



Steeper discounting of delayed rewards in schizophrenia but not first-degree relatives



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ARTICLE INFO

Keywords:

Genetic risk
Decision-making
Cognitive
Delay discounting

ABSTRACT

Excessive discounting of future rewards has been related to a variety of risky behaviors and adverse clinical conditions. Prior work examining delay discounting in schizophrenia suggests an elevated discount rate. However, it remains uncertain whether this reflects the disease process itself or an underlying genetic vulnerability, whether it is selective for delay discounting or reflects pervasive changes in decision-making, and whether it is driven by specific clinical dimensions such as cognitive impairment. Here we investigated delay discounting, as well as loss aversion and risk aversion, in three groups: schizophrenia (SZ), unaffected first-degree family members (FM), and controls without a family history of psychosis (NC). SZ had elevated discounting, without changes in loss aversion or risk aversion. Contrary to expectations, the FM group did not show an intermediate phenotype in discounting. Higher discount rates correlated with lower cognitive performance on verbal reasoning, but this did not explain elevated discount rates in SZ. Group differences were driven primarily by the non-smoking majority of the sample. This study provides further evidence for elevated discounting in schizophrenia, and demonstrates that steeper discounting is not necessarily associated with familial risk, cannot be wholly accounted for by cognitive deficits, and is not attributable to smoking-related impulsivity.

1. Introduction

There is increased focus on studying the basic neuropsychological processes that are altered in mental illness (Insel et al., 2010). One process that is widely affected across mental illnesses is decision-making (Montague et al., 2012; Mukherjee and Kable, 2014). This observation is especially true of individuals with schizophrenia, who differ from healthy comparison subjects in several decision-making tasks (Ahn et al., 2011; Heerey et al., 2007, 2008, 2011; Treméau et al., 2008; Waltz and Gold, 2007; Weller et al., 2014; Wolf et al., 2014). In particular, individuals with schizophrenia discount delayed rewards more than healthy subjects, placing greater relative value on immediate rewards (Ahn et al., 2011; Gold et al., 2013; Heerey et al., 2007, 2011; Weller et al., 2014). Reduced preference for future rewards in schizophrenia is important to understand, as this could contribute to impulsive behaviors, interfere with long-term planning, and reduce motivation for long-term treatment benefits.

An open question is whether decision-making differences in schizophrenia are specific to delayed rewards or are more general

(Rachlin, 2009; Sozou, 1998). One study found that individuals with schizophrenia treated gains similarly, but exhibited reduced weighting of losses (Heerey et al., 2008). The specificity of effects of schizophrenia can be clarified by examining sensitivity to delayed rewards, probabilistic rewards, and gains and losses in the same individuals.

In addition to changes in reward valuation, decision-making in schizophrenia may reflect impaired cognition (Aukes et al., 2009; Glahn et al., 2003; Irani et al., 2012; Niendam et al., 2006; Wood et al., 2003), leading to a failure to hold reward representations in mind or implement the complex reasoning necessary to optimally integrate costs and benefits (Gold et al., 2008; Strauss et al., 2014). In delay discounting tasks, working memory and complex reasoning may enable one to integrate multiple dimensions of rewards in order to choose delayed outcomes with larger rewards (Hinson et al., 2003). Cognitive abilities are inversely correlated with delay discounting in healthy individuals (Olson et al., 2007; Shamosh et al., 2008) and individuals with schizophrenia (Ahn et al., 2011; Heerey et al., 2007, 2011). However, while some studies find that group differences in decision-making are secondary to cognitive impairments in schizophrenia

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<http://dx.doi.org/10.1016/j.psychres.2017.02.062>

Received 25 June 2016; Received in revised form 5 February 2017; Accepted 28 February 2017

Available online 07 March 2017

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(Heerey et al., 2008, 2011), others do not (Ahn et al., 2011). Thus, it remains unclear to what extent differences in decision-making can be explained by cognitive deficits.

Another issue with studying reward-related processes in individuals with schizophrenia is that a large proportion of them smoke (de Leon, 1996; Forchuk et al., 1997). Smoking impacts reward pathways (Barr et al., 2008), and is associated with increased discounting (Baker et al., 2003; Bickel et al., 1999; MacKillop et al., 2011; Reynolds, 2006). Therefore, differences in reward-related cognition in schizophrenia may be attributable to nicotine use (Pizzagalli, 2010). While one study found that individuals with schizophrenia who smoke are more impulsive than those who do not (Wing et al., 2012), other studies have found that discounting in schizophrenia is unrelated to smoking (MacKillop and Tidey, 2011; Weller et al., 2014).

Finally, it remains unknown whether altered decision-making in schizophrenia is a consequence of the disease itself, or constitutes an endophenotype reflecting underlying genetic vulnerability. Schizophrenia is highly heritable (Kendler and Diehl, 1993), and delay discounting is also a heritable phenotype (Anokhin et al., 2015). Functional imaging in unaffected first-degree relatives has linked familial risk for schizophrenia to dysfunction in fronto-striatal regions involved in decision-making (Grimm et al., 2014; Vink et al., 2016). This suggests genetic vulnerability to schizophrenia could be associated with elevated delay discounting; however, no prior studies have examined delay discounting (or risk-aversion or loss-aversion) in family members of individuals with schizophrenia.

To address these open questions, we studied individuals with schizophrenia, unaffected first-degree family members and healthy controls using a delay discounting task in concert with loss aversion and risk aversion tasks. While these decision-making constructs have been tested in select studies with patients with schizophrenia (e.g. Reddy et al., 2014; Treméau et al., 2008; Shurman et al., 2005), results are often mixed, and it is not clear how deficits could relate to each other. Testing multiple dimensions of decision-making allowed us to determine whether alterations in decision-making are widespread, or restricted to delay discounting. We also assessed multiple cognitive domains (Gur et al., 2010; Moore et al., 2015) to examine whether altered decision-making in schizophrenia can be accounted for by cognitive deficits. Finally, by including unaffected first-degree relatives, we evaluated whether altered decision-making is part of a broader genetic risk factor for schizophrenia or is more likely due to the impact of the disease itself.

2. Methods

2.1. Participants

We gathered data for 131 participants age 18–60, including 51 clinically stable individuals affected by schizophrenia (N=47) or schizoaffective disorder depressed type (N=4), 36 unaffected first-degree family members of individuals with schizophrenia (not necessarily participants with schizophrenia in the present study), and 44 controls without any first-degree family history of psychosis.

Antipsychotic dosages in chlorpromazine equivalents were determined with routine conversion calculations (described in Supplementary Materials). Groups did not differ on demographic variables except for the expected trend toward lower education in SZ (Table 1). Written informed consent was obtained and all study procedures were approved by the University of Pennsylvania's Institutional Review Board.

2.1.1. Subject exclusions

Subjects could not be enrolled if they had serious or unstable medical or neurological conditions, a history of substance abuse or dependence (excluding nicotine) in the past six months by history or a positive urine drug screen on the day of the study, or a history of

Table 1

Demographic, cognitive, and clinical description of analyzed study participants.

Variable	NC (N=42) ^a	FM (N=35)	SZ (N=49)	p-value
Age (mean, years)	39.9 (11.7)	44.4 (14.3)	40.6 (10.5)	0.31 ^{b,c}
Gender (% female)	54%	63%	47%	0.39 ^d
Smoke (% yes)	33%	12%	43%	0.008
Education (mean, yrs)	14.6 (2.2)	14.4 (2.5)	13.6 (2.2)	0.08
Parental Education (mean, yrs)	13.9 (2.5)	13.1 (3.7)	13.3 (3.1)	0.40
Mean Z-Scored Verbal Reasoning (PVRT)	0.14 (1.1)	0.09 (1.0)	-0.4 (1.0)	0.02
Trait Social Anhedonia (RSAS)	7.8 (6.2)	8.3 (6.2)	13.7 (7.2)	< 0.001
Trait Physical Anhedonia (RPAS)	11.4 (7.4)	11.1 (7.4)	18.0 (8.6)	< 0.001
Mean negative symptoms (SAPS)	0.07 (0.24)	0.21 (0.42)	1.12 (0.94)	< 0.001
Mean positive symptoms (SANS)	0.37 (0.62)	0.77 (0.74)	2.04 (0.94)	< 0.001
Mean negative symptoms (CAINS)	0.61 (0.38)	0.72 (0.47)	1.31 (0.65)	< 0.001
Total depressive symptoms (CDSS)	0.81 (1.78)	2.23 (2.71)	2.90 (3.10)	< 0.001
Antipsychotic Dosage ^e	na	na	522 (359)	na

PVRT: Penn Verbal Reasoning Test; RSAS: Revised Chapman Anhedonia Scale – Social; RPAS: Revised Chapman Anhedonia Scale – Physical; SAPS: Scale for Assessment of Positive Symptoms; SANS: Scale for Assessment of Negative Symptoms; CAINS: Clinical Assessment Interview of Negative Systems; CDSS: Calgary Depressive Symptoms Scale

^a Table includes all subjects with analyzed data from any of the three tasks.

^b 2-tailed p-values, testing for differences among the three groups

^c ANOVA used to compare group means for dimensional variables

^d Fisher's Exact Test was used to compare proportions for categorical variables

^e Chlorpromazine mg equivalents. 41 were on atypical, 11 on typical, 6 on both, 3 on no antipsychotic

pathological gambling screened using items from the South Oaks Gambling Screen (Lesieur and Blume, 1987). Family member and control subjects were additionally excluded if they met criteria for any Axis I psychiatric disorder except depressive disorders, or any Axis II disorder other than Cluster A personality disorders.

Participants were also excluded from analyses on a task-by-task basis, based on either missing data points or poor quality data indicative of task non-adherence/random responding (see Quality Control section below). For the delay discounting task, one participant was excluded for missing data and 7 for poor task adherence. For the loss aversion task, 4 participants were excluded for missing data and 13 for poor task adherence. For the risk aversion task, 3 participants were excluded for missing data and 18 for poor task adherence.

2.2. Study design and assessment procedures

Cognitive performance was assessed using z-scored accuracy measures from the Penn Computerized Neurocognitive Battery (CNB; Moore et al., 2015; Gur et al., 2010). We also measured trait anhedonia, depression, and positive and negative symptoms of schizophrenia (see Supplementary Materials for further assessment details).

2.3. Tasks

Participants' delay discounting was assessed with an intertemporal choice task (Senecal et al., 2012; Kirby and Maraković, 1996) (Fig. 1A). The task consists of 51 choices, and has a similar structure to the short questionnaire from Kirby and Maraković (1996). In the task, participants have to choose between two options: one is a smaller amount of money given immediately, and the other is a larger amount of money given at a specified delay. The immediate amount ranges from \$10 to \$34. The delayed amount is always one of three possibilities (\$25, \$30, \$35), and the delay ranges from 1 to 180 days. The side the delayed and immediate options are presented on the screen are randomized across

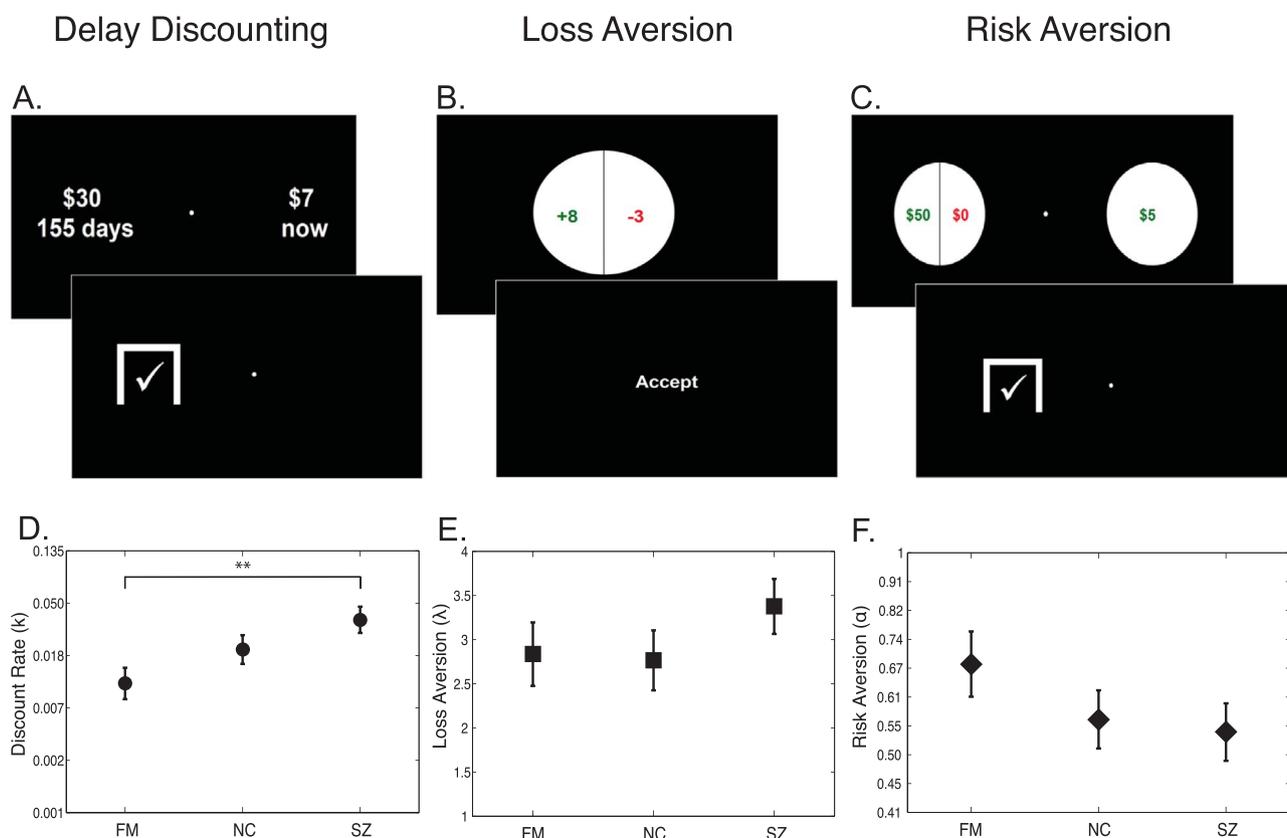


Fig. 1. Panels A-C: Participants performed three tasks: A) delay discounting; B) loss aversion; C) risk aversion. Panels D-F: Group difference in performance in the three tasks D) delay discounting; E) loss aversion; F) risk aversion. Discount rates and risk aversion rates are on log scale. SZ=patients with schizophrenia; FM=first degree relatives; NC=normal controls. Error bars are standard errors of the mean.

trials. The participant is given unlimited time to answer, then 500 ms of feedback marking the option the participant has chosen, followed by an intertrial interval (ITI) of 1000 ms.

Loss aversion was assessed with a task consisting of 64 choices (Tom et al., 2007) (Fig. 1B). In this task, participants see a circle on the screen, divided in half. This circle represents a 50-50 gamble, with the amount one could win with a 50% chance shown in green, and the amount one could lose with a 50% chance shown in red. Amount to win ranges from \$10-\$41 (sampled uniformly), and amount to lose ranges from \$5-\$20 (sampled uniformly), both in increments of \$1. The sides of the amount to win and lose are counterbalanced across trials. Participants choose to accept or to reject the gamble. They have unlimited time to respond, followed by 1000 ms of feedback showing whether they accepted or rejected, and then an ITI of 1000 ms.

Risk aversion was assessed with a binary choice task consisting of 60 choices (Levy et al., 2010; Gilaie-Dotan et al., 2014) (Fig. 1C). In this task, participants choose between a smaller amount of money (ranging between \$1 and \$68) that is certain, and a larger amount of money (from \$10 to \$100) that is risky. All risky options have a 50% chance of receiving the larger amount and a 50% chance of receiving nothing. The certain amount of money is represented within a complete circle on one side of the screen, and the 50% gamble is represented as a circle divided in half, with the amount to win on one side of the divide, and \$0 on the other side. The side that each option is presented on the screen is counterbalanced. Participants again have unlimited time to respond, after which they view 500 ms of feedback indicating the option they have chosen, followed by an ITI of 1000 ms.

The risk aversion and loss aversion tasks were incentive compatible: at the end of the study, the experimenter randomly selected one task and drew a random trial from that task to play out for real. The participants received the option they had chosen on that trial, and 50-50 gambles were resolved with a coin flip. If the participant lost money

on a loss aversion trial, the loss was deducted from his or her payment for participation and winnings from other tasks (but he or she always made money overall). The delay discounting task was hypothetical. Past studies examining discount rates in schizophrenia (Ahn et al., 2011; Heeey et al., 2011, 2007; Weller et al., 2014) regularly used hypothetical questions, and evidence suggests that discount rates are similar for real and hypothetical rewards (Bickel et al., 2009; Madden et al., 2003).

2.4. Data analysis

We used MATLAB (Mathworks), SPSS (Version 20, IBM), and R (CRAN) for analysis.

2.4.1. Quality control

To calculate a quality control measure, we fit a logistic regression model with MATLAB's built-in function (mnrfit) that included the following predictors: an intercept, all task variables, and the squares of all task variables. This model was used to estimate how much choice behavior was a systematic function of the task variables. For the ITC task, the terms were the intercept, the delayed amount, the immediate amount, the delay, and the squares of the two amounts and delay. In the loss aversion task, the terms were the intercept, the gain amount, the loss amount, and the squares of the two amounts. In the risk aversion task, the terms were the risky amount, the certain amount, and the squares of the two amounts:

$$P_1 = \frac{1}{1 + e^{-U_{task}}}$$

$$U_{ITC} = \beta_0 + \beta_1 A_{delayed} + \beta_2 A_{immediate} + \beta_3 D + \beta_4 A_{delayed}^2 + \beta_5 A_{immediate}^2 + \beta_6 D^2$$

$$U_{loss-aversion} = \beta_0 + \beta_1 A_{gain} + \beta_2 A_{loss} + \beta_3 A_{gain}^2 + \beta_4 A_{loss}^2$$

$$U_{\text{risk-aversion}} = \beta_0 + \beta_1 A_{\text{risky}} + \beta_2 A_{\text{certain}} + \beta_3 A_{\text{risky}}^2 + \beta_4 A_{\text{certain}}^2$$

A goodness of fit cutoff for these logistic models was used to eliminate data that could be indicative of poor task adherence or random responding. The goodness-of-fit was assessed with McFadden's pseudo- R^2 , which is calculated as 1 minus the log likelihood ratio of the full model compared to an intercept-only model. Most of the mass in the distribution of pseudo- R^2 for each task was between 0.3 and 1 with a long tail extending from 0 to 0.3. Additionally, by visual inspection of individual-level data, it was clear that behavior was notably less consistent when the pseudo- R^2 was below 0.3. When we applied this threshold to a different dataset comprised of healthy young adult participants, less than 5% of participants fell below this threshold. Hence participants who were below a pseudo- R^2 of 0.3 were excluded from further analysis.

With the above criterion, 4 participants were excluded from all three tasks (2 in schizophrenia group - SZ, 1 in family member group - FM, 1 in normal controls group - NC), 9 participants were excluded from two of the three tasks (SZ: 5, FM: 2, NC: 2), and 16 participants were excluded from a single task (SZ: 6, FM: 3, NC: 7). For the delay discounting task, the final N for analysis was 123, with 47 in the SZ group, 34 in the FM group, and 42 in the NC group. For loss aversion, the final N was 114, with 44 SZ, 33 FM and 37 NC. For risk aversion, the final N was 110, with 40 SZ, 31 FM, and 39 NC.

2.4.2. Parameter estimation

Participants' individual choice data for each task was fit with the following logistic function using maximum likelihood estimation with function minimization routines in MATLAB:

$$P_1 = \frac{1}{1 + e^{-\sigma(SV_1 - SV_2)}}, \quad P_2 = 1 - P_1$$

where P_1 refers to the probability that the participant chose option 1, and P_2 refers to the probability that the participant chose option 2. SV_1 and SV_2 refer to the participant's estimated subjective value of option 1 and option 2 respectively. σ was a scaling factor and fitted for each individual task.

In the delay discounting task, P_1 was the probability of choosing the delayed option, and the subjective value of the options (i.e., SV_1 and SV_2) were estimated using a hyperbolic function:

$$SV = \frac{A}{1 + kD}$$

where A is the amount of the option, D is the delay until the receipt of the reward (for immediate choice, $D = 0$) and k is a discount rate parameter that varies across subjects. Higher k indicates higher discounting and less tolerance of delay.

In the loss aversion task, P_1 was the probability of accepting the given bet. SV_1 and SV_2 referred to the subjective value of the gamble and that of nothing respectively. The subjective value of the gamble was calculated as the offered gain amount in the gamble minus the loss amount times a multiplier:

$$SV = A_{\text{gain}} - \lambda A_{\text{loss}}$$

where A_{gain} and A_{loss} would be 0 for the option of rejecting the given bet, and λ is a loss aversion parameter that varies across subjects. Higher λ indicates a greater weighting of potential losses compared to potential gains.

Finally, in the risk aversion task, P_1 was the probability of choosing the risky option. SV_1 and SV_2 (subjective values for the risky option and safe option, respectively) were calculated using the power utility function in which subjective value is calculated by multiplying the probability of winning by the amount to win raised to a power:

$$SV = pA^\alpha$$

where $p=0.5$ for the risky option, $p=1$ for the certain option, and α is a

risk aversion parameter that varies across subjects. Higher α indicates a larger risk tolerance and lesser degree of risk aversion.

Hence, two parameters for each task were estimated for every individual. One was the scaling parameter σ present in the logistic function, and another was the parameter associated with individual differences in delay discounting, loss aversion, or risk aversion: k , λ , or α respectively.

2.4.3. Group level analysis and hypothesis testing

We used a natural log transform on the discounting (k) and risk aversion (α) parameters, because these are not normally distributed. For correlations with clinical and cognitive variables that are not normally distributed, we used the non-parametric Spearman's rho (ρ). For correlations between binary variables and continuous variables, we used Pearson's point-biserial correlation (r). To correct for multiple comparisons, we used the Holm-Bonferroni method (Holm, 1979) to adjust all p -values. In the Holm's method, the Bonferroni correction is applied sequentially starting with the smallest p -value in a series, then the next smallest, and so on until the testing procedure stops at the p -value where the null hypothesis cannot be rejected. All non-significant p -values then take on that value in R's implementation of the method.

Where there were significant relationships between a measure of cognitive ability and decision-making, we used that measure in a one-way analysis of covariance (ANCOVA) to test for group differences. Where no cognitive or demographic measures were significantly correlated, we performed one-way analysis of variance (ANOVA) instead. We further investigated the role of smoking status in group differences by entering smoking as a covariate in an ANCOVA and by performing separate ANOVAs in either smokers or non-smokers.

3. Results

3.1. Correlation between cognitive variables and decision-making measures

In order to control for cognitive effects, we first determined which cognitive variables were significantly correlated with each of the decision-making measures, using Spearman correlations. Across all subjects, verbal reasoning (PVRT) from the CNB was the only cognitive measure significantly correlated with log discount rate after correcting for multiple comparisons ($\rho = -0.39$, $p = 0.0002$, $N = 110$). The n-back working memory task was nominally significant but did not survive multiple comparison correction ($\rho = -0.22$, $p = 0.147$, $N = 109$), and other CNB tests showed no significant correlation with discount rate (all $0 < \rho \leq -0.19$). None of the cognitive measures were significantly correlated with loss aversion ($-0.06 \leq \rho \leq 0.13$) or risk aversion ($-0.02 \leq \rho \leq 0.14$). Exploring the PVRT correlation separately within each group, the relationship with delay discounting was significant in SZ ($\rho = -0.37$, $p = 0.04$, $N = 44$) and NC ($\rho = -0.42$, $p = 0.04$, $N = 36$), but not FM ($\rho = -0.18$, $p = 0.35$, $N = 30$).

3.2. Analysis of variance in decision-making tasks

We found elevated discount rates in SZ compared to FM. In a one-way ANCOVA investigating group differences in discount rate while covarying for cognitive ability (PVRT), Group was significant ($F(2, 106) = 4.73$, $p = 0.01$; $\eta_p^2 = 0.08$). Post-hoc testing showed significantly higher discounting [$t(72) = -3.08$, $p = 0.009$] in SZ (log k adjusted mean = -3.31 ; 95% C.I.: $[-3.81, -2.82]$) compared to FM (adjusted mean log $k = -4.53$; 95% C.I.: $[-5.12, -3.94]$) (Fig. 1D). The difference between SZ and NC (adjusted mean = -3.89 ; 95% C.I.: $[-4.42, -3.35]$) was not significant ($p = 0.226$), nor was the difference between FM and NC ($p = 0.226$).

In contrast, in a one-way ANOVA, we found no group differences for loss aversion λ ($F(2, 111) = 1.06$, $p = 0.35$; $\eta_p^2 = 0.02$); or for risk aversion α ($F(2, 107) = 1.33$, $p = 0.27$; $\eta_p^2 = 0.02$) (Fig. 1E and F).

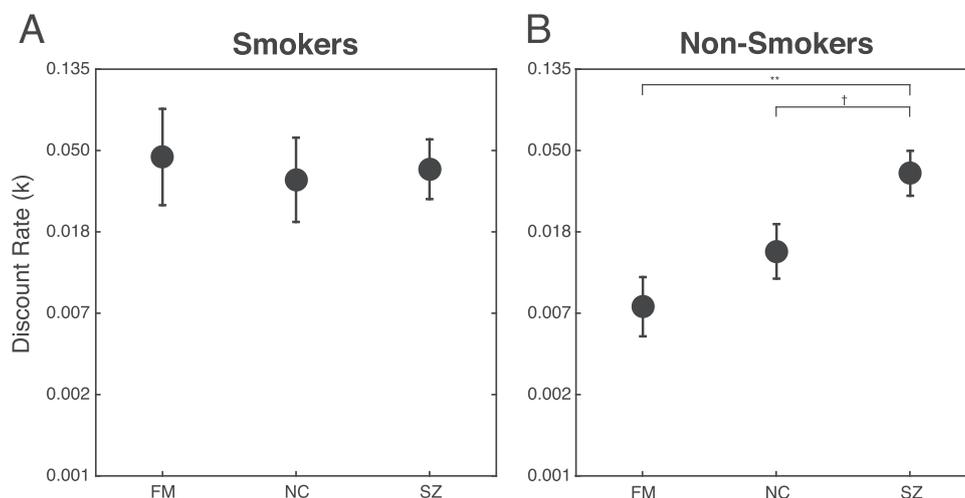


Fig. 2. Group differences in discounting for A) smokers and B) non-smokers. Error bars are standard errors of the mean.

3.3. Relationship of smoking and other variables to decision-making

Across all participants, smoking status (a binary measure) was significantly correlated with $\log k$ using a Pearson point-biserial correlation ($r=0.23$, $p=0.012$, $N=123$). Group differences remained significant when covarying for both cognitive ability (PVRT) and smoking status in a one-way ANCOVA ($F(2, 106)=3.32$, $p=0.04$; $\eta_p^2=0.06$). Splitting participants into smoking and non-smoking groups, diagnostic group differences in $\log k$ (examined with one-way ANOVAs) were significant in the non-smoking group ($F(2, 34)=6.25$, $p=0.003$; $\eta_p^2=0.132$) but not in the smoking group ($F(2, 34)=0.13$, $p=0.96$, $\eta_p^2=0.003$). Post-hoc tests revealed that in the non-smoking group, SZ (mean $\log k=-3.28$; 95% C.I.: $[-3.82, -2.74]$) discounted at a significantly higher rate than FM (mean $\log k=-4.92$; 95% C.I.: $[-5.63, -4.21]$) ($t(55)=3.54$, $p=0.003$), and showed a similar trend towards higher discounting compared with NC (mean $\log k=-4.24$; 95% C.I.: $[-4.9, -3.58]$) ($t(53)=2.21$, $p=0.062$) after correcting for multiple comparisons (Fig. 2).

4. Discussion

We find that delay discounting is elevated in schizophrenia, an effect that is actually more robust in comparison to unaffected family members than in comparison to controls without familial risk, providing initial evidence that discounting does not constitute a genetic vulnerability endophenotype. We also show that steeper discounting in schizophrenia is not solely attributable to smoking status, cognitive impairment, or pervasive non-specific abnormalities in decision-making. Our finding of elevated discount rates in schizophrenia replicates several previous reports (Heerey et al., 2007, 2011; Ahn et al., 2011; Weller et al., 2014), and together the evidence points to higher discounting in schizophrenia as a consequence of manifest illness or its treatment.

Our family group had the lowest discounting rates of the three groups. The fact that FM did not have intermediate discount rates goes against an account of steeper discounting as a part of the genetic endophenotype of schizophrenia. It is possible that compensatory processes in family members obscure underlying genetic vulnerabilities, but the simplest interpretation is that higher discounting in schizophrenia is associated with the illness itself, or its treatment. Drugs that enhance dopamine signaling decrease discounting (de Wit et al., 2002; Foerde et al., 2016). Antipsychotics generally block dopamine (D2) receptors, and decreased D2 receptor availability is associated with increased discounting (Ballard et al., 2015). While we did not find an effect of antipsychotic dose, decision-making studies directly examining the effect of antipsychotics and examining medication-free populations

are needed to tease apart medication effects from effects of the disease.

It is well-established that smoking status is related to higher discount rates (Bickel et al., 1999, 2003; Reynolds, 2006; MacKillop et al., 2011). This raises the possibility that schizophrenia is associated on average with higher discount rates simply because such a high proportion of individuals with schizophrenia are smokers (Forchuk et al., 1997). By including an analysis stratified according to smoking status, we demonstrate that the pattern of variation in discounting levels we see across our three groups is driven by non-smokers, and therefore cannot be attributed to differential rate of smoking. Group differences are reduced when analysis is limited to smokers versus non-smokers or the full sample, because discounting levels are elevated as expected in association with smoking in the NC and FM groups, while discounting was equally high in SZ regardless of smoking status. This contributed to the failure to find a significant SZ-NC difference in the full sample; indeed, in the non-smoking subsample, the SZ-NC difference shows a statistical trend in the expected direction (significant prior to multiple comparisons correction). However, our finding that FM have the lowest discounting rate is not explained by smoking status. Although we had fewer smokers in the FM group than the other groups due to recruitment limitations, FM had the lowest discount rates even when the analysis was limited to non-smokers.

The lack of differences in discounting between smokers with or without schizophrenia has also been reported in prior studies (Weller et al., 2014; MacKillop and Tidey, 2011; Wing et al., 2012). One possible explanation is that schizophrenia and nicotine addiction may have similar effects on pathways involved in delay discounting, resulting in an occlusive effect producing similar discounting in smokers and non-smokers with schizophrenia. Alternatively, smoking may have competing relationships with discounting in SZ, with pro-cognitive effects leading to lower discounting and counteracting the normal positive association between smoking and elevated discounting. Indeed, Weller et al. (2014) reported that discounting rates were actually lower in smokers than nonsmokers with schizophrenia. Future studies will need to investigate the mechanisms impacting complex inter-relationships between nicotine addiction, schizophrenia, and discounting.

One explanation for changes in decision-making in schizophrenia is disruption in reward representations stemming from impaired cognitive abilities (Gold et al., 2008). Supporting this contention, Heerey and colleagues found that differences between healthy individuals and individuals with schizophrenia in the weighting of losses (Heerey et al., 2008) or in a composite measure of future orientation (Heerey et al., 2011) disappeared after controlling for working memory ability. In addition, Weller et al. (2014) found that individuals with schizophrenia who were “inconsistent responders” had both higher

discounting rates and lower cognitive scores. Here we assessed several different aspects of cognition, and found a significant correlation between discount rates and verbal reasoning. This relationship fits with several previous studies, which find that working memory and IQ measures correlate with discounting in both healthy and psychiatric populations (Ahn et al., 2011; Bobova et al., 2009; Burks et al., 2009; Heerey et al., 2011, 2007; Shamosh et al., 2008; Weller et al., 2014). Critically, when we excluded inconsistent responders and controlled for cognitive differences, individuals with schizophrenia were still significantly higher discounters than family members. Thus, cognitive impairments cannot fully explain steeper discounting in schizophrenia.

Finally, we did not find any robust correlations between our decision-making tasks and any of the clinical measures (see [Supplementary Materials](#)). The literature on associations between discounting and symptom measures is quite mixed, with some studies finding correlations with negative symptoms (Heerey et al., 2007) or anhedonia (Heerey et al., 2011; Lempert and Pizzagalli, 2010), others with positive symptoms (Weller et al., 2014), and still others no correlations (Ahn et al., 2011). We examined measures of anhedonia, negative symptoms, positive symptoms, and depression; however, there are other clinical dimensions related to enhanced reward sensitivity, such as mania and impulsivity, that may have a stronger relationship with discounting.

Of the aspects of decision-making we tested, individuals with schizophrenia differed only on delay discounting. This is not to say that delay discounting is the only aspect of decision-making affected by schizophrenia. There is also evidence for steeper discounting of rewards requiring effort, which is correlated with negative symptom severity (Fervaha et al., 2013; Gold et al., 2013; Wolf et al., 2014). However, our study demonstrates that elevated delay discounting in schizophrenia is not due to pervasive changes in decision-making or to the processing of uncertain rewards.

Our finding of no reduction in loss aversion in schizophrenia is contrary to two previous reports (Heerey et al., 2008; Treméau et al., 2008). However, there were significant methodological differences between these two prior studies and ours. Higher task complexity due to varying probabilities (Heerey et al., 2008) and differences in the specific loss-related construct examined (Treméau et al., 2008) may contribute to the disparate results. In Heerey et al. (2008), group differences disappeared after working memory measures were taken into account, indicating that the complexity of the task may explain differences in loss aversion in their study. Our findings using simple gambles provide strong evidence that schizophrenia is not associated with robust reductions in loss aversion.

We also did not find any group differences in risk aversion. Schizophrenia has previously been associated with altered decision-making in the balloon analogue risk task (Cheng et al., 2012; Reddy et al., 2014) and the Iowa Gambling Task (Kester et al., 2006; Ritter et al., 2004; Sevy et al., 2007; Shurman et al., 2005; Yip et al., 2009; though see Cavallaro et al. (2003), Evans et al. (2005), Rodríguez-Sánchez et al. (2005), Turnbull et al. (2006) and Wilder et al. (1998)). However, both of these tasks involve ambiguity, losses, and learning in addition to risk, and therefore altered decision-making could arise from many sources, not just differences in risk aversion.

4.1. Limitations

There were several limitations in our study. The sample sizes in each group were not particularly large, limiting our ability to detect smaller effects. Relatedly, although group differences in discounting remain significant after controlling for PVRT, we cannot rule out the possibility of residual confounding, which larger studies should address in the future with more complex structural equation modeling (Westfall and Yarkoni, 2016). We only collected a binary measure of current smoking status in the full sample, and therefore did not examine the effect of former smoking or current smoking severity which may

influence discount rates (Wing et al., 2012). Furthermore, although we enriched our NC sample with smokers to more adequately compare to the SZ group, we could not recruit enough smokers in the FM group to match smoking across all groups. While our analysis in non-smokers shows that our conclusions are not attributable to the difference in smoking rates across groups, future studies will need to confirm these conclusions, especially regarding the lack of a genetic endophenotype in FM, using samples well-matched on severity of current and former smoking.

4.2. Conclusion

Many explanations have been put forth for steeper discounting of future rewards in schizophrenia: cognitive impairments, genetic endophenotypes, smoking, antipsychotic medication, and disease symptoms. Here we tested many of these hypotheses. We find that cognitive impairments explain part of the difference between groups, but do not completely account for elevated discounting. Increased discounting rates were not found in close genetic relatives of individuals with schizophrenia. Increased discounting was not attributable to greater prevalence of smoking in schizophrenia, and in fact smoking status was not associated with discounting in schizophrenia, contrary to the case in controls. Steeper discounting of future rewards therefore seems to be a feature of the disease or its treatment.

Conflicts of interest

The authors report no conflicts of interest.

Funding

This work was supported by the National Institutes of Mental Health [grant numbers R01MH101111, R01MH107703, K23MH085096, and K23MH098130]; the Brain and Behavior Research Foundation; and the Penn Medicine Neuroscience Center.

Acknowledgements

We would like to thank all of the study subjects for their participation.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.psychres.2017.02.062](https://doi.org/10.1016/j.psychres.2017.02.062).

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