can be expected in decision-making tasks (Frost & McNaughton, 2017). Decision-making involves an instrumental aspect similar to MID tasks (reacting to a cue to obtain a desired outcome) and may therefore confound findings of non-difference between DRD and DLD such as reported by Bickel et al. (2009). So far, no study has attempted to disentangle outcome anticipation and decision-making in an fMRI comparison of DRD and DLD. In summary, neural studies currently do not provide much evidence on differences between DRD and DLD.

3.3.7 Delayed Aversion Discounting and Addiction

The literature on the link between DLD and addiction presents few and conflicting findings. In an early study, both alcohol-dependent and healthy participants learned button press patterns to gain rewards,

rewards paired with immediate shocks, or rewards paired with shocks delayed by 30 seconds. While alcohol-dependent individuals generally took longer to learn avoidance of punishment, there was no interaction with delay. This suggested a broad disinhibition to avoid aversive consequences when seeking rewards among alcohol-dependent individuals (Vogel-Sprott & Banks, 1965).

In a healthy sample of 33 subjects, a correlation between discounting and alcohol use was only observed for delayed losses, but not rewards (Takahashi et al., 2009). A more recent study compared 78 AUD patients with 51 healthy controls and found steeper DRD and DLD in the AUD group (Bailey et al., 2018). For nicotine dependence, two studies reported steeper monetary and health DLD in smokers compared to non-smokers (Baker et al., 2003; Odum et al., 2002), whereas two studies did not find a difference (Johnson et al., 2007; Ohmura et al., 2005). One study reported steeper DLD and DRD rates in cocaine-dependent versus healthy participants across commodities (money, health and drug-related outcomes), albeit with a stronger effect for rewarding outcomes (Cox et al., 2020). In contrast, Mejìa-Cruz and colleagues (2016) compared 77 cocaine-dependent, 44 cannabis-dependent and 40 healthy participants and found no differences in DLD. One possible explanation for these inconsistencies is that addiction-related studies on DLD focused on group comparisons using rather small sample sizes, and that the DLD subgroups mentioned above were not analyzed. No study has investigated neural correlates of DLD in individuals with addiction. In conclusion, aversion discounting stands out as a promising yet understudied pathomechanism for addiction research.

3.4 Aims and Research Questions

As previously explained, the role of aversion discounting within addiction remains an open gap in the state of knowledge. Filling this gap was the goal of the present dissertation project. As reward discounting is robustly associated with addiction, commonalities and differences between Delay Discounting of aversive and rewarding consequences were first investigated on a behavioral and neural level. The goal was to first elucidate whether aversion discounting is an inherently different process than reward discounting, as some differences between DRD and DLD seem to suggest. To this end, the project aimed at the development of a novel intertemporal choice task to reliably infer DRD and DLD parameters and allow for a systematic comparison of discounting models. This task should then be used to find associations between DLD and addiction. The project focused on alcohol use due to the high prevalence of AUD. As the literature on Delay Discounting, especially studies on addiction, is often based on small sample sizes and intransparent data handling (e.g. exclusion of non-systematic discounting), the project aimed at endorsing open science practices by preregistering all studies, publishing raw data and aiming at sufficient sample sizes. This also allowed for replication of prior findings such as the association between DRD and addiction.

Following the literature summarized earlier, five overarching research questions guided the project:

- **Q_1** Are monetary losses subject to hyperbolic/hyperboloid Delay Discounting?
- **Q_2** Are DLD and DRD different cognitive mechanisms, as reflected by dissociable behavioral patterns (sign effect, correlation between DRD and DLD, discounting functions, non-discounting)?
- **Q_3** Are dissociable brain regions recruited during DRD and DLD decision-making?
- **Q_4** Is steepness of DLD associated with severity of Alcohol Use Disorder and alcohol consumption?
- **Q_5** Does the neural processing of DLD and DRD differ between Alcohol Use Disorder patients and healthy controls?

4 Study 1

Title: Comparing Discounting of Potentially Real Rewards and Lossesby Means of Functional Magnetic Resonance Imaging

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Comparing Discounting of Potentially Real Rewards and Losses by Means of Functional Magnetic Resonance Imaging

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Aim: Delay discounting (DD) has often been investigated in the context of decision making whereby individuals attribute decreasing value to rewards in the distant future. Less is known about DD in the context of negative consequences. The aim of this pilot study was to identify commonalities and differences between reward and loss discounting on the behavioral as well as the neural level by means of computational modeling and functional Magnetic Resonance Imaging (fMRI). We furthermore compared the neural activation between anticipation of rewards and losses.

Method: We conducted a study combining an intertemporal choice task for potentially real rewards and losses (decision-making) with a monetary incentive/loss delay task (reward/loss anticipation). Thirty healthy participants (age 18-35, 14 female) completed the study. In each trial, participants had to choose between a smaller immediate loss/win and a larger loss/win at a fixed delay of two weeks. Task-related brain activation was measured with fMRI.

Results: Hyperbolic discounting parameters of loss and reward conditions were correlated (r = 0.56). During decision-making, BOLD activation was observed in the parietal and prefrontal cortex, with no differences between reward and loss conditions. During reward and loss anticipation, dissociable activation was observed in the striatum, the anterior insula and the anterior cingulate cortex.

Conclusion: We observed behavior concurrent with DD in both the reward and loss condition, with evidence for similar behavioral and neural patterns in the two conditions. Intertemporal decision-making recruited the fronto-parietal network, whilst reward and loss anticipation were related to activation in the salience network. The interpretation of these findings may be limited to short delays and small monetary outcomes.

Keywords: delay discounting, monetary incentive delay task, reward, aversion, fMRI

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INTRODUCTION

Imagine having to choose between two monetary rewards: win €50 today or €100 in three months. What would you choose? Intertemporal choice tasks (ICTs) like these are used to assess *delay discounting* (DD), an aspect of decision-making whereby individuals attribute decreasing value to outcomes in the future (Gonçalves and Silva, 2015; Myerson et al., 2017; Yeh et al., 2020). This decrease over time is most commonly described with a hyperbolic discounting function (Myerson and Green, 1995). Inter-individual differences in the temporal discounting rates are associated with economic behavior, but also mental disorders like substance use disorder (Story et al., 2014; Cruz Rambaud et al., 2017; Amlung et al., 2019).

Compare the decision above with the following one: Lose €50 today or €100 in three months. What would you choose now? It is still an open question whether the cognitive decision-making process between these potential losses are the same as in the first example, only in the opposite direction. Therefore, comparing the behavioral and neural processes between temporal loss discounting (LD) and temporal reward discounting (RD) was the main goal of this study.

On a behavioral level, there appear to be inherent differences between LD and RD. Losses are discounted less steeply than rewards (Loewenstein and Prelec, 1992; Frederick et al., 2002; Estle et al., 2006; Mitchell and Wilson, 2010; Green et al., 2014). In other words, it appears as if losses in the distant future remain aversive. Not only are losses discounted less steeply, but also less frequently: around 20% of participants do not discount losses at all, another 20% exhibit reverse discounting, i.e., gravitating more towards immediate choices with increasing delay. In contrast, future rewards are discounted by more than 90% of participants (Gonçalves and Silva, 2015; Myerson et al., 2017; Yeh et al., 2020). Another commonly found difference between RD and LD is the lack of magnitude effects in LD: in RD, very large wins are less steeply discounted than small wins, whereas for LD it was found to be constant over a wide range of monetary outcomes (Johnson and Bickel, 2002; Mitchell and Wilson, 2010; Green et al., 2014; Yeh et al., 2020).

There also appear to be similarities between both processes. A stronger tendency to discount future losses has been associated with substance use disorder (Johnson et al., 2015; Cox et al., 2020). Different studies report vastly different correlation coefficients between discounting rates of losses and reward, ranging from strong to none at all (Chapman, 1996; Mitchell and Wilson, 2010; Halfmann et al., 2013; Myerson et al., 2017). To summarize, it remains unclear whether LD and RD represent the same cognitive process.

This uncertainty translates to the neural underpinnings of LD and RD, with only very few studies comparing neural correlates of RD and LD. There is considerable literature only for the neural correlates of RD: RD typically recruits brain areas which are related to executive control (frontal and parietal cortex, supplementary motor area), reward valuation (ventral striatum, amygdala, orbitofrontal cortex) and salience (insula, anterior cingulate cortex (Wesley and Bickel, 2014; Owens et al., 2019). Moreover, steeper RD is associated with altered activity in regions including the ventral striatum (VS), inferior frontal gyrus, anterior cingulate and medial PFC (Schüller et al., 2019).

Directly comparing LD and RD, Bickel et al. (2009) reported no significant differences between BOLD responses in RD and LD. Xu et al. (2009) reported a stronger BOLD response in the dorsolateral PFC and the posterior cingulate, the insula, the thalamus and the striatum during LD trials as compared with RD trials. Using dynamic causal modeling, the same group found distinct networks for gains and losses, whereby the valuation of losses and gains relies more on dorsolateral PFC and medial cortical regions, respectively (Zhang et al., 2018).

Whereas the neural underpinnings of reward- and aversion-related discounting have been rarely compared, a large number of studies have compared other processes that involve both rewarding and aversive consequences. One of these is reward and loss anticipation as measured by monetary incentive delay (MID) tasks (Kirsch et al., 2003; Knutson et al., 2005). Cognitive processes during this task include the valuation of possible outcomes and instrumental behavior to obtain a given outcome. For this task, recent meta-analyses have demonstrated comparable activation for trials involving losses and rewards, but also stronger activation in the ventral striatum during reward compared to loss anticipation (Dugré et al., 2018; Oldham et al., 2018). Like outcome anticipation, intertemporal decision-making usually includes an evaluation process and instrumental approach behavior (see also Scheres et al. (2013)). Therefore, differences in neural activation between loss and reward decision-making could be confounded with differences in the motivational value of the reward or loss as reflected in the activation during reward and loss anticipation (Algermissen et al., 2021). To this end, we developed a sequence of decision-making and outcome anticipation by combining intertemporal choice tasks with a MID task (Kirsch et al., 2003).This further allowed us to conduct a MID task with highly salient outcomes which have been chosen by the participants themselves.

In addition, behavioral modeling of discounting parameters allowed us to derive subjective values which we could associate with brain activation during the MID task. During decision-making, the subjective value of monetary wins is associated with stronger activation in the MPFC, the VS, the PCC, the ACC and other regions throughout the frontal and parietal cortex (Sripada et al., 2011; Schüller et al., 2019).

Most analyses were performed in an exploratory manner. We focused on investigating differences and correlations between behavior and neural activation during decision-making between rewards and losses. We further collected data on self-perceived impulsivity via the Barratt Impulsivity Scale-15 (Meule et al., 2011) to investigate its association with delay discounting. We preregistered seven hypotheses based on the results of an unpublished pilot study (for further information)[1]. Hypotheses included the presence of delay discounting in both reward and loss conditions, a replication of ventral striatal activation during reward anticipation, and more ventral striatal activity during reward anticipation than during loss anticipation. Furthermore, we hypothesized to see no correlation between

[1]https://osf.io/cj35t

behavioral parameters for LD and RD. Lastly, we expected an association between stronger RD and higher activation during the anticipation of immediate rewards (compared to delayed rewards), and an association between stronger LD and reduced prefrontal activation during decision-making.

METHODS

Sample

We recruited 30 healthy participants from local universities via social media, public notices and registers of participants from earlier studies. Eligibility criteria included: absence of acute severe medical diseases, absence of acute psychiatric disorders, and MRI suitability. Eligibility criteria were assessed using a standardized telephone screening protocol. Eligible participants signed written informed consent prior to the study. There was no financial compensation, but participants could win money based on their responses during the experiment. On average, participants won €15.20 during the study.

The study was approved by the ethics committee of the Medical Faculty Mannheim, University of Heidelberg (2019-633N).

Study Procedure

A standardized information sheet was used to explain the behavioral task before the MRI session. Participants were informed that they would be compensated based on their decisions in the behavioral task.

Each participant completed the experiment in the fMRI scanner. The experiment consisted of two sessions of 32 trials each. Within each trial, the participant first had to choose between two monetary options (decision phase) and then respond quickly enough after an anticipation period to receive the chosen option (anticipation phase). The trial procedure is described below and illustrated in **Figure 1**.

The two sessions were identical in every aspect (amounts to choose from, order of stimuli) except for valence: participants had to choose between and anticipate monetary wins in one session (reward condition) and losses in the other session (loss condition). The order of the two sessions was counter-balanced across participants.

Decision Phase (Intertemporal Choice Task): At the beginning of each trial, participants had to choose between a smaller immediate or a larger later amount of money to be received/lost in two weeks. The delay was always fixed at two weeks to allow for manageable payment. If no choice was made within 3 seconds, the trial was excluded for analysis. The phase was followed by a jittered 1-2 sec inter-stimulus interval.

The 32 trial options were calculated for eight fixed amounts for the immediate option (€1, €1.25, €1.50, €1.75, €2, €2.25, €2.50 and €2.75) and four ratios between the immediate and delayed options (0.2, 0.4, 0.6, 0.8). For example, the delayed options in the four trials offering €1 immediately were: €5, €2.5, €1.66, and €1.25.

Anticipation Phase (Incentive Delay Task): After making a choice, the chosen amount of money and the chosen delay (immediate or 2 weeks) were cued for 6 seconds. Subsequently, a short flash of 50 ms duration prompted the participant to respond as fast as possible by pressing a button to receive the chosen outcome. The threshold for a fast response was adaptive for each trial, targeting a 50% probability of success: starting with 300 ms, the required reaction time was increased/decreased by 5% after a slow/fast response. Then the feedback was presented for 1.5 seconds. In case of no or a too slow response, the chosen reward was replaced with €0, whereas chosen losses were doubled. Lastly, the jittered inter-trial interval of 1.5 to 5 seconds followed.

For each task, two trials were randomly selected and paid out. For the trials of the loss discounting experiment, participants were given a baseline balance of €8.20 for immediate choices and €10 for delayed choices, from which the selected loss was subtracted. An equal balance for both choices would have resulted in a trivial task where the smaller loss would constantly yield a larger win. We selected different balances so that choosing the delayed loss would result in a higher win in 50% of trials.

After the MRI session, participants were asked to fill out the Barratt Impulsivity Scale-15 (BIS-15, German Short Version; Meule et al. (2011)) and two open questions for each task: 1) *Did you have a strategy (if yes, please describe)?* 2) *Did you switch your preference for an immediate or delayed win/loss at a specific difference between the two amounts?* These questions were used to assess whether we successfully induced discounting of losses despite the possibility of winning money in both tasks.

Behavioral data extracted from logfiles included individual trial-wise choices and reaction times during the decision and anticipation phases.

Behavioral Modeling

We inferred hyperbolic delay discounting models on the sequence of behavioral choices of each subject (Mazur, 1987; Davison and McCarthy, 1988), as commonly done in human research (Mazur, 1987; Davison and McCarthy, 1988; Kirby and Herrnstein, 1995; Myerson and Green, 1995; Johnson and Bickel, 2002; Ballard and Knutson, 2009; Bernhardt et al., 2019; Ahn et al., 2020; Croote et al., 2020). Since we have presented only two delays, robust estimation of discounting models is limited. Therefore, we did not run model comparisons between different discounting models and instead applied the commonly used hyperobic model to remain comparable to other studies. The model assumes that the internal (subjective) values V of a delayed choice a_2 decline hyperbolically over time, i.e., according to $V(a_2) = \left(\frac{1}{1+ \cdot \kappa^l D}\right) r_2$, where r_2 represents the outcome of the delayed option, κ^l is a free (discounting) parameter reflecting the individual tendency of discounting the delayed outcome in the reward or loss condition (indexed by l), and D represents the temporal delay. The value of the immediate choice $V(a_1)$ is simply given by the outcome r_1 itself.

By connecting these values to behavioral choices in the task through a probabilistic process, we describe the probability p for choosing an action a_i as $p\,(a_i) = \frac{e^{\frac{1}{\beta^l} V(a_i)}}{\sum_j e^{\frac{1}{\beta^l} V(a_j)}}$, where β^l describes the individuals tendency to exploit or explore choices (separately

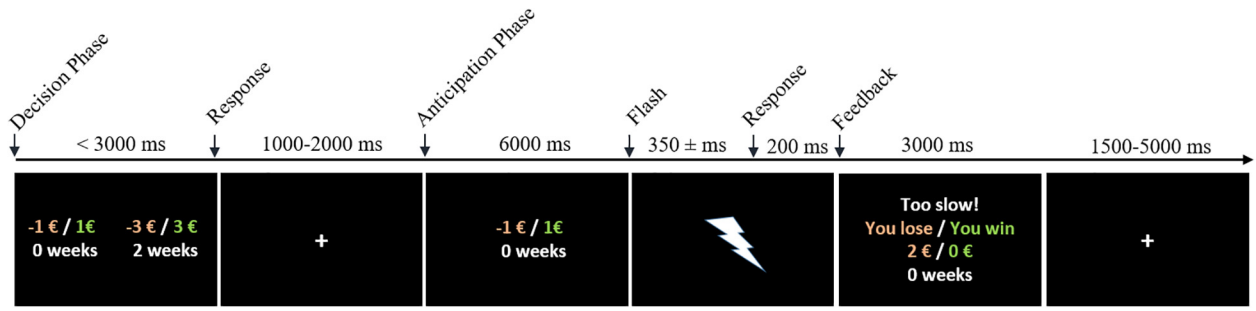

FIGURE 1 | Experimental design. Arrows indicate onsets of GLM regressors. Participants had to choose between two losses (red) or two wins (green) within 3 seconds (*decision phase*). The chosen outcome was then cued for 6 seconds (*anticipation phase*), after which a short flash (50 ms) occurred. If participants pressed the button within an adaptive response window (starting with 300 ms), they received the outcome. If not, the win was reduced to €0 (reward condition) and losses were doubled (loss condition), as presented in the example.

for reward and loss conditions). Parameters were inferred via maximum likelihood estimation using constrained parameter optimization (with inbuilt MATLAB routines) and parameter constraints on $\beta^l \in [0, 1]$, and $\kappa^l \in [0, \infty)$.

Furthermore, the (negative) subjective values of chosen losses were transformed to absolute subjective values for easier interpretation (so that a higher absolute subjective value reflects a higher loss).

Behavioral Data Analysis

To evaluate discounting behavior during the decision phase, we first counted the individual number of discounted choices by condition, that is, all immediate choices in the reward condition and all delayed choices in the loss condition. To test the hypothesis that the frequency of discounted choices increased as a function of a higher immediate/delayed ratio, we aggregated the data by obtaining the relative frequency of discounted choices for each participant, condition and ratio.

Based on these data, we set up a linear mixed model (LMM, Singmann and Kellen (2019)) to test for the effect of ratio (between the immediate and delayed options) and condition on the number of discounted choices. The LMM was chosen to take into account the hierarchical data structure and possible interaction effects. Here, the outcome variable was the relative frequency of discounted choices, with condition (i.e., reward/loss) and ratio between immediate and delayed amount (i.e., 0.2, 0.4, 0.6, 0.8) as fixed effect predictors. Furthermore, we added a per-participant random intercept, a random slope per participant for both fixed effects, and the correlation between the random effects, resulting in the following formula:

```
Relative _ frequency ~ condition + ratio
+ (condition + ratio | subject)
```

Next, we tested whether the behavioral parameters κ and β from the hyperbolic model were significantly different or associated between conditions. To this end, paired t-tests and Pearson's correlation coefficient were calculated. To rule out potential bias from non-converging behavioral models, these statistics were repeated excluding participants without choice variability in at least one condition. Lastly, correlations between the model parameters, the number of discounted choices, and BIS-15 scores were calculated.

To investigate other possible differences between loss and reward trials, we statistically compared reaction times during loss and reward trials, both for the decision phase and the anticipation phase. Here we also took into account the ratio between monetary options (decision phase) and the reward/loss magnitude (anticipation phase) as possible predictors of reaction time. To this end, we fit LMMs to the data of both phases.

For the decision phase, we set up a LMM with the reaction time during decision-making as outcome variable. Fixed effect predictors were condition (reward/loss) and ratio between immediate and delayed amount (i.e., 0.2; 0.4, 0.6, 0.8). Furthermore, we added a per-participant random intercept, a random slope per participant for both fixed effects, and the correlation between the random effects, resulting in the following formula:

```
Reaction_time ~ condition + ratio +
(condition + ratio | subject)
```

For the anticipation phase, we set up a LMM with the reaction time after the flash as an outcome variable. Fixed effect predictors were condition (reward/loss) and outcome magnitude, which we obtained from the subjective values derived from the hyperbolic model. A random intercept per participant was included, resulting in the formula:

```
Reaction_time ~ condition +
subjective_value + (1 | subject)
```

A significance threshold of $p < .05$ (two-sided) was used for all behavioral analyses. All behavioral analyses were performed using R (version 4.1.2). Linear mixed models were fit using the packages *lme4* (Bates et al., 2015). F-statistics and p-values for LMMs were estimated using the Satterthwaite method as implemented in the statistical R package *lmertest* (Kuznetsova et al., 2017).

Brain Imaging

Functional imaging data were acquired using a 3 Tesla Siemens Magnetom Trio Scanner (Siemens Medical Systems, Erlangen, Germany) with a 32 channel head coil. Morphological brain data was assessed by high-resolution 3-dimensional T1-weighted anatomical images (MPRAGE) (repetition time (TR) = 2300 ms,

eco time (TE) = 3.03 ms, flip angle = 9°, field of view (FOV) = 256 mm, 192 slices, slice thickness = 1.00 mm, voxel dimension = 1.0 × 1.0 × 1.0 mm, matrix size = 256 × 256).

The individuals blood oxygen level dependent (BOLD) signal was measured with two 9:36 min T2*-weighted echo-planar image (EPI) sequences with 285 volumes (TR = 2000 ms, TE = 30 ms, flip angle = 80°, FOV = 192 mm, 28 sagittal slices, slice thickness = 4.0 mm, 1 mm gap, voxel dimension = 3.00 x 3.00 x 4.00 mm, matrix size = 64 x 64). The behavioral tasks were presented using the Presentation software package (Version 21.1, Neurobehavioral Systems, Inc., Albany, CA, United States).

Functional Magnetic Resonance Imaging Data Analysis

Preprocessing

We used SPM 12 (Wellcome Department of Cognitive Neurology, London, United Kingdom) implemented in MATLAB R2019a (MathWorks Inc., Sherborn, MA, United States) for preprocessing and analysis of functional images. The first four volumes of functional data were discarded. Preprocessing included normalization of the anatomical image to the SPM TPM template, and for the functional images slice-time correction, realignment to the mean image, co-registration to the anatomical image, spatial normalization to the SPM TPM template, rescaling to a resolution of 2 mm × 2 mm × 2 mm, and spatial smoothing with a 8x8x8 mm Gaussian kernel.

Modeling

For subject-specific first-level analyses, we set up three general linear models (GLMs). The reward and loss conditions were modeled as separate sessions within the GLMs described below. The respective regressors were the same for both sessions and are illustrated in **Figure 1**. Regressor onsets were convolved with the default SPM canonical hemodynamic response function. Six estimated movement parameters were included as regressors of non-interest in all models. The following GLMs were specified:

(1). A *phase-related GLM* was set up to compare task-related activation between conditions (i.e., loss/reward) and implicit baseline. Two phase related-regressors of interest were specified: the *decision phase* (onset of the decision phase modeled with the respective reaction time) and the *anticipation phase* (onset of the cue during the anticipation phase modeled with a fixed duration of 6 s). Trials in which the participants failed to choose an option during the decision phase were excluded from the regressors of interest by adding two dummy regressors of non-interests. To account for additional activation variance of no interest, we added several regressors of no interest, including the button press during the decision phase, the flash after the anticipation phase, the button press after the flash, and the feedback.
The following contrasts were specified to detect activation related to the reward decision phase (RDec), the loss decision phase (LDec), reward anticipation (RA) and loss anticipation (LA):
Decision Phase: RDec > Implicit Baseline; LDec > Implicit Baseline; RDec > LDec; LDec > RDec.
Anticipation Phase: RA > Implicit Baseline; LA > Implicit Baseline; RA > LA; LA > RA.

(2). A *parametric decision-related GLM* was set up to assess changes in brain activation in response to trial difficulty, which was operationalized as the difference between the subjective values (SV) of the immediate and delayed options. Here, a smaller difference indicates that the immediate option and the discounted delayed option have a more similar subjective value, which is considered a more difficult decision. The subjective value difference (SV_Diff) was added as a parametric modulator for the decision phase.
Following contrasts were specified in this model:
Decision Phase: SV_Diff_{reward} > Baseline; SV_Diff_{loss} > Baseline.

(3). A *parametric anticipation-related GLM* was set up to characterize the association between phase-related activation during the anticipation phase and the internal value representation of the cued amount of money. For this purpose, the subjective value of the chosen option was added as a parametric modulator for the anticipation phase.
Following contrasts were specified in this model:
Anticipation Phase: SV_{reward} > Baseline; SV_{loss} > Baseline.

(4). A *choice-related GLM* was set up to compare choice-related activation within conditions. The regressors were identical with the first model, with the two phase-related regressors of interest (decision phase and anticipation phase) being split into four regressors based on the participant's choice for the immediate or delayed option. Participants with less than 20% discounted choices (6 out of 32 trials) were excluded from respective contrasts.
The following contrasts were specified in this model:
Decision Phase: Immediate > Delayed, Delayed > Immediate (separately for reward and loss).
Anticipation Phase: Immediate > Delayed, Delayed > Immediate (separately for reward and loss).

Linear contrast estimates were then entered into a second-level random effects model. One-sample *t*-tests were used to detect within-group activation. Inferences were conducted on the whole-brain level with a cluster-corrected significance threshold of $p < 0.05$ and a cluster-defining threshold of $p < 0.001$ uncorrected. We also conducted all contrasts at a family-wise peak voxel-corrected threshold of $p < 0.05$. Both cluster-corrected and peak voxel-corrected *p*-values are reported in the (**Supplementary Tables 1**, **2**). The contrasts for the *decision phase* (task-related GLM) yielded very large clusters (> 60.000 voxels), therefore we only report regions which remained significant at the peak voxel-corrected threshold.

In order to test the hypotheses regarding ventral striatal activation during reward and loss anticipation, an a priori defined ROI analysis was conducted for two contrasts of the first model:

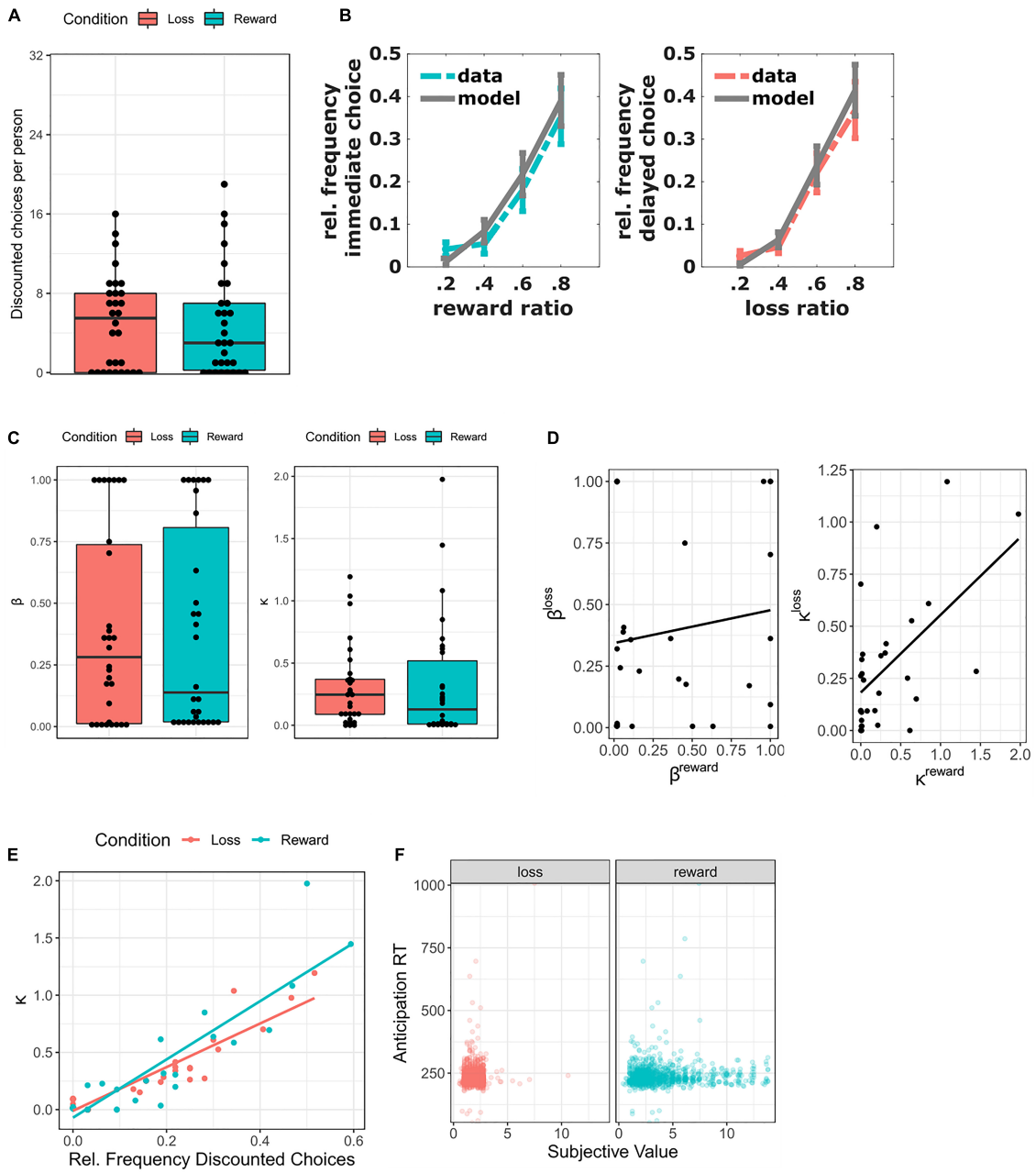

FIGURE 2 | Behavioral results ($N = 30$). **(A)** Number of discounted choices per person (reward = immediate choices; loss = delayed choices). **(B)** Relative frequency of discounted choices per ratio between immediate and delayed options (means and standard errors of the mean). Gray: means and standard errors of the subject-wise hyperbolic model predictions. **(C)**: Distribution of κ and β values. **(D)**: Associations of κ and β between conditions. **(E)**: Association between κ parameters and relative frequency of discounted choices. **(F)**: Associations between reaction time during the anticipation phase and hyperbolic model-derived subjective values (note: absolute subjective values used for loss condition, "see Behavioral Modeling").

"Reward > Implicit Baseline" (Hypothesis 2) and "Reward > Loss" (Hypothesis 3). The mask for the ROI analysis covering the bilateral nucleus accumbens was based on the automated anatomical atlas (AAL, Tzourio-Mazoyer et al. (2002)) and comprised a volume of 9506 mm^3 (1189 voxels). Inference for ROI analyses was conducted with a significance threshold of $p < 0.05$ corrected for small volume.

To test for associations between individual discounting tendency and brain activation during the *decision phase*, model-derived discounting parameters (κ) were entered as covariates of interest in the second level models. Lastly, to test the hypothesis of stronger RD and higher activation during the anticipation of immediate rewards (compared to delayed rewards), the discounting parameter κ^{reward}

was entered as a covariate of interest in the second level of the *choice-related* contrast Immediate > Delayed Reward Anticipation.

RESULTS

Study Population

The study sample consisted of 30 undergraduate university students (mean age ± SD = 24 ± 3.46 years; range 19 to 33; 14 female) from different fields.

Missing Data

MRI data from two participants had to be excluded due to an incidental finding and excessive head movement. Behavioral analyses are reported with N = 30, fMRI analyses with N = 28.

A total of 30 trials (1.56% of all trials) had to be excluded from further analyses due to no decision within 3s.

Behavior

For the decision phase, the number of discounted choices per condition is illustrated in **Figure 2A**. The average number of discounted choices (out of 32 trials) was 4.93 in the reward condition and 5.12 in the loss condition (**Table 1**), with a correlation of $r = 0.47$ ($p = 0.01$) between the two. Almost a third of all participants (8 in the loss condition, 9 in the reward condition) never chose the discounted option. In both conditions, the relative discounting frequency increased as the ratio between immediate and delayed options approximated 1, as illustrated by **Figure 2B**. This is further confirmed by the statistically significant effect of ratio ($t(29.31) = 5.62$, $p < 0.001$) in the LMM predicting relative discounting frequency by ratio and condition (**Table 2**). In contrast, the effect of condition was not significant ($t(29.05 = 0.03$, $p = 0.79$), indicating no difference between loss and reward trials with regard to number of discounted choices.

The descriptive statistics for the behavioral model parameters κ and β are presented in **Table 1** (see also **Figure 2C**). Paired t-tests revealed that discounting parameters κ ($t(29) = -0.31$, $p = 0.76$) and choice parameters β ($t(29) = 0.16$, $p = 0.88$) did not differ significantly between conditions. Excluding participants showing no behavioral variability yielded the same results (all $p > 0.44$). Instead, model-derived discounting parameters κ ($r = 0.56$, $p < 0.01$), but not choice parameters β ($r = 0.14$, $p = 0.46$), were significantly correlated between conditions (**Table 1** and **Figure 2D**). The correlation between discounting parameters κ did not remain significant after excluding participants without behavioral variability in at least one of the two conditions ($r = 0.43$, $p = 0.09$, $n = 17$).

Correlations between the behavioral model parameters and number of discounted choices are presented in **Table 1**. Discounting parameters κ based on the hyperbolic model were highly correlated with the number of discounted choices, both for the loss ($r = 0.92$, $p < 0.001$) and the reward condition ($r = 0.90$; $p < 0.001$; **Figure 2E**). The correlation remained constant after

TABLE 1 | Means, standard deviations, and correlations of behavioral data ($N = 30$).

Variable	*M*	*SD*	1	2	3	4	5	6	7	8	9
(1). κ (Reward)	0.33	0.48									
(2). κ (Loss)	0.30	0.32	0.56** [0.25, 0.77]								
(3). β (Reward)	0.38	0.41	0.26 [−0.11, 0.57]	0.39* [0.03, 0.66]							
(4). β (Loss)	0.39	0.39	0.28 [−0.09, 0.58]	0.18 [−0.20, 0.50]	0.14 [−0.23, 0.48]						
(5). Number of discounted choices (Reward)	4.93	5.40	0.90** [0.80, 0.95]	0.56** [0.25, 0.76]	0.30 [−0.07, 0.60]	0.20 [−0.17, 0.52]					
(6). Number of discounted choices (Loss)	5.13	4.79	0.42* [0.07, 0.68]	0.92** [0.83, 0.96]	0.29 [−0.08, 0.59]	0.33 [−0.03, 0.62]	0.47** [0.14, 0.71]				
(7). BIS: Non-Planning	9.50	2.81	−0.15 [−0.49, 0.22]	0.03 [−0.34, 0.38]	−0.24 [−0.55, 0.13]	0.02 [−0.34, 0.38]	−0.20 [−0.52, 0.17]	0.13 [−0.25, 0.46]			
(8). BIS: Motor	10.83	2.29	−0.32 [−0.61, 0.04]	0.00 [−0.36, 0.36]	0.08 [−0.29, 0.42]	−0.04 [−0.39, 0.33]	−0.27 [−0.58, 0.10]	0.01 [−0.35, 0.37]	0.34 [−0.02, 0.62]		
(9). BIS: Attentional	8.73	1.64	0.11 [−0.26, 0.45]	0.01 [−0.35, 0.37]	-0.08 [−0.43, 0.29]	-0.25 [−0.56, 0.12]	0.05 [−0.32, 0.40]	-0.03 [−0.38, 0.34]	0.09 [−0.28, 0.44]	0.09 [−0.28, 0.44]	
(10). BIS: Total	29.07	4.66	−0.21 [−0.53, 0.16]	0.02 [−0.34, 0.38]	−0.14 [−0.47, 0.24]	−0.09 [−0.44, 0.28]	−0.24 [−0.55, 0.13]	0.07 [−0.30, 0.42]	0.80** [0.62, 0.90]	0.73** [0.50, 0.86]	0.45* [0.11, 0.70]

*M and SD are used to represent mean and standard deviation, respectively. BIS = Barrat Impulsivity Scale. * indicates $p < .05$. ** indicates $p < .01$.*

TABLE 2 | Linear Mixed Model for the effect of condition (Loss = 0, Reward = 1) and ratio between immediate and delayed options (0.2, 0.4, 0.6, 0.8) on relative frequency of discounted choices during the decision phase (*N* = 30).

Level	Effect	Estimate	SE	t	*df*	P	5% CI	95% CI
Group	Intercept	−0.12	0.03	−3.43	35.36	< 0.01	−0.19	−0.05
Group	Condition	−0.01	0.03	−0.27	29.05	0.79	−0.07	0.05
Group	Ratio	0.57	0.10	5.62	29.31	< 0.01	0.36	0.77
Subject	SD (Intercept)	0.13						
Subject	Intercept*Condition	−0.40						
Subject	Intercept*Ratio	−0.92						
Subject	SD (Condition)	0.13						
Subject	Condition*Ratio	0.02						
Subject	SD (Ratio)	0.50						
Residual	SD	0.14						

Estimates are in relative frequencies (0 to 1).

removing data from participants without behavioral variability (reward: $r = 0.89$; loss: $r = 0.92$, both $p < 0.001$). Taken together, the hyperbolic discounting parameters were a good indicator of observed discounting behavior.

No behavioral index of discounting behavior showed a significant association with any of the subscales nor the total scale of the BIS-15 (**Table 1**), indicating no linear relationship between self-rated impulsivity and observed discounting behavior.

Lastly, there was no effect of condition (reward/loss) on the reaction times in the decision phase and the anticipation phase. For the decision phase, the LMM revealed a statistically significant effect of ratio ($t(28.67) = 4.06$, $p < 0.001$)), but not condition ($t(28.99) = -0.97$, $p = 0.34$; **Table 3**), indicating slower decision-making in trials with higher ratio between the immediate and delayed option.

For the anticipation phase, the LMM revealed no significant effects of condition ($t(1852.64) = 0.01$, $p = 0.99$) or subjective value ($t(1856.64) = 0.29$, $p = 0.77$; **Table 4**). The reaction time after the flash was therefore unrelated to valence or magnitude, as illustrated by **Figure 2F**.

Functional Magnetic Resonance Imaging

Decision Phase

Reward Condition

The *phase-related GLM* contrast "RDec > Implicit Baseline" revealed clusters of activation in the visual cortex, the cerebellum, the anterior insula, the operculum, the primary and supplementary motor areas, the superior and posterior parietal cortex, and the anterior cingulate cortex (see **Figure 3A** and **Supplementary Table 1**).

In no brain region was task-related activation significantly correlated to the individual discounting parameter κ^{reward} (*phase-related GLM* contrast 'RDec > Implicit Baseline) * κ^{reward} '). This result remained unchanged after excluding participants without behavioral variability (remaining $n = 21$).

The *choice-related GLM* contrasts "Immediate > Delayed Choices" and vice versa revealed no significant clusters of brain activation. However, due to the low behavioral variance, data of only 12 participants were included in this contrast.

The *parametric modulation* of RDec with the subjective value difference between immediate and delayed options revealed no significant clusters of activation.

Loss Condition

The *phase-related GLM* contrast "LDec> Implicit Baseline" revealed clusters of activation in the visual cortex, the cerebellum, the anterior insula, the operculum, the primary and supplementary motor areas, the superior and posterior parietal cortex, and the anterior cingulate cortex (see **Figure 3B** and **Supplementary Table 1**).

No brain region showed activation in significant relation with the individual discounting parameter κ^{loss} (*phase-related GLM* contrast 'LDec > Implicit Baseline) * κ^{loss} '). This result remained unchanged after excluding participants without behavioral variability (remaining $n = 22$).

The *choice-related GLM* contrasts "Immediate > Delayed Choices" and vice versa revealed no significant clusters of brain activation. However, due to the low behavioral variance, data of only 15 participants were included in this contrast.

The *parametric modulation* of LDec with the subjective value difference between immediate and delayed options revealed no significant clusters of activation.

Reward Condition vs. Loss Condition

There were no significant clusters in the *phase-related GLM* contrasts "LDec > RDec" and vice versa. An exploratory contrast combining loss and reward ('LDec + RDec > Baseline') revealed activation throughout the same regions as during the individual conditions (**Supplementary Figure 1** and **Supplementary Table 3**).

Anticipation Phase

Reward Anticipation

In the *phase-related GLM* contrast "RA > Implicit Baseline," significant activation was present in the anterior insula, anterior cingulate cortex, putamen, pallidum, operculum, cerebellum, thalamus as well as primary and supplementary motor areas (see **Figure 4A** and **Supplementary Table 2**). Furthermore, the a priori ROI analysis revealed significant activation in the ventral striatum (**Supplementary Table 2**).

TABLE 3 | Linear Mixed Model for the effect of condition (Loss = 0, Reward = 1) and ratio between immediate and delayed options (0.2, 0.4, 0.6, 0.8) on reaction times during the decision phase (*N* = 30).

Level	Effect	Estimate	SE	t	*df*	P	5% CI	95% CI
Fixed	Intercept	1,043.17	35.58	29.32	28.90	< 0.01	970.40	1,115.95
Fixed	Condition	−34.82	35.81	−0.97	26.99	0.34	−108.07	38.42
Fixed	Ratio	241.67	59.57	4.06	28.68	< 0.01	119.77	363.57
Subject	SD (Intercept)	167.13						
Subject	Intercept*Condition	−0.52						
Subject	Intercept*Ratio	0.59						
Subject	SD (Condition)	181.01						
Subject	Condition*Ratio	−0.02						
Subject	SD (Ratio)	279.04						
Residual	SD	299.79						

Estimates are in milliseconds.

TABLE 4 | Linear Mixed Model for the effect of condition (Loss = 0, Reward = 1) and subjective value of outcome on reaction times during the anticipation phase. Subjective values of the chosen option were derived from the hyperbolic model ("see Behavioral Modeling") (*N* = 30).

Level	Effect	Estimate	SE	t	*Df*	p	5% CI	95% CI
Fixed	Intercept	239.72	3.91	61.32	39.40	0.00	231.82	247.63
Fixed	Condition	0.05	3.81	0.01	1,853.64	0.99	−7.42	7.53
Fixed	Subjective Value	0.16	0.53	0.29	1,857.64	0.77	−0.89	1.20
Subject	SD (Intercept)	18.91						
Residual	SD	46.86						

Estimates are in milliseconds.

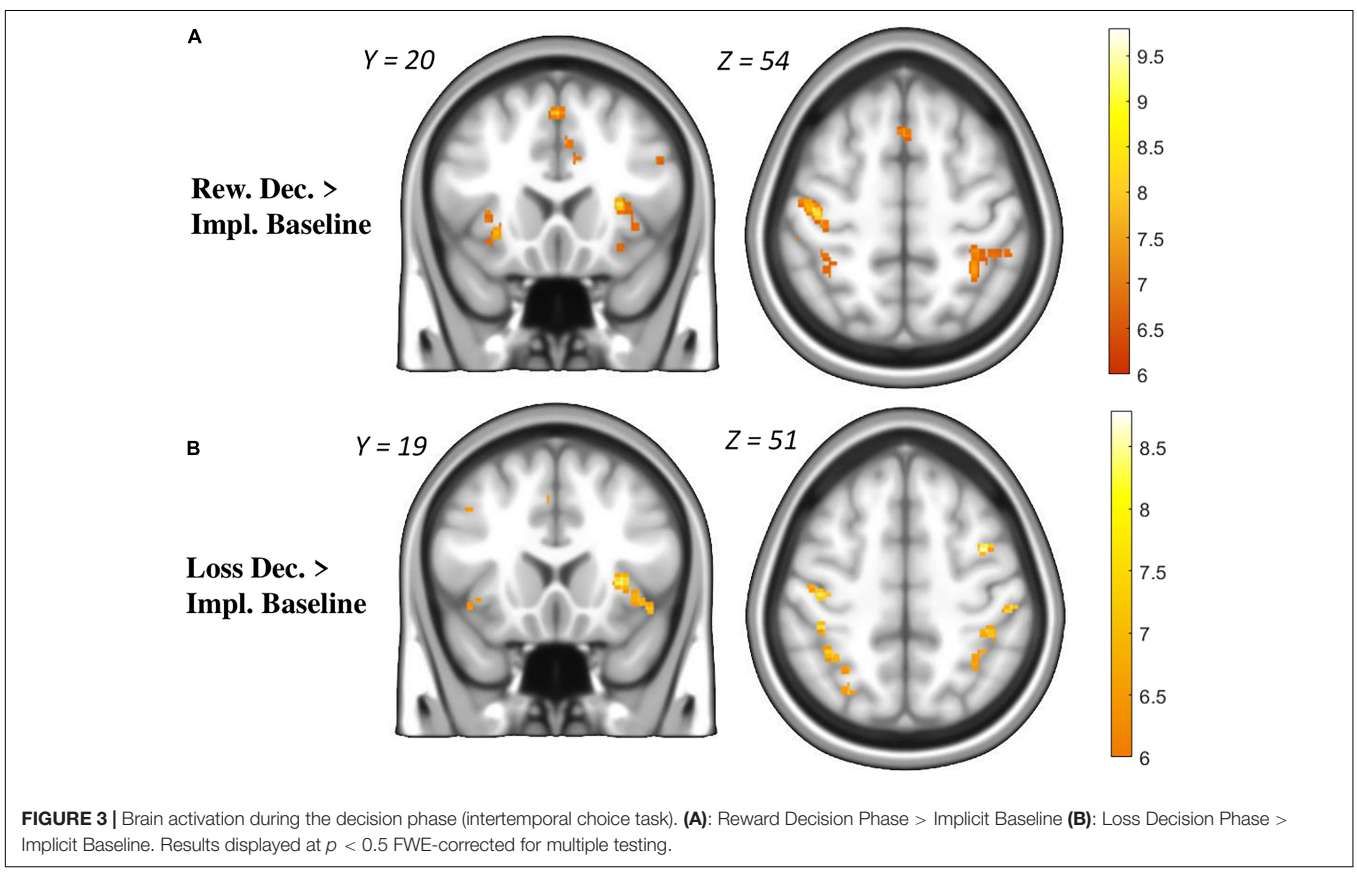

FIGURE 3 | Brain activation during the decision phase (intertemporal choice task). **(A)**: Reward Decision Phase > Implicit Baseline **(B)**: Loss Decision Phase > Implicit Baseline. Results displayed at $p < 0.5$ FWE-corrected for multiple testing.

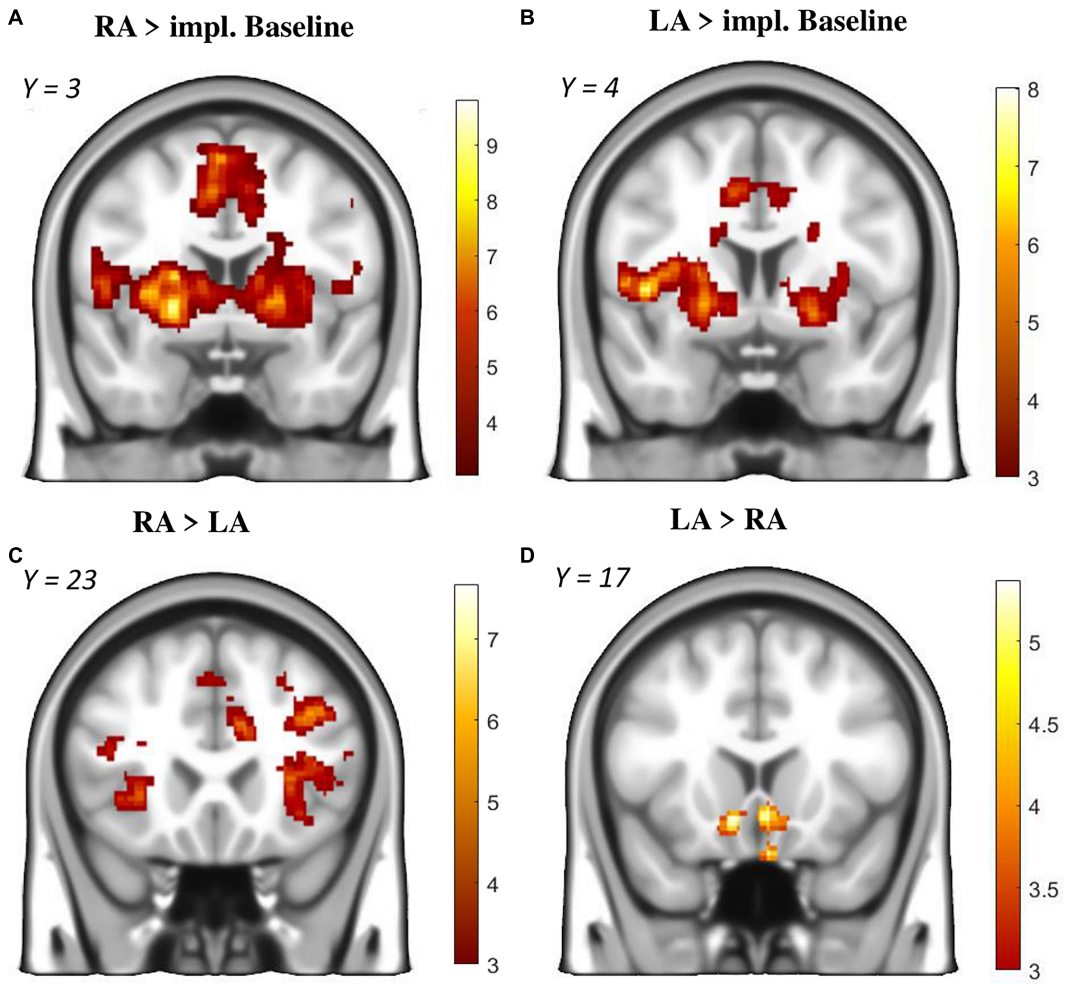

FIGURE 4 | Brain activation during the anticipation phase (monetary incentive delay task). **(A)**: Reward Anticipation (RA) > Implicit Baseline. **(B)**: Loss Anticipation (LA) > Implicit Baseline. **(C)**: RA > LA. **(D)**: LA > RA. Only voxels from significant clusters (cluster-size $p < 0.05$ corrected for multiple testing and $p < 0.001$ as cluster-defining threshold) are displayed.

The *parametric modulation* of RA with subjective value revealed three clusters in the anterior insula + striatum, the cerebellum and the anterior cingulate cortex (**Figure 5A** and **Supplementary Table 2**). In other words, the chance of winning higher rewards was associated with more activity in salience-related regions.

The *choice-related GLM* contrasts "Immediate > Delayed Choices" and vice versa revealed no significant clusters of brain activation. However, due to the low behavioral variance, data of only 12 participants could be included in this contrast.

The *choice-related* brain-behavior correlation '(Immediate > Delayed) * κ^{reward} revealed no significant clusters of activation.

Loss Anticipation

The *phase-related GLM* contrast "LA > Implicit Baseline" revealed significant clusters in the anterior insula, anterior cingulate cortex, putamen, pallidum, operculum, cerebellum, visual cortex as well as and primary and supplementary motor areas (**Supplementary Table 2** and **Figure 4B**).

The *parametric modulation* of LA with subjective value revealed five clusters associated with the chance of preventing higher losses: the prefrontal cortex, middle cingulate cortex, thalamus and precuneus (**Supplementary Table 2** and **Figure 5B**).

The *choice-related GLM* contrasts "Immediate > Delayed Choices" and vice versa revealed no significant clusters of brain activation. However, due to the low behavioral variance, data of only 15 participants reward could be included in this contrast.

Reward Anticipation vs. Loss Anticipation

The *phase-related GLM* contrast "RA >LA" revealed significantly more activation during RA throughout the prefrontal and parietal cortex, anterior insula, putamen, anterior cingulate cortex and motor areas (**Supplementary Table 2** and **Figure 4C**). The opposite contrast "LA > RA" revealed significantly more activation during LA in the ventral striatum (**Supplementary Table 2** and **Figure 4D**).

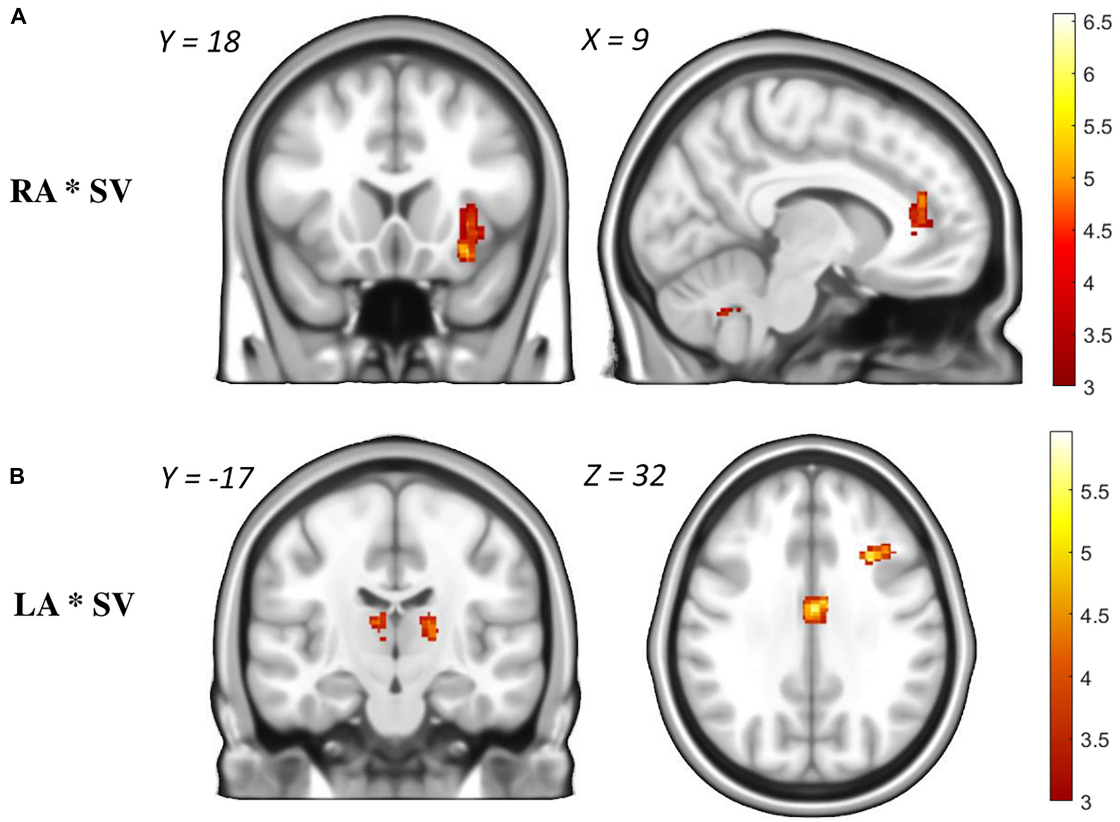

FIGURE 5 | Parametric modulation of brain activation during the anticipation phase with hyperbolic model-derived subjective values ("see Behavioral Modeling"). **(A)**: Brain regions that show more activation during Reward Anticipation (RA) when subjectively higher rewards could be won. **(B)**: Brain regions that show more activation during Loss Anticipation (LA) when subjectively higher losses could be avoided. Only voxels from significant clusters (cluster-size $p < 0.05$ corrected for multiple testing and $p < 0.001$ as cluster-defining threshold) are displayed.

DISCUSSION

General Discussion

In this study, we aimed to investigate the differences and/or associations between temporal discounting of losses and rewards on a behavioral and neural level. We combined an intertemporal choice task with a monetary incentive delay task in an fMRI experiment. That is, participants had to choose between two potentially real losses or rewards in the *decision phase* of each trial, and respond quickly to receive the chosen option in the *anticipation phase* of each trial. Individual discounting parameters were estimated based on the hyperbolic discounting model. Based on these parameters, we were able to obtain subjective values for the chosen rewards and losses and used these as parametric modulators in the fMRI models.

Statistical analyses focused on the exploratory comparison of the behavior and neural activation during the loss and reward conditions. During the decision phase of the task, we observed correlated LD and RD behavior and no neural differences between the loss and reward condition. During the anticipation phase, the ventral striatum was more strongly activated during the loss condition, whereas several regions including ACC and anterior insula were more strongly activated during the reward condition. Higher subjective losses and rewards were found to be associated with stronger activation in several regions during the anticipation phase.

Our a priori-defined analyses regarding correlations between neural activation and individual discounting parameters did not yield any significant finding. As discussed further below, this might be explained by the overall low rate of discounting behavior.

Comparing Discounting of Rewards and Losses

We observed discounting of both losses (LD) and rewards (RD): participants gravitated more towards the discounted option in trials where the immediate and delayed option were more similar, i.e., where the ratio between options was closer to 1 (**Table 2**). The general discounting frequency in our experiment was low, which is why key analyses were repeated excluding non-discounters. However, at least for the loss task, the discounting rates seem in line with prior literature reporting about 30% non-discounters (Mitchell and Wilson, 2010; Myerson et al., 2017; Yeh et al., 2020; Thome et al., 2022).

In general, the observed data in both conditions matched the pattern predicted by the hyperbolic model (**Figure 2B**).

Note that the hyperbolic model was chosen based on the literature ("see Behavioral Modeling"). With only one delay, it could not be compared to other models like the exponential or hyperboloid function. However, hyperbolic κ parameters were strongly correlated with the number of discounted choices in both reward (r = 0.90) and loss (r = 0.92) conditions, a result which remained unchanged after excluding non-discounting participants. These findings support our hypothesis of some form of discounting behavior in both conditions.

Contrary to our expectations, we found very similar behavior during loss and reward trials. The condition had no significant effect on the number of discounted trials (**Table 2**). Further, loss and reward behavior was highly correlated, as reflected by the correlation between conditions regarding number of discounted choices (r = 0.47, **Table 1**) and κ values (r = 0.56, **Figure 2D**). The strong correlation between κ values did not remain significant after excluding non-discounters, yet the effect size remained comparable (r = 0.46). Power analyses revealed that our full sample of N = 30 yielded 96% power to detect the strong correlation of r = 0.55 reported for middle-aged adults by Halfmann et al. (2013), but only 73% power to replicate the moderate correlation of r = 0.39 reported by Mitchell and Wilson (2010). Therefore, the lack of significance after reduction of the sample size can most likely be attributed to a lack of power.

Like the number of discounted choices, the behavioral model parameters κ and β did not significantly differ between conditions. However, prior studies (Chapman, 1996; Engelmann et al., 2013) reported differences between LD and RD only for large but not for small delays, matching our data which is only based on small delays. In addition, post-hoc power analyses revealed only 48% power to find a small difference of d = 0.3 between RD and LD in our sample. Consequently, our finding of no behavioral difference should not be generalized to large delays and small effects.

Another similarity between conditions was found in reaction times during the decision phase, which were highly variable, but not related with the reward/loss condition (**Tables 3**, **4**). Together, this suggests commonalities between cognitive processes involved in reward and loss discounting, if only for short delays and small monetary outcomes.

Successful Induction of Loss Perception

The implementation of real losses is not a straightforward enterprise if participants start with upfront money that can be won. Using one balance for both immediate and delayed losses would motivate participants to exploit the immediate loss to receive more money at the end. Here we tested a system with different balances for immediate and delayed losses: In this study, two random choices per condition were selected and paid out. Chosen losses were subtracted from a fixed balance if the reaction time during the anticipation phase task was fast enough and doubled if the reaction time was too slow. However, this means that participants could actually win money in the loss condition. By choosing different balances for the immediate (€8.20) and delayed loss (€10), we tried to prevent an obvious winning strategy. However, theoretically participants could always opt for the maximum win if they followed an optimal strategy. This means that we could not guarantee that the loss ICT actually induced a perception of losing money, rather than of potentially winning more money.

To evaluate our success in inducing a perception of loss (and consequently loss discounting), participants answered open questions about their strategy after completing all measurements. In the reward condition, 24 participants stated an overall strategy of always choosing the higher win, whereas 12 participants explicitly named a variable strategy based on time and reward ratio (discounting behavior). In the loss condition, 19 participants stated an overall strategy of always choosing the smaller loss, with 11 participants naming variable strategies based on time and reward ratio. Here, a variable strategy could be the result of both discounting and a win-oriented strategy. However, only one participant explicitly described choosing the loss that resulted in the larger win. Notably, 19 participants explicitly used the word "loss" when talking about their strategy, indicating a perception of actual losses, rather than absolute wins. Few studies have investigated LD in the fMRI, and to our knowledge, none have used real losses. This is understandable, given the obvious ethical problems of inflicting monetary losses on participants. Here we tried to mask the "optimal" choice by using different balances from which immediate and delayed losses were subtracted. This enabled us to follow up the intertemporal choice task by means of an incentive delay task with real losses. Taken together, the quantitative and qualitative results clearly indicate that the behavioral variance in the loss condition was indeed due to LD and not win-orientation.

Brain Activation During Intertemporal Decision-Making

During the decision phase, a pattern of regions related to networks of salience (e.g., anterior insula and cingulate cortex), decision-making (e.g., parietal and frontal cortex) and motor control (e.g., precentral gyrus and SMA) was observed in both conditions (**Figure 3** and **Supplementary Figure 1**). This activation pattern closely matches the overlap of three different discounting tasks against baseline reported by Koffarnus et al. (2017). In line with the behavioral results, we observed no significant differences between the loss and reward conditions. Furthermore, we found no brain-behavior correlation with the model-derived κ parameters. Again, the low behavioral variability observed throughout the experiment may have impeded the statistical comparison of neural discounting processes. Indeed, the few studies comparing neural correlates of LD and RD have reported inconsistent results (Bickel et al., 2009; Xu et al., 2009) which might suggest only subtle differences in neural activity during LD and RD.

We did not find any evidence for a modulation of brain activation by the difference between the two subjective values presented in each trial. Very difficult trials (i.e., trials close to the indifference point, therefore small difference) have been shown to elicit more activation in the ACC and dlPFC, than very easy trials (Monterosso et al., 2007; Koffarnus et al., 2017). Again, this result may be best explained by the small monetary outcomes and low

behavioral variability, yielding only few trials with very hard and very easy choices.

Delay Discounting and Impulsivity

No subscale or total score of the BIS-15 was significantly associated with discounting behavior. Excessive delay discounting is associated with "impulsive" behavior such as obesity and substance use disorders (Story et al., 2014). However, the term impulsivity is multi-faceted and contains different constructs with inconsistent associations (Moreira and Barbosa, 2019). Stahl et al. (2014) found no association between delay discounting and other measures of impulsivity and argue that "impulsivity" is an umbrella term of limited usability. The BIS-15 is a common self-rating instrument with weak associations to discounting at best (Reynolds et al., 2006; de Wit et al., 2007; Mobini et al., 2007). In conclusion, rather than reflecting impulsivity, discounting might better be understood as a construct on its own (Odum, 2011).

Brain Activity During the Anticipation Phase

The observed activity during the anticipation phase in both conditions (**Figure 4**) matches the very typical pattern associated with motivational salience and monetary incentive delay tasks (Kirsch et al., 2003; Bjork et al., 2012; Oldham et al., 2018). The anterior insula and cingulate cortex are thought to modulate attention and goal-directed behavior towards context-relevant stimuli. Indeed, activity in these two regions was furthermore associated with subjective value, indicating a neuronal reflection of salience increasing with the amount of money that can be won or lost. In contrast, a study by Diekhof et al. (2012) found increased striatal response during the MID in response to an increased subjective value of the presented outcome. In our study, ventral striatal activation was surprisingly limited during reward anticipation, as reflected by the small cluster which only remained significant in the ROI analysis (**Supplementary Table 2**). A reason for this might be our overall experimental design with two tasks that are known to activate the ventral striatum (Kirsch et al., 2003; Schüller et al., 2019). In addition to this, the anticipation task lacked an explicit control condition, leaving only the implicit baseline contrast with possibly low residual variance.

Comparing Reward and Loss Anticipation

Comparing baseline contrasts side by side, activity during loss anticipation was focused around the same salience hubs as during reward anticipation (**Figure 4**). This is in line with recent meta-analyses suggesting a valence-independent processing of motivational salience (Dugré et al., 2018; Oldham et al., 2018). However, a direct contrast of reward anticipation >loss anticipation and vice versa revealed differentiated activity during the two conditions (**Figures 4C, D**). The aforementioned salience regions and several clusters throughout the cortex were significantly more activated during reward trials, whilst loss trials were associated with more activation in the ventral striatum. The former effect is less surprising if we take into account the average subjective value: participants chose smaller losses and larger rewards (see also **Figure 2F**). Therefore, reward trials (with an average win of €4.02) were possibly more salient than loss trials (with an average loss of €1.89), reflected by more activity on corresponding brain networks. Indeed, brain regions involved in evaluating the motivational relevance of states have been theorized to act as valence-independent salience networks (Oldham et al., 2018).

Though plausible, this cannot explain the increased ventral striatal response during loss anticipation. In fact, we were expecting the opposite, as a recent meta-analysis reported more ventral striatal activity during reward anticipation (Oldham et al., 2018). However, given that the incentive delay task allows the participants to prevent an anticipated loss, increased activation in a core region of motivational processing might reflect a higher motivational value of the prevention of a potential loss compared to a potential win. Such a response pattern would be predicted by prospect theory (Kahneman and Tversky, 1979) in the context of loss aversion.

Limitations

Our study used potentially real rewards and losses, trading external validity against a low monetary range and no variation in the delay, due to practical considerations. This combination probably resulted in a very low discounting rate, and hence statistical power. Moreover, generalization to large delays and monetary outcomes is limited. For most participants, the calculation of discounting parameters relied on few trials, limiting the reliability of the obtained parameters. Importantly, the lack of different delays made it impossible to compare different discounting models, e.g., the hyperbolical and the hyperboloid function.

Although we demonstrate a successful induction of loss discounting using real outcomes, this could possibly introduce a bias of upfront money, which might increase the validity of the monetary domain and hence reduce discounting (Jiang et al., 2016). Another possible bias comes from the payment procedure, where chosen losses were doubled if the anticipation time was too short. This unproportionally increased the potential loss associated with the (larger) delayed option.

Lastly, some methodological issues arise from our combination of an ICT with a MID. The contingency of the ICT outcome on performance in the MID induced ambiguity, i.e., an implicit and changing probability of ∼50% to not receive the chosen reward or even receive a higher loss. This may have biased participants to prefer a smaller loss. In addition, ambiguity may have influenced neural processes during the ICT, limiting the comparison to neuroimaging studies investigating pure delay discounting or risky decision-making (Ikink et al., 2019; Ortiz-Teran et al., 2019). Another limitation is that the behavioral paradigm was not designed to directly contrast brain activation during the decision phase and the anticipation phase.

Therefore, the separation of decision-making and instrumental behavior is only conceptual, but cannot be backed up by more intricate statistical analyses.

Future Research

A proper comparison of loss and reward discounting requires an adaptation of the paradigm with respect to inter- and intra-individual differences. Delay discounting is a decision-making process assumed to involve a valuation of options. Comparing subjective valuation requires comparable subjective values. This means taking into account global differences between RD and LD (e.g., magnitude effect, loss aversion) and individual discounting behavior to create intertemporal decisions with comparable subjective value. To this end, we recently developed a model-based framework to evoke predicted responses in RD and LD (Thome et al., 2022). As a next step, we plan to apply this adaptive task in the fMRI to allow for more fine-grained analysis of the neural differences between RD and LD.

CONCLUSION

We found similar behavior in intertemporal choice tasks involving potentially real losses and rewards. Whilst the overall discounting rate was low, losses were discounted as frequently as rewards. There was a considerable correlation ($r = 0.56$) between hyperbolic discounting parameters κ during loss and reward discounting. In line with this finding, brain activation during reward- and loss-related decision-making were not significantly different from another. In contrast to that, reward anticipation recruited more salience-related brain regions like the anterior insula and the ACC, with the exception of more ventral striatal activation during loss anticipation. In line with prior research we demonstrate that brain activation in salience-related regions during reward and loss anticipation was associated with model-derived subjective values. Taken together, the general results of our study seem to support the account that LD and RD rely on similar or at least overlapping cognitive and neural processes. However, this similarity is yet to be demonstrated for an extensive range of delays and monetary outcomes.

DATA AVAILABILITY STATEMENT

The behavioral datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: https://osf.io/kmer3/. The fMRI datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of the Medical Faculty Mannheim, University of Heidelberg (2019-633N). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

GK, PK, and WS conceptualized the study. MP and PH collected the data. MP, JT, and GK performed the statistical analyses. MP wrote the manuscript. All authors contributed to conception and the design of the study, read, revised, and approved the submitted manuscript.

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Study 1: Supplementary Material

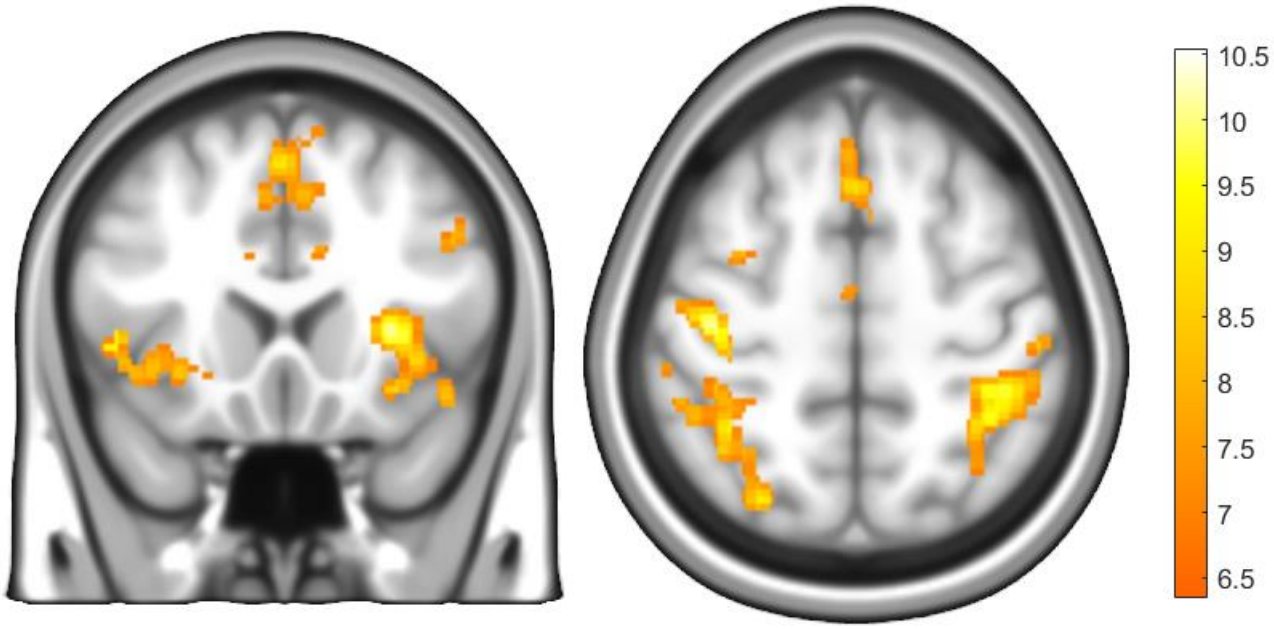

Figure S1. Brain activation during the decision phase (intertemporal choice task). Reward Decision Phase + Loss Decision Phase > Baseline

Tables S1, S2, S3: Due to table size and format, please download from https://www.frontiersin.org/articles/10.3389/fnsys. 2022.867202/full#supplementary-material

5 Study 2

Title: A Model Guided Approach to Evoke Homogeneous Behavior During Temporal Reward and Loss Discounting

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A Model Guided Approach to Evoke Homogeneous Behavior During Temporal Reward and Loss Discounting

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Background: The tendency to devaluate future options as a function of time, known as delay discounting, is associated with various factors such as psychiatric illness and personality. Under identical experimental conditions, individuals may therefore strongly differ in the degree to which they discount future options. In delay discounting tasks, this inter-individual variability inevitably results in an unequal number of discounted trials per subject, generating difficulties in linking delay discounting to psychophysiological and neural correlates. Many studies have therefore focused on assessing delay discounting adaptively. Here, we extend these approaches by developing an adaptive paradigm which aims at inducing more comparable and homogeneous discounting frequencies across participants on a dimensional scale.

Method: The proposed approach probabilistically links a (common) discounting function to behavior to obtain a probabilistic model, and then exploits the model to obtain a formal condition which defines how to construe experimental trials so as to induce any desired discounting probability. We first infer subject-level models on behavior on a non-adaptive delay discounting task and then use these models to generate adaptive trials designed to evoke graded relative discounting frequencies of 0.3, 0.5, and 0.7 in each participant. We further compare and evaluate common models in the field through out-of-sample prediction error estimates, to iteratively improve the trial-generating model and paradigm.

Results: The developed paradigm successfully increases discounting behavior during both reward and loss discounting. Moreover, it evokes graded relative choice frequencies in line with model-based expectations (i.e., 0.3, 0.5, and 0.7) suggesting that we can successfully homogenize behavior. Our model comparison analyses indicate that hyperboloid models are superior in predicting unseen discounting behavior to more conventional hyperbolic and exponential models. We report out-of-sample error estimates as well as commonalities and differences between reward and loss discounting, demonstrating for instance lower discounting rates, as well as differences in delay perception in loss discounting.

Conclusion: The present work proposes a model-based framework to evoke graded responses linked to cognitive function at a single subject level. Such a framework may be used in the future to measure cognitive functions on a dimensional rather than dichotomous scale.

Keywords: temporal discounting, loss discounting, design optimization, reward discounting, computational modeling, computational psychiatry

INTRODUCTION

Evaluating and deciding between alternative outcomes available at different points in time forms one critical aspect of human decision making (1). Outcomes which lie in the distant future are typically devaluated in this context, a phenomenon widely known as temporal or delay discounting (1–3).

Devaluation of future outcomes is *per se* a rational choice strategy as time comes at a cost (2, 4–6), however, some forms of temporal discounting as well as overly steep discounting may result in non-optimal and potentially harmful choices. For instance, it has been argued that steeper (hyperbolic) delay discounting may explain why individuals choose a cigarette now over a long-term healthy life, that is, why they prefer a smaller immediate over a delayed larger reward [(7–9); for overviews see (10, 11)].

In line with this argument, individuals with impulsive disorders and addiction show steeper discounting of future rewards such as monetary gains [for overviews see (12–15)]. Moreover, steeper discounting does not only differentiate between addiction disorders and healthy individuals, but it also predicts entry into drug use as well as therapy outcome (16, 17), and has accordingly been described as a behavioral biomarker of addiction and its treatment (18). Alterations in the discounting of future monetary losses are less well investigated which is surprising given that "continued use despite aversive consequences" is a primary symptom of addiction (19). In any case, understanding the neurobiological mechanisms underlying both temporal reward and loss discounting is therefore of particular clinical concern in the addiction field.

The common way to assess temporal (reward) discounting is the intertemporal choice task (ICT), in which an individual is presented with a series of trials and asked to choose between an immediate smaller vs. a delayed larger reward, or between two options delayed at different time points [(20); for overviews see (3, 21, 22)]. Immediate choices are then taken as an indicator of temporal discounting.

Individuals strongly vary in their tendency to discount due to various factors such as psychiatric illness, but also gender, or personality traits [(12, 23, 24); for overviews see (25, 26)]. In the ICT, this inter-individual variability results in an unequal number of discounted trials per participant, generating difficulties in linking the temporal discount process to psychophysiological and neural correlates. For instance, investigating the underlying neurobiological substrates by comparing differences between immediate and delayed choices may fall short of statistical power given highly unbalanced trial types and the high variability in discounting strength across individuals [e.g., (27–32); for an overview see (21)]. At times, participants even have to be excluded from analyses due to not discounting at all [e.g., (31, 33–45)].

To remedy this problem, delay discounting has often been investigated within adaptive experimental designs. Earlier studies have focused on applying titration procedures [originally introduced by Oldfield (46)] where reward or delay schedules are adjusted on a trial-by-trial basis depending on the participant's choice history in order to find the points at which immediate and delayed choices are displayed with equal probability, the so called 'indifference points' (since at these points the participant is indifferent toward either choice [e.g., (7, 9, 20, 27–29, 37, 47–51)]).

More recently, several behavioral model-based approaches have been proposed which aim at adapting the ICT trials to the individual so as to elicit (more) comparable levels of discounting and assess discounting more efficiently (31, 32, 36, 43, 52–56). Ordinarily these approaches make the assumption that the devaluation of future outcomes follows a hyperbolic curve such that the perceived outcome values monotonically decrease with increasing delay. Consequently, there are unique points on this curve where the perceived value of a delayed larger outcome and an immediate smaller outcome intersect, that is, where immediate and delayed outcome values are equal, corresponding to the individual's indifference points.

While some of these approaches infer discount parameters with a remarkably low number of trials [e.g., (36, 57)], their primary goal lies in the efficient inference of subject-wise discounting parameters and/or in determining inter-individual indifference points. The latter are then used to contrast neural activation toward "hard" as compared to "easy" adaptive trials (i.e., trials close to vs. far from the indifference point) (58), or to compare immediate and delayed responses with comparable frequency at the indifference points. However, since discounting is described by a continuous monotone function, it may in principle be interesting to study the neural response not only at the indifference point of a subject at which we expect a 0.5 discounting probability [see also (59, 60)]. By parametrically mapping the individual discounting curves onto behavioral probabilities comparable across subjects, we may construe experimental trials which allow us to examine discounting behavior and its neural correlates dimensionally. At the same time, by constructing customized trials for a given discounting probability, we may create more homogeneous experimental conditions on the behavioral discounting continuum, and thereby increase statistical power

needed to compare discounting behavior at different levels (e.g., low, medium, and high).

Another caveat of the model-based approaches is that they almost exclusively rely on the hyperbolic discounting model (with one exception (53)), and thus depend on the implicit assumption of this model being 'true', or at least on it accounting for a substantial proportion of intra-individual variability. However, studies primarily focusing on comparing the goodness-of-fit of different discounting functions have suggested that this may not be the case [(53); see also (38, 49, 61–63)], such that multiple alternatives to the hyperbolic model have been proposed [(53); see also (5, 27, 64–69)]. Adaptive design procedures may therefore benefit from taking into account model comparison results.

Here, we propose a generic framework which generates individualized experimental trials based on a proposed model, and subsequently evaluates a variety of models in order to create an adaptive experimental (discounting) paradigm (following the pre-registered protocol: https://doi.org/10.17605/OSF.IO/PMWXB). In contrast to previous studies, our framework provides a formal condition to generate trials which are expected to elicit graded discounting probabilities on a dimensional scale. Models are selected based on out-of-sample estimates of the prediction error (70), such that we can report how well the tested models perform at predicting unseen data. We also extend the paradigm to loss discounting. The proposed framework may be transferred to generate experimental paradigms tailored to the assessment of other cognitive or emotional functions.

MATERIALS AND METHODS

Study Design

The designed temporal discounting paradigm went as follows: Participants were asked to solve an ICT in two separate runs. The ICTs consisted of both reward discounting and loss discounting trials presented within alternating blocks (see **Figure 1A**). The behavioral choices on the first run (referred to as "run A" in the following) were used to infer subject-level behavioral discounting models. These models were employed to generate the trials of the second run (referred to as "run B"; see also **Figure 1B**). Trials in run B were generated so as to elicit immediate choice probabilities (and correspondingly relative discounting frequencies) of 0.3, 0.5, and 0.7 in each participant. The probabilities were selected to obtain three behavioral gradings of low, medium, and high discounting probabilities. High and low discounting probabilities reflect "easy," while 0.5 probabilities reflect "hard" trials in analogy to previous studies. In principle though, the probabilities are arbitrarily tunable.

This paradigm was assessed online and optimized in a series of experiments. After collecting data on one experiment (i.e., run A and run B), several alternative discounting models were separately inferred on the two runs and their ability to predict the behavior of the opposing run was assessed. The current model was then used to adjust and improve trials of run A, or a superior model was selected to update the trial-generating process for the successive experiment (see **Figure 1B**).

Run A

Individuals were instructed to choose between a smaller immediate or a larger later reward or loss. The magnitude of the delayed rewards and losses, as well as the delay duration was varied across trials. Each trial comprised a decision phase of up to 10 s (otherwise self-paced), as well as visual feedback of the selected choice and an inter-stimulus-interval of 1 s each.

In the initial experiment (exp 1), the delays were set to $D = \{2, 7, 30, 90, 180\}$ days and the delayed outcomes to $r_2 = +/-\{2, 5, 10, 20\}$ £ (UK) for the reward and loss condition, respectively, following frequently used delays and delayed outcomes in previous studies (47, 71). Immediate outcomes were selected which - according to the hyperbolic discounting model - were expected to elicit an equal probability for immediate and delayed choices at different hypothetical discounting parameter values $\kappa = \{0.01, 0.1, 0.2, 0.6\}$, that is, to generate trials at the corresponding indifference points (see Equation 3 for details, where β was fixed to 1). Run A in exp 1 thus comprised 5 (delays) × 4 (delayed outcomes) × 4 (discounting parameters) × 2 (conditions: reward and loss) = 160 trials. Reward and loss trials were presented in blocks of 40 trials each. The trial order within blocks was fully randomized.

Run B

After completing run A, behavioral discounting models were inferred on the behavioral choices of each participant. We set out with the perhaps most commonly applied discounting model, the hyperbolic model, widely applied to study human choice in the ICT [e.g., (8, 9, 20, 36, 37, 44, 72–74)]. The model assumes that the values V for the delayed options a_2 are discounted according to a hyperbolic function, that is, according to

$$V(a_2|s_j) = \left(\frac{1}{1 + \kappa \cdot D}\right) r_2, \quad (1)$$

while the values for the immediate options a_1 correspond to the actual outcomes, $V(a_1|s_j) = r_1$ (temporal delay $D = 0$ at this point). Here, the state s_j indexes the reward (s_1) or loss (s_2) condition, κ captures the inter-individual discounting degree (where high values indicate strong discounting), D the temporal delay, and r_i the actual outcome for the respective choice ($i = 1$ = immediate, $i = 2$ = delayed). We further refer to the factor in front of r_2 which captures the devaluation strength as the discount factor.

While the majority of studies infer κ by fitting a sigmoid function to the behavioral performance under this model via least squares [see e.g., (31, 38, 43, 62, 63, 74)], we use the sigmoid to link the discount model to immediate choice probabilities and infer parameters via maximum likelihood estimation [see also (36, 75–80)]. The probability of an immediate choice a_1 at any time t is given by

$$p\left(a_1|s_j\right) = \frac{1}{1 + e^{\beta(V(a_2|s_j) - V(a_1|s_j))}}, \quad (2)$$

where β indicates the tendency to exploit ($\beta \to \infty$) or explore ($\beta \to 0$) choices (81), and $p(a_2|s_j) = 1 - p(a_1|s_j)$. This sigmoid is akin to a psychometric function used in psychology to map

(differences in) stimulus intensity on to behavioral response probabilities, where here, we map differences in subjective values to the probability of an immediate response. Models were inferred (online) with constrained parameter optimization (using optimize.minimize() from the SciPy library, https://scipy.org/citing-scipy/, and $\kappa \in [0, 10]$ and $\beta \in [0, 100]$).

The benefit of linking a sigmoid function to immediate choice probabilities is that we can rearrange Equation 2 and explicitly solve for immediate outcomes which elicit a predetermined choice probability in a given participant. Defining $p_1 := p(a_1|s_j)$ as the probability for the immediate choice (the one we want to adjust), and inserting the model values (Equation 1) into Equation 2, then rearranging for immediate outcomes r_1, we obtain the condition

$$\begin{aligned} r_1 &= V(a_2|s_j) + \frac{\log\left(\frac{p_1}{1-p_1}\right)}{\beta} \\ &= \left(\frac{1}{1 + \kappa \cdot D}\right) r_2 + \frac{\log\left(\frac{p_1}{1-p_1}\right)}{\beta} \end{aligned} \quad (3)$$

for the hyperbolic model (defined for $0 < p_1 < 1$). Intuitively, at $p_1 = 0.5$, that is, if we want to induce an equal probability for an immediate and delayed option (to e.g., generate trials at the indifference points), the right part of Equation 3 drops such that the immediate value (and correspondingly the immediate reward) becomes equal to the discounted value. Increasing/decreasing immediate choice probability above/below 0.5, on the other hand, results in increasing/decreasing the immediate outcome. The condition in the middle further holds for all models which only differ in their expression of the discounted value. Note that we rearranged Equation 2 to solve for the immediate reward given an immediate choice probability p_1 (see also **Figures 1C,D** for an illustration of the method's operating principle). One may however also apply this approach to solve for the appropriate delay (see **Supplementary Methods S1** and **Supplementary Figure S1**).

Trials of run B were generated using this condition (Equation 3). Three trial types were defined, namely trials which were expected to evoke immediate choice probabilities of $p_1 = \{0.3, 0.5, 0.7\}$, corresponding to trials in which we expected participants to mainly choose the delayed option (with $p_1 = 0.3$), choose both options with equal probability ($p_1 = 0.5$), or mainly choose the immediate option (with $p_1 = 0.7$). Note that in the reward task p_1 also corresponds to the discounting probability (as the immediate choice corresponds to the discounted choice) while for loss, the discounting probability is equal to $p_2 = 1 - p_1$ (as the delayed choice corresponds to the discounted choice).

For each choice probability, each delay D, and each delayed outcome r_2 (as used in run A), immediate outcomes were thus determined according to the inferred subject specific model parameters κ and β. The initial run B thus comprised 5 (delays) × 4 (delayed outcomes) × 3 (choice probabilities) × 2 (condition: reward and loss) = 120 trials.

Note that a few parameter constellations could result in atypical trials with (1) negative immediate reward (corresponding to losses in reward trials) or positive immediate loss (corresponding to rewards in loss trials), (2) equal immediate and delayed reward/loss, or (3) larger immediate compared to delayed reward or smaller immediate compared to delayed loss. To avoid these trials, immediate outcomes were adjusted by iteratively increasing/ decreasing the delay durations by 1 until these cases were dissolved, or the minimum or maximum delay was reached. If still not dissolved, negative immediate rewards or positive immediate losses were set to 1 or -1 penny, while immediate rewards/losses which were equal to delayed rewards/losses were reduced/increased by 1 penny, respectively. All choice outcomes were hypothetical.

For the successive experiments, delays, outcomes, and discounting models were adapted to optimize the paradigm in agreement with the interim results (see section "RESULTS").

Sample

Healthy participants were recruited to participate in the online study via the Prolific website (https://www.prolific.co/). Eligibility criteria included age 18–65 and current residency in the United Kingdom (UK). Participants received £7.50 per hour as compensation for study participation. In total, 200 participants took part in the study (see **Supplementary Table S1**). Data were collected in batches of 50 individuals each. After each batch, the developed paradigm was evaluated and adjusted in line with the interim results and the proposed framework (see **Figure 1B**). Specifically, batch 1 and 2 were combined into one experiment (exp 1, $N = 100$), batch 3 represents the second experiment (exp 2, $N = 50$) and batch 4 represents the third experiment (exp 3, $N = 50$). Individuals were excluded from further analyses in case of not completing the first run, not completing the second run, or not responding to more than 10% of the trials during each run.

Data Collection and Online Setup

The online study was programmed in JavaScript using the open-source package "jsPsych" (82) and was hosted on a custom virtual server using a Linux-Apache-PHP-MySQL stack (see **Supplementary Figure S2**). Model parameter inference and trial generation of run B was written in Python. All code needed for the setup and execution of the study can be found here: https://github.com/MathieuPinger/discounting-online.

Participants entered the study through a link on the Prolific website. Participant IDs were randomly generated for data storage. Additionally, a separate password-protected database associated each participant with a Prolific internal ID to ensure a study completion checkup.

After completing the consent form, participants filled out sociodemographic information (age, gender, education, employment, country of current residency). Subsequently, run A was presented, after which participants completed the alcohol use disorder identification questionnaire (AUDIT; (83)) and the short version of the Barratt-Impulsiveness-Scale (BIS-15; (84)). During this time, subject-level behavioral models were inferred on data from run A, and used to generate trials for run B which was presented immediately after the questionnaires.

The study was approved by the ethics committee of the Medical Faculty Mannheim, University of Heidelberg (2019-633N).

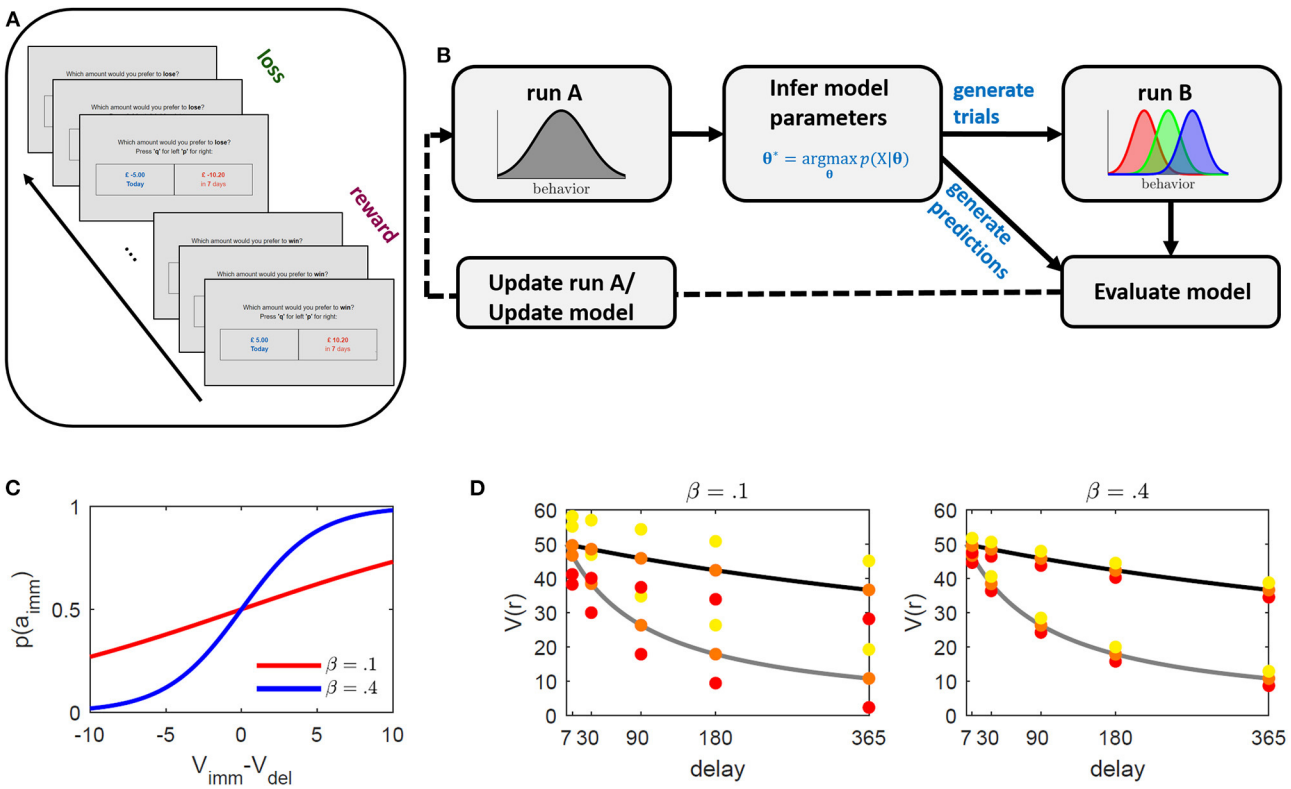

FIGURE 1 | Illustration of the intertemporal choice task (ICT) and proposed paradigm adaptation framework. **(A)** Schematic illustration of the ICT. Subjects were faced with a series of binary choice trials between an immediate and a delayed outcome. The absolute value of the delayed outcome was always higher. Reward and loss trials were presented within alternating blocks of 40 trials each. **(B)** Paradigm development framework. Subjects perform an ICT with equal trials across subjects (run A). The task is used to infer subject-level parameters based on a proposed underlying behavioral model. These parameters are used to generate individualized trials designed to elicit relative immediate choice frequencies of 0.3, 0.5, and 0.7 of run B (schematically displayed as red, green, and blue, respectively), and to generate behavioral predictions along with other common discounting models. By comparing observed and predicted behavior in run B, the task underlying model is either updated, or trials of run A are optimized to improve parameter inference. The procedure may be repeated until no further improvement is observed. **(C, D)** Illustration of method's operating principle. **(C)** Immediate choice probability $p(a_{imm})$ (cf. Equation 2) as a function of the difference between immediate (V_{imm}) and delayed (V_{del}) value for $\beta = 0.1$ (red), and $\beta = 0.4$ (blue). The indifference point where $V_{imm} = V_{del}$ is at 0. If $V_{imm} > / < V_{del}$, immediate choice probability is below/above 0.5. β regulates the steepness of the curve and thus the sensitivity toward differences in values. Lower β values require larger value differences (x-axis) to obtain a comparable probability (y-axis). **(D)** Discounted value (y-axis) for different delays (x-axis) for two hypothetical discount parameter values ($\kappa = 0.05$ in gray and $\kappa = 0.005$ in black). The colored dots represent the method's selected immediate rewards ($= V_{imm}$) at a given delay for the different induced immediate choice probabilities 0.3 (red), 0.5 (orange), and 0.7 (yellow). The distances between immediate values (colored dots) and delayed values (discounting curve) is constant across all delays to ensure equally induced probabilities across delays (see graph **(C)**). This also indicates that for subjects with different κ's, the reward and value ratios will vary. The left graph depicts selected rewards for a hypothetical $\beta = 0.1$ and the right graph for $\beta = 0.4$. While β regulates discounted value of the delayed reward V_{del}, κ regulates the distance of the selected immediate reward around V_{del} with higher β resulting in smaller differences, making the differentiation between the two more difficult (that is, requiring higher sensitivity).

Data Analysis

Behavioral Models and Model Parameters

The initial experiment was conducted with the most frequently used delay discounting model in human research, the hyperbolic discounting model (see Equation 1). The model was compared with several other proposed models in the field. These models differ in the assumption of how an individual devaluates the delayed outcome (see Equation 1). For completeness, the compared models include

- The hyperbolic model (20, 85), where $V(a_2|s_j) = \left(\frac{1}{1+\kappa \cdot D}\right) r_2$, with $\kappa \in [0, \infty)$.
- The exponential model (68), where $V(a_2|s_j) = \kappa^D r_2$, with $\kappa \in [0, 1]$, implying that the perceived value of a delayed outcome is discounted exponentially scaled by the individual discounting rate κ.
- The quasi-hyperbolic model [also known as the beta-delta model; (5, 69)], where $V(a_2|s_j) = \gamma\, \kappa^D r_2$, for $D > 0$, with $\gamma, \kappa \in [0, 1]$, where the exponential discounting of the delayed outcome is additionally modulated by a second linear discount parameter γ.
- The hyperboloid model (27, 65), where $V(a_2|s_j) = \frac{1}{(1+\kappa \cdot D)^s} r_2$, with $\kappa \in [0, \infty)$ and $s \in [0, 1]$, similar to the hyperbolic discounting model, only that the discounting factor is scaled by an additional parameter s.

- The modified hyperboloid model (20, 86), where $V(a_2|s_j) = \frac{1}{(1+\kappa \cdot D^s)} r_2$, with $\kappa \in [0, \infty)$ and $s \in [0, 1]$, which is a slight modification of the hyperboloid model, suggesting that s solely scales the delay and thus may account for differences in perceived time.
- The double-exponential model (87), where $V(a_2|s_j) = (w{\kappa_1}^D + (1-w){\kappa_2}^D)r_2$, with $w, \kappa_i \in [0, 1]$, which is inspired by the evidence that choices result from the competition between two neurobiological systems (referred to as valuation and control) scaled by their own decay rates (κ_1 and κ_2), each contributing by a factor w and 1 – w, respectively, and,
- The constant-sensitivity model (64), where $V(a_2|s_j) = exp(-(\kappa \cdot D)^\delta) r_2$, with $\kappa, \delta > 0$. This model accounts for decision heuristics by including the κ parameter as an indicator of impatience, and δ reflecting time sensitivity. Note that this model differs from model (3) in terms of parameter constraints.

Models were compared by inferring each model on each experimental run (A and B) and condition (reward and loss) of each participant and using the inferred parameters to assess the out-of-sample prediction error (PE) on the respective contrary run (i.e., predicting behavior in B when inferring models on A and vice versa). The PE here was defined as $1-\hat{p}_j$, where $\hat{p}_j = \frac{1}{T}\sum_t^T p(a_t|s_j)$, i.e., is defined as the average over the predicted probabilities of observed choices per condition j. For simpler interpretability, only $\hat{p}_j$ is reported.

Note that the predicted probability will depend on trial difficulty where more difficult choices (i.e., trials closer to the indifference point of a subject), should by definition be predicted with a lower probability. We thus do not expect an average predicted probability close to 1 in either run. Particularly in run B, where by condition we generate trials eliciting immediate choice probabilities of 0.3, 0.5, and 0.7, the expected prediction should lie around $(0.7 + 0.5 + 0.7)/3 = 0.63$ (see also **Supplementary Figure S5** right), and may slightly deviate due to slight trail adjustments (see Section Run B) or to using a model not used for trial generation.

Behavioral Variables and Data Analysis

Temporal discounting was measured by assessing the frequency of discounted choices for each run, each condition, and each manipulated (immediate choice) probability (cf. p_1), as well as the median reaction time (RT) for these conditions. Individuals which discounted in < 5% of all trials were defined as "non-discounters."

We further assessed subjective impulsivity by averaging across all items of the BIS-15 (i.e., BIS-total), as well as across items related to the three sub-scales, namely attentional impulsivity (i.e., the difficulties to focus attention or concentrate), motor impulsivity (i.e., acting without thinking), and non-planning impulsivity (i.e., lack of future orientation), respectively (84). We also assessed abusive or harmful alcohol consumption by the alcohol use disorders identification test (AUDIT; (83)).

Model parameters and behavioral variables such as discounting parameters, choice frequencies, as well as (absolute) deviations between observed and expected choice frequencies, were compared via t-tests for paired or unpaired samples (i.e., for comparisons between conditions and runs vs. comparisons between experiments; please note, absolute deviations were used when comparing experiments) in case of normally distributed variables, or nonparametric Wilcoxon signed-rank tests for paired and Wilcoxon rank-sum tests for unpaired samples in case of normality violation. Variables were correlated via Pearson's or Spearman's correlation coefficient, respectively. The number of discounters vs. non-discounters across experiments was compared via Chi-square tests for equal and Fisher's exact test for unequal sample sizes. Statistical significance was set to $p < 0.05$ (two-tailed) for all tests. Individuals repeating either option in more than 95% of all trials during run A, making it difficult to obtain valid parameter estimates, were removed from analyses on run B where deemed necessary (explicitly mentioned in the Results Section). Individuals with extreme discounting parameters $\kappa > 2$ were removed from all analyses related to this parameter.

RESULTS

Experiment 1

Two separate batches of 50 individuals each were collected for exp 1. After collecting the first sample ($N = 50$), we observed a minor bug in the paradigm code which resulted in the generation of run B trials with equal immediate and delayed outcomes. These trials occurred in < 1.2% of all trials (around 2–3 trials in 24 participants). We thus immediately collected a second sample ($N = 50$) with this bug fixed and removed the afore-mentioned trials from the first sample in the behavioral measures analyses. Two individuals were excluded from further analyses since they had > 30% missing values in one condition. Exp 1 thus included $N = 98$ individuals.

As reported in multiple other studies [e.g., 31, 33–35, 38–40], we observed a high percentage of individuals, namely 58%, which showed no temporal discounting in at least one condition of the initial run A (see **Figures 2A,B**). This was particularly evident for the loss discounting condition which yielded 53% of non-discounters (see **Figure 2B**; non-discounters being defined as individuals which discounted in < 5% of all trials, cf. Behavioral Variables and Data Analysis).

After adapting the experimental trials to the individual participants in run B, we observed a considerable reduction in non-discounters (from 26 to 13% in the reward, and from 53 to 42% in the loss condition), and a significant increase in the frequency of discounted choices in both reward ($Z = 5.06$, $p < 0.001$; see **Figure 2A**), and loss ($Z = 4.85$, $p < 0.001$; see **Figure 2B**) conditions. This was accompanied by a significant increase in the inferred discount parameters κ, signaling higher discounting (reward: $Z = 2.83$, $p = 0.005$, loss: $Z = 4.57$, $p < 0.001$).

The observed choice frequencies in run B, moreover, aligned with the experimentally manipulated probabilities. That is, the frequency of immediate choices increased in response to trials with $p_1 = 0.7$ compared to $p_1 = 0.5$ (reward: $Z = 5.43$, $p < 0.001$; loss: $Z = 4.91$, $p < 0.001$), and to trials with $p_1 = 0.5$ to $p_1 = 0.3$ (reward: $Z = 6.21$, $p < 0.001$; loss: $Z = 3.72$, $p < 0.001$).

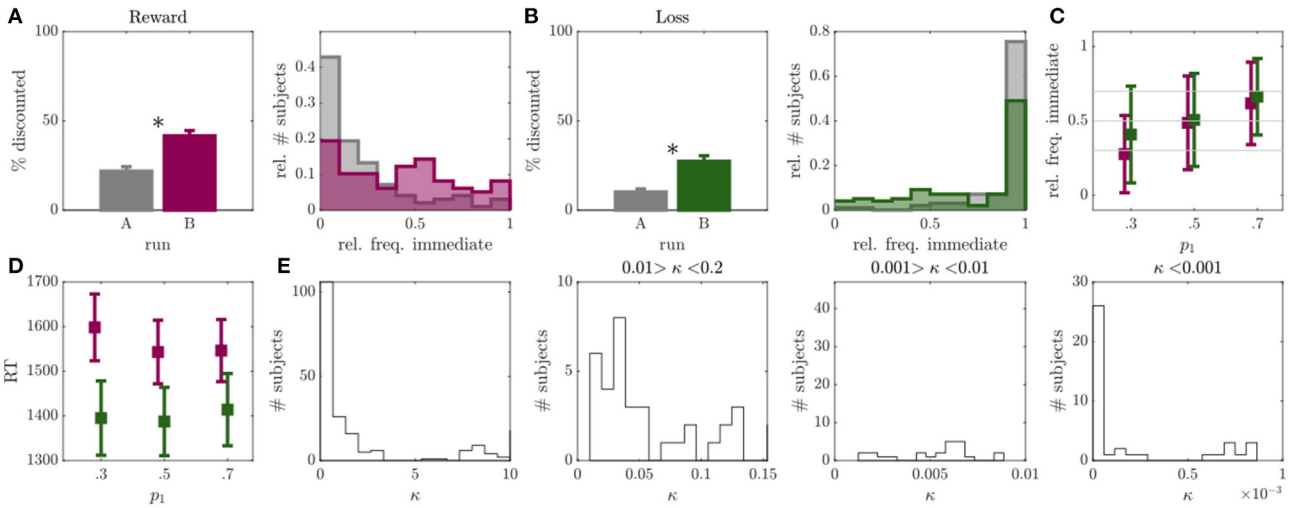

FIGURE 2 | Results of experiment 1. **(A)** Left: Percentage of discounted choices in run A (gray) and run B (magenta) for reward condition. Right: Histograms over relative frequency of immediate choices in run A (gray) and run B (magenta) for reward condition. Asterisks indicate significant differences. **(B)** Same as A for loss condition with run B displayed in green. **(C)** Mean and standard deviation of observed relative frequency of immediate choices for the experimentally evoked probabilities $p_1 = \{0.3, 0.5, 0.7\}$ (x-axis) in run B (individuals with >95% or <5% immediate choices were removed, $N = 28$ or 29% in reward, $N = 52$ or 53% in loss condition). **(D)** Mean and standard deviation of median reaction time (RT; y-axis) for $p_1 = \{0.3, 0.5, 0.7.\}$ trials (x-axis) in run B for reward (magenta) and loss (green) conditions. **(E)** Histograms over discounting parameter κ of the hyperboloid model for both loss and reward conditions, displayed at different resolutions and bin widths.

However, the observed choice frequencies deviated significantly from the model expectations w.r.t. all three trial types in the loss condition ($p_1 = 0.3$: $Z = 6.52$, $p < 0.001$; $p_1 = 0.5$: $Z = 5.63$, $p < 0.001$; $p_1 = 0.7$: $Z = 4.27$, $p < 0.001$), as well as for $p_1 = 0.7$ in the reward condition ($Z = 3.35$, $p < 0.001$; other comparisons $p > 0.05$). This was somewhat due to individuals who consistently chose only one option showing no behavioral variation in general (concerning $N = 28$ in the reward and $N = 52$ in the loss condition). After removing these individuals from the analysis, the mean of the choice frequency distributions moved closer to the model expectations (see **Figure 2C**), although still significantly deviating for $p_1 = 0.7$ in the reward ($Z = 3.35$, $p < 0.001$) and for $p_1 = 0.3$ in the loss condition ($Z = 2.21$, $p = 0.027$; all other p's > 0.05). We did not observe an increase in RT toward $p_1 = 0.5$ trials (defined as "hard" trials in the field) as compared to the other two trial types (amounting to "easy" trials here; reward: p's > 0.329; loss: p's > 0.290; see also **Figure 2D**).

In conclusion, the first experiment indicated that by applying the condition in Equation 3, we were able to reduce the number of non-discounters and evoke higher discounting frequencies. We could also show that for individuals which generally showed behavioral variation in run A, the observed immediate choice frequencies on average largely centered around the model expectations in run B. However, the standard deviation of these choice frequencies was rather high. Also, RT's did not reflect a clear separation between 'hard' and 'easy' trials (see **Figure 2D**).

Two possible (non-exclusive) explanations may account for these findings. First, the hyperbolic model may not have captured the entire systematic data variation, such that the model predictions and thus the generated model-based (run B) trials were somewhat biased. In fact, the hyperbolic model performed worse in predicting (out-of-sample) behavior than several other tested models (see **Supplementary Figure S3**), achieving a prediction of only 0.55 for both reward and loss (as compared to predictions > 0.7, see **Supplementary Figure S3**). Second, going one step back, trials in run A may not have evoked enough behavioral variability to infer valid model parameters required to generate subject specific trials. Since the percentage of discounted choices during run A was rather low for both reward and loss conditions (**Figures 2A,B**), and we obtained a higher behavioral model agreement after excluding individuals with low behavioral variability from analysis (**Figure 2C**), the second explanation seemed rather likely. A poor (hyperbolic) model fit could therefore also be due to a poor selection of run A trials. As an initial step to further improve the paradigm, we thus first focused on improving trials of run A to promote valid parameter inference, before altering the underlying trial-generating model.

Modification

Trials of run A were initially generated by using common delays and delayed outcomes found in the literature and finding the indifference points to these values, given a set of hypothetical discounting parameters κ (cf. Section Run A). To improve this run, we now focused on generating trials which more closely matched the actually observed discounting parameters and behavior in run B (since we observed more discounting in this run). We observed a bimodal κ distribution, with the majority of individuals being characterized by κ's ranging between 2.6×10^{-11} and 3, and a few above 7 (see **Figure 2E** left). The dominance of the left mode indicates that most participants were characterized by rather low discounting rates (see also **Figures 2A,B**), and, in particular, far lower than the ones used for

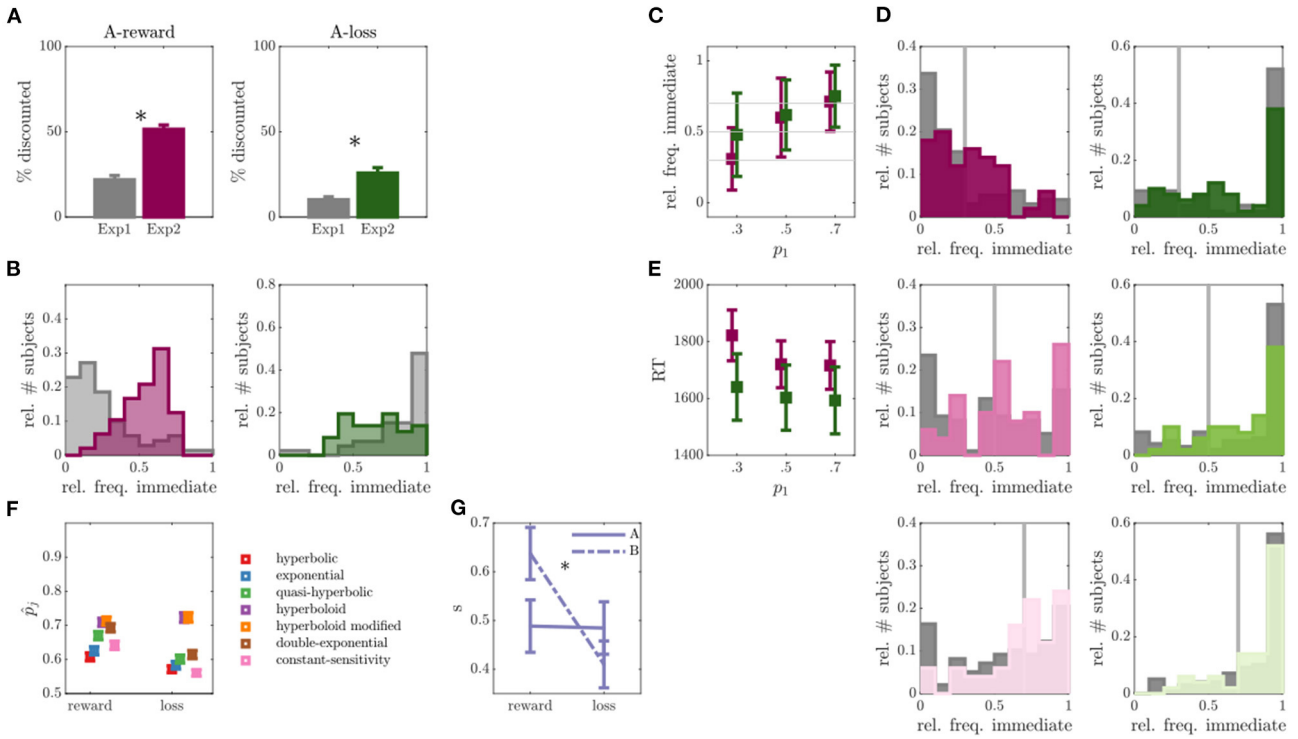

FIGURE 3 | Results of experiment 2. **(A)** Percentage of discounted choices in run A for experiment (exp) 1 and exp 2 for reward (left) and loss (right) discounting. Asterisks indicate significant differences. **(B)** Empirical distribution of the relative frequency of immediate choices for reward (left) and loss (right) conditions in run A of exp 1 (gray) and exp 2 (colors). **(C)** Relative frequency of immediate choices (*y*-axis) in run B of exp 2 as a function of experimentally manipulated probabilities (*x*-axis) for reward (magenta) and loss (green) conditions (individuals without behavioral variability were removed, $N = 2$ for reward, $N = 14$ for loss condition). **(D)** Empirical distributions of the relative frequency of immediate choices in run B for trials with immediate choice probability 0.3 (top), 0.5 (middle) and 0.7 (bottom), as also indicated by the gray line. Reward condition is displayed left, loss right, exp 1 in gray and exp 2 in color. **(E)** Average over median reaction times (RT) for the three experimentally manipulated immediate choice probabilities for reward (magenta) and loss (green) conditions. **(F)** Average predicted (out-of-sample) probability of observed responses $\hat{p}_j$ (*y*-axis) for reward and loss conditions (x-axis) for different models. **(G)** Inferred scaling parameters *s* of the modified hyperboloid model for reward and loss discounting conditions.

the initial run generation (cf. Run A). Run A was thus modified to better represent the left mode of the actually observed κ distribution (see **Figure 2E** for a high resolution of the true κ distribution). Around half the sample was characterized by a $\kappa < 0.2$ (reward: $N = 67$; loss: $N = 62$). Of these, 20 participants in the reward and 16 participants in the loss condition exhibited κ's between 0.01 and 0.2, 17 participants in the reward and 16 participants in the loss condition ranged between 0.001 and 0.01, and 20 participants in the reward and 21 participants in the loss condition were characterized by κ's < 0.001 (among which 10 in the reward and 16 participants in the loss condition were characterized by κ's < 0.00001; see **Figure 2E**). To cover this range of the parameter distribution, we updated the set of hypothetical discounting parameters in run A (cf. Section Run A) to $\kappa = \{0.00001, 0.001, 0.01, 0.6\}$.

We further exchanged the shortest delay (2 days delay) with a long delay (365 days delay) as longer delays additionally encourage discounting (cf. Equation 3) such that the new set of delays was set to $D = \{7, 30, 90, 180, 365\}$. Lastly, we removed the lowest delayed outcome and replaced it by a higher delayed outcome such that the new set of delayed rewards and losses was $r_2 = +/-\{5, 10, 20, 50\}$£.

Experiment 2

Fifty individuals completed exp 2 with altered trials of run A. In run A of exp 2, compared to exp 1, we observed a considerably lower percentage of non-discounters in the reward condition ($N = 2$, that is, a drop from 26% to 4%; OR $= 8.67$, $p < 0.001$), as well as in the loss condition ($N = 14$, a drop from 53% to 28%; OR $= 2.91$, $p = 0.005$) (see also **Figure 3A**). The average percentage of discounted choices also significantly increased in run A of exp 2 compared with run A of exp 1, for both reward and loss conditions (reward: $Z = 6.58$, $p < 0.001$; loss: $Z = 3.93$, $p < 0.001$; see **Figures 3A,B**). In fact, for the reward condition it amounted to 51%, rendering more optimal conditions for parameter inference. In the loss task, this percentage remained lower, however, with around 26%. In both conditions, we furthermore observed a significant increase in RT compared with exp 1 (reward $Z = 4.47$, $p < 0.001$; loss: $Z = 4.26$, $p < 0.001$), suggesting that choices became more difficult, closer to the indifference points of each participant. We conclude that by model based adaptation of run A, we were able to reduce the number of non-discounters and increase behavioral variability within participants (see also **Figures 3A,B**).

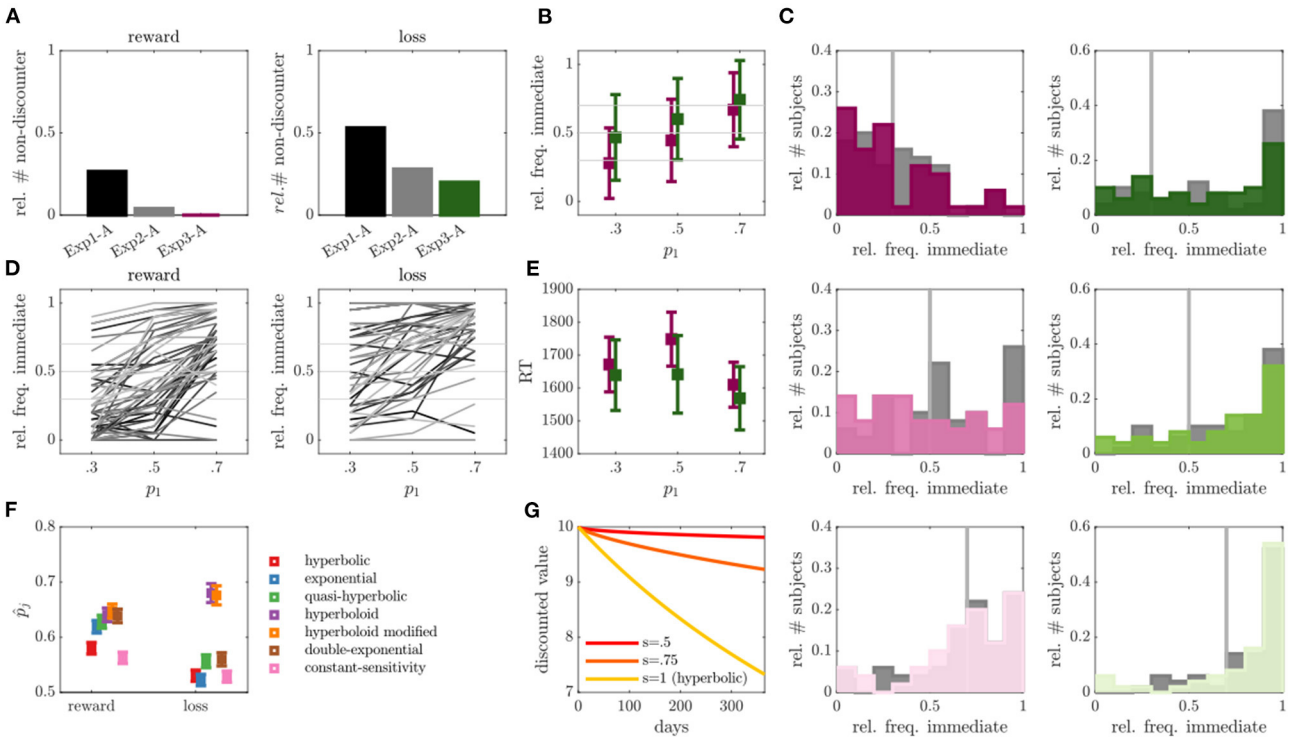

FIGURE 4 | Results of experiment 3. **(A)** Relative number of non-discounter in run A across experiments for reward (left) and loss (right) conditions. **(B)** Relative frequency of immediate choices (*y*-axis) in run B of exp 3 as a function of experimentally manipulated probabilities (*x*-axis) for reward (magenta) and loss (green) conditions (individuals without behavioral variability were removed, $N = 0$ for reward, $N = 10$ for loss condition). **(C)** Empirical distributions of the relative frequency of immediate choices in run B for trials with immediate choice probability 0.3 (top), 0.5 (middle) and 0.7 (bottom), as also indicated by the gray line. Reward condition is displayed left, loss right, exp 2 in gray and exp 3 in color. **(D)** Average relative frequencies of immediate choices per subject across the three experimentally manipulated immediate choice probabilities. **(E)** Average over median reaction times (RT) for the three experimentally manipulated immediate choice probabilities for reward (magenta) and loss (green) conditions. **(F)** Average predicted (out-of-sample) probability of observed responses $\hat{p}_j$ (*y*-axis) for reward and loss conditions (*x*-axis) for different models averaged over run A and B. **(G)** Hypothetical discounting curves in the modified hyperboloid model for $\kappa = 0.01$, $r_1 = 10$, and different values of scaling parameter *s*.

Regarding run B, the observed immediate choice frequencies in the reward condition centered around the model expectations (see **Figure 3C**; reward: $p_1 = 0.3$: $Z = 0.50$, $p = 0.615$; $p_1 = 0.5$: $Z = 1.46$, $p = 0.145$; $p_1 = 0.7$: $Z = 0.09$, $p = 0.923$), while still significantly deviating in the loss condition ($p_1 = 0.3$: $Z = 4.93$, $p < 0.001$; $p_1 = 0.5$: $Z = 4.55$, $p < 0.001$; $p_1 = 0.7$: $Z = 3.22$, $p = 0.001$). Nonetheless, for both reward and loss conditions, the absolute deviations between expected and observed relative immediate choice frequencies were lower in exp 2 compared with exp 1 (statistically significant for reward: $p_1 = 0.3$: $Z = 2.64$, $p = 0.008$; $p_1 = 0.5$: $Z = 1.67$, $p = 0.096$; $p_1 = 0.7$: $Z = 2.65$, $p = 0.008$; and loss: $p_1 = 0.5$: $Z = 2.24$, $p = 0.025$; see **Figure 3D**), suggesting an improvement in the proposed paradigm. However, many non-discounters remained in the loss condition of run B ($N = 14$, **Figure 3D**).

Given that run A now rendered better conditions for parameter inference, we next focused on evaluating and improving the paradigm underlying model. For this, we inferred several discounting models suggested by the literature on run A and run B separately (cf. Section Behavioral Models and Model Parameters) and assessed their ability to predict the behavior in the opposing run, that is, inferring parameters on run A and predicting behavior in run B and vice versa. The two experimental runs thus allowed us to assess an estimate of the out-of-sample PE which is less biased and preferred over in-sample estimates (70, 88), commonly used in the field [e.g., (38, 61, 89)]. **Figure 3F** shows the model comparison results averaged over predictions in both runs. The hyperboloid and the modified hyperboloid model outperformed all other models in both reward and loss conditions, with a slight preference for the modified hyperboloid model (20, 86). On average, the modified hyperboloid model predicted responses successfully with 0.71 probability in the reward, and 0.72 probability in the loss condition. In contrast, the most commonly used hyperbolic and exponential models performed comparatively poorly (exponential model: $\hat{p}_{reward} = 0.64$, loss $\hat{p}_{loss} = 0.58$, hyperbolic model: $\hat{p}_{reward} = 0.61$, $\hat{p}_{loss} = 0.57$; see also **Figure 3F** and **Supplementary Figure S6**). These results held true when evaluating a weighted PE where the response probability was averaged over predictions for immediate and delayed choices (ensuring that predictions were not only good in predicting a dominant response, sometimes referred to as the majority class, see **Supplementary Figure S4**). Note that the hyperboloid models also outperformed the exponential

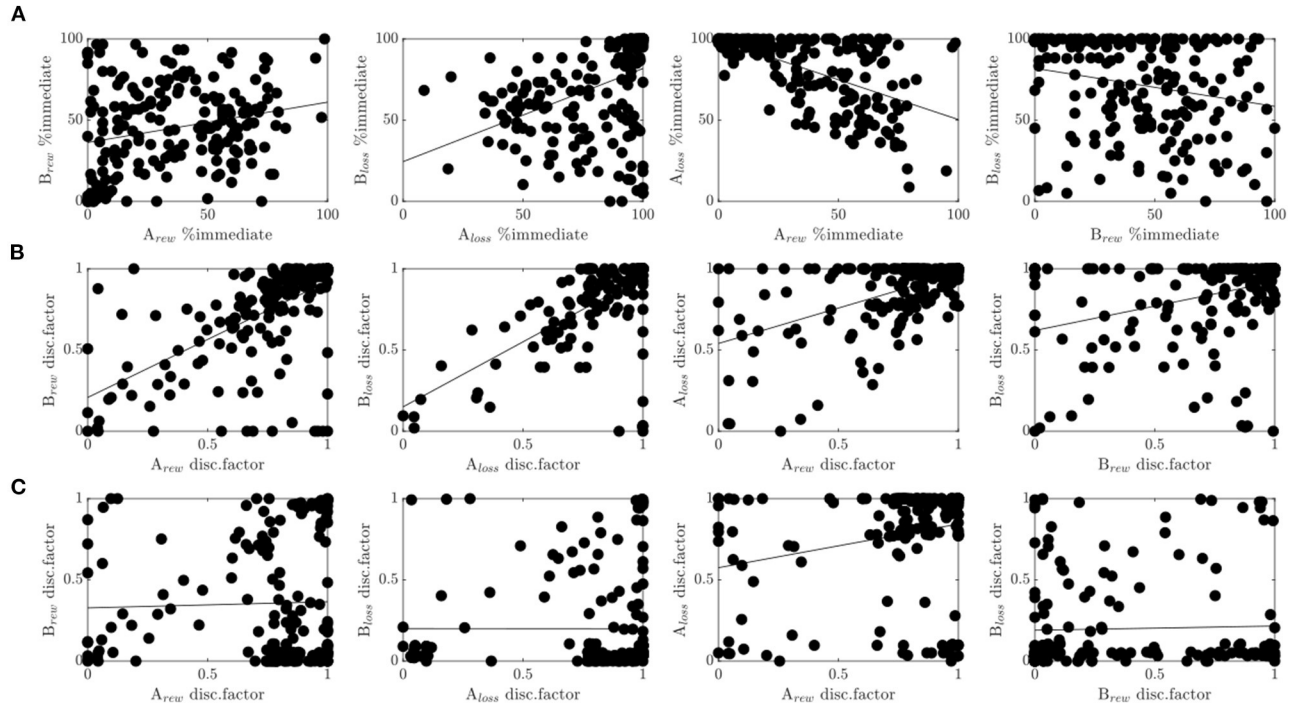

FIGURE 5 | Cross-experimental results. **(A)** Correlations of the percentage of immediate choices between run A and run B for the reward condition (1st plot), and the loss condition (2nd plot), and between reward and loss conditions within run A (3rd plot), and run B (4th plot). **(B)** Same as in **(A)** only with the discount factor evaluated at delay $D = 30$ for the hyperboloid model. **(C)** Same as in **(B)** for the hyperbolic model.

and hyperbolic models on predicting the data of exp 1 (see **Supplementary Figure S3**).

Evaluating the parameters of the modified hyperboloid model (cf. Behavioral Models and Model Parameters) also revealed some interesting insights into behavior. The additional scaling parameter s distinguishing this model was extremely reliable, observed in terms of a high correlation in s between runs (for reward: $r = 0.44$, $p = 0.001$; for loss: $r = 0.44$, $p = 0.001$) and conditions (run A: $r = 0.26$, $p = 0.064$; run B: $r = 0.24$, $p = 0.091$), and pointing toward a trait like scaling of delay. Apart from that, s was higher in the reward compared with the loss condition ($Z = 3.43$, $p < 0.001$; see **Figure 3G**).

Modification

Following these results, we updated the paradigm to now generate trials of run B according to the modified hyperboloid model (20, 86). The lower values in the scaling parameter s observed for the loss condition effectively reduce discounting (by shrinking the delay duration). To further encourage discounting in the loss task, we therefore also exchanged the shortest delay (7 days delay) with a long delay (3 years) in the loss condition only. The new set of delays for the loss condition was set to $D = \{30, 90, 180, 365, 1095\}$.

Experiment 3

Fifty individuals completed exp 3 with altered trials of run A in the loss condition and an altered trial-generating discounting model for run B (now using the modified hyperboloid model).

In run A, we observed a slight reduction in the number of non-discounters compared with exp 2, with 0 non-discounters observed in the reward and 10 non-discounters observed in the loss condition, although this was statistically not significant ($p > 0.875$; see **Figure 4A**). The average frequency of discounted choices did also not significantly differ in run A of exp 2 compared with run A of exp 3, neither for the reward ($Z = 1.08$, $p = 0.277$), nor for the loss condition ($Z = 0.33$, $p = 0.740$). We observed an average of 48% discounted choices in the reward and 27% in the loss condition in exp 3.

In run B, we also observed a slight, but statistically not significant reduction in the number of non-discounters (reward: $N = 2$ or 4%; loss: $N = 12$ or 24%). The observed immediate choice frequencies again increased with increasing model expectations (i.e., from 0.3 to 0.5, and from 0.5 to 0.7) both on average (all p's < 0.001), as well as (largely) on a single subject level (see **Figures 4B,D**). For the reward condition, the observed frequencies seemed to moreover center around the model-based expectations (see **Figure 4B**; $p_1 = 0.3$: $Z = 0.88$, $p = 0.378$; $p_1 = 0.5$: $Z = 1.23$, $p = 0.221$; $p_1 = 0.7$: $Z = 0.37$, $p = 0.712$), while still deviating significantly for the loss condition (see **Figure 4B**; $p_1 = 0.3$: $Z = 4.27$, $p < 0.001$; $p_1 = 0.5$: $Z = 3.60$, $p < 0.001$; $p_1 = 0.7$: $Z = 3.31$, $p < 0.001$). The absolute deviations between observed and expected immediate choice frequencies were again lower than those in exp 1, indicating choice frequencies were more consistent with model expectations (statistically verifiable

for reward $p_1 = 0.7$: $Z = 2.67$, $p = 0.008$; loss $p_1 = 0.3$: $Z = 2.05$, $p = 0.040$; $p_1 = 0.5$: $Z = 1.89$, $p = 0.059$), but remained comparable to those in exp 2 (that is, no significant differences were observed, p's > 0.2; see also **Figure 4C**). In contrast to exp 1 and 2, RTs were however more in line with theoretical expectations by which RT increases toward "harder" trials (see **Figure 4E** and **Figure 3E** in comparison). Individuals responded slower to reward trials close to the indifference point (i.e., $p_1 = 0.5$) as compared to trials far from the indifference point ($p_1 = 0.7$: $Z = 3.20$, $p = 0.001$; $p_1 = 0.3$: $Z = 1.70$, $p = 0.089$). Although this was statistically not verifiable for the loss condition (p's > 0.237), a qualitatively consistent picture was observed (see **Figure 4E**).

The out-of-sample based model comparison analysis suggested once more that the hyperboloid models outperformed all other tested models in both the reward and loss conditions (see **Figure 4F**; hyperboloid model $\hat{p}_{reward} = 0.64$ and $\hat{p}_{loss} = 0.68$, modified hyperboloid model $\hat{p}_{reward} = 0.65$ and $\hat{p}_{loss} = 0.68$). Similar to exp 2, the hyperbolic and exponential models performed rather poorly, particularly in the loss condition (hyperbolic model $\hat{p}_{reward} = 0.58$ and $\hat{p}_{loss}$t $= 0.53$, exponential model $\hat{p}_{reward} = 0.62$ and $\hat{p}_{loss} = 0.52$). Once more, the scaling parameter s was lower in the loss compared with reward condition in run B ($Z = 3.17$, $p = 0.002$).

Joint Analysis of Experiments 1, 2, and 3

Lastly, we investigated correlations between behavioral variables and model parameters across all three experiments to gain a deeper understanding of involved mechanisms during reward and loss discounting. First of all, there was a moderate correlation between the immediate choice frequencies of run A and B (reward: $r = 0.24$, $p = 0.001$, loss: $r = 0.42$, $p < 0.001$, see **Figure 5A**) suggesting at least some reliability in delay discounting processes as assessed in terms of choice frequency. Second, there was a considerable (expected negative) correlation between loss and reward (run A: $r = -0.59$, $p < 0.001$, run B: $r = -0.22$, $p = 0.002$, see **Figure 5A**), suggesting commonalities in the processing of reward and loss discounting.

In agreement with these results, the discount factor of the modified hyperboloid model (evaluated at delay $D = 30$) was highly correlated across runs and conditions (see **Figure 5B**). We observed a considerable correlation between run A and run B (reward: $r = 0.6$, $p < 0.001$; loss: $r = 0.65$, $p < 0.001$), and between reward and loss conditions (run A: $r = 0.53$, $p < 0.001$, run B: $r = 0.35$, $p < 0.001$). The correlations assessed on the discount factors were even higher than when assessed on the choice frequencies (Z's > 3.24, p's < 0.001). Discounting parameters κ were similarly correlated across runs (reward: $r = 0.43$, $p < 0.001$; loss: $r = 0.48$, $p < 0.001$) and conditions (run A: $r = 0.37$, $p < 0.001$; run B: $r = 0.46$, $p < 0.001$), although significantly less so (Z's > 1.97, p's < 0.024), with exception of the correlation between conditions during run B ($Z = 1.21$, $p = 0.112$).

In contrast, the discount factor of the hyperbolic model (evaluated at delay $D = 30$) did not correlate across runs (reward: $r = 0.03$, $p = 0.698$; loss: $r = 0$, $p = 0.991$, see **Figure 5C**). It correlated moderately between reward and loss conditions of run B ($r = 0.24$, $p < 0.001$), but not run A ($r = 0.03$, $p = 0.633$). The correlations observed for the hyperbolic model were therefore also significantly lower than the ones observed for the hyperboloid model (Z's > 3.33, p's < 0.001). A qualitatively similar picture held true when evaluating the discount parameter κ which is proportional to the discount factor in the hyperbolic model. These results suggest that cognitive processes related to delay discounting were only captured reliably in the superior model, that is, the model with superior prediction performance. Note that the scaling parameter s of the hyperboloid model was also reliable, that is, correlated across reward and loss conditions (run A: $r = 0.19$, $p = 0.006$, run B: $r = 0.25$, $p < 0.001$), and across runs (reward: $r = 0.31$, $p < 0.001$; loss: $r = 0.26$, $p < 0.001$).

We also observed several differences between reward and loss conditions. The discount parameters κ and the scaling parameters s, were higher in the reward compared with the loss condition (κ run A: $Z = 5.72$, $p < 0.001$; κ run B: $Z = 2.71$, $p < 0.001$; s run A: $Z = 1.99$, $p = 0.046$; s run B: $Z = 5.53$, $p < 0.001$), while the discount factor was lower in the reward condition (run A: $Z = 7.05$, $p < 0.001$; run B: $Z = 5.53$, $p < 0.001$). Note though that despite the parameter constraints on scaling parameter s, we did observe moderate correlations between s and κ in the reward condition (run A: $r = -0.31$, $p < 0.001$; run B: $r = -0.31$, $p < 0.001$), suggesting slight issues with parameter identifiability.

W.*r*.t. subjective reports, we did not observe any associations between model parameters and subjective reported impulsivity or alcohol use behavior (p's > 0.147). We did also not observe any correlations between subjective reports and the discount factors of the hyperbolic model (all p's > 0.105). Exploratory analyses revealed a weak negative association between the loss discounting factor of the modified hyperboloid model (evaluated at $D = 30$) in run A and impulsivity (BIS-total: $r = -0.15$, $p = 0.037$), and between the loss discounting factor of the modified hyperboloid model in run B and alcohol use behavior (AUDIT-total: $r = -0.14$, $p = 0.044$; see **Supplementary Figure S7**).

DISCUSSION

A long-standing problem with the experimental measurement of cognitive functions based on group statistics is that an identical experimental trial presented to different subjects may elicit very different levels of functioning due to high inter-individual variability [(90–94); see also (95)]. This aggravates the reliable measurement of cognitive mechanisms and limits the comparability of results between subjects. For example, the same aversive stimulus in a fear conditioning paradigm can lead to very different degrees of fear association across individuals (93, 94). To remedy this problem, a common approach is to adapt experimental conditions such as stimulus intensities to the subject, making the experimental condition more comparable and less heterogenous across individuals (94, 96). Similarly, in delay discounting, the extent of discounting behavior is known to vary widely between subjects [(97, 98); for review see (25, 26)]. In an ICT, adjusted experimental settings for delays and outcome values per subject are therefore required to map a similar magnitude of discounting between subjects (31, 32, 36, 43, 53, 54), whereby poorly adaptive or non-adaptive experimental designs may even lead to subjects entirely not discounting. This

may result in the exclusion of these subjects from further analyses [similar to conditioning paradigms (94)]. Here, we attempt to address this problem and propose a general approach to tailor experimental trials to the single subject. The underlying idea of this approach is that by modeling behavior as being probabilistically generated by the experiment and the cognitive function of interest, we can use the model to alter experimental components so as to align behavior. Besides reducing variance between subjects within an experimental condition, the proposed approach offers an additional advantage to current adaptive designs. It allows to generate trials associated with the entire range of discounting probabilities thus enabling to measure graded levels of discounting behavior. Both the model and the experimental components are optimized in an iterative process. We apply the proposed approach here to reward and loss delay discounting.

Our experimental paradigm is divided into two runs, run A and run B, which both consist of an identically structured delay discounting task which differs only in the prompted outcomes and delays (but could also be extended to other tasks and processes). From the behavioral results of run A, we infer subject-level models that probabilistically explain each participant's behavior. The modeled behavioral probabilities are then used to design (that is, solve for) experimental trials of run B to elicit discounting behavior with a predetermined probability. Here, we chose trials that, according to the applied model, should elicit a probability for the discounted option of 0.3, 0.5, and 0.7, although the approach principally allows for an arbitrary grading. The behavior in run B was then in turn used to (i) optimize run A based on the current model and (ii) evaluate and adjust the model-by-model comparison analyses. We tested the protocol in three sequential experiments.

Overall, we were able to significantly reduce the number of individuals showing no behavioral discounting. In addition, we were able to largely induce graded levels of discounting behavior on a single subject level. That is, the observed frequency of immediate choices in both the reward and the loss condition increased within participants with increasing immediate choice probability predicted by the behavioral model. In the reward task, this choice frequency was not only graded, but on average also consistent with the specific model expectation.

The match between model expectation and behavior improved across the successive experiments. In the first experiment we observed that the participants' behavior in run B was graded with respect to the predetermined probabilities, although the actual deviation from these probabilities was rather high. We also observed a high number of non-discounters in both conditions. By model-based adjustment of run A trials, we were able to drastically reduce this number in experiment 2, an issue commonly reported in the delay discounting literature, whereby studies report various rates of non-systematic discounting behavior ranging from 7% up to 50% of the investigated samples (31, 35–45, 89). In addition, the adjustments led to higher behavioral variability within participants, rendering better conditions to validly infer model parameters in run A. This in turn resulted in lower deviations between observed behavior and model predictions in run B of exp 2. Our procedure therefore successfully generated graded response conditions with lower variance, that is, higher behavioral homogeneity within conditions of exp 2.

After systematic model comparison analyses, we then additionally adjusted the underlying trial-generating model in the 3rd (and last) experiment. Again, we observed significantly smaller behavioral deviations from model predictions within run B of exp 3 compared to run B of exp 1. The deviation was comparable to that of exp 2. The total number of non-discounters further decreased on a descriptive level, although this was not confirmed statistically. In contrast to exp 2 (see **Figure 3E**), reaction times of exp 3 (see **Figure 4E**), however, were more in line with theoretical expectations by which reaction times close to the indifference point, that is, close to difficult choices, are slower compared with easy choices.

Interestingly, one of the most commonly applied models, the hyperbolic model, performed among the worst in predicting out-of-sample behavior (see also **Supplementary Figure S6**). With a correct prediction probability of on average $\hat{p}_{reward} = 0.57$ and $\hat{p}_{loss} = 0.55$ (evaluated across all runs and experiments, see **Supplementary Figure S5** left), it performed only marginally above chance level. Overall, the hyperboloid models provided the highest prediction probability, averaged across experiments. The modified hyperboloid model was able to correctly predict behavior on average with 0.68 probability in the reward and 0.71 in the loss condition (see **Supplementary Figure S5** left). It particularly excelled at predicting behavior in run A while staying close to the theoretical expectation in run B (see **Supplementary Figure S5** right), as observed for several other models as well.

As most studies in the field do not report out-of-sample prediction errors (9, 21, 38, 41, 44, 49, 61, 63, 72, 74, 99–101), or report predicted log-likelihood (40), or predicted accuracies (54), which may be far above the predicted probabilities reported here, and since the prediction error depends on trial difficulty (i.e., on how close trials are to the indifference point and therefore on the precise experimental manipulation, cf. Section Behavioral Models and Model Parameters), the obtained values are difficult to compare. However, the results are in line with the few studies who have considered the modified hyperboloid model and have shown its superiority [(49, 61–63, 100); but see also (44)], and which show that the hyperbolic model is not a comparably good fit (61–63, 100).

The modified hyperboloid model is characterized by an additional free parameter s which scales the delay period in the discount factor (cf. Section Behavioral Models and Model Parameters) analogous to a psychophysiological power function [(9); see also (102)]. The power law, originating from psychophysics, describes the relationship between the intensity of a stimulus and the perceived magnitude increase in the sensation induced by the stimulus, which is modulated exponentially by a parameter, here s (102). In the present investigation, as often observed, s on average was smaller than 1 (38, 49, 61, 62), indicating a flattening of the discounting curve (cf. **Figure 4G**). This indicates that delay durations may not be perceived similarly, that is, objectively, across participants as indicated by e.g., the hyperbolic and exponential models, but there is

additional inter-individual variability w.r.t. delay perceptions. This is in line with studies indicating that time perception plays a significant role in delay discounting [(103–107); see also (108)].

This scaling parameter s, as well as the discount parameter κ, moreover differed significantly between the reward and the loss condition. Both parameters were on average lower in the loss condition. Since the scaling parameter s was restricted between 0 and 1 [see also (109, 110)], smaller values here lead to a shrinking of the objectively experienced delay and thus to a lower degree of devaluation. Small κ values in the hyperboloid model similarly cause the discount factor to approach 1 such that effectively devaluation decreases. The fact that we found differences in both parameters, together with the fact that the hyperboloid model was superior to the hyperbolic at predicting the data, suggests that lower κ values alone were not sufficient to capture the weaker devaluation process observed in the loss condition. One may therefore speculate whether lower s values during loss discounting may be associated to a subjectively shorter perception of delays in this condition. Note though that this interpretation should be evaluated with caution since we observed a moderate correlation between s and κ in the reward condition. While a previous study evaluating the modified hyperboloid model did not find differences in the scaling parameter s between discounted rewards and losses (49), while others did not explicitly compare the parameters between tasks (38, 61, 62), the obtained results are in line with the frequent observation of lower discounting rates during loss discounting, also termed "sign-effect" [see also (41, 111); for an overview see (112)]. This sign-effect was also reflected in the lower frequency of discounted choices for the loss condition as compared to the reward condition observed for all runs and experiments despite explicitly prolonging delays for this condition (see **Supplementary Results S2.1–S2.3**).

Interestingly, the discount factor of the modified hyperboloid model was significantly related to subjective measurements: Subjectively reported impulsive behavior, as well as alcohol use behavior was negatively related to the discount factor, indicating that stronger temporal discounting was related to higher impulsivity and more alcohol use behavior. While this is in line with studies linking stronger discounting behavior to higher impulsivity as well as increased alcohol use behavior [(113–117); for an overview see (26, 118, 119)], other studies did not provide evidence for a direct link (120–122).

A crucial difference between our framework and other adaptive designs is that previous studies were mainly interested in the two-level comparison between hard and easy trials, i.e., trials close and far from the indifference point (31, 32, 43, 52, 54), or interested in choices around the indifference points [e.g., (31, 32, 43)]. By providing a formal condition for trial generation, our approach in contrast allows a more highly resolved and targeted grading of discounting probabilities. This includes the assessment of hard and easy trials, that is, trials with discounting probability 0.5 vs. discounting probability unequal to 0.5, as well as any other selected discounting probability on the probability measure (i.e., between 0 and 1). By inducing graded behavior, one presumably induces graded levels of cognition and associated neuronal responses. This facilitates the identification of brain regions or networks which co-vary with discounting probabilities, resolving the neural response at a finer scale and thus providing stronger evidence of the underlying neuronal mechanism (123–127). In addition, from a statistical point of view, generating more homogeneous experimental conditions across different levels of discounting behavior within subjects, should increase the statistical power needed to detect (differences in) the associated brain responses (128–130).

While most studies to date continue to focus on reward (rather than loss) discounting, we provide a general framework which is easily transferable to other scenarios. Although our approach did not work as well for the loss condition, that is, the average discounting frequency deviated somewhat from the model expectation, we did observe graded choice frequencies in response to the three experimentally manipulated levels for both reward and loss conditions. This (and even finer) gradation at the within subject level could be particularly helpful when studying the neurobiological underpinnings of a cognitive process, by providing a dimensional mapping from experimental trial to discounting probabilities.

Beyond that, many previous studies have focused on addressing the question of which discounting model best fits empirical data and how to adapt experimental trials to the individual. However, these studies mostly focused either on model comparisons [e.g., (38, 40, 49, 61, 72, 74, 89)], or on model-based trial adaptation [(31, 32, 36, 43, 54); but see (53)], but not on both. The latter is important though, since the success of model-based trial adaptation should naturally depend on the suitability of the model (see also **Supplementary Figure S5**). To our knowledge, only one study performed both model selection and design optimization simultaneously (53), selecting models on a subject-specific (as compared to group) level (which comes with its own advantages and disadvantages). However, this study as well as the other model comparison studies have mainly selected models based on in-sample error estimates [(9, 21, 38, 41, 44, 49, 61, 63, 72, 74, 99–101); but see also (40, 54)]. In-sample errors are susceptible to under-estimation of the PE due to e. g. overfitting, whereas out-of-sample errors represent more conservative and unbiased estimates (70, 88). They thus do not allow to quantify how well the models actually work at predicting unseen data (70). On the other hand, the studies focusing on adaptive designs have mainly focused on the hyperbolic model [e.g., hyperbolic only: (31, 32, 43, 54)], which performed particularly poorly in other studies [e.g., (53)], and yielded poor predictions as well as unreliable parameter estimates here.

One caveat of comparing multiple models as done in the present study is that it requires a sufficient number of trials. Other adaptive approaches which are often tuned to a single model have focused on optimizing efficiency and require a lower number of trials. A lower number of trials with equal reliability is desirable as it exerts less experimental burden on the participant. Overall, the applied number of trials varies highly between adaptive studies though, ranging from 5, ∼10 and 98 trials in more recent approaches (31, 36) up to over 300 trials in more classical titration procedures [e.g., (32, 40, 43, 44, 47–50, 54, 89, 131, 132); with an average of around 95 trials (+/−77)]. The exact trial

numbers may depend on subject specific parameters, and on how many delays and outcomes are applied. In an appealing Bayesian framework, Pooseh et al. (32) performed simulation analyses investigating the number of iterations necessary for parameter estimates to converge to their true values. Their results illustrate the dependency on the true parameter values and indicate that the classic amount adjusting method converges after 20–200 iterations (with high variance). Their Bayesian approach on the other hand starts to converge after around 50 trials for both κ and β evaluated on experimental data (32). Using adaptive design optimization [ADO; (36, 53)], recent studies demonstrated remarkable efficiency in measuring κ with high reliability in <10 trials, although the β parameter is inferred less reliably and likely requires more trials. Having now established a suitable model for our parametric method, one could perhaps improve the proposed framework by combining run A with one of these more efficient methods to further reduce the number of trials necessary in run A.

An interesting observation of the present study is that we noticed a high agreement in the discount factor of the hyperboloid model between both experimental runs and between reward and loss conditions. This agreement suggests that temporal discounting may be reliably measured (and may bear similarities in the processing of loss and reward) and is consistent with (the significantly) lower correlation of behavioral frequencies. In contrast, in the commonly used hyperbolic model, the relation between discount factors across runs (and partly across conditions), as well as the associations to discounting relevant measures such as impulsivity and alcohol use, vanished. On the one hand, this suggests that poorer behavioral models may provide more unreliable and biased parameter estimates, potentially also explaining difficulties in reproducibility between studies [see also e.g., (133) restricted reliability for hypothetical monetary outcomes; see also (36)]. On the other hand, it also shows that using appropriate behavioral models in combination with adaptive designs may even improve the valid and reliable measurement of cognitive function (superior to for instance behavioral frequencies). Especially considering the reproducibility crisis in psychological experiments [for overviews see (134–138)], such approaches could prove particularly beneficial [see also (139)].

Finally, we also address several limitations of the current study. First, our sample was highly dominated by women (with $N = 145$ women and $N = 51$ men). Although we found no differences in discounting behavior between women and men (cf. **Supplementary Table S2**), we cannot exclude that our findings generalize better to women. Second, although the proposed framework performed well within the reward condition, many non-discounters remained in the loss condition. It is unclear whether this may be attributed to yet suboptimal run A trial settings, inadequate to identify each participant's indifference point, or whether there is a true proportion of individuals in the population who do not exhibit loss discounting. The latter is not unlikely, as other studies with different settings have also found constant high rates of non-discounters (31, 33–35, 38, 40). However, it is also possible that the delays used in the current experiment were simply not long enough to tempt participants to discount future losses, masking the true proportion of non-discounters in the population. Future studies that explore the relationship of non-discounting to other subjective factors such as risk aversion, punishment sensitivity, reward sensitivity, preference uncertainty, and temporal uncertainty, or that systematically examine other trial settings, may help shed light on this question and reveal potential alternative discounting "styles."

We also recognize that even in the reward condition, where choice frequencies on average matched well with model expectations, the behavioral variation was quite high. This could either be due to natural noise in the behavioral process, or that the true behavior generating model was not amongst the tested set. We cannot exclude that there is another model that describes the data better and would potentially further reduce the observed variation [see also 53]. For example, there is evidence that temporal discounting also depends on the tendency to avoid risks, often referred to as risk aversion (32, 40, 52, 73). Lopez-Guzman et al. (40) could for instance show that by inferring the individual's risk attitude on an independent task and adding it as an additional parameter to the discounting function, they could account for more behavioral variance in a temporal discounting task. It may also be reasonable to assume that individual participants are best described by different models (53), although inferring models on the single subject level limits comparability of associated neurobiological correlates.

CONCLUSION

The present work proposes a model guided framework to evoke graded responses linked to cognitive function at a single subject level. Such a framework may be used in psychology, neuroscience, or psychiatry in the future to (a) measure cognitive function on a dimensional rather than dichotomous scale, (b) homogenize behavior across participants, (c) test the validity of a behavioral model, or (d) investigate the causal differences underlying heterogeneous behavior, which may benefit the investigation of cognitive mechanisms [see e.g., (140)]. Importantly, temporal discounting is a fundamental process underlying decision making and largely comparable between species (13). Given that similar decay functions of reward delay discounting have been observed in humans and rats (141), application of the here proposed adaptive experimental design to appropriate behavioral animal models may significantly enhance insights to the circuitry and molecular underpinnings of various neuropsychiatric disorders (142). Future studies are needed to assess whether our approach is suitable to dissolve discounting behavior on more than three levels, that is, on a more fine-grained dimensional spectrum of behavioral probabilities. We also propose a more general approach to create adaptive experimental designs based on the combination of behavioral models and model selection techniques. Our framework was tested in the context of temporal reward and loss discounting.

It may however be generalized to other cognitive functions by using similar models which map actions probabilistically to an underlying cognitive process.

DATA AVAILABILITY STATEMENT

The datasets presented in this study, as well as the code needed to reproduce the findings presented in this study, can be found at https://github.com/GKoppe.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Medical Faculty Mannheim, University of Heidelberg (2019-633N). The participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

GK, PK, and WHS conceptualized the study. GK, JT, MP, PH, PK, and WHS contributed to the design of the study. MP compiled the online experiment and collected the data. GK and JT performed the statistical analyses and wrote the manuscript. DD, GK, JT, MP, PH, PK, and WHS contributed to reading, revising, and approving the submitted manuscript. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2022.846119/full#supplementary-material

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Study 2: Supplementary Material

S1 Methods

S1.1 Generating trials by varying delays across subjects.

Eqn. (3) in the main manuscript may be rewritten as $V_2 = r_1 + \frac{\log(\frac{1-p_1}{p_1})}{\beta}$, where r_1 is the immediate outcome, p_1 is the (desired) immediate choice probability, and V_2 is the discounted value, implicitly containing the delay and the discount parameter. If we insert V_2, defined by the respective model, we may solve for the adaptive delay given a set of immediate and delayed outcomes, model parameters, and desired immediate choice probabilities. For instance, inserting V_2 of the hyperbolic model, yields $(\frac{1}{1+\kappa D})r_2 = r_1 + \frac{\log(\frac{1-p_1}{p_1})}{\beta}$, from which we can derive

$$D = \left(\left(\frac{r_1}{r_2} + \frac{\log(1-p_1)}{\beta r_2} - \frac{\log(p_1)}{\beta r_2}\right)^{-1} - 1\right)\left(\frac{1}{\kappa}\right),$$

as trial generating condition, where D is the delay, and κ and β are model parameters.

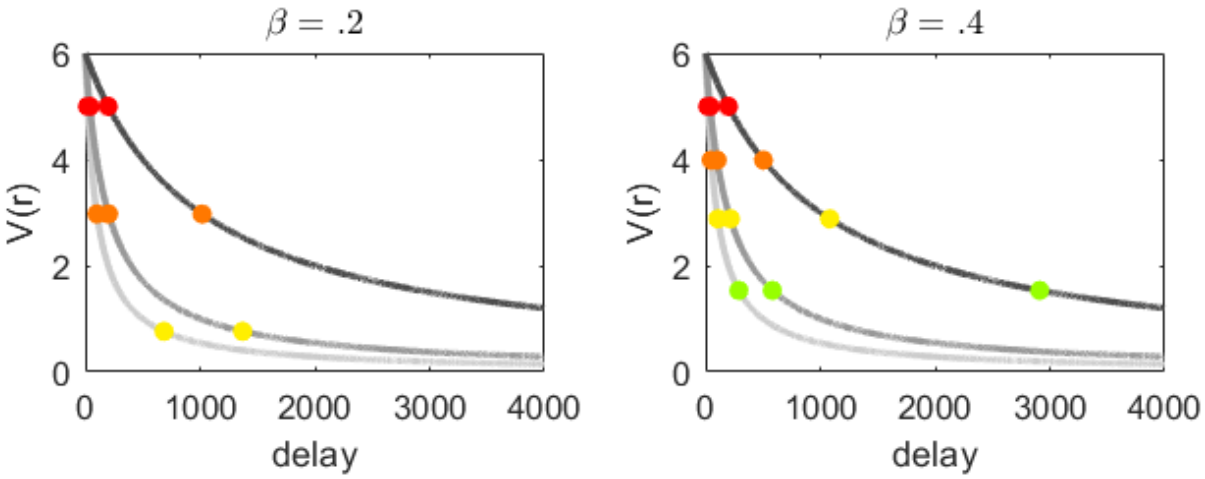

Fig S1. Illustration of method's operating principle when solving for delay rather than immediate outcome. In this example, the immediate reward was set to 5, and the delayed reward to 6. The 3 lines correspond to hypothetical κ values of .01 (light gray), .005 (gray), and .001 (dark grey). Colored dots mark the respective delays selected for each theoretical κ to obtain immediate choice probabilities of .5 (red), .6 (orange), .7 (yellow), and .8 (green). The left graph corresponds to subjects with β=.2 and the right to β=.4 (i.e., high sensitivity). To obtain similar discounting probabilities for subjects with different κ values (with same β), delays are selected such that the discounted value is equal across subjects (i.e., lies on a horizontal line). β tunes the difference between immediate and discounted outcomes, shifting the dots on the curves (i.e., discounted values) to the left. For larger β, shorter delays are necessary to discriminate between outcomes, consistent with higher sensitivity.

S2 Results

S2.1 Experiment 1

The frequency of discounted choices was lower in loss as compared to reward discounting in run A (Z=6.07, p<0.001), as well as run B (Z=3.59, p<0.001).

S2.2 Experiment 2

The frequency of discounted choices was lower in loss as compared to reward discounting in run A (Z=5.89, p<0.001), as well as run B (Z=4.14, p<0.001).

S2.3 Experiment 3

The frequency of discounted choices was lower in loss as compared to reward discounting in run A (Z=4.99, p<0.001), as well as run B (Z=3.14, p=0.002).

Table S1. Socio-demographic and subjective reports.

		Exp 1		**Exp 2**		**Exp 3**	
		N=98		N=50		N=50	
age (mean/SD)		32.44	11.55	31.38	9.79	31.86	9.24
gender (N)	female	65		37		43	
	male	32		12		7	
	diverse	1		1		0	
education (N)	primary	0		1		0	
	alevel	44		16		12	
	gcse	6		6		1	
	undergrad	32		15		25	
	grad	15		12		11	
	phd	1		0		1	
AUDIT-total		5.58	5.15	4.4	3.52	4.56	4.19
BIS-total		31.34	6.99	30.86	7.02	31.22	6.14
BIS-non-planning		11.29	3.19	10.6	3.41	10.9	2.84
BIS-motor		14	4.34	9.92	2.87	10.3	2.35
BIS-attentional		10.23	2.78	10.34	2.91	10.02	2.39

Legend. AUDIT = Alcohol Use Disorder Identification Test, BIS = Barratt Impulsiveness Scale; Exp = experiment; gcse = general certificates of secondary education

Table S2. Socio-demographic information across experiments with respect to gender (binary)

	female		**male**		**test-statistic**	
	N=145		N=51		Z	*p*
age (mean/SD)	31.49	12.09	33.94	9.89	1.09	0.275
run A						
% non-discounter	46.89		49.02			
% non-discounter reward	16.55		13.73			
% non-discounter loss	46.89		41.18			
reward imm choice freq (mean/SD)	37.21	25.21	32.98	26.09	0.88	0.381
loss imm choice freq (mean/SD)	80.53	16.94	84.72	22.83	0.39	0.693
reward explo-exploitan (mean/SD)	11.69	26.81	9.76	29.72	1.04	0.299
reward discounting par (median/perc)	0.02	[0.01,0.14]	0.01	[0.004,0.13]	0.87	0.382
reward scaling par (mean/SD)	0.57	0.38	0.60	0.37	0.49	0.618
loss explo-exploitan par (mean/SD)	27.36	42.04	28.49	42.9339	0.78	0.433
loss discounting par (median/perc)	0.002	[<0.001,0.03]	0.007	[<0.001,0.02]	0.79	0.424
loss scaling par (mean/SD)	0.52	0.35	0.53	0.36	0.19	0.845
run B						
% non-discounter	44.14		39.22			
% non-discounter reward	13.10		3.92			
% non-discounter loss	39.31		37.25			
reward imm choice freq (mean/SD)	42.96	24.53	50.04	27.25	1.74	0.081
loss imm choice freq (mean/SD)	71.92	30.19	68.76	28.94	0.72	0.469
reward explo-exploitan (mean/SD)	10.17	24.58	9.88	26.31	0.33	0.739
reward discounting par (median/perc)	0.01	[0.001,0.05]	0.02	[0.004,0.09]	0.28	0.781
reward scaling par (mean/SD)	0.65	0.37	0.65	0.36	0.01	0.995
loss explo-exploitan par (mean/SD)	33.68	43.65	30.75	44.87	0.19	0.844
loss discounting par (median/perc)	9.5x10-5	[<0.001,0.04]	0.004	[<0.001,0.04]	0.35	0.725
loss scaling par (mean/SD)	0.43	0.39	0.5	0.37	1.18	0.238

Legend. discount = discounting; explo = exploration; exploit = exploitation; imm = immediate; freq = frequency; par = parameter; SD = standard deviation; perc = percentile (25% - 75%); % = percentage

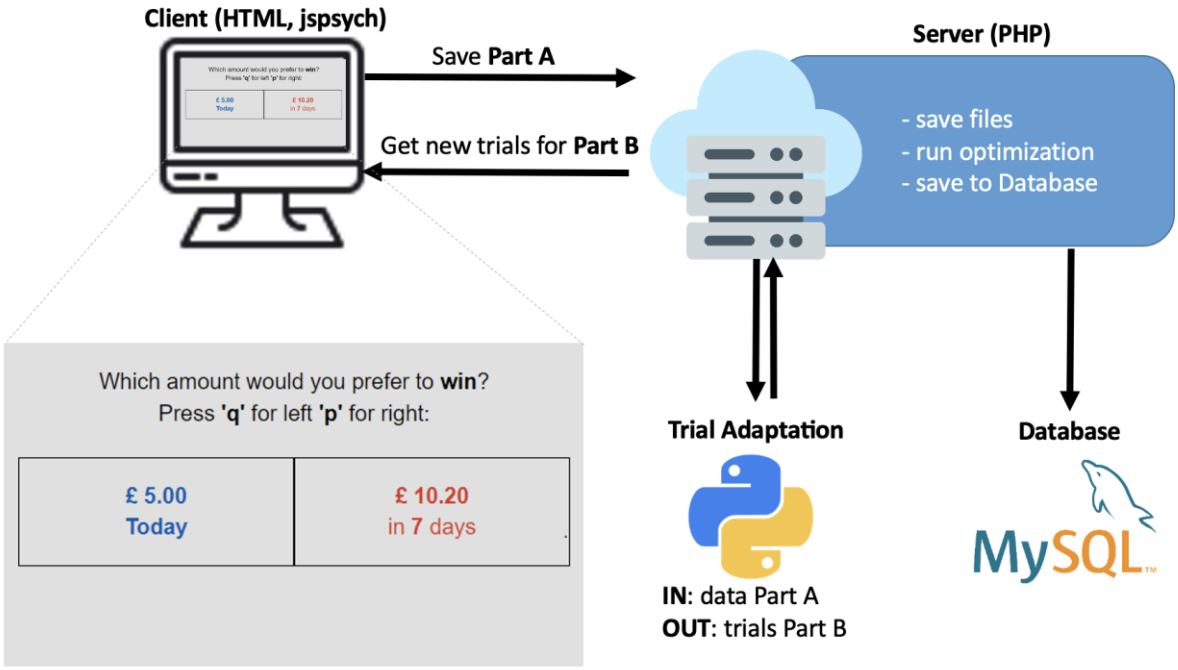

Fig. S2. Illustration of online paradigm technical information flow. Upper left: The reward and loss discounting paradigm was programmed in JavaScript using the open-source package 'jsPsych'. Lower left: Exemplary reward discounting trial prompting the participant to either press ‘q’ or ‘p’, if she/he wants to win £5 today (blue) or £10.20 in 7 days (red). Upper right: The experiment was hosted on a custom virtual server using Linux-Apache-PHP-MySQL. Lower right: Model inference on data from run A and trial generation for run B was realized on the custom virtual server using self-written Python scripts. Data was stored on the open-source data management system MySQL.

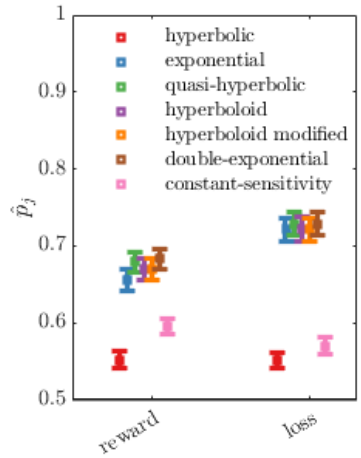

Fig. S3. Model comparison for experiment 1. Average predicted (out-of-sample) probability of observed responses $\hat{p}_j$ (y-axis) for reward and loss conditions (x-axis) for different models averaged over run A and B. Choice behavior of run B was predicted based on model parameters inferred on run A and vice versa. Choice behavior of the reward discounting condition was predicted by the hyperbolic model with $\hat{p}_{reward}$=.55, by the exponential model with $\hat{p}_{reward}$=.66, by the quasi-hyperbolic model with $\hat{p}$=.68, by the hyperboloid model with $\hat{p}_{reward}$=.67, by the modified hyperboloid model with $\hat{p}_{reward}$=.67, by the double-exponential model with $\hat{p}_{reward}$ =.68, and by the constant-sensitivity model with $\hat{p}_{reward}$=.60 (in order of legend). Choice behavior of the loss discounting condition was predicted by the hyperbolic model with $\hat{p}_{loss}$=.55, by the exponential model with $\hat{p}_{loss}$=.72, by the quasi-hyperbolic model with $\hat{p}_{loss}$=.73, by the hyperboloid model with $\hat{p}_{loss}$=.72, by the modified hyperboloid model with $\hat{p}_{loss}$=.72, by the double-exponential model with $\hat{p}_{loss}$=.73, and by the constant-sensitivity model with $\hat{p}_{loss}$=.57.

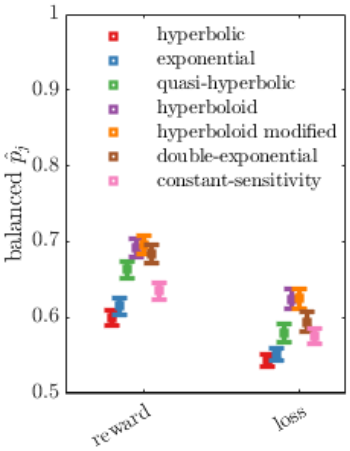

Fig. S4. Model comparison for experiment 2. Average predicted (out-of-sample) probability of observed responses $\hat{p}_j$ (y-axis) for reward and loss conditions (x-axis) for different models averaged over run A and B. Choice behavior of run B was predicted based on model parameters inferred on run A and vice versa. Choice behavior of the reward discounting condition was predicted by the hyperbolic model with $\hat{p}_{reward}$=.6, by the exponential model with $\hat{p}_{reward}$=.62, by the quasi-hyperbolic model with $\hat{p}$=.66, by the hyperboloid model with $\hat{p}_{reward}$=.69, by the modified hyperboloid model with $\hat{p}_{reward}$=.7, by the double-exponential model with $\hat{p}_{reward}$=.68, and by the constant-sensitivity model with $\hat{p}_{reward}$=.64 (in order of legend). Choice behavior of the loss discounting condition was predicted by the hyperbolic model with $\hat{p}_{loss}$=.54, by the exponential model with $\hat{p}_{loss}$=.55, by the quasi-hyperbolic model with $\hat{p}_{loss}$=.58, by the hyperboloid model with $\hat{p}_{loss}$=.62, by the modified hyperboloid model with $\hat{p}_{loss}$=.63, by the double-exponential model with $\hat{p}_{loss}$=.59, and by the constant-sensitivity model with $\hat{p}_{loss}$=.58.

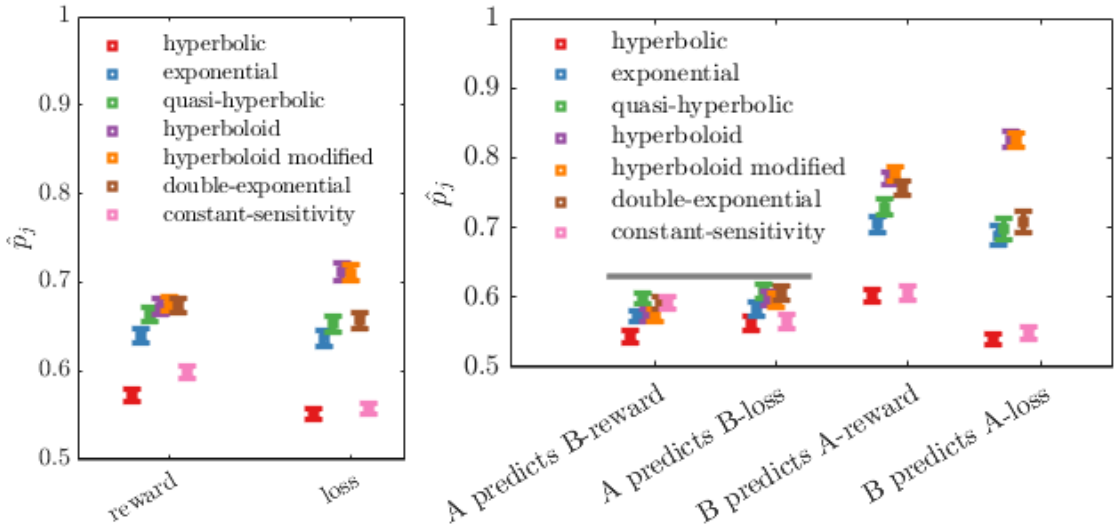

Fig. S5. Model comparison across all experiments. Left: Average predicted (out-of-sample) probability of observed responses $\hat{p}_j$ (y-axis) for reward and loss conditions (x-axis) for different models averaged over run A and B. Choice behavior of run B was predicted based on model parameters inferred on run A and vice versa. Choice behavior of the reward discounting condition was predicted by the hyperbolic model with $\hat{p}_{reward}$=.57, by the exponential model with $\hat{p}_{reward}$=.64, by the quasi-hyperbolic model with $\hat{p}$=.66, by the hyperboloid model with $\hat{p}_{reward}$=.67, by the modified hyperboloid model with $\hat{p}_{reward}$=.68, by the double-exponential model with $\hat{p}_{reward}$=.67, and by the constant-sensitivity model with $\hat{p}_{reward}$=.59 (in order of legend). Choice behavior of the loss discounting condition was predicted by the hyperbolic model with $\hat{p}_{loss}$=.55, by the exponential model with $\hat{p}_{loss}$=.64, by the quasi-hyperbolic model with $\hat{p}_{loss}$=.65, by the hyperboloid model with $\hat{p}_{loss}$=.71, by the modified hyperboloid model with $\hat{p}_{loss}$=.71, by the double-exponential model with $\hat{p}_{loss}$=.66, and by the constant-sensitivity model with $\hat{p}_{loss}$=.56. Right: Same as left separated for predictions on run A and run B. When predicting run B based on models inferred on run A, all models perform below and close to the upper bound given by the theoretical expectation (horizontal grey line). When predicting behavior in run A based on models inferred on run B, the hyperboloid models show the highest prediction performance, while the common hyperbolic model performs particularly poorly.

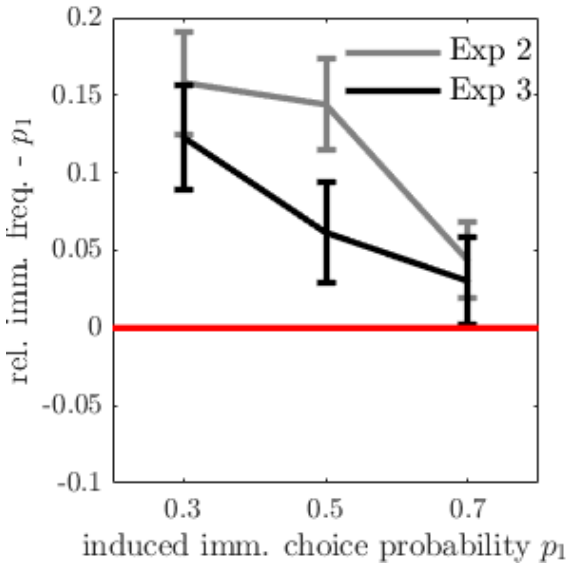

Fig S6. Investigation of model bias. The figure displays the deviation between observed relative immediate choice frequencies and induced immediate choice probabilities (y-axis), as a function of observed immediate choice probabilities (y-axis) in experiment 2 (grey) and experiment 3 (black), averaged across reward and loss conditions. The experiments differ w.r.t to whether choice probabilities were induced via the hyperbolic (experiment 2) or the modified hyperboloid (experiment 3) models. Descriptively, observed deviations are closer to 0 in experiment 3 indicating a lower bias in the induction of behavior for the modified hyperboloid model and thus indicating higher model validity. Statistically, we see a marginal difference within the .5 trail condition (p=.06).

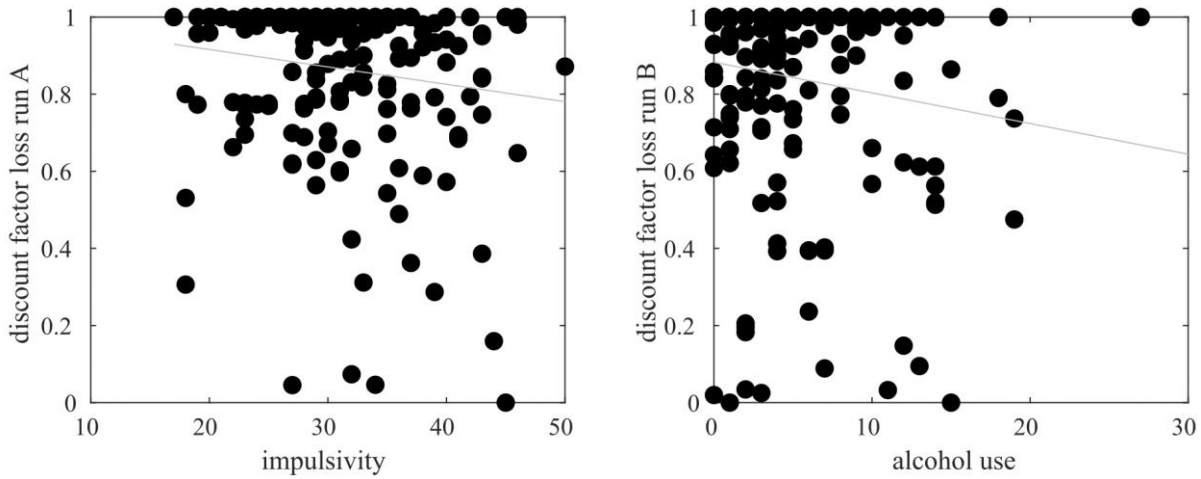

Fig S7. Correlation between subjective reports and discount factor of the modified hyperboloid model across all experiments. Left: Negative association between the discount factor (loss, run A) and impulsivity (BIS-total: r=-0.15, *p*=0.037). Right: Negative association between the discount factor (loss, run B) and alcohol use (AUDIT-total: r=-0.14, *p*=0.044).

7 Study 3

Title: The Association between Reward and Loss discounting, Alcohol Use and Socioeconomic Status

Under Review in: Alcohol, Clinical and Experimental Research (as of 16.04.2024)

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Abstract

Background: Delay Discounting refers to the devaluation of future outcomes over time and has been linked to problematic alcohol and substance use. Prior studies show modest yet consistent associations between problematic alcohol use and delayed reward discounting (DRD). This study aims to replicate these correlations and expand the scope to include delayed loss discounting (DLD). Additionally, it explores the potential confounding influence of socioeconomic status (SES).

Methods: We collected data from 341 moderately-drinking participants (mean alcohol consumption = 27.92g/day) in a cross-sectional online study. DRD and DLD were measured using an intertemporal choice task. Questionnaires encompassed problematic alcohol use (AUDIT), education and income, among further exploratory measures of past and present SES, quantity-frequency of drinking, and impulsivity.

Results: We found a correlation (r = .15) between DRD, but not DLD, and alcohol use. SES indicators were negatively associated with both DRD (education) and alcohol use (education, income). The partial effect of DRD on alcohol use remained significant after accounting for SES, explaining 1.5% of variance in AUDIT scores. Impulsivity was not associated with either DRD or DLD, but with alcohol use (r = .36).

Conclusions: We replicated a small but robust association between alcohol use and DRD, but not DLD. DRD explained incremental variance in AUDIT scores above and beyond several potential confounding variables. Given the small effect sizes, investigation of more complex relationships between alcohol use, DRD and SES may require larger sample sizes.

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Introduction

Reward Discounting, Addiction and Socioeconomic Status

Numerous studies have established a link between Delayed Reward Discounting (DRD) and alcohol use disorder (AUD), demonstrating that individuals with more AUD symptoms and higher drinking levels tend to favor short-term rewards in monetary intertemporal choice tasks (MacKillop *et al.*, 2011; Amlung *et al.*, 2017). Consequently, DRD has been proposed as a behavioral marker of addiction and a potential target for therapeutic interventions (Bickel *et al.*, 2014; Story *et al.*, 2014).

However, steep DRD could also be a rational behavior in response to limited resources, when waiting for a delayed reward is not feasible (Becker and Mulligan, 1997). This might explain why lower socioeconomic status (SES), such as low education and income, is associated with steeper DRD (de Wit *et al.*, 2007; Reimers *et al.*, 2009; Green *et al.*, 2014; Tunney, 2022). Some studies suggest a causal link between income and DRD, as hypothetical income declines are associated with increased DRD rates (Bickel *et al.*, 2016; Mellis *et al.*, 2018), demonstrating that DRD reflects more than impulsivity traits.

Individuals with low SES not only discount rewards more steeply, but also have a higher risk of AUD and mental disorders (Jenkins *et al.*, 2008; Grant *et al.*, 2015; Beard *et al.*, 2019). Moreover, their risk for alcohol-related harm is disproportionally higher when compared to individuals with higher SES and equal drinking levels. This alcohol harm paradox may be partly explained by an increased incidence of aversive experiences and mental health problems among socioeconomically deprived individuals, leading to alcohol consumption as a coping mechanism (Lee *et al.*, 2013; Probst *et al.*, 2020; Shuai *et al.*, 2022). Notably, subjective measures of SES have been shown to have a stronger link to alcohol use and psychological well-being compared to objective measures, underscoring the relevance of subjective perceptions of SES (Adler *et al.*, 2000; Ishii, 2015; Garza *et al.*, 2017; Ishii, Eisen and Hitokoto, 2017; Najdzionek *et al.*, 2023).

In summary, experiencing socioeconomic hardship increases both DRD rates and the vulnerability for AUD. Existing studies on the association between DRD and alcohol use often lack statistical power to address this potential confound, or do not systematically incorporate SES as an additional predictor. Additionally, many studies are limited to clinical populations that have already experienced significant socioeconomic consequences due to AUD.

Delayed Loss Discounting and AUD

Decisions about alcohol consumption involve assessing both the positive and negative consequences. Therefore, high-risk drinkers may devaluate both benefits of abstinence and long-term harms of drinking. However, research on alcohol use and Delayed Loss Discounting (DLD) is scarce. In a study of 33 students, DLD was moderately linked to alcohol consumption frequency (Takahashi *et al.*, 2009). Bailey et al. (2018) and Gerst et al. (2017) found that individuals with AUD discount future losses more than healthy controls. Those who steeply discount rewards also tend to discount losses (DeHart *et al.*, 2020; Thome, Pinger, Halli, *et al.*, 2022). However, Myerson et al. (2017) found significant associations between AUD and DRD, but not DLD. Interestingly, in a prior exploratory analysis in a healthy sample, we observed the opposite pattern (Thome, Pinger, Halli, *et al.*, 2022). However, evidence from larger samples with problematic alcohol use is lacking.

Aims and Hypotheses

Here we aim to address two key questions related to DRD and its association with AUD. Firstly, we seek to investigate to which degree the relationship between DRD and alcohol use is confounded by socioeconomic status (SES) with the objective to determine whether DRD contributes additional explanatory power to alcohol use after accounting for socioeconomic influences. We pursued a varied sample of individuals with moderate to heavy drinking patterns. This methodology allows for statistical models to explore quantitative effects among high-functioning individuals exhibiting high drinking quantities.

Secondly, we aim to investigate a potential relationship between alcohol use and the discounting of aversive consequences. For this, we employed a previously established DLD task (Thome et al 2022), using financial losses at different time points.

Hypotheses and methods were preregistered (https://aspredicted.org/ac46k.pdf). We hypothesized to replicate the positive association between alcohol use (measured by AUDIT scores) and DRD steepness (H1) and extend this to DLD steepness (H2). Furthermore, we hypothesized that SES (yearly income and education) is negatively associated with DRD (H3) and AUD severity (H4). Lastly, we hypothesized that controlling for these SES diminishes the association between DRD and alcohol use (H5).

Materials and Methods

Sample

Participants used personal computers at home and were recruited in June 2022 via the online participant platform Prolific (https://www.prolific.co). Eligibility criteria were filtered using Prolific's custom prescreening tools and included age 18-65, current residency in the UK and minimum weekly alcohol consumption of 10 alcohol units. Participants received £9 per hour as compensation and provided informed consent prior to the study. The ethics committee of the Medical Faculty Mannheim, University of Heidelberg (2019-633N), approved the study.

A priori power analysis determined a required sample size of 311 participants for 80% power to replicate the correlation of r = .14 between DRD and alcohol use found in a recent meta-analysis (Amlung *et al.*, 2017). We targeted a sample size of 350 participants.

Study Materials

Delay Discounting of Rewards and Losses

Participants completed an intertemporal choice task developed by our group (Thome, Pinger, Halli, *et al.*, 2022), making decisions between hypothetical monetary rewards (reward condition, 96 trials) or losses (loss condition, 96 trials). Each choice involved an immediate smaller outcome and a delayed larger outcome, with varying delays (D = {7, 30, 90, 180, 365, 109} days), immediate reward/loss magnitudes (r_{a1}), and delayed reward/loss magnitudes (r_{a2} = {5, 10, 20 50} £UK). Immediate magnitudes (r_{a1}) were determined a priori through a computational model solving for magnitudes for a range of hypothetical discounting parameters and predicted choice probabilities. We could show that this procedure, compared to other fixed-trial procedures as in Rachlin et al. (1991), samples sufficient variance in behavior across a broad range of plausible discounting rates (for details, see Thome, Pinger, Halli, et al., 2022, and Thome, Pinger, Durstewitz, et al., 2022).

The 96 trials of each condition were randomized and split into two blocks of 48 trials each.
Reward and loss blocks were presented in alternating order, starting randomly with either condition. Within each trial, the two options were randomly presented on the left and the right side of the screen. Participants indicated their choices by pressing either "Q" (for the left option) or "P" (for the right option) within 10 seconds of stimulus presentation. The chosen option was then highlighted for one second, followed by a fixation cross for another second. After each block, participants were allowed to take a break for a self-chosen duration.

Self-report measures

Problematic alcohol use was assessed using the Alcohol Use Disorder Identification Test (AUDIT, Saunders et al., 1993). To enhance standardization, the term "a drink" was replaced with "a standard unit", accompanied by a visual aid retrieved from the UK Department of Health and Social Care (2020). Using the Daily Drinking Questionnaire (DDQ; Collins et al., 1985), participants reported average standard units of alcohol consumed on each day of the week over the past three month.

Assessment of income was based on gross income in the last twelve months, including earnings from all sources of income, separately for personal and household level. Income was assessed using levels from "less than £10,000" to "more than £250,000", using £10,000 increments up to £100,000, and thereafter in £50,000 increments (Diemer *et al.*, 2013). Education was assessed as the highest level of education according to the International Standard Classification of Education (ISCED) levels adapted for the UK (Schneider, 2013), ranging from 0 ("no formal education") to 8 ("doctoral degree or higher"). Education of primary and secondary (if applicable) caregivers during adolescence was assessed using the same levels. Subjective adolescent financial well-being was measured using the single-item question "Please rate your family's or household's financial wellbeing during your adolescence" and a Likert scale with 5 steps ("not at all well-off", "not very well-off", "average", "somewhat well-off" and "very well-off"). Subjective SES was measured using the MacArthur scale, a visual 10-step ladder representing relative societal standing including education, income and occupation (Adler *et al.*, 2000).

Impulsivity was measured using the short-form Barratt-Impulsiveness-Scale (BIS-15; Spinella, 2007).

Data Collection and Study Procedure

The online study was programmed in JavaScript using the open source package jsPsych, version 6.2 (de Leeuw, 2015) and was hosted on a custom virtual server using a Linux-Apache-PHP-MySQL stack (see Thome et al., 2022 for details). Participants entered the study through a link on the Prolific website. After completing the consent form and filling out sociodemographic information, participants received an introduction into the intertemporal choice tasks, including six example trials. After finishing the the task, participants completed the remaining questionnaires.

Data Analysis

Data Preprocessing

Data from participants who completed less than 80% of the discounting trials within one condition, who displayed stereotypical key press patterns (only pressing "Q" or "P") or who had average reaction times below 500ms in the discounting trials were excluded from all analyses. Data exclusion was preregistered.

Sum scores were calculated for the AUDIT, the BIS-15 and the DDQ. Education and income were treated as continuous variables. To this end, the character-based income levels (e.g., "£10,000-20,000") were transformed into numerical values by using mid-points of each income category, (£15,000 for the example above). The ISCED education categories were treated as a Likert scale. Educational levels of primary and secondary caregivers during adolescence were averaged to obtain single-value parental education levels.

Intertemporal decision-making was investigated using discounting frequencies and hyperboloid model parameters. To this end, hyperboloid discounting models were inferred on the behavioral choices of each participant (see Thome, Pinger, Durstewitz, et al., 2022; Thome, Pinger, Halli, et al., 2022 for details). The modified hyperboloid model (Mazur, 1987; Rachlin, 2006) posits that the values V for the delayed choices a_2 are discounted according to

$$V(a_2) = \frac{1}{1 + \kappa \cdot D^s} r_2 \qquad (1)$$

while the values for the immediate options a_1 correspond to the actual outcomes, $V(a_1) = r_1$. Here, κ indexes the individual discounting parameter, s represents an individual temporal scaling parameter, D the temporal delay in days, and r_1 and r_2 are the immediate and delayed outcomes, respectively. Values were translated into immediate choice probabilities via a sigmoid function

$$p(a_1|V) = \frac{1}{1 + e^{\beta(V(a_2) - V(a_1))}}, \qquad (2)$$

where β indicates the disposition to exploit ($\beta \to \infty$) or explore ($\beta \to 0$) choices (Sutton & Barton, 2018), and $p(a_2) = 1 - p(a_1)$. Parameters were then inferred via maximum likelihood estimation (see also Ahn et al., 2020; Thome et al., 2022), implemented via optimize.minimize() from the SciPy library in Python, with constraints $\kappa \in [0, 1000]$ and $\beta \in [0.01, 2]$). Separate discounting and scaling parameters were inferred for DRD and DLD trials.

This resulted in three indices of discounting behavior:

1.) Hypotheses were tested using natural log-transformed κ parameter obtained from hyperboloid model (see above) after adding a constant of 0.0001 to account for zero-values. Higher log(κ) values indicate steeper discounting.
2.) The discounting factor $df := \frac{1}{1+\kappa \cdot D^s} \in [0, 1]$ at delay $D = 365$ days was used as an exploratory measure. Lower discounting factors indicate steeper discounting.
3.) Frequency of discounted choices relative to all completed trials was used as an exploratory behavioral measure. Discounted choices were defined as immediate choices in the reward condition and delayed choices in the loss condition.

Hypothesis Testing

All data were analyzed using R, Version 4.2.1 (R Core Team, 2022). Hypothesis testing was conducted with two-tailed tests (α = 0.05).

The predictive effects of DRD (H1) and DLD (H2) on problematic alcohol use were assessed through simple linear regressions with AUDIT sum scores as the dependent variable and log(κ_R) for DRD or log(κ_L) for DLD as the independent variables. Predictive effects of SES on DRD (H3) and problematic alcohol use (H4) were tested through multiple linear regressions, using education and personal income as independent variables and log(κ_R) and AUDIT scores as dependent variables, respectively. Confounding effects of SES on the association between DRD and problematic alcohol use (H5) were tested through hierarchical linear regression. Personal income and education were introduced as dependent variables, followed by log(κ_R) in a subsequent step. F-tests were used to test whether the addition of log(κ_R) explained significantly more variance than SES alone.

Exploratory Analyses

Pearson correlation coefficients were obtained for pairwise combinations of all variables.

Regression models for hypothesis testing were repeated for the two exploratory measures of DRD and further socioeconomic variables significantly associated with both delay discounting and alcohol use.

We examined gender effects via t-tests on AUDIT scores, DDQ scores, discounting, impulsivity, education, and income. Additionally, we employed a multiple regression model with log(κR), gender (dummy-coded with 0 = female, 1 = male), their interaction as independent variables, and AUDIT scores as the dependent variable.

Participants with a relative discounting frequency below 5% in the intertemporal choice tasks were defined as non-discounters. T-tests were conducted to compare discounters and non-discounters with respect to age, impulsivity, alcohol use, income and education.

Results

Sample Description and Missing Data

A total of 347 participants completed the online study. Due to technical problems, data from six participants could not be retrieved from the server, therefore, the final sample size is N = 341. Table 1 and Table 2 provide descriptive statistics of all variables. On average, participants had an AUDIT score of 11.76 and have been drinking 24.43 alcohol units per week or 27.92g/day of alcohol within the 3 months precluding the study. Average alcohol consumption by weekday is illustrated in Figure 1. The sample was balances with respect to gender (170 female participants = 50%). The majority of participants reported being employed (65.7%) or self-employed (14.7%), while 4.4% were retired, 4.1% were students, 7.3% were unemployed and 3.8% used alternative self-descriptive terminology.

No participants had to be excluded based on reaction times or key press patterns in the delay discounting tasks. One participant exceeded the exclusion criteria of more than 20% missing trials in the loss condition.

Due to few missing data entries, participants with missing data points were excluded from analyses with the missing variable.

Preregistered Hypotheses

Pearson correlation coefficients between the five variables preregistered for hypothesis testing are given in Table 3.

H1: DRD and Problematic Alcohol Use. We found a small but significant positive correlation between the DRD parameter $\log(\kappa_R)$ and AUDIT sum scores ($r = .15$, $p = .01$, Figure 2). Linear regression revealed a significant prediction of AUDIT scores by $\log(\kappa_R)$ ($R^2 = .023$, $F(1, 339) = 7.81$, $p < .01$).

H2: DLD and Problematic Alcohol Use. The correlation between the DLD parameter $\log(\kappa_L)$ and AUDIT sum scores was not significant ($r = .09$, $p = .10$, Figure 2), therefore no linear regression was computed.

H3: DRD and SES. We found a significant negative correlation between the DRD parameter $\log(\kappa_R)$ and level of education ($r = -.19$, $p < .01$), but not between $\log(\kappa_R)$ and yearly personal income ($r = -.10$, $p = .07$). Linear regression revealed a significant prediction of $\log(\kappa_R)$ by education ($R^2 = .031$, $F(1, 339) = 12.04$, $p < .01$).

H4: SES and Problematic Alcohol Use. AUDIT sum scores were significantly and negatively correlated with both level of education (r = -.15, p < .01) and yearly personal income (r = -.12, p = .03), with the latter two also showing a significant intercorrelation (r = .26, p < .01). Employing both education and income as independent variables and AUDIT scores as dependent variable in a multiple regression, only education remained a significant predictor (β = -0.11, t(327) = -2.03, p = .04). The fitted model accounted for 2.6% of variance in AUDIT scores (R^2 = .026, F(2, 327) = 4.43, p = .01, see Table 4).

H5: DRD, SES and Problematic Alcohol Use. When the DRD parameter log(κ_R) was included as an independent variable after testing education and income alone, the extended model explained significantly more variance in AUDIT sum scores than the simpler model (Delta R^2 = .015, Total R^2 = .041, F(3, 326 = 5.16), p = .02, see Table 4). In addition, log(κ_R) remained the only significant predictor of AUDIT scores (β = 0.13, t(326) = 2.27, p = .02).

Exploratory Analyses

Secondary measures of DRD, Alcohol Use and SES

Pairwise correlations between all measures of alcohol consumption, delay discounting, SES and demographic variables are given in Appendix S1.

In addition to the tested hypotheses, subjective SES and age were found to be significantly associated with AUDIT scores and log(κ_R) (Appendix S1). Additionally, all three indices of DRD (log(κ_R), relative frequency of discounted choices, discounting factor at one-year delay) were highly intercorrelated, as well as the two measures of alcohol use (AUDIT, DDQ). Therefore, the regression models used to test H4 and H5 were repeated for these secondary measures. To this end, we ran two-step hierarchical regressions with AUDIT or DDQ as dependent variable, education with subjective SES or age as first-level independent variables, and discounting factor, relative discounting frequency or log(κ_R) as second-level independent variables. Results are provided in Appendix S2. All measures of DRD remained significant predictors of alcohol use when controlling for SES. However, when age and education were entered as first-step predictors, 7.1% of variance in AUDIT scores could be explained (F(2, 338) = 13, p < .01), with both predictors reaching significance. The addition of log(κ_R) accounted for an additional 0.7% of variance, but did not reach statistical significance (F(1,337) = 2.40, p = .12).

Loss Discounting

The three indices of DLD ($\log(\kappa_L)$, relative frequency of discounted choices, discounting factor at one-year delay) were highly intercorrelated (see Appendix S1). Small but significant correlations were present between DRD and DLD (e.g., $r = .25$ between $\log(\kappa_R)$ and $\log(\kappa_L)$). In contrast to DRD, no measure of DLD was significantly correlated with any of the socioeconomic or alcohol-related variables.

On average, DLD was less steep than DRD, as indicated by lower discounting frequencies (46.88% in DRD vs. 25.08% in DLD). Importantly, 29.7% of participants were non-discounters in the DLD condition, compared to only 2.9% of participants in the DRD condition. Paired t-tests revealed that non-DLD-discounters did not differ in age, alcohol use, impulsivity, education, income from other participants (Appendix S3). Lastly, when we excluded non-discounters from the correlation analysis for H2 to rule out a possible sub-group effect, the association between $\log(\kappa_L)$ and AUDIT sum scores remained non-significant ($r = .07$, $p = .31$).

Adolescent SES

In contrast to measures of momentary SES (income, education, subjective SES), we found no significant correlations between adolescent SES (subjective adolescent SES, average parental education) and alcohol use or delay discounting.

Impulsivity

BIS-15 sum scores were weakly correlated with indices of DRD (e.g., for $\log(\kappa_R)$: $r = .17$, $p < .01$), education ($r = -.25$, $p < .01$), personal income ($r = -.19$, $p < .01$), subjective SES ($r = -.29$, $p < .01$), and moderately correlated with AUDIT sum scores ($r = .36$, $p < .01$).

Gender

On average, women had significantly lower AUDIT scores, drinking quantities and personal income (Appendix S4). Women and men did not differ significantly with respect to $\log(\kappa_R)$ and $\log(\kappa_L)$. Upon visual inspection, the association between $\log(\kappa_R)$ and AUDIT scores appeared higher in men ($r = .25$, $p < .01$) than in women ($r = .05$, $p = .55$) (Figure 3). However, the difference in correlation coefficients was not significant when applying Fisher's z-transformation ($z = 1.91$, $p = .056$). A multiple regression revealed a significant main effect of gender ($t = 2.98$, $p < .01$), but no significant interaction between gender and $\log(\kappa_R)$ ($t = 1.79$, $p = .07$). Regarding $\log(\kappa_L)$, neither the correlation within the male ($r = .14$, $p = .08$) nor in the female subsample ($r = .06$, $p = .47$) reached significance, and there was no significant difference in correlation coefficients ($z = .73$, $p = .46$).

Discussion

Our study sought to elucidate the complex relationship between delay discounting, socioeconomic status (SES), and the severity of problematic alcohol use. Namely, we investigated 1) the influence of SES on the association between Delayed Reward Discounting (DRD) and problematic alcohol use, and 2) the relationship between Delayed Loss Discounting (DLD) and problematic alcohol use. Our findings revealed that DRD, but not DLD, accounted for a certain proportion of AUDIT scores. However, the small size of this effect does not endorse the practicality of a DRD task as a biomarker for precision medicine approaches in addressing AUD.

DRD, Problematic Alcohol Use and SES

Consistent with our hypotheses and previous research, our findings revealed significant associations between DRD, alcohol use and SES. The small, yet significant positive correlations between $\log(\kappa_R)$ and AUDIT ($r = .15$) and weekly drinking quantity ($r = .11$) replicate the meta-analytic effects of $r = .14$ between DRD and AUDIT and $r = .11$ between DRD and drinking quantity (Amlung *et al.*, 2017). Our findings also confirmed the expected negative association between DRD and education. Contrary to prior findings (Amlung and MacKillop, 2014), income was not related to DRD. Yet, both income and education correlated negatively with AUDIT scores. Education notably emerged as the stronger predictor of alcohol use, which replicates the main finding from a large UK-based survey (Beard *et al.*, 2019).

In addressing our first research question, we discovered that DRD significantly contributes to explaining alcohol use, even after accounting for education and income. This finding remained robust in exploratory models using various measures of DRD and alcohol use, and accounting for subjective SES. However, when education and age were accounted for in an exploratory model, DRD did not explain additional variation. Older and more educated individuals reported lower problematic alcohol use and discounted rewards less steeply. As a recent meta-analysis did not find a systematic association between DRD and age (Seaman *et al.*, 2020), this effect should be carefully confirmed in a subsequent study. Taken together, our results suggest that the link between DRD and alcohol use is not entirely confounded by SES.

Lately, there has been a burgeoning debate regarding the validity of DRD as a construct in addiction research (Bailey et al., 2021; Exum et al., 2023, but see also Martínez-Loredo, 2023; Stein et al., 2023). Responding to the methodological recommendations brought up in this debate, we employed a fixed-trial intertemporal choice task which samples behavior across a sufficiently large variety of decisions, and report several measures of DRD/DLD. Importantly, we developed and validated our task using out-of-sample prediction estimates in a prior study (Thome, Pinger, Halli, *et al.*, 2022) and found that the

modified hyperboloid model predicts behavior better than other discounting models, but not perfectly (prediction probability of 0.68 in DRD and 0.71 in DLD). In the present study, hyperboloid model parameters and behavioral frequencies seem to yield the same results, supporting the robustness of our findings.

Our results reinforce the need to critically evaluate the predictive power of DRD in relation to potential confounders. Due to small effect sizes (DRD explained 1.5% of variance when education and income were controlled for), even larger sample sizes would be needed to disentangle the complex relationship between DRD and alcohol use when more potential confounders are addressed.

Adolescent SES showed no substantial association with alcohol use or delay discounting. This contrasts with previous findings linking addiction and monetary decision-making to socioeconomic hardship in childhood and youth (Hardaway and Cornelius, 2014; Tunney, 2022). The questions we utilized (parental education and subjective SES during adolescence) might be susceptible to biased memory or may not encompass all dimensions of adolescent SES.

DLD and Problematic Alcohol Use

Contrary to our expectations (H2), neither the Delayed Loss Discounting (DLD) parameter $\log(\kappa_L)$ nor the two other measures of DLD showed a significant correlation with problematic alcohol use or drinking quantity. As in our earlier study (Thome, Pinger, Halli, *et al.*, 2022), we observed a large percentage (29.7%) of participants who almost never chose the larger-later loss, compared to only 2.9% of participants who almost never chose the smaller-sooner reward. These non-discounters did not differ significantly from "regular" discounters in education, income, age, drinking level or impulsivity, and their exclusion did not change the overall result. Taken together, we did not find any evidence that DLD is a relevant predictor of problematic alcohol use. However, this does not rule out a potential link between discounting of aversive consequences in other modalities (such as health). Arguably, negative consequences of alcohol cannot be reduced to monetary losses only, psychologically aversive outcomes such as craving, withdrawal and health problems may play a greater role. Therefore, using monetary DLD to measure flawed decision-making in addiction may not be entirely valid. While the same problem applies to monetary DRD, studies show moderate correlations between various reward discounting forms (e.g., money, health) and both hypothetical and real rewards. DLD lacks such evidence due to ethical or scalability issues in studying aversive consequences.

Impulsivity and Delay Discounting

Delay discounting is commonly subsumed under the construct of impulsivity. However, some authors have criticized impulsivity as an arbitrary umbrella term for only loosely related processes (Stahl et al., 2014). A popular solution to this issue is to interpret DRD as a facet of "impulsive choice" as compared to "impulsive action" etc. (McCarthy *et al.*, 2016). Based on the weak correlations between BIS-15 scores and DRD rates in our study, we agree that delay discounting and impulsivity should not be used synonymously. Interestingly, BIS-15 scores were more strongly associated with alcohol use than any other variable (r = .36).

Gender Differences

We found no significant main effects of gender on DRD or DLD, but a main effect on AUDIT scores and drinking quantities. Visual inspection of the data suggested that the relationship between DRD and AUDIT scores is driven by male individuals, as indicated by a correlation coefficient of r = .25 for men compared to r = .05 for women (Figure 3). However, neither the difference in correlation coefficients nor the interaction between gender and DRD reached significance. Therefore, this observation warrants confirmation in a study with higher power.

An early meta-analysis by Silverman (2003) suggested a small advantage for women in Delay of Gratification, whereas a later review by Weafer and de Wit (2014) concluded that women tend to discount rewards more steeply than men. In contrast, a recent meta-analysis reported steeper DRD and higher internet addiction rates among male participants (Cheng *et al.*, 2021). Interestingly, two studies observed male-specific associations between DRD and AUD (Myerson *et al.*, 2015) and expectations for alcohol analgesia (Ferguson *et al.*, 2022), aligning with our observations.

Women have lower rates of AUD and seek treatment less frequently, therefore being less represented in AUD research (Agabio *et al.*, 2017). Notably, prominent meta-analyses by Amlung et al. (2017) and MacKillop et al. (2011) did not investigate gender differences. Our exploratory analysis suggest that gender differences should be considered in studies investigating dysregulated decision-making and AUD.

Strengths and Limitations

Using an online experiment, we were able to collect data from a sufficiently large sample to achieve 80% power for replication of the main effects. The sample can best be described as moderate drinkers with weekly drinking quantities (mean 24.43 alcohol units per week or 27.92g/day) and AUDIT scores (mean 11.76) above commonly reported thresholds for risky drinking (AUDIT > 10, weekly consumption of >

14 units). Female participants averaged 20.80 alcohol units per week (or 23.8 g/day), exceeding the WHO threshold of 20g/day for low risk drinking in women. In contrast, male participants consumed 28.1 alcohol units per week (or 32.1 g/day), below the WHO threshold of 40 g/day for low-risk drinking in men. Figure 1 reveals a pattern of weekend drinking for most participants. Our data, lacking diagnostic criteria, allow conclusions about the association between delay discounting and alcohol use rather than addiction specifically. In addition to that, the study sample is biased towards highly educated (61.3% university degree) and employed (80.4%) participants. Taken together, this possibly reduced our ability to detect strong socioeconomic effects. On the other hand, many DRD studies are confined to heavily affected patient groups, despite only a minority of individuals with alcohol use disorder seeking treatment. Our study therefore allows for the important exploration of DRD's influence on high-functioning heavy drinkers, contributing significantly to the field. Nonetheless, the absence of longitudinal data limits our ability to establish causal relationships between DRD and alcohol use.

Data availability

Raw data, analysis scripts and a codebook of all variables are publicly available at https://osf.io/85k3h/. All code needed for the setup and execution of the online study is available at https://github.com/MathieuPinger/discounting-online/tree/main/Discounting_AUD_Socioeconomic.

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Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Study 3

Table 1

Descriptive Statistics (Numeric)

Variable	N	Mean	SD	SE	Min	Max	Skew	Kurtosis
Age	341	43.48	11.90	0.64	19.00	65.00	-0.19	-0.89
Education	341	4.31	1.57	0.08	1.00	7.00	-0.40	-1.04
AUDIT	341	11.76	6.06	0.33	0.00	39.00	1.04	1.70
DDQ (8g Alc. Units per Week)	341	24.43	18.48	1.00	0.00	91.00	1.50	2.28
Income Personal (£)	330	28000.00	22846.79	1257.67	5000.00	175000.00	2.24	8.11
Income Household (£)	329	53541.03	39586.26	2182.46	5000.00	250000.00	2.09	6.48
No. of Household Members	341	2.60	1.25	0.07	1.00	7.00	0.88	0.72
Subjective SES	341	5.53	1.63	0.09	1.00	10.00	-0.33	-0.31
Adolescent Well-Being	341	1.77	0.93	0.05	0.00	4.00	0.11	-0.32
Avg. Parental Education	318	2.43	1.73	0.10	0.00	7.00	0.55	-0.63
BIS-15	341	30.65	6.65	0.36	16.00	52.00	0.30	0.02
Reward Discounting								
Rel. Discounting Frequency	341	46.88	18.54	1.00	0.00	100.00	-0.17	0.07
β	341	0.89	0.68	0.04	0.00	2.00	0.52	-1.17
s	341	0.49	0.37	0.02	0.00	1.00	0.02	-1.48
log(κ)	341	-3.44	3.40	0.18	-9.21	6.91	0.63	0.81
Discounting Factor	341	0.57	0.31	0.02	0.00	1.00	-0.38	-1.10
Loss Discounting								
Rel. Discounting Frequency	340	25.08	22.20	1.20	0.00	100.00	0.53	-0.61
β	340	1.11	0.78	0.04	0.00	2.00	0.04	-1.73
s	340	0.30	0.38	0.02	0.00	1.00	0.83	-0.91
log(κ)	340	-5.99	3.77	0.20	-9.21	6.91	1.07	0.54
Discounting Factor	340	0.77	0.30	0.02	0.00	1.00	-1.24	0.34

Note. SD = Standard Deviation, SE = Mean Standard Error, AUDIT = Alcohol Use Disorders Identification Test, DDQ = Daily Drinking Questionnaire, SES = Socioeconomic Status, BIS-15 = Barratt Impulsiveness Scale (Short Version).

Table 2

Descriptive Statistics (Categorical)

Variable	Categories	N	%
Gender	Female	170	49.9
	Male	171	50.1
Employment	Employed	224	65.7
	Self-Employed	50	14.7
	Retired	15	4.4
	Student	14	4.1
	Unemployed	25	7.3
	Other	13	3.8

Table 2

Means, standard deviations, and correlations with confidence intervals for the variables used in hypothesis testing.

Variable	AUDIT	log(κ) - Reward	log(κ) – Loss	Personal Income
AUDIT				
log(κ) - Reward	.15** [.04, .25]			
log(κ) – Loss	.09 [-.02, .19]	.25** [.15, .35]		
Personal Income	-.12* [-.22, -.01]	-.10 [-.20, .01]	.00 [-.10, .11]	
Education	-.15** [-.25, -.05]	-.19** [-.29, -.08]	-.07 [-.17, .04]	.26** [.16, .36]

Note. Values in square brackets indicate the 95% confidence interval for each correlation. * $p < .05$. ** $p < .01$.

Table 3
Hierarchical Regression results using AUDIT sum scores as the criterion.

Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	sr^2 95% CI [LL, UL]	*r*	Fit	Difference
Step 1 (Intercept)	14.45**	[12.51, 16.40]							
Education	-0.45*	[-0.88, -0.01]	-0.11	[-0.23, -0.00]	.01	[-.01, .04]	-.14*		
Personal Income	-0.00	[-0.00, 0.00]	-0.09	[-0.20, 0.02]	.01	[-.01, .03]	-.12*		
								R^2 = .026* 95% CI[.00,.07]	
Step 2 (Intercept)	14.79**	[12.83, 16.74]							
Education	-0.36	[-0.80, 0.08]	-0.09	[-0.20, 0.02]	.01	[-.01, .03]	-.14*		
Personal Income	-0.00	[-0.00, 0.00]	-0.08	[-0.19, 0.03]	.01	[-.01, .02]	-.12*		
log(κR)	0.22*	[0.03, 0.42]	0.13	[0.02, 0.23]	.02	[-.01, .04]	.15**		
								R^2 = .042** 95% CI[.01,.08]	ΔR^2 = .015* 95% CI[-.01, .04]

Note. b represents unstandardized regression weights. *beta* indicates the standardized regression weights. sr^2 represents the semi-partial correlation squared. *r* represents the zero-order correlation. *LL* and *UL* indicate the lower and upper limits of a confidence interval, respectively.
* indicates $p < .05$. ** indicates $p < .01$

Figures

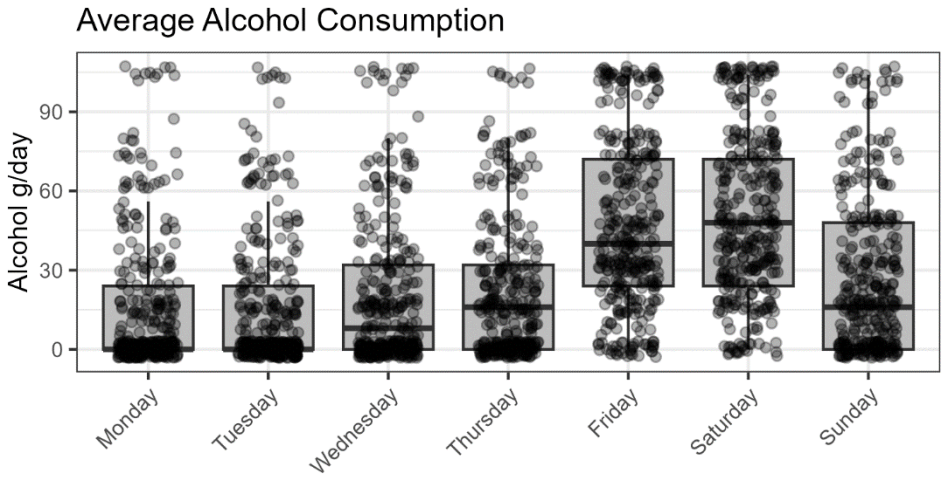

Figure 1. Average self-report drinking quantities over the course of the last 3 months as assessed by the Daily Drinking Questionnaire (DDQ). For easier interpretation, UK alcohol units (= 8g) were transformed into grams per day.

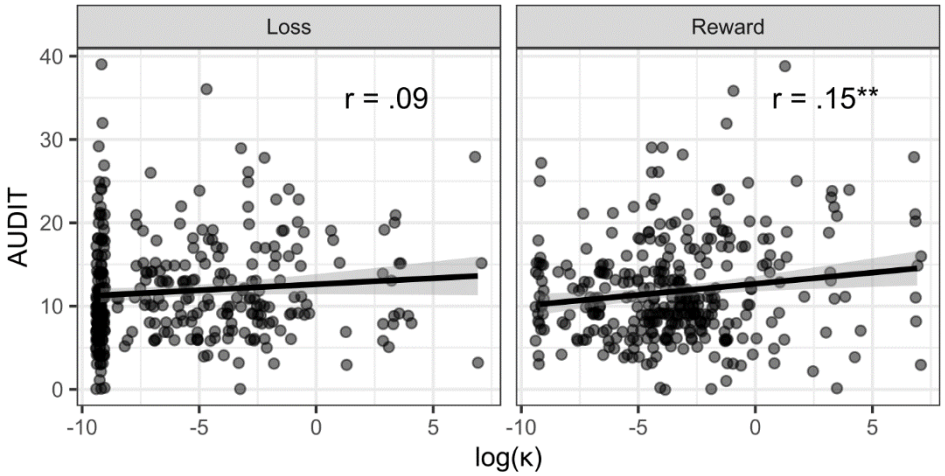

Figure 2. Associations between hyperboloid discounting parameters log(κ) and AUDIT sum scores in the reward (N = 341) and loss (N = 340) condition. Higher log(κ) indicates steeper discounting. *Note*. * $p < .05$, ** $p < .01$.

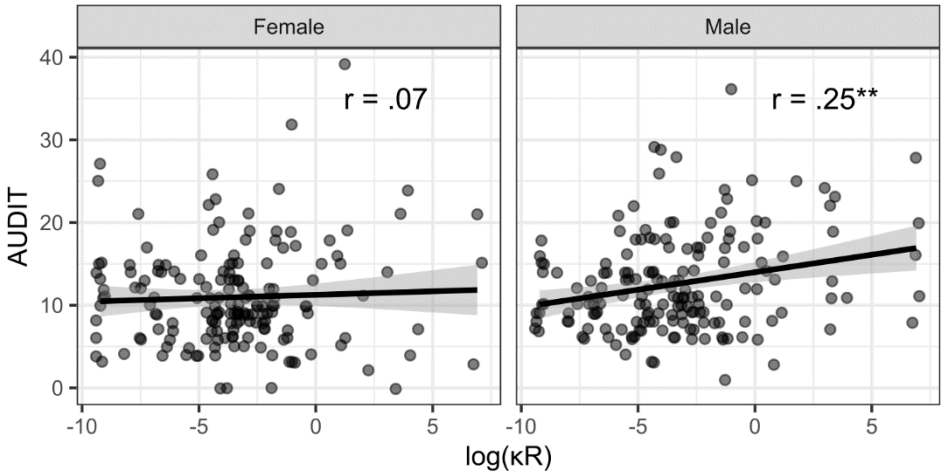

Figure 3. Associations between hyperboloid discounting parameters log(κ) and AUDIT sum scores in the male (N = 171) and female (N = 170) sub-groups. Higher log(κ) indicates steeper reward discounting. * $p < .05$, ** $p < .01$.

Study 3: Supplementary Material

Table S1

Means, standard deviations, and correlations of all variables

Variable	*M*	*SD*	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. log(κR)	-3.44	3.4															
2. Disc.Factor (Reward)	0.57	0.31	-.71** [-.76, -.66]														
3. Rel. Frequency of Reward Discounting	46.88	18.54	.68** [.62, .73]	-.84** [-.87, -.81]													
4. log(κL)	-5.99	3.77	.25** [.15, .35]	-.30** [-.39, -.20]	.38** [.29, .47]												
5. Disc.Factor (Loss)	0.77	0.3	-.21** [-.31, -.11]	.35** [.26, .44]	-.41** [-.50, -.32]	-.87** [-.89, -.84]											
6. Rel. Frequency of Loss Discounting	25.08	22.2	.27** [.17, .37]	-.39** [-.48, -.30]	.45** [.36, .53]	.84** [.80, .87]	-.85** [-.87, -.81]										
7. AUDIT	11.76	6.06	.15** [.04, .25]	-.13* [-.23, -.03]	.14** [.03, .24]	0.09 [-.02, .19]	-0.06 [-.17, .04]	0.1 [-.01, .20]									
8. DDQ (8g Alcohol Units / week)	24.43	18.48	.12* [.02, .23]	-0.1 [-.21, .00]	0.09 [-.02, .19]	-0.01 [-.11, .10]	-0.01 [-.11, .10]	0.06 [-.05, .16]	.68** [.62, .74]								
9. Education	4.31	1.57	-.19** [-.29, -.08]	.13* [.03, .24]	-.18** [-.28, -.08]	-0.07 [-.17, .04]	0.07 [-.04, .18]	-0.08 [-.19, .02]	-.15** [-.25, -.05]	-0.1 [-.20, .01]							
10. Income Personal	28000	22846.79	-0.1	.14*	-.15**	0	0.01	0.02	-.12*	-0.06	.26**						

Study 3

Variable	*M*	*SD*	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
			[-.20, .01]	[.03, .24]	[-.25, -.04]	[-.10, .11]	[-.10, .12]	[-.09, .13]	[-.22, -.01]	[-.17, .05]	[.16, .36]						
11. Income Household	53541.03	39586.26	-0.05	.12*	-.12*	-0.01	0.04	-0.01	-.13*	-.12*	.28**	.65**					
			[-.15, .06]	[.01, .22]	[-.22, -.01]	[-.12, .10]	[-.07, .15]	[-.12, .10]	[-.23, -.02]	[-.23, -.01]	[.17, .37]	[.58, .71]					
12. Subjective Socioeconomic Status	5.53	1.63	-.19**	.21**	-.26**	-0.06	0.1	-0.09	-.14*	-.11*	.30**	.43**	.55**				
			[-.29, -.08]	[.10, .31]	[-.36, -.16]	[-.16, .05]	[-.00, .21]	[-.19, .02]	[-.24, -.03]	[-.22, -.01]	[.20, .40]	[.33, .51]	[.47, .62]				
13. Adolescent Socioeonomic Status	1.77	0.93	-0.07	0.04	-0.06	0.01	-0.04	0.03	-0.06	-0.08	.14*	0.09	.20**	.20**			
			[-.18, .03]	[-.07, .14]	[-.16, .05]	[-.09, .12]	[-.14, .07]	[-.07, .14]	[-.16, .05]	[-.18, .03]	[.03, .24]	[-.02, .19]	[.10, .31]	[.09, .30]			
14. Average Parental Education	2.43	1.73	-0.08	0.08	-0.07	0.05	0.02	0.01	-0.07	-.12*	.23**	.11*	.12*	.13*	.38**		
			[-.19, .03]	[-.03, .19]	[-.18, .04]	[-.06, .16]	[-.09, .13]	[-.10, .12]	[-.18, .04]	[-.22, -.01]	[.12, .33]	[.00, .22]	[.01, .23]	[.02, .24]	[.28, .47]		
15. BIS-15	30.65	6.65	.17**	-.17**	.17**	0.07	-0.05	0.08	.36**	.15**	-.25**	-.19**	-.25**	-.29**	-0.06	-0.09	
			[.06, .27]	[-.27, -.07]	[.07, .28]	[-.04, .18]	[-.16, .06]	[-.03, .19]	[.27, .45]	[.05, .25]	[-.35, -.15]	[-.29, -.09]	[-.35, -.14]	[-.38, -.19]	[-.16, .05]	[-.20, .02]	
16. Age	43.48	11.9	-.20**	.12*	-.12*	-0.1	0.05	-0.07	-.22**	0.02	0	0.03	-0.06	0	-.21**	-.24**	-.22**
			[-.30, -.09]	[.01, .22]	[-.23, -.02]	[-.21, .00]	[-.05, .16]	[-.17, .04]	[-.32, -.12]	[-.09, .13]	[-.11, .10]	[-.08, .14]	[-.17, .05]	[-.10, .11]	[-.31, -.11]	[-.34, -.13]	[-.32, -.11]

Note. M and *SD* are used to represent mean and standard deviation, respectively.

Values in square brackets indicate the 95% confidence interval for each correlation.

* indicates $p < .05$. ** indicates $p < .01$.

AUDIT = Alcohol Use Disorders Identification Test, BIS-15 = Barratt Impulsiveness Scale (Short Version)

Table S2.1

Regression results using AUDIT as the criterion and Education and the Reward Discounting Factor as predictors

Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	sr^2 95% CI [LL, UL]	*r*	Fit	Difference
(Intercept)	14.31**	[12.43, 16.18]							
Education	-0.59**	[-1.00, -0.18]	-0.15	[-0.26, -0.05]	.02	[.00, .06]	-.15**		
								R^2 = .023** 95% CI[.00,.06]	
(Intercept)	15.34**	[13.24, 17.44]							
Education	-0.53*	[-0.94, -0.12]	-0.14	[-0.24, -0.03]	.02	[-.01, .05]	-.15**		
Reward Discounting Factor	-2.24*	[-4.33, -0.14]	-0.11	[-0.22, -0.01]	.01	[-.01, .04]	-.13*		
								R^2 = .036** 95% CI[.01,.08]	ΔR^2 = .013* 95% CI[-.01, .04]

Note. b represents unstandardized regression weights. *beta* indicates the standardized regression weights. sr^2 represents the semi-partial correlation squared. *r* represents the zero-order correlation. *LL* and *UL* indicate the lower and upper limits of a confidence interval, respectively. * indicates $p < .05$. ** indicates $p < .01$.

Table S2.2

Regression results using AUDIT as the criterion and Education and Relative Frequency of Reward Discounting as predictors

Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	sr^2 95% CI [LL, UL]	*r*	Fit	Difference
(Intercept)	14.31**	[12.43, 16.18]							
Education	-0.59**	[-1.00, -0.18]	-0.15	[-0.26, -0.05]	.02	[.00, .06]	-.15**		
								R^2 = .023** 95% CI[.00,.06]	
(Intercept)	12.18**	[9.48, 14.89]							
Education	-0.51*	[-0.92, -0.10]	-0.13	[-0.24, -0.02]	.02	[-.01, .04]	-.15**		
Rel. Frequency of Reward Discounting	0.04*	[0.00, 0.07]	0.12	[0.01, 0.22]	.01	[-.01, .04]	.14**		
								R^2 = .036** 95% CI[.01,.08]	ΔR^2 = .013* 95% CI[-.01, .04]

Note. b represents unstandardized regression weights. *beta* indicates the standardized regression weights. sr^2 represents the semi-partial correlation squared. *r* represents the zero-order correlation. *LL* and *UL* indicate the lower and upper limits of a confidence interval, respectively. * indicates $p < .05$. ** indicates $p < .01$.

Table S2.3

Regression results using AUDIT as the criterion and Education, Subjective Socioeconomic Status and log(kR) as predictors

Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	sr^2 95% CI [LL, UL]	*r*	Fit	Difference
(Intercept)	15.88**	[13.35, 18.41]							
Education	-0.47*	[-0.90, -0.04]	-0.12	[-0.23, -0.01]	.01	[-.01, .04]	-.15**		
SSS	-0.38	[-0.79, 0.03]	-0.10	[-0.21, 0.01]	.01	[-.01, .03]	-.14*		
								R^2 = .033** 95% CI[.00,.07]	
(Intercept)	15.97**	[13.45, 18.49]							
Education	-0.41	[-0.84, 0.02]	-0.11	[-0.22, 0.01]	.01	[-.01, .03]	-.15**		
SSS	-0.32	[-0.73, 0.10]	-0.09	[-0.20, 0.03]	.01	[-.01, .02]	-.14*		
log(kR)	0.20*	[0.01, 0.40]	0.11	[0.01, 0.22]	.01	[-.01, .04]	.15**		
								R^2 = .045** 95% CI[.01,.09]	ΔR^2 = .012* 95% CI[-.01, .04]

Note. b represents unstandardized regression weights. *beta* indicates the standardized regression weights. sr^2 represents the semi-partial correlation squared. *r* represents the zero-order correlation. *LL* and *UL* indicate the lower and upper limits of a confidence interval, respectively.
* indicates $p < .05$. ** indicates $p < .01$.
SSS = Subjective Socioeconomic Status

Table S2.4

Regression results using DDQ scores (= average weekly 8g alcohol units over the last 3 months) as the criterion and Education and log(kR) as predictors

Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	sr^2 95% CI [LL, UL]	*r*	Fit	Difference
(Intercept)	29.36**	[23.61, 35.12]							
Education	-1.14	[-2.40, 0.11]	-0.10	[-0.20, 0.01]	.01	[.00, .04]	-.10		
								R^2 = .009 95% CI[.00,.04]	
(Intercept)	30.36**	[24.55, 36.18]							
Education	-0.91	[-2.18, 0.37]	-0.08	[-0.18, 0.03]	.01	[-.01, .02]	-.10		
log(kR)	0.59*	[0.00, 1.17]	0.11	[0.00, 0.22]	.01	[-.01, .03]	.12*		
								R^2 = .021* 95% CI[.00,.06]	ΔR^2 = .011* 95% CI[-.01, .03]

Note. b represents unstandardized regression weights. *beta* indicates the standardized regression weights. sr^2 represents the semi-partial correlation squared. *r* represents the zero-order correlation. *LL* and *UL* indicate the lower and upper limits of a confidence interval, respectively. * indicates $p < .05$. ** indicates $p < .01$.

Table S2.5

Regression results using AUDIT scores as the criterion and Education, Age and log(kR) as predictors

Predictor	*b*	*b* 95% CI [LL, UL]	*beta*	*beta* 95% CI [LL, UL]	sr^2	sr^2 95% CI [LL, UL]	*r*	Fit	Difference
(Intercept)	19.17**	[16.24, 22.10]							
Age	-0.11**	[-0.16, -0.06]	-0.22	[-0.32, -0.12]	.05	[.00, .09]	-.22**		
Education	-0.59**	[-0.99, -0.19]	-0.15	[-0.26, -0.05]	.02	[-.01, .05]	-.15**		
								R^2 = .071** 95% CI[.03,.13]	
(Intercept)	19.06**	[16.13, 21.98]							
Age	-0.10**	[-0.16, -0.05]	-0.20	[-0.31, -0.10]	.04	[-.00, .08]	-.22**		
Education	-0.53*	[-0.94, -0.13]	-0.14	[-0.24, -0.03]	.02	[-.01, .05]	-.15**		
log(kR)	0.15	[-0.04, 0.34]	0.08	[-0.02, 0.19]	.01	[-.01, .02]	.15**		
								R^2 = .078** 95% CI[.03,.13]	ΔR^2 = .007 95% CI[-.01, .02]

Note. b represents unstandardized regression weights. *beta* indicates the standardized regression weights. sr^2 represents the semi-partial correlation squared. *r* represents the zero-order correlation. *LL* and *UL* indicate the lower and upper limits of a confidence interval, respectively. * indicates $p < .05$. ** indicates $p < .01$.

Table S3

T-tests of selected variables between DLD non-discounters (n = 101, defined as <5% discounting) and DLD discounters (n = 239)

	Mean (Non-Disc.)	Mean (Disc.)	Difference	t	*df*	*p*
Age	43.80	42.94	0.86	0.64	210.31	.523
AUDIT	12.07	11.03	1.04	1.45	190.74	.148
BIS-15	30.83	30.25	0.58	0.75	194.91	.456
Education	4.33	4.26	0.07	0.39	189.70	.694
Income Personal	29,206.01	24,895.83	4,310.18	1.81	254.32	.071

Note. AUDIT = Alcohol Use Disorders Identification Test, BIS-15 = Barratt Impulsiveness Scale (Short Version)

Table S4

T-tests of selected variables between male (n = 171) and female (n = 170) subgroups

	Mean (Male)	Mean (Female)	Difference	t	*df*	*p*
AUDIT	10.96	12.56	-1.59	-2.44	338.76	.015*
DDQ	23.75	32.07	-8.32	-3.71	322.72	< .001***
BIS-15	30.42	30.88	-0.46	-0.64	327.66	.524
Education	4.32	4.30	0.01	0.08	336.75	.936
Income Personal	22,826.09	32,928.99	-10,102.91	-4.14	308.90	< .001***
log(κL)	-5.88	-6.09	0.22	0.53	336.87	.597
log(κR)	-3.49	-3.39	-0.09	-0.25	338.07	.802

Note. AUDIT = Alcohol Use Disorders Identification Test, DDQ = Daily Drinking Questionnaire, BIS-15 = Barratt Impulsiveness Scale (Short Version)

8 General Discussion

8.1 Summary of the Study Results

8.1.1 Study 1: Comparing Discounting of Potentially Real Rewards and Losses by Means of Functional Resonance Imaging

The first study investigated decision-making during a monetary intertemporal choice task in 30 healthy participants. Using a rather basic fixed-amount procedure, the study served as a baseline comparison between DRD and DLD both on a behavioral and neural level and informed the subsequent studies.

Two novelties were employed: Firstly, decision-making was separated from outcome anticipation by combining a fixed-amount monetary ITC task with a MID task. This allowed for a relatively unbiased comparison of neural activity during decision-making in DRD and DLD and potentially eliminated the confounding differences between reward and loss anticipation (Oldham et al., 2018). Secondly, potentially real outcomes were used, rather than hypothetical outcomes as in most studies, as no study has compared real and hypothetical DLD. In the presented study, qualitative and behavioral data suggest that the induction of loss perception in the DLD task was successful, enabling a comparison between DRD und DLD in an ecologically valid manner. This however comes at the cost of reducing the span of temporal delays, thus not allowing for a comparison of discounting models.

Behavior in DRD and DLD was significantly correlated, yielding effect sizes at the upper end of those reported in the literature (r = .56 for hyperbolic κ parameters). Interestingly, a substantial group of non-discounting participants was present in both DRD and DLD, and no influence of task condition on behavior was found. Therefore, the commonly observed sign effect was not present in this study, which could be due to small monetary amounts and short delays. No difference in decision-related brain activity between DRD and DLD was observed. Decision-making elicited activity in fronto-parietal brain areas commonly associated with the executive control network. No difference of brain activity during immediate and delayed choices was observed, challenging the Competing Neurobehavioral Systems Theory described earlier. Regarding the overarching research questions of this dissertations, the first study replicated that monetary losses are subject to Delay Discounting (**Q_1**), but did not provide information on the underlying discounting function. There was no evidence for dissociable behavioral patterns (**Q_2**) or dissociable brain activity for DLD and DRD (**Q_3**). Taken together, the study provided evidence for similar processes underlying DRD and DLD.

8.1.2 Study 2: A Model Guided Approach to Evoke Homogeneous Behavior During Temporal Reward and Loss Discounting

The second study aimed at thoroughly comparing DRD and DLD in 198 healthy participants, using a novel adaptive intertemporal choice task. The task was implemented in a custom full-stack web framework developed by the author of the dissertation project. Behavior was sampled in two experimental runs: in the first run, participants performed a fixed-amount task sampling a wide array of possible monetary amounts and delays. After the first run, participants completed surveys. Meanwhile, a server-based script inferred individual behavioral models and generated individualized trials with predicted choice probabilities for the second run. This procedure is unique and differs from other adaptive Delay Discounting tasks which adapt parameters on a trial-by-trial basis (Ahn et al., 2020; Pooseh et al., 2018). In contrast to these trial-by-trial procedures, the new paradigm enables calculation of out-of-sample prediction errors to compare behavioral models. The online setting further enabled a series of three experimental iterations, each modifying the procedure based on the results of the last one. An influential commentary by Bailey et al. (2021) recently criticized the use of short and adaptive discounting tasks which do not sample a wide range of behavior and do not allow for a falsification of the assumed discounting model. The presented procedure offers a promising new alternative.

The study provides strong evidence in favor of hyperboloid models, with a slight advantage for the modification suggested by Rachlin (2006) whereby the scaling parameter s is only raised to the delay component. Importantly, the same winning model was found in DRD and DLD, indicating similar behavioral patterns. The study replicated both the sign effect (less DLD than DRD) and a percentage of DLD-non-discounters (24% in the last experiment) almost exactly matching the numbers observed by previous studies (Myerson et al., 2017; Yeh et al., 2020). Similar to Study 1, the moderate correlations of DRD and DLD (r = .53 in the first run, r = .35 in the second run) again point towards similar behavioral patterns. The significant negative correlation between AUDIT scores and DLD discount factors in the second run (r = -.14), but not DRD, should be interpreted with caution, as the distribution of AUDIT scores demonstrates a heavy floor effect. Note that discount factors present an opposite polarity to other measures of discounting, i.e. a higher discount factor indicates less discounting.

The variation in effects between the first and second run could be explained by the moderate reliability and accuracy of all DRD parameters. Overall, the between-run correlation of inferred discount factors was r = .60 for DRD and r = .65 for DLD, indicating significant inconsistencies in choice behavior. Indeed, a substantial prediction error remained throughout all experiments, and hyperboloid models were able to predict choice behavior with 68% (DRD) and 71% (DLD) probability. Crucially, using the hyperbolic model reduced prediction accuracies to 57% (DRD) and 55% (DLD), and inferred hyperbolic discount factors did not correlate between the first and second run. Similarly, the correlation coefficients

between DRD and DLD obtained from the hyperbolic model were significantly lower than those from the hyperboloid model (r = .03 in the first run, r = .24 in the second run). As explained earlier, the literature provides very inconsistent correlations between DRD and DLD. Study 2 clearly demonstrates that measures of Delay Discounting are only moderately reliable, and that model selection has a large influence on effect sizes. The hyperbolic model, on which a majority of findings in the literature is based on, performed especially weakly. Combined with small sample sizes, inconsistent findings are readily explained. Regarding the overarching research questions of the project, Study 2 provided rich evidence on the best fitting discounting function for DLD (**Q_1**) as well as differences and similarities between DLD and DRD behavior patterns (**Q_2**). Limited and exploratory evidence also hinted at an association between DLD and alcohol use (**Q_4**), but note the low variance in AUDIT scores.

8.1.3 Study 3: The Association between Reward and Loss Discounting, Socioeconomic Status and Alcohol Use

The third study applied the previously developed web-framework to a sample of 347 moderate-to-heavy drinking participants. The sample size provided sufficient power to find small correlations between Delay Discounting and alcohol use, as present in the literature. The aim was to 1.) replicate the association between problematic alcohol use and DRD, 2.) expand the scope to DLD and 3.) investigate the potential confounding influence of socioeconomic status (SES) on these associations. The study revealed a significant correlation between DRD and alcohol use consistent with previously reported effect sizes (r = .15). Importantly, DRD remained a significant predictor when accounting for a variety of SES, explaining 1.7% of incremental variance. However, the study findings indicates that a number of factors (education, age and gender) should be considered in future studies, which would necessitate even larger sample sizes.

In this study, DLD did not emerge as a significant predictor of alcohol use, neither was it significantly associated with any sociodemographic or socioeconomic measure. Importantly, a bias stemming from the 29% DLD-non-discounters could be excluded. Similar to Study 2, a moderate association between DRD and DLD could be observed (r = .35 for discount factors).

In summary, the study replicates the findings of Study 2 and provides robust evidence against an association between DLD and alcohol use (**Q_4**).

8.1.4 Evaluation of Research Questions

Taken together, the presented studies demonstrated a systematic and time-dependent devaluation of future losses (**Q_1**) and replicated common patterns of DRD and DLD, namely, the sign effect and a substantial proportion of non-discounting in DLD. Apart from these differences, DRD and DLD rates

appeared to be consistently correlated with moderate effect sizes, and the same modified hyperboloid model predicted behavior in both tasks most successfully (**Q_2**). Importantly, the moderate reliability of discounting parameters (Study 2) sets a natural upper boundary for correlations between DRD and DLD. In addition, no differences in brain activity during DRD and DLD tasks were found (**Q_3**). In the light of these findings, despite differences in behavioral patterns, it can be argued that DRD and DLD share more commonalities than differences, and rely on the same underlying neuro-cognitive processes. The difference between DRD and DLD appears to be driven by more shallow DLD and non-discounters, who did not differ from other participants in any analyzed measure.

DLD was not found to be a predictor of either quantity of alcohol use or severity of alcohol-related problems in a large and varied sample (**Q_4**). Therefore, the continuation of the DLD paradigm in form of an fMRI study with AUD patients was discarded, and **Q_5** will not be followed. Note that this project did not realize a comparison of DLD in AUD patients versus in healthy controls. A small difference cannot be ruled out completely, as group comparisons in extreme groups typically yield larger effect sizes than dimensional analyses. However, the goal of this work was to investigate DLD as a possible pathomechanism. If a behavioral construct does not explain significant variance in alcohol use despite efforts to maximize measurement accuracy (Study 2), variance in the dependent variable and statistical power (Study 3), it is difficult to argue in favor of resource-intensive patient and fMRI studies.

Two possible conclusions can be drawn: Either aversion discounting is simply not a relevant pathomechanism in addiction, or aversion discounting is a relevant pathomechanism, albeit inadequately operationalized as monetary DLD. The following sections will examine both directions in more detail. First, an integrated theory of Delay Discounting (both DRD and DLD) as a functional pathomechanism will be presented. Then, the question of operationalization will be further examined. Despite a plethora of research on associations between Delay Discounting and addiction, the mechanistic role of discounting in addiction, i.e., what the mechanism "actually does", is rarely addressed. To qualify for a pathomechanism, the precise psychopathological function of Delay Discounting needs to be delineated, in other words, a causal theory is needed. The claim that Delay Discounting is a behavioral marker of virtually all aspects of addiction (Bickel et al., 2014) and many other disorders (Amlung et al., 2019) hints at a lack of such a specific and testable theory. Insufficient theory building encourages vague hypotheses, weak operationalization and arbitrary interpretation of results (Oberauer & Lewandowsky, 2019). The Competing Neurobehavioral Systems Theory (Bickel et al., 2018) of addiction posits an overactive impulsive valuation system which is correlated with increased Delay Discounting. Overall, the meta-analytic evidence for the fundamental assumption of this theory is weak (Schüller et al., 2019; Souther et al., 2022), and the theory does not explain how the proposed neurobehavioral systems become

dysregulated. Therefore, the next section attempts to delineate how and when Delay Discounting (both of positive and negative consequences) could function as a mechanism in addiction.

8.2 A Mechanistic Model of Delay Discounting

Reward Discounting is posited only as a predisposing factor rather than a gauge of severity and a behavioral marker of all stages of addiction, including treatment success, as claimed by Bickel et al. (2014). Steep DRD results in a choice bias in favor of smaller-sooner rewards due to devaluation of larger-later rewards. This may arguably not be relevant once an alcohol use pattern has manifested into a pathological AUD. At this juncture, the subjective incentive value of drug use is not a small immediate reward weighed against larger later rewards anymore, but instead a very large immediate reward. This is a central assumption of the Incentive Sensitization theory (Berridge & Robinson, 2016) and receives support from neurobiological alterations in the valuation system of humans and animals facing drug cues (Ray & Roche, 2018; Schultz, 2011), as well as clinical observations of subjective craving as an early symptom of addiction (Morgenstern et al., 2016). Abstinence and especially withdrawal further increase subjective drug reward values due to negative emotional states (Nesse & Berridge, 1997; Verharen et al., 2020). Intuitively, the finding of increased DRD rates (for both monetary and substance rewards) in heroin- and nicotine-dependent individuals undergoing withdrawal (Field et al., 2006; Giordano et al., 2002) does not necessarily reflect an increased *de*valuation of delayed rewards, but could be due to an *up*valuation of immediate rewards during an acute negative state.

However, the choice bias of DRD does fill a theoretical gap during the onset of addiction. According to all major theories, a necessary step to develop addiction is learning the positive value of drug consumption in specific contexts (e.g., anxiety reduction). Mechanisms such as operant conditioning subsequently amplify the likelihood of selecting drug use in similar situations. However, while many individuals learn at least some positive associations with alcohol over time, not all progress to AUD. This phenomenon is not completely explained by habit formation or incentive sensitization. In these initial stages, individuals with pronounced DRD may tend to favor the immediate value offered by drug use more frequently due to discounting alternative options (e.g., meditation, sports, socializing) perceived to require more time. Consequently, this pattern could result in repeated consumption and thus increased reinforcement. Therefore, susceptibility of developing a vicious circle may be increased for individuals with steeper DRD. This model is supported by the observation that DRD rates seem to predict future substance use, but not vice versa (Fröhner et al., 2022), and higher DRD rates in individuals with a family history of addiction (Rodriguez-Moreno et al., 2021). It would also deliver an explanation why DRD rates do not consistently predict treatment outcomes (Exum et al., 2023).

Within this model, a prominent role for aversion discounting would not be assumed. At the onset of the addiction circle, negative consequences of drug use are not imminent nor expected. For instance, drinking a few cans of beer to fend off anxiety would not lead to any health consequences and probably not even to a hangover. Therefore, abstaining from drinking is not a minor aversive option weighed against future negative consequences. As the vicious circle progresses, future negative consequences become increasingly imminent, yet abstaining from drinking also becomes more aversive for multiple reasons. Again, withdrawal and craving increase the aversive value of abstaining from drug use. In later stages, compromised mental well-being and socio-economic stability as a consequence of addiction may further diminish the subjective aversive value of drug consumption, as individuals have "less to lose" (Pickard & Ahmed, 2016; Verharen et al., 2020). Consequently, abstaining from consumption becomes a highly aversive immediate option weighed against future adverse events. Therefore, aversion discounting is not expected to be influential during either early or late stages of addiction.

The proposed model is in line with the presented studies and previous findings, as it provides a causal explanation for both small effects of DRD and a lack of consistent DLD effects. Moreover, the model does not rely on inherent differences between neuro-cognitive processes involved in DRD and DLD, but rather on different mechanistic functions in the psychopathology of addiction. Lastly, the model seamlessly integrates with existing theories of addiction. It fills open gaps in theories centered around learning processes without conflicting with currently debated models of habit formation (Ersche et al., 2016) and goal-directed behavior under negative states (Hogarth, 2020). The same holds true for reward deficiency theories, as steep DRD could interact with or follow from blunted dopaminergic responses, thus forming a related risk factor for addiction. Moreover, if later stages of addiction result in a decline in the dopamine-driven incentive value of alternative rewards, the significance of DRD would be further diminished, as the subjective value of larger-later rewards from abstinence diminishes. Instead of contrasting contradictory theories against each other or suggesting a completely new theory, the model demonstrates an integration of existing theories. Not every observed association with addiction requires its own causal theory for the development of addiction.

8.2.1 Methodological Considerations and Future Perspectives

The second possible conclusion from the presented study is that aversion discounting could play a role in addiction but is not adequately represented by monetary DLD. The first limitation stems from the use of monetary outcomes. Although financial losses are certainly among the aversive consequences of addiction, other domains such as health or social life may be more prominent. However, given that discounting rates in other domains such as health and pain are comparable to or lower than those for monetary losses (Chapman, 1996; Harris, 2012), it is unlikely that the absence of effects is solely

attributable to the monetary DLD task utilized in the presented studies. Nevertheless, discounting rates in different domains are only moderately correlated (Chapman & Elstein, 1995), and the discounting of other aversive consequences in addiction remains an open question.

The second limitation pertains to the complexity of decision-making in real-life situations. In contrast to discounting paradigms, actual decisions in addiction involve both rewarding and aversive outcomes at different delays and probabilities. Drugs offer an immediate, certain and strong reward paired with uncertain negative future consequences. Drinking alcohol to deal with stress has a quick and reliable positive effect, but one may not know whether this single drinking occasion will lead to negative consequences, and if so, when and how likely that would happen. In the same example, abstinence would be immediately and certainly aversive, whereas its future benefits remain ambiguous and uncertain.

Research has historically concentrated on separate discounting of delays and probabilities (Kyonka & Schutte, 2018; Odum et al., 2020), which have been robustly identified as distinct and largely uncorrelated processes (Mitchell & Wilson, 2010; Yeh et al., 2020). Additionally, dissociable activation between Probability and Delay Discounting has been observed in the posterior cingulate cortex (Peters & Büchel, 2009; Weber & Huettel, 2008). However, recent studies have attempted to combine Delay and Probability Discounting into one paradigm and revealed that both dimensions appear to interact in a multiplicative (rather than additive) fashion (Białaszek et al., 2020; Cox & Dallery, 2016). A number of studies have stressed that even pure Delay Discounting tasks involve implicit ambiguity and risk, therefore an explicit operationalization of these dimensions might lead to a unifying model (Epper & Fehr-Duda, 2012; Ikink et al., 2019).

Neuroscientific investigations support this notion. Experiments with non-human primates have revealed distinct yet interacting neural populations encoding delayed reward value and uncertainty processing (O'Neill & Schultz, 2010). It has been proposed that a conflation of value and uncertainty signals serves as a pathomechanism in addiction decision-making (Schultz, 2011). Human fMRI studies have further underscored this by demonstrating shared substrates for subjective value signals across discounting modalities (probability, delay, effort) in the medial prefrontal cortex and ventral striatum (Miedl et al., 2012; Seaman et al., 2018). In summary, behavioral and neural findings strongly indicate dissociable yet interacting processes associated with the evaluation of different aspects of decision-making components. If aversive consequences are subject to more subtle and complex discounting processes involving gain-loss trade-offs as described above, pure DLD tasks may not capture them. Therefore, as a direct continuation of this dissertation's project, a model-based task to predict complex decision-making in combined delay and probability discounting is currently under development. That is, participants will have to decide between immediate-certain (e.g. "lose 5€ now with 100% probability) and later-uncertain rewards and losses (e.g. "lose 10€ in 1 year with 70% probability").

As a last note, the symptom of "continued consumption despite negative consequences" could be explained without any discounting at all. It could be simpler, such as a difference in the estimation of outcome probabilities and delays. For instance, an individual anticipating meditation to be swift and effective might opt for meditation over drinking, while another who perceives meditation as time-consuming, challenging to learn, and occasionally ineffective might choose drinking instead. In this scenario, the mechanism would involve the estimation of expectations rather than discounting. Likewise, one person may assess that alcohol results in swift and highly likely negative health consequences, while another might highlight well-known individuals who have never experienced alcohol-related issues despite drinking. The fundamental mechanism in this context would be outcome *evaluation* rather than *discounting*.

8.2.2 Clinical Implications

As evidenced by most psychiatric classification systems such as the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), diagnosis and treatment of mental health problems is traditionally based on categorical definitions of disorders that root in observable symptoms. For instance, the DSM-5 splits addictions into nine substance categories and gambling disorder, with other putative behavioral disorders still missing (American Psychiatric Association, 2013). Consequently, recommendations for and development of evidence-based therapy largely rely on these categories (Chambless & Hollon, 1998). In recent years, the validity of diagnostic categories has been questioned, and underlying transdiagnostic processes have come under the spotlight (Hayes et al., 2020; Schaeuffele et al., 2021). For instance, neurobiological, epidemiological and behavioral research suggests common underlying processes within substance-based and behavioral addictive disorders (Grant & Chamberlain, 2016). In 2008, RDoC was proposed as a framework of fundamental mechanisms for investigating mental health and advancing treatment modalities. RDoC aimed to identify underlying brain circuits across disorders using behavioral, biological and genetic markers (Cuthbert, 2022; Insel et al., 2010). Within these developments, Delay Discounting has been a popular target mechanism to improve understanding and treatment of addiction (Lempert et al., 2019). As this dissertation has attempted to integrate Delay Discounting as a functional mechanism within existing theories, does Delay Discounting cater towards mechanism-based addiction treatment?

First, it needs to be acknowledged that evaluation of short- and long-term consequences of behavior is already a core concept of cognitive behavioral therapy. In fact, behavioral analysis systematically weighs future consequences of behavior (such as drug use) against each other to understand vicious circles and develop alternatives (Abbruzzese & Kübler, 2013). In addiction therapy, negative and positive consequences of drug use and abstinence are assessed using a 4-field schema (Lindenmeyer, 2016;

Mann et al., 2006). This begs the question whether more research on Delay Discounting can contribute further advantages to the current addiction therapy. A straightforward translation from research to practice would involve precisely evaluating temporal delays (and probabilites) of future outcomes when applying behavioral analysis. This would prompt explicit decision-making between outcomes at different delays and probabilities, enabling the use of other cognitive techniques to modify behavior. However, the evidence for a direct manipulation of Delay Discounting and its influence on therapy outcomes is mixed (Exum et al., 2023; Scholten et al., 2019).

Following the integrative model of Delay Discounting suggested earlier, specific Delay Discounting-oriented interventions may be an ideal target during initial steps of addiction therapy, e.g. detoxification treatment. In this stage, it would be expected that devaluation of future outcomes plays a minor role compared to the excessive overvaluation of drug rewards and incentive sensitization to drug cues. However, over longer periods of abstinence, assuming that craving and the associated overvaluation of drug rewards diminish (Wang et al., 2013), Delay Discounting of rewards might become a fruitful target to support long-term abstinence, especially in patients with steep DRD. For instance, interventions could target the anticipated delay and effect of alternatives to drug use in situations of acute stress, i.e. emphasizing that these strategies can be quick and rewarding. Interestingly, even Delay Discounting of aversive consequences could prove to be a useful target in such a long-term rehabilitation setting. Patients who have experienced negative consequences of addiction and who excessively discount future events could be more vulnerable to relapsing. However, longitudinal data and improved methodology are necessary to evaluate a clinical relevance of aversion discounting beyond the findings reported in this dissertation.

8.2.3 Final Remarks

The first conceptual study on discounting of aversive consequences noted that “studies […] fail to indicate any characteristic common to the alcoholic” (Vogel-Sprott & Banks, 1965). Sixty years later, it can be concluded that addiction is a highly complex process wherein no single variable can explain more than a fraction of variance in the development and continuation of AUD (Whelan et al., 2014). What holds true from Vogel-Sprott and Bank’s statement is that Delay Discounting does not qualify as a “characteristic common to the alcoholic”, i.e. a behavioral marker of addiction (Bickel et al., 2014). With its small effect sizes, Delay Discounting of rewards should be considered as one among many risk factors, and Delay Discounting of aversive consequences might be an even smaller one, if relevant at all. Future studies will need to clarify whether more intricate decision models can better encapsulate the various facets of addiction.

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