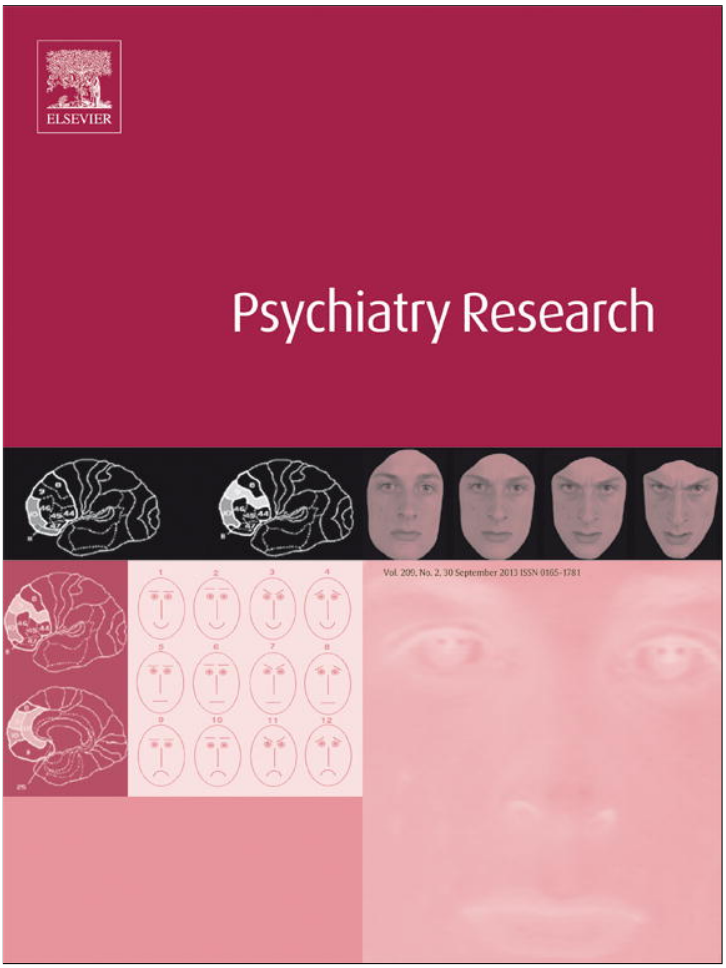

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Hypothetical decision making in schizophrenia: The role of expected value computation and "irrational" biases

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ABSTRACT

The aim of the present study was to examine the contributions to decision making (DM) deficits in schizophrenia (SZ) patients of expected value (EV) estimation and loss aversion. Patients diagnosed with SZ ($n=46$) and healthy controls ($n=34$) completed two gambling tasks. In one task, participants chose between two options with the same EV across two conditions: Loss frames and Keep frames. A second task involved accepting or rejecting gambles, in which gain and loss amounts varied, determining the EV of each trial. SZ patients showed a reduced "framing effect" relative to controls, as they did not show an increased tendency to gamble when faced with a certain loss. SZ patients also showed a reduced tendency to modify behavior as a function of EV. The degree to which choices tracked EV correlated significantly with several cognitive measures in both patients and controls. SZ patients show distinct deviations from normal behavior under risk when their decisions are based on prospective outcomes. These deviations are two-fold: cognitive deficits prevent value-based DM in more-impaired patients, and in less-impaired patients there is a lack of influence from well-established subjective biases found in healthy people. These abnormalities likely affect everyday DM strategies in schizophrenia patients.

1. Introduction

Cognitive and motivational problems are some of the most debilitating aspects of schizophrenia (SZ), contributing greatly to functional deficits in patients with the illness (Dickinson et al., 2007). Based, in part, on evidence that SZ patients exhibit normal hedonic responses to the experience of rewards (Heerey et al., 2008; Cohen and Minor, 2010), it has been suggested that motivational deficits in SZ may be driven by a relative inability to accurately and adaptively represent the expected value (EV) of response alternatives, outcomes, and stimuli predictive of reward availability. Such representations are needed to guide effective decision-making (DM).

A growing body of research points to abnormalities in value-based DM in SZ. Over the last decade, multiple studies have shown that chronic SZ patients make lower rates of optimal choices on tasks of risky DM (Hutton et al., 2002; Cheng et al., 2012; Fond et al., 2013). For example, most, but not all studies using the Iowa Gambling Task (IGT; Bechara et al., 1994) point to impaired value-based DM in SZ (for a review see Sevy et al., 2007). Because advantageous and disadvantageous decks in the IGT are distinguished by the magnitudes of punishments associated with each, poor performance on the IGT has been interpreted as reflecting reduced sensitivity to punishments in clinical populations (Bechara et al., 1995). With the IGT, however, it is difficult to discern whether DM abnormalities result from reduced sensitivity to punishments (and thus a preference for risky choices), or an inability to process the simultaneous rewards and punishments administered on every trial, or a reduced ability to update and integrate value representations based on a long series of outcomes.

To isolate alterations in DM, as opposed to alterations in outcome processing, it is useful to study risky DM under hypothetical conditions, in which learning from feedback does not play a role. Experimental work into this type of DM has determined that expected utility, as defined by von Neumann and Morgenstern (1947), is not the only factor influencing choice behavior, as healthy people often fail to choose options offering the highest EV (by virtue of either reward magnitude, probability of receipt, or both). Prospect theory (Kahneman and Tversky, 1979; Tversky and Kahneman, 1981; Trepel et al., 2005) accounts for these examples of non-rational DM by emphasizing the role of perceptual factors and subjective biases about the relative value of different outcomes. Most importantly, DM behavior in healthy subjects is often influenced by a greater bias to avoid losses, than to seek gains.

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That is, when faced with the choice between a certain loss and an uncertain loss that has a larger magnitude, but the same EV, most subjects are willing to gamble (i.e., take on risk) in order to avoid the certain loss. In contrast, when subjects have the choice between a certain gain and the chance for a larger, but uncertain, gain, loss aversion leads to an unwillingness to gamble (De Martino et al., 2006). To the same end, when faced with the choice to play a gamble or accept a neutral outcome, loss aversion leads subjects to avoid risking a loss, unless the proposed gamble offers a potential gain that is significantly greater than the potential loss (when the EV is significantly greater than zero; Tom et al., 2007). Thus, the same bias leads to different decisions depending on the context (a phenomenon called the "framing effect"; Kahneman and Tversky, 1979). While this bias is not "rational," it is a well-established pattern of choice behavior in healthy subjects (Rabin and Thaler, 2001; Kahneman, 2003).

We were interested in examining this issue in schizophrenia for several reasons. First, there is suggestive evidence that people with schizophrenia may undervalue potential losses in uncertain DM contexts (Heerey et al., 2008), and show a reduced endowment effect (whereby people tend to overestimate the value of a good that is already in their possession; Tremeau et al., 2008). A reduced sensitivity to potential losses might result in abnormal (albeit more rational DM) in SZ patients. Interestingly, Heerey et al. (2008) reported that reduced loss sensitivity was related to measures of working memory capacity, suggesting that patients may lack some of the cognitive capacities that are needed to evaluate all the features involved in representing comparative choices, which might also be expected to impact the appearance of framing effects.

Suspicion that SZ patients might show altered loss aversion in DM is bolstered by recent neuroimaging studies that have examined the neural basis of this phenomenon and implicated a set of regions, many of which are likely to be compromised in schizophrenia. For example, a functional magnetic resonance imaging (fMRI) study by Tom et al. (2007) has linked loss aversion to the targets of the mesolimbic and mesocortical dopamine (DA) pathways, such as the ventral striatum (VS), ventromedial prefrontal cortex (VMPFC), and medial orbitofrontal cortex (OFC). Other fMRI studies (De Martino et al., 2006, 2010) have found activity in the amygdala – a region involved in processing affective information (for a review see Phan et al., 2004) – to be most predictive of loss-averse behavior. Evidence that all of these brain areas may be implicated in schizophrenia (Grace, 2000) further supports the idea that many patients with SZ may not exhibit normal DM behavior based on loss-aversion biases.

In order to examine the issue of loss aversion in SZ, we adapted two tasks from the recent functional imaging literature on loss-aversion biases. In one task, adapted from De Martino et al. (2006), subjects were given a varying amount of money at the start of each trial and were asked to choose between a certain outcome, which was to retain a portion of the original amount, and a probabilistic outcome, which was to accept a gamble. On two-thirds of trials, both options had the same EV and were presented in either a certain gain (or Keep frame) or a certain Loss frame (Fig. 1). The task was designed to test the effect of the framing of the choice (independent of the EV of the choice) on subjects' willingness to gamble. In a second task, adapted from Tom et al. (2007), subjects chose either to accept or reject a gamble involving a 50% chance of gaining a certain amount and a 50% chance of losing a certain amount. In this task, potential gains and losses varied from trial to trial, such that the absolute value of the potential gain magnitude could exceed, be the same as, or be less than, the absolute value of the potential loss magnitude. This task was designed to identify the ratio of potential loss magnitude to potential gain magnitude at which each individual subject was indifferent to accepting or rejecting a gamble. This ratio serves as a quantitative measure of loss aversion in individual subjects.

We predicted that loss aversion would be attenuated in schizophrenia, resulting in a reduced framing effect. In short, we expected that SZs would gamble more or less equally in Keep and Loss frames, and not exhibit the "irrational bias" observed in controls in the De Martino et al. (2006) task. In the context of the Tom et al. (2007) task, we expected SZ patients to show less

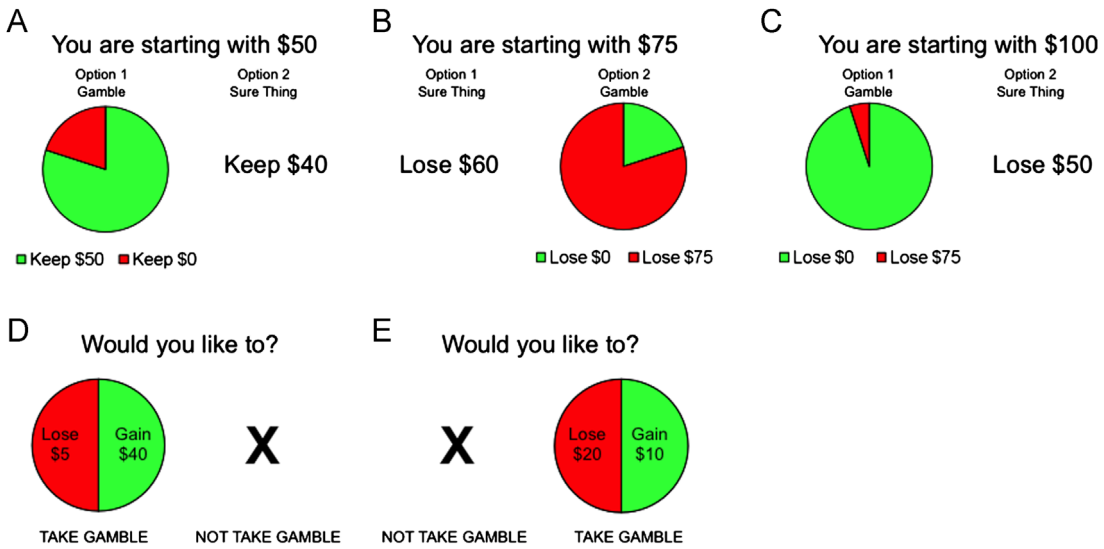

Fig. 1. Illustration of behavioral tasks. (A) A trial involving a Keep frame from the DeMartino Framing Task (2006). In this example, participants started with $50 and had to decide whether they would rather keep $40 certainly, or accept a gamble with an 80% of keeping the entire $50 and a 20% chance of keeping nothing. (B) A trial involving a loss frame from the DeMartino Framing Task (2006). In this example, participants started with $75 and had to decide whether they would rather lose $60 certainly, or accept a gamble with an 80% of losing the entire $75 and a 20% chance of losing nothing. (C) Illustration of a "Catch" trial from the DeMartino Framing Task (2006). In this example, participants started with $100 and had to decide whether they would rather lose $50 certainly, or accept a gamble with a 5% chance of losing the entire $100 and a 95% chance of losing nothing. (D) Trial with an advantageous gamble from Tom et al. (2007). The gamble option from this trial had a very positive EV (17.5), due to large potential gain and small potential loss. (E) Trial from Tom et al. (2007) with a disadvantageous gamble (EV=−5), due to large potential loss and small potential gain.

lawful modification of gambling rates based on changes in EV, due to reduced precision in representing both expected rewards and expected punishments. Because negative symptoms have been associated with neural signals in striatum and PFC (Wolkin et al., 1992; Ehrlich et al., 2012), we additionally predicted that an increased severity of negative symptoms in SZ patients would lead to less loss-averse behavior than both controls and patients with milder negative symptoms.

2. Methods

2.1. Participants

Forty-six patients meeting DSM-IV-TR criteria for schizophrenia or schizoaffective disorder (SZ) as determined by the Structural Interview for the DSM-IV (SCID-I; First et al., 1997), and 34 healthy control (NC) subjects, volunteered to participate in the study and provided written informed consent. All subjects were compensated for study participation. All SZ patients were recruited from the Maryland Psychiatric Research Center (MPRC) and were clinically stable (as determined by their treating physician) and medically stable (no changes in medication type or dose within 4 weeks of study; see Table 1). Normal control participants were recruited from the community via random digit dialing and advertisements and were screened for Axis I and II disorders using the SCID-I (First et al., 1997). All control participants were free of any significant personal psychiatric and medical history, had no history of severe mental illness in first-degree relatives, and did not meet criteria for current substance abuse or dependence.

2.2. General procedures

Study participants completed a standard cognitive batteries including the MATRICS battery (Green et al., 2004), Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999), Wide Range Achievement Test Four (WRAT4; Wilkinson and Robertson, 2006), and Wechsler Test of Adult Reading (WTAR; Wechsler, 2001). All study participants were required to achieve 100% accuracy on a short quiz utilizing pie charts to represent their chances of winning and losing prior to the administration of both gambling tasks in order to ensure comprehension.

Overall symptom severity in patients was characterized using the Brief Psychiatric Ratings Scale (BPRS; Overall and Gorman, 1962), and negative symptom severity was quantified using the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1984) and the Brief Negative Symptom Scale (BNSS; Kirkpatrick et al., 2011).

2.2.1. Framing effects task

Participants completed a gambling task, based on the work of De Martino et al. (2006); (see Fig. 1). Ninety-six trials (32 Loss frame, 32 Keep frame, and 32 Catch trials) were presented randomly over one block, without feedback. On each trial, text indicated the amount of money the subject started with for that trial (four starting amounts were used: $100, $75, $50, and $25). Participants were told that on each trial, they would have to choose between a sure option and a gamble option and that they would not see the outcome of their choices. They were also told to choose carefully, as they would receive a bonus at the end of the experiment (all subjects received $5.00). The sure option in Keep frame trials involved keeping a portion of the starting amount; in Loss frame trials, the sure option involved losing a portion of the starting amount. The gamble option was represented by a pie-chart, depicting the probability of keeping or losing all of the money in Keep and Loss frames, respectively. Within the gamble option, four different probabilities of keeping or losing the starting amount were used (20%, 40%, 60%, or 80%). For example: on a given trial, a subject could be told they were starting with $50 and presented with a choice between accepting a gamble, representing a 40% chance of keeping the entire $50, or taking a certain $20 (40% of $50). A Loss frame would involve a choice between accepting a gamble, representing a 60% chance of losing the entire $50, and taking a certain loss of $30 (60% of $50). All experimental variables (total starting amount, percentage of the money kept or lost, number of trials) were identical between the Loss and Keep frame conditions. The EVs of sure and gamble options were always equivalent in each Loss and Keep frame trial, and also mathematically equivalent between frames.

Thirty-two Catch trials were included in the experimental design to ensure that participants were actively engaged and understood the task. Catch trials presented subjects with two clearly unbalanced options, such that there was an obvious preferable choice if participants computed EV properly (e.g. starting with $100, choose between a 95% chance of keeping the entire $100, or keep a certain $50; see Fig. 1C). The 32 Catch trials were split evenly across the Keep and Loss frames, and the advantageous choices were split evenly across gamble and certain options.

2.2.2. Loss aversion task

Participants were presented with a second gambling paradigm adapted from a study by Tom et al. (2007). In each trial, the subject was presented with a choice of accepting or rejecting a gamble, each gamble having a 50% chance of gaining one amount of money and a 50% chance of losing another amount (choosing either a pie chart or an "X", as illustrated in Fig. 1D and E). Possible gains ranged from $10 to $40 (in $2 increments) and possible losses ranged from $5 to $20 (in $1 increments). All 256 possible combinations of gain and loss amounts (16 possible loss amounts × 16 possible gain amounts) were presented over four blocks of 64 trials. The EV of the gambles ranged from a minimum of −$5 (gain amount = $10,

Table 1
Demographic, cognitive, and clinical characteristics of study participants.

Measure	All SZs (N=46) Mean	(S.D.)	All NCs (N=34) Mean	(S.D.)	p of t/χ^2
Demographic					
Age	40.570	(10.697)	38.500	(10.732)	0.397
Gender	18 F, 28 M		14 F, 20 M		1.000
Race	27 C, 17 AA, 2 O		19 C, 14 AA, 1 O		0.896
Sub education (years)	12.610	(2.206)	14.680	(1.902)	< 0.001
Father's education (years)	13.900	(3.506)	13.210	(2.571)	0.332
Cognitive					
Average Reading Score (WRAT4-Reading+WTAR)	94.696	(13.722)	108.132	(12.370)	< 0.001
WASI Estimated IQ	95.800	(15.970)	116.500	(10.396)	< 0.001
MDS-WM	37.670	(11.074)	51.350	(10.383)	< 0.001
Clinical					
BPRS Total	35.341	(1.218)			
BPRS Positive	2.280	(0.180)			
BPRS Negative	1.790	(0.102)			
BPRS Disorganization	1.364	(0.052)			
SANS Total	34.128	(2.615)			
SANS Anhedonia+Avolition	20.833	(1.453)			
BNSS Total	22.022	(2.750)			
Antipsychotic drugs					
Clozapinemonotherapy	17				
Other SGA monotherapy	15				
Multiple SGAs	5				
FGA monotherapy	8				
FGA+SGA	1				

Abbreviations: SZs, schizophrenia patients; NCs, normal controls; WRAT4, Wide Range Achievement Test—Version 4; WTAR, Wechsler Test of Adult Reading; WASI Estimated IQ, Estimated IQ from the Wechsler Abbreviated Scale of Intelligence; MDS-WM, MATRICS Domain Score—Working Memory; BPRS, Brief Psychiatric Rating Scale; SANS, Scale for the Assessment of Negative Symptoms; BNSS, Brief Negative Symptom Scale; SGA, second-generation antipsychotic; FGA, first-generation antipsychotic.

loss amount=$20) to a maximum of +$17.5 (gain amount=$40, loss amount=$5). Rejection of a gamble was understood as a neutral outcome, and subjects were not shown the results of accepted gambles. Participants were instructed to choose carefully, as they would receive a bonus at the end of the experiment (all subjects also received $5.00 for completion of this task).

2.3. Analysis of behavioral data

2.3.1. DeMartino task

Percentage of gamble choices was calculated for each subject separately in Keep frame trials, Loss frame trials, and Catch trials. Statistical analyses were done using Statistical Package for Social Sciences (SPSS) 11.0. For each subject, we computed a difference score contrasting the rates of accepting gambles in Loss and Keep frames, which served as a quantification of the framing effect. Because the distributions of outcome values from this task were markedly kurtotic (kurtosis values >2), analyses were performed with non-parametric tests. The main test of a group difference was a Mann–Whitney *U*-test on the framing effect, or contrast of gambling rates across Keep and Loss frames. In comparing framing effect indices across groups, we included only subjects who achieved above-chance performance on Catch trials. Binomial expansion determined that subjects who made greater than 62.5% (20) optimal choices on the 32 Catch trials performed beyond the limits of chance with $>95\%$ certainty.

2.3.2. Tom task

In order to examine correspondences between gamble parameters and trial-by-trial choices, we performed, separately for each subject, Firth Logistic Regression (Firth, 1993), using the R statistical package (http://www.r-project.org). Four regressors were used: magnitudes of the potential gain and loss on that trial, and the change in the magnitude of the potential gain and loss from the last trial. Standardized regression coefficients (beta-values) were submitted to second-level analyses, along with a behavioral loss-aversion index (λ), which was calculated by dividing the negative of the beta for losses by the beta for gains ($\lambda=-\beta_{loss}/\beta_{gain}$). Because the distributions of outcome values from this task were also kurtotic, analyses were performed with Mann–Whitney *U*-tests. In comparing lambda-values across groups, we included only subjects who satisfied the following criteria: (1) they showed above-chance performance on Catch trials from the DeMartino task; (2) they had a negative beta-coefficient for loss amounts (β_{loss}), from the Tom task; (3) they had a positive beta-coefficient for gain amounts (β_{gain}), from the Tom task; and (4) at least one of β_{loss} and β_{gain} differed significantly from zero.

2.4. Analyses of variability within the sample of SZ patients

For SZ patients and controls that showed above-chance performance on Catch trials, we examined correlations between clinical and neuropsychological variables and several of the task variables mentioned above. We examined correlations between measures of experimental task performance and summary variables from the BPRS, SANS, and BNSS, to assess four symptom domains: positive, negative, disorganized, and depressed. We examined correlations between measures of experimental task performance and three summary variables from standard neuropsychological tests: an averaged reading score (the means of the scaled scores from the WRAT4-Reading and WTAR), the estimate of IQ from the WASI, and the MATRICS working memory domain score. Using a one-way ANOVA, we also compared the subgroup of patients who showed Catch trial performance not differing from chance, with controls and the patients and controls who showed above-chance performance on Catch trials, on a number of demographic, clinical, and neuropsychological variables.

To examine effects of antipsychotic drug (APD) dose, we calculated a standardized APD dose for each patient by transforming APD type and dose into haloperidol equivalents using the formula implemented by Andreasen et al. (2010). This method was chosen over the traditional standardized chlorpromazine equivalent because many clinicians and researchers are not familiar with chlorpromazine dosing strategies, and are more familiar with those of haloperidol (Andreasen et al., 2010).

3. Results

3.1. DeMartino task

3.1.1. Performance on Catch trials

We found that, out of 46 SZ patients and 33 healthy controls, 12 patients and two controls failed to perform beyond the limits of chance on the 32 Catch trials. Although the remaining subjects (34 patients and 31 controls) averaged over 90% optimal responses on Catch trials, the groups showed a trend toward a significant difference in their performance on Catch trials (patients' median=96.9%; controls' median=100%, $Z=-1.776$, $P=0.076$).

3.1.2. Gambling in Keep and Loss frames

As described above, the framing effect is operationalized in this paradigm as the relative willingness to gamble in Loss frames, when compared with Keep frames. As shown in Fig. 2, we observed a significant group difference in the direct measure of the framing effect (the [percentage gamble in Loss frames −percentage gamble in Keep frames] contrast; patients' median=−3.1%; controls' median=+3.1%, $Z=-2.155$, $P=0.031$). This group difference in the contrast was driven by a significant group difference in gambling rates in Keep frames, as patients were significantly more likely to gamble in Keep frames, as compared to controls ($Z=-2.592$, $P=0.010$). By contrast, we observed no group difference in gambling rates in Loss frames ($Z=-0.947$, $P=0.344$).

When we examined within-group effects, using Wilcoxon tests, we found that controls were significantly more likely to gamble in Loss frames as compared to Keep frames ($Z=-2.435$, $P=0.015$), replicating the results of De Martino et al. (2006), and indicating that our framing manipulation was effective. Importantly, however, patients did not show an increased willingness to gamble in Loss frames, relative to Keep frames ($Z=-0.795$, $P=0.427$).

3.2. Tom task

3.2.1. Tracking of expected value

In characterizing the tracking of expected value and loss aversion, we again only considered the 34 patients and 31 controls that performed significantly above chance on the Catch trials from the DeMartino task. Patients and controls differed significantly in their betas for losses (patients' median=−0.402, controls' median=−0.638, $Z=-3.123$, $P=0.002$). Patients and controls also differed in their betas for gains (patients' median=0.259, controls' median=0.478, $Z=-2.456$, $P=0.014$). These results confirm the general impression from panels A–E of Fig. 3 that SZ patients were both less likely to accept the most favorable gambles, involving the largest gains and smallest losses, and more likely to accept the least favorable gambles, involving the largest losses and smallest gains.

3.2.2. Loss-aversion indices

We next compared loss-aversion indices (lambda values) across groups, in 28 patients and 31 controls who both showed above-chance Catch trial performance and who had valid lambda-values

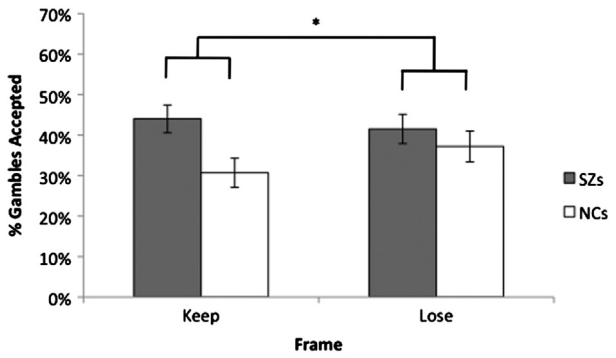

Fig. 2. Results from DeMartino Task. When we examined gambling performance on the DeMartino task in the 34 patients and 31 controls who showed valid Catch trial performance, we observed a significant group difference in the direct measure of the framing effect (the [percentage gamble in Loss frames−percentage gamble in Keep frames] contrast.

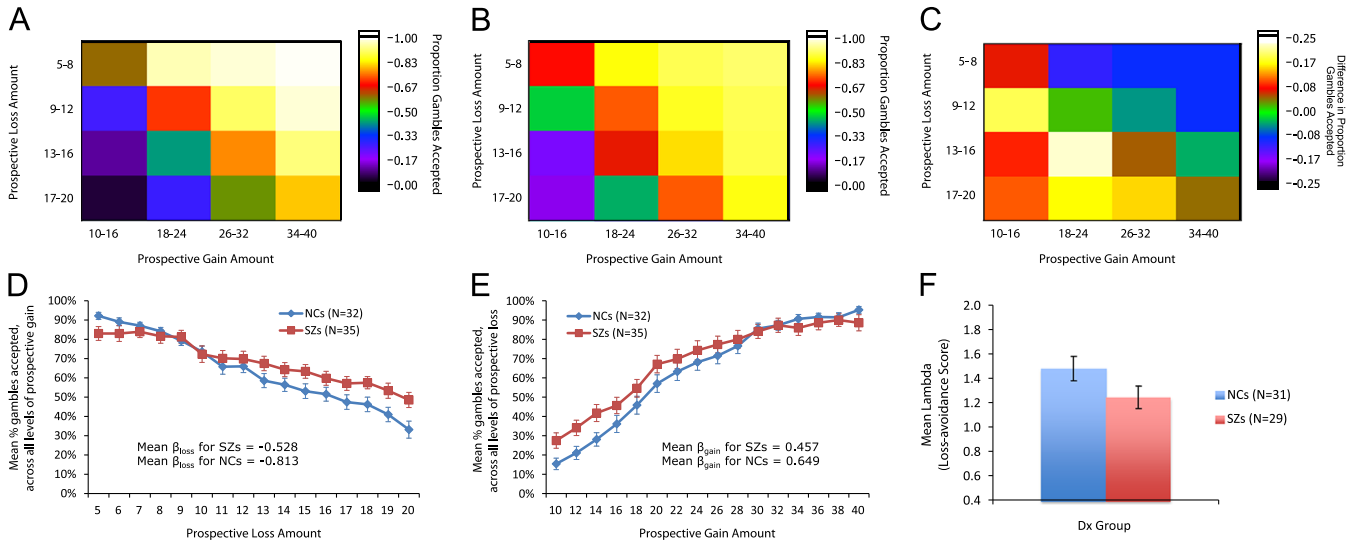

Fig. 3. Results from Tom Loss-aversion Task. (A) Heat maps showing gradients of gamble acceptance, according to trial gain and loss magnitude, in controls and (B) patients, as well as (C) the contrast [controls–patients]. (D) Plots showing proportions of gambles accepted by loss magnitude, collapsed across all levels of gain magnitude. (E) Plots showing proportions of gambles accepted by gain-magnitude, collapsed across all levels of loss magnitude. (F) Measures of loss-aversion (λ) in patients and controls with valid β-values for gain and loss magnitude.

Table 2
Demographic, cognitive, and clinical characteristics of study participants, who did and did not show above-chance performance on Catch-trials from the De Martino et al. (2006) task.

Measure	SZ fail	($N=12$)	SZ pass	($N=34$)	NC pass	($N=31$)	
	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)	p of $F/t/\chi^2$
Demographic							
Age	45.670	(6.840)	38.760	(11.298)	38.030	(11.137)	<0.040
Gender	6 F, 6 M		12 F, 22 M		14 F, 17 M		0.587
Race	2 C, 10 AA		25 C, 7 AA, 2 O		18 C, 12 AA, 1 O		0.005
Subject's education (years)	11.330	(2.188)	13.060	(2.059)	14.740	(1.932)	<0.015[abc]
Father's education (years)	11.640	(1.963)	14.730	(3.600)	13.330	(2.670)	0.005[cd]
Cognitive							
Average reading score (WRAT4-Reading+WTAR)	85.208	(11.680)	98.044	(12.923)	109.952	(11.372)	<0.001[abc]
WASI estimated IQ	85.170	(13.341)	99.560	(15.258)	117.520	(9.996)	<0.002[abc]
MDS-WM	31.580	(10.740)	39.880	(10.490)	52.350	(10.167)	<0.025[abc]
Clinical							
BPRS Total	31.273	(5.217)	36.697	(8.461)			0.053
BPRS Positive	1.610	(0.793)	2.500	(1.228)			0.031
BPRS Negative	1.862	(0.692)	1.765	(0.678)			0.680
BPRS Disorganized	1.236	(0.175)	1.406	(0.375)			0.158
SANS Total	39.180	(17.713)	32.000	(16.583)			0.231
SANS Anhedonia+Avolition	23.181	(9.516)	20.000	(9.398)			0.342
BNSS Total	26.416	(22.362)	20.424	(16.917)			0.341
Antipsychotic drugs							0.124
Avg haloperidol-equivalent dose	14.287	(8.081)	10.859	(5.956)			0.126
Clozapine monotherapy	1		16				
Other SGA monotherapy	5		10				
Multiple SGAs	2		3				
FGA monotherapy	4		4				
FGA+SGA	0		1				

Abbreviations: WRAT4, Wide-ranging Achievement Test—Version 4; WTAR, Wechsler Test of Adult Reading; WASI estimated IQ, estimated IQ from the Wechsler Abbreviated Scale of Intelligence; MDS-WM, MATRICS Domain Score—Working Memory; BPRS, Brief Psychiatric Rating Scale; SANS, Scale for the Assessment of Negative Symptoms; BNSS, Brief Negative Symptom Scale; SGA, second-generation antipsychotic; Anhed, anhedonia; Avol, avolition; HD, haloperidol; Eq, equivalent; monoth, monotherapy; SGA, second-generation antipsychotic; FGA, first-generation antipsychotic; SZF, SZ Fail, schizophrenia patients who failed Catch trials; SZP, SZ Pass, schizophrenia patients who passed Catch trials; NCP, NC Pass, normal controls who passed Catch trials.

[a] =NCP > SZP.
[b] =NCP > SZF.
[c] =SZP > SZF.
[d] =SZP > SZF (trend, $P=0.077$).

on the Tom task, according to the criteria discussed in Section 2. Patients and controls did not differ in their loss-aversion indices, according to a Mann–Whitney U-test (patients' median= 1.211; controls' median=1.402, $Z=-1.351$, $P=0.177$; Fig. 3F).

3.3. Correlation analyses

Based on our hypothesis that the computation of EV is a function heavily dependent on general intellectual function, we

assessed the relationships among experimental variables from both tasks and measures of intellectual function in patients and controls who showed above-chance performance on Catch trials. In patients, there were significant correlations between Catch trial performance and WASI estimated IQ (r_s=0.450, P=0.008), and mean reading scores (average of WTAR and WRAT4-Reading scaled scores; r_s=0.0451, P=0.007). Additionally, patients showed a significant correlation between betas for losses and WASI estimated IQ (r_s=−0.434, P=0.010), and mean reading scores (r_s=−0.374, P=0.030), and a trend toward significance between betas for gains and WASI estimated IQ (r_s=0.338, P=0.051), and mean reading scores (r_s=0.333, P=0.055). Lambda was not correlated with any cognitive measures in either group (all P > 0.100). Notably, there were no correlations between the framing effect and any standard measure of intellectual functioning in patients (for WASI estimated IQ, r_s=−0.023, P=0.897; for the MATRICS working memory domain score, r_s=−0.052, P=0.775; for mean reading scores, r_s=0.006, P=0.975). In controls, only one systematic relationship was found between betas for losses and WASI estimated IQ (r_s=−0.437, P=0.014). Again, of note, there were no correlations between the framing effect and any standard measure of intellectual functioning in the control group (for WASI estimated IQ, r_s=−0.107, P=0.565; for the MATRICS working memory domain score, r_s=−0.139, P=0.455; for mean reading scores, r_s=−0.035, P=0.853).

When we tested for relationships between clinical measures and task performance, we observed no significant correlations between negative or positive symptom ratings and variables from either task (all P > 0.100). When we tested for relationships between haloperidol-equivalent APD doses and experimental task performance, we observed no significant correlations between APD doses and variables from the DeMartino task (for Catch trial performance, r_s=−0.003, P=0.985; for framing effect, r_s=0.229, P=0.193). However, we observed significant correlations between standardized APD dose and beta loss (r_s=0.432, P=0.011), and between APD dose and beta gain (r_s=−0.351, P=0.042). This result suggests that higher APD dose correlates with decreased sensitivity to gains and an increased sensitivity to losses.

3.4. Analysis of differences within the sample of SZ patients

When we examined the clinical and intellectual characteristics of patients showing chance-level performance on Catch trials, we found that relative to patients showing above-chance performance, these patients had higher ratings for negative symptoms and much significantly-lower scores on three cognitive measures: WASI estimated IQ, MATRICS Working Memory Domain Score, and the average of scaled scores from the WRAT4 Reading subtest and the WTAR (Table 2). Demographically, patients in the at-chance group were predominantly African American, were significantly older, were significantly less-educated, and had less parental education than patients who performed above-chance on Catch trials (Table 2).

4. Discussion

Taken together, the results of these two DM tasks reveal specific abnormalities in the way patients with schizophrenia approach choice under uncertainty. Most previous research has focused on DM behavior in SZ patients in learning environments; this study sought to investigate the roles of EV computation and subjective biases on hypothetical risk-taking behavior in schizophrenia. We found that patients with schizophrenia exhibited abnormal behavior in performing two different gambling tasks. We attribute this both to a limited capacity to prospectively calculate EV and a reduced influence of classic “irrational” biases on behavior.

4.1. Patients with schizophrenia do not show an increased willingness to gamble in Loss frames, relative to Keep frames

The group of SZ patients who were able to compute basic EV did not exhibit subjective biases consistent with traditional Prospect Theory (as defined by Kahneman and Tversky (1979)). That is, they showed no increase in risk-seeking behavior in Loss frames, relative to Keep frames, on the De Martino et al., 2006 task, when prompted to choose between options of equal EV. Rather, SZ patients showed similar risk-seeking behavior in Loss frames, and Keep frames. For example, when faced with the choice between losing 80% of $75 ($60) for certain or having an 80% chance of losing the whole $75 (and a 20% chance of losing nothing), patients did not show an increase in willingness to gamble, as controls did. This reduced sensitivity to losses in SZ patients is consistent with other studies of DM under uncertainty in this population (Heerey et al., 2008; Tremeau et al., 2008).

4.2. The role of intellectual function in expected value computation

While the entire sample of SZ patients showed significantly poorer Catch trial performance and significantly lower beta values for tracking variations in gain and loss magnitude, when compared with healthy controls, the lack of loss-aversion biases in SZ patients should be considered with caution. The capacity to estimate the EV of a hypothetical choice, through integration of the probabilities and magnitudes of potential outcomes, relies on working memory function and general intellectual ability (Frank and Claus, 2006). Given the fact that working memory deficits are well-documented in schizophrenia (Park and Holzman, 1992; Goldman-Rakic, 1994; Carter et al., 1998; Barch et al., 2001), we anticipated that patients might show great difficulty in adaptively estimating the value of options. This suspicion was confirmed as the patients showed numerous significant correlations between measures of EV computation (Catch trial performance, beta-values for both gains and losses) and standard measures of intellectual function (including WASI estimated IQ, reading scores, and the Working Memory Domain Score from the MATRICS). Furthermore, a subset of patients who were entirely unable to compute EV in performing these tasks had, on average, lower estimated IQs and lower working memory scores.

Notably, the correlations observed in patients between task measures and measure of intellectual function were strictly limited to those requiring basic EV computation, and did not extend to the measure of the framing effect. This finding reiterates the point that the computation of EV in the context of DM relates closely to other cognitive capacities, such as working memory, and that a basic level of intellectual function is required to make optimal decisions, even when the two options differ greatly in their EV. Additionally, this finding illustrates that the lack of a framing effect in patients is not due to differences in intellectual functioning, and can be better explained by a lack of loss aversion biases.

4.3. Loss aversion and psychopathology measures

One aim of this research was to investigate loss aversion in schizophrenia as it relates to symptom severity. Unfortunately, we are unable to make a definitive claim regarding this issue, as we were unable to include a sizeable number of our recruited patient group in our analyses, due to severely impaired Catch trial performance. Interestingly, these severely impaired patients tended to have less severe positive symptoms as well as more

severe negative symptoms, suggesting a relationship between negative symptom severity and EV calculation. In the group of patients who met the Catch trial inclusion criteria, however, we did not observe any evidence of a negative symptom signal. It is unclear if this resulted from censoring the informative part of the patient distribution for poor Catch trial performance or a genuine lack of relationship. Further work, using DM paradigms that are less sensitive to general intellectual impairment, will be needed to address this important issue.

4.4. Accounting for discrepancies in the decision-making literature in schizophrenia

Patients in our study clearly exhibit deficits in the computation of EV based on the integration of reward magnitude and probability in a non-learning task environment. In this type of task, the EV computation is used to guide behavior in a prospective way, without feedback from choices. By contrast, there is some evidence that, in environments where incremental reinforcement learning is possible, some aspects of reward-based DM are intact, such as loss-avoidant behavior (Waltz et al., 2007; Cheng et al., 2012; Gold et al., 2012). This discrepancy between risk-taking behavior based on hypothetical descriptions of reward and feedback-driven behavior based on experience has also been observed in healthy individuals (Ludvig and Spetch, 2011). Thus, it appears that patients are most likely to exhibit normal DM behavior when they experience the outcomes of their choices, and apply fairly simple reinforcement learning mechanisms. In contrast, patients are less likely to exhibit normal DM behavior when faced with hypothetical scenarios that require a decision. It appears that the DM processes involved in such hypothetical scenarios require contributions from cognitive capacities, such as working memory (Frank and Claus, 2006), that are impaired in schizophrenia, and possibly account for their abnormal performance.

Another important direction for research would be to examine loss aversion in unmedicated patients with schizophrenia. Because antipsychotic drugs directly modulate activity in dopamine pathways, we examined relationships between standardized APD dose using the method of Andreasen et al. (2010) and task measures in patients. Our results showed that patients taking higher doses of APD were less likely to be influenced by gain amount when deciding to accept or reject a given gamble, but were more likely to be influenced to loss amount. However, this result is difficult to interpret as it was only observed in one of the paradigms. Additionally, drug dose and type were not randomly assigned to patients in this study, fully confounding drug dose and the clinical illness features that likely led to the use of higher medication doses. Further investigation of APD effects on loss aversion in schizophrenia, in the context of randomized clinical trials, is warranted, as their effects are impossible to disambiguate from those of the underlying pathology.

4.5. General conclusion

In sum, there are clear abnormalities in the manner in which patients with schizophrenia approach risky choices, when they must make decisions based on prospective outcomes. Certain aspects of abnormal DM behavior exhibited by patients are clearly linked to general intellectual impairments, while others appear to be independent of these broad cognitive deficits. More impaired patients have a clear inability to gauge the EV of choices presented to them, making meaningful DM impossible. Less impaired patients who demonstrate an ability to weigh two options still show abnormalities, in that they do not guide behavior based on the well-established subjective biases employed by healthy people. These deficits in evaluating value and applying normal subjective biases are likely factors that impact the everyday DM of patients with schizophrenia.

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References

Andreasen, N.C., 1984. The Scale for the Assessment of Negative Symptoms (SANS). University of Iowa, Iowa City, IA.
Andreasen, N.C., Pressler, M., Nopoulos, P., Miller, D., Ho, B.C., 2010. Antipsychotic dose equivalents and dose-years: a standardized method for comparing exposure to different drugs. Biological Psychiatry 67 (3), 255–262.
Barch, D.M., Carter, C.S., Braver, T.S., Sabb, F.W., MacDonald 3rd, A., Noll, D.C., Cohen, J.D., 2001. Selective deficits in prefrontal cortex function in medication-naive patients with schizophrenia. Archives of General Psychiatry 58 (3), 280–288.
Bechara, A., Damasio, A.R., Damasio, H., Anderson, S.W., 1994. Insensitivity to future consequences following damage to human prefrontal cortex. Cognition 50 (1–3), 7–15.
Bechara, A., Tranel, D., Damasio, H., Adolphs, R., Rockland, C., Damasio, A.R., 1995. Double dissociation of conditioning and declarative knowledge relative to the amygdala and hippocampus in humans. Science 269 (5227), 1115–1118.
Carter, C.S., Perlstein, W.M., Ganguli, R., Brar, J., Mintun, M.A., Cohen, J., 1998. Functional hypofrontality and working memory dysfunction in schizophrenia. American Journal of Psychiatry 155 (9), 1285–1287.
Cheng, G.L., Tang, J.C., Li, F.W., Lau, E.Y., Lee, T.M., 2012. Schizophrenia and risk-taking: impaired reward but preserved punishment processing. Schizophrenia Research 136 (1–3), 122–127.
Cohen, A.S., Minor, K.S., 2010. Emotional experience in patients with schizophrenia revisited: meta-analysis of laboratory studies. Schizophrenia Bulletin 36 (1), 143–150.
De Martino, B., Camerer, C.F., Adolphs, R., 2010. Amygdala damage eliminates monetary loss aversion. Proceedings of the National Academy of Sciences of the United States of America 107 (8), 3788–3792.
De Martino, B., Kumaran, D., Seymour, B., Dolan, R.J., 2006. Frames, biases, and rational decision-making in the human brain. Science 313 (5787), 684–687.
Dickinson, D., Bellack, A.S., Gold, J.M., 2007. Social/communication skills, cognition, and vocational functioning in schizophrenia. Schizophrenia Bulletin 33 (5), 1213–1220.
Ehrlich, S., Yendiki, A., Greve, D.N., Manoch, D.S., Ho, B.C., White, T.L., Schulz, S.C., Goff, D.C., Gollub, R.L., Holt, D.J., 2012. Striatal function in relation to negative symptoms in schizophrenia. Psychological Medicine 42, 267–282.
First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 1997. Structured Clinical Interview for DSM-IV-Axis I Disorders (SCID-I). American Psychiatric Press, Washington, DC.
Firth, D., 1993. Bias reduction of maximum likelihood estimates. Biometrika 80 (1), 27–38.
Fond, G., Bayard, S., Capdevielle, D., Del-Monte, J., Mimoun, N., Macgregor, A., Boulenger, J.P., Gely-Nargeot, M.C., Raffard, S., 2013. A further evaluation of decision-making under risk and under ambiguity in schizophrenia. European Archives of Psychiatry and Clinical Neurosciences 263 (3), 249–257.
Frank, M.J., Claus, E.D., 2006. Anatomy of a decision: striato-orbitofrontal interactions in reinforcement learning, decision making, and reversal. Psychological Review 113, 300–326.
Gold, J.M., Waltz, J.A., Kasanova, Z., Strauss, G.P., Matveeva, T.M., Herbener, E.S., Frank, M.J., 2012. Negative symptoms and the failure to represent the expected reward value of actions: behavioral and computational modeling evidence. Archives of General Psychiatry 69 (2), 129–138.
Goldman-Rakic, P.S., 1994. Working memory dysfunction in schizophrenia. Journal of Neuropsychiatry and Clinical Neuroscience 6 (4), 348–357.
Grace, A.A., 2000. Gating of information flow within the limbic system and the pathophysiology of schizophrenia. Brain Research Reviews 31 (2–3), 330–341.
Green, M.F., Nuechterlein, K.H., Gold, J.M., Barch, D.M., Cohen, J., Essock, S., Fenton, W.S., Frese, F., Goldberg, T.E., Heaton, R.K., Keefe, R.S., Kern, R.S., Kraemer, H., Stover, E., Weinberger, D.R., Zalcman, S., Marder, S.R., 2004. Approaching a consensus cognitive battery for clinical trials in schizophrenia: the NIMH-MATRICS conference to select cognitive domains and test criteria. Biological Psychiatry 56 (5), 301–307.
Heerey, E.A., Bell-Warren, K.R., Gold, J.M., 2008. Decision-making impairments in the context of intact reward sensitivity in schizophrenia. Biological Psychiatry 64 (1), 62–69.
Hutton, S.B., Murphy, F.C., Joyce, E.M., Rogers, R.D., Cuthbert, I., Barnes, T.R., McKenna, P.J., Sahakian, B.J., Robbins, T.W., 2002. Decision making deficits in patients with first-episode and chronic schizophrenia. Schizophrenia Research 55 (3), 249–257.
Kahneman, D., 2003. A perspective on judgment and choice: mapping bounded rationality. American Psychologist 58 (9), 697–720.

Kahneman, D., Tversky, A., 1979. Prospect theory: an analysis of decision under risk. Econometrica 47, 263–291.
Kirkpatrick, B., Strauss, G.P., Nguyen, L., Fischer, B.A., Daniel, D.G., Cienfuegos, A., Marder, S.R., 2011. The brief negative symptom scale: psychometric properties. Schizophrenia Bulletin 37 (2), 300–305.
Ludvig, E.A., Spetch, M.L., 2011. Of black swans and tossed coins: is the description-experience gap in risky choice limited to rare events? PLoS One 6 (6), e20262.
Overall, J.E., Gorman, D.R., 1962. The Brief Psychiatric Rating Scale. Psychological Reports 10, 799–812.
Park, S., Holzman, P.S., 1992. Schizophrenics show spatial working memory deficits. Archives of General Psychiatry 49 (12), 975–982.
Phan, K.L., Wager, T.D., Taylor, S.F., Liberzon, I., 2004. Functional neuroimaging studies of human emotions. CNS Spectrum 9 (4), 258–266.
Rabin, M., Thaler, R.H., 2001. Anomalies: risk aversion. Journal of Economic Perspectives 15 (1), 219–232.
Sevy, S., Burdick, K.E., Visweswaraiah, H., Abdelmessih, S., Lukin, M., Yechiam, E., Bechara, A., 2007. Iowa gambling task in schizophrenia: a review and new data in patients with schizophrenia and co-occurring cannabis use disorders. Schizophrenia Research 92 (1–3), 74–84.
Tom, S.M., Fox, C.R., Trepel, C., Poldrack, R.A., 2007. The neural basis of loss aversion in decision-making under risk. Science 315 (5811), 515–518.
Tremeau, F., Brady, M., Saccente, E., Moreno, A., Epstein, H., Citrome, L., Malaspina, D., Javitt, D., 2008. Loss aversion in schizophrenia. Schizophrenia Research 103 (1–3), 121–128.
Trepel, C., Fox, C.R., Poldrack, R.A., 2005. Prospect theory on the brain? Toward a cognitive neuroscience of decision under risk. Brain Research Cognition and Computation 23 (1), 34–50.
Tversky, A., Kahneman, D., 1981. The framing of decisions and the psychology of choice. Science 211 (4481), 453–458.
von Neumann, J., Morgenstern, O., 1947. Theory of Games and Economic Behavior. Princeton University Press, Princeton, NJ.
Waltz, J.A., Frank, M.J., Robinson, B.M., Gold, J.M., 2007. Selective reinforcement learning deficits in schizophrenia support predictions from computational models of striatal-cortical dysfunction. Biological Psychiatry 62 (7), 756–764.
Wechsler, D., 1999. Wechsler Abbreviated Scale of Intelligence (WASI). The Psychological Corporation, San Antonio TX.
Wechsler, D., 2001. Wechsler Test of Adult Reading (WTAR). The Psychological Corporation, San Antonio, TX.
Wilkinson, G.S., Robertson, G.J., 2006. Wide Range Achievement Test 4: Professional Manual. Psychological Assessment Resources, Inc, Lutz, FL.
Wolkin, A., Sanfilipo, M., Wolf, A.P., Angrist, B., Brodie, J.D., Rotrosen, J., 1992. Negative symptoms and hypofrontality in chronic schizophrenia. Archives of General Psychiatry 49 (12), 959–965.