

# Negative Symptoms of Schizophrenia Are Associated with Abnormal Effort-Cost Computations

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**Background:** Decision-making studies show that response selection is influenced by the “effort cost” associated with response alternatives. These effort-cost calculations seem to be mediated by a distributed neural circuit including the anterior cingulate cortex and subcortical targets of dopamine neurons. On the basis of evidence of dysfunction in these systems in schizophrenia (SZ), we examined whether effort-cost computations were impaired in SZ patients and whether these deficits were associated with negative symptoms.

**Methods:** Effort-cost decision-making performance was evaluated in 44 patients with SZ and 36 demographically matched control subjects. Subjects performed a computerized task where they were presented with a series of 30 trials in which they could choose between making 20 button presses for \$1 or 100 button presses for higher amounts (varying from \$3 to \$7 across trials). Probability of reward receipt was also manipulated to determine whether certain (100%) or uncertain (50%) reward affected effort-based decision-making.

**Results:** Patients were less likely than control subjects to select the high-effort response alternative during the 100% probability condition, particularly when the value payoff was highest (i.e., \$6 and \$7). Patients were also less likely to select the high-effort option on trials after reward in the 50% probability condition. Furthermore, these impairments in effort-cost computations were greatest among patients with elevated negative symptoms. There was no association with haloperidol equivalent dosage.

**Conclusions:** The motivational impairments of SZ might be associated with abnormalities in estimating the “cost” of effortful behavior. This increased effort cost might undermine volition.

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**Key Words:** Decision-making, effort-cost, psychosis, reward, schizophrenia, value

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Many people with schizophrenia (SZ) demonstrate persistent negative symptoms such as reductions in emotional expressivity, spontaneous speech, initiation of goal-directed behavior, and seeking out rewarding experiences (1). Although the functional importance of negative symptoms is well-established (2,3), their cause remains unclear. The idea that reduced hedonic experience might underlie in negative symptoms has long been assumed (4,5). However, recent laboratory-based [see, for example, Cohen and Minor (6)] and real-world experience sampling studies (7,8) demonstrating surprisingly intact in-the-moment hedonic experience in SZ seem to undermine this causal explanation [see Strauss and Gold (9) for a recent review]. Although hedonic experience might be intact in SZ, it is clear that many patients display reductions in behaviors motivated by goals and rewards. Thus, the question of why patients with a normal capacity for pleasure fail to pursue rewarding activities remains unanswered.

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One possible explanation for why individuals with SZ have difficulty translating normal hedonic experiences into motivated behavior is that they have difficulty forming mental representations of prospective reward value that are crucial for decision-making (10,11). Evidence for this comes from studies demonstrating that patients have impairments in linking reward value to different stimuli and response alternatives and that these deficits are associated with working memory ability and clinically rated negative symptoms, particularly anhedonia and avolition (11–19). In essence, the “pull” from the future prospect of a reward is too weak to invigorate and direct behavior in the present. This leads to a reduced tendency to exploit favorable contingencies and reduced facilitation of behaviors in the service of reward pursuit (11,18,19). Although this account is supported by experimental data, it fails to consider an important aspect of decision making—the “cost” of the effort that is involved in pursuing a future goal. One could have a clear representation of the value of a future goal but fail to pursue that goal, because the cost of the required effort outweighs the anticipated benefit.

There are several reasons to suspect that effort-cost computations might be altered in SZ. There is a large body of behavioral research in rodents and functional neuroimaging in humans that suggest that the effort computations involve a distributed neural circuit that involves the cingulate cortex and subcortical targets of dopamine neurons (20,21), neural systems implicated in SZ (22,23). Furthermore, in healthy volunteers, higher scores on a trait anhedonia measure correlated with increased effort-cost computations, with additional evidence that willingness to expend effort for low probability outcomes is directly related to individual differences in striatal dopamine activity (24,25). Interestingly, the transgenic mouse model that over-expresses striatal dopamine D2 receptors shows intact hedonics coupled with reduced reward-seeking effort (26). Additionally, there is robust evidence that dopamine D2 antagonists reduce reward-seeking

effort (21). Thus, altered effort-cost computations might be expected as a function of the diagnosis of SZ, negative symptom severity, or as a consequence of antipsychotic treatment. This experiment was designed to explore these three paths to increased effort-cost computations, guided by the hypothesis that negative symptom severity will be related to decreased willingness to expend effort to gain rewards.

## Methods and Materials

### Participants

Forty-four individuals (42 outpatients, 2 inpatients) meeting DSM-IV (27) criteria for SZ ( $n = 36$ ) or schizoaffective disorder ( $n = 8$ , none in mood episode at time of testing) and 36 healthy control subjects (CN) participated in the study. Patient and control groups did not significantly differ on age, parental education, gender, or ethnicity (Table 1). All patients were taking stable doses of medication for at least 4 weeks at the time of testing and were considered to be clinically stable by treatment providers. The outpatients were recruited from the Maryland Psychiatric Research Center outpatient clinics, other local clinics, and inpatients from the Maryland Psychiatric Research Center Treatment Research Unit as they were awaiting discharge.

Healthy control participants were recruited from the community via random digit dialing, word of mouth among participants, and newspaper advertisements. Control subjects had no current Axis I or II diagnoses as established by the Structured Clinical Interview for DSM-IV Axis I Disorders (28) and Structured Interview for DSM-IV Personality (29), no family history of psychosis, and were not taking psychotropic medications. All participants denied a history of significant neurological injury or disease and significant medical or substance use disorders within the last 6 months. All participants provided informed consent for a protocol approved by the University of Maryland School of Medicine Institutional Review Board.

To examine the role of negative symptoms, the patients were divided into high (HI-NEG) and low negative symptom (LOW-NEG) sub-groups with a median split on the Brief Negative Symptom Scale (BNSS) (30) total score (split score = 21). The three groups did not significantly differ in age, gender, parental education, or ethnicity (Table 1). Control subjects completed significantly more years of education than both patient groups, whereas the patient groups did not differ from each other. Both patient groups displayed moderate symptom severity on the Brief Psychiatric Rating Scale (BPRS) (31) total scores. The two patient groups differed on the severity of the BPRS negative symptom factor but not BPRS psychosis, disorganization, or total symptom scores. There were no differences between the two patient groups on the proportion of patients prescribed conventional or atypical antipsychotics or haloperidol equivalent dosage (32).

### Effort-Cost Computation Task

Participants completed a computerized effort-cost decision-making task that examined the effects of reward value and probability on making "high" and "low" effort decisions. In this task, participants were told that they would be making decisions between two response alternatives: an easy option with a lower reward and a more difficult option with a higher reward (see Figure 1 for trial example). The effortful task that they had to perform was to use a game controller to press alternating left-right buttons to inflate a balloon on the computer screen until it popped. They were free to pick either balloon, with each alternative explicitly indicating the number of pumps required and corresponding value for popping it continuously displayed on the screen. For each trial, the probability (either 50% or 100%) for receiving a reward from the choice of either response was displayed between the two choice locations, and was the same for both choices. Participants were told that they would receive a task bonus at the end of the study that was based upon their choices. In actuality, all subjects were paid a \$5 bonus.

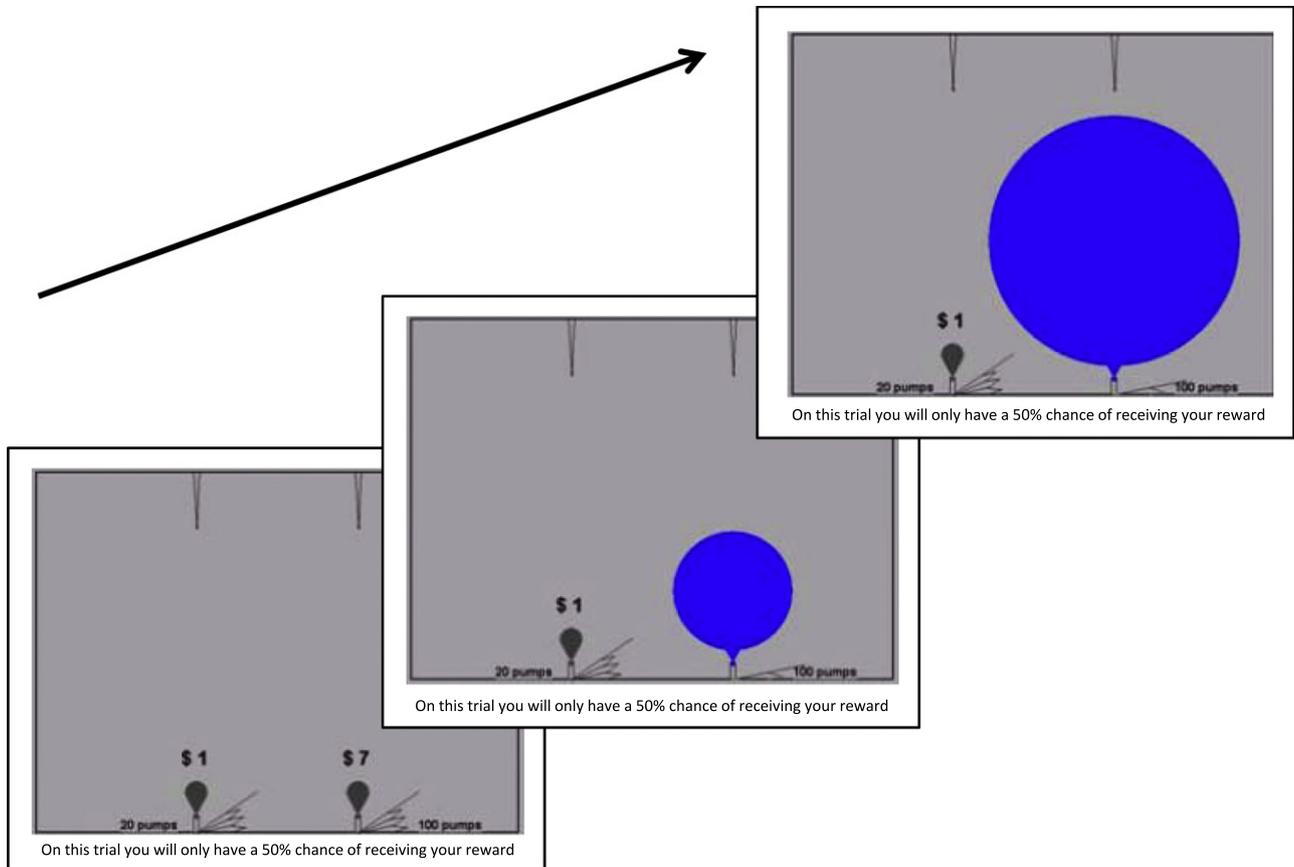
**Table 1.** Demographic and Clinical Characteristics for SZ and CN Groups

	SZ ( $n = 44$ )	CN ( $n = 36$ )	Test Statistic	$p$	HI-NEG	LOW-NEG	Test Statistic <sup>a</sup>	$p^a$
Age	41.0 (10.8)	39.4 (11.0)	$F = .46$	.50	40.3 (11.0)	42.2 (10.8)	$F = .46$	.64
Participant Education	12.5 (2.2)	14.8 (1.9)	$F = 24.2$	<.001	12.14 (11.0)	12.95 (10.8)	$F = 12.5$	<.001
Parental Education	13.4 (2.5)	13.3 (1.9)	$F = .04$	.85	12.82 (2.3)	13.93 (2.7)	$F = 1.3$	.28
% Male	63.6%	61.1%	$\chi^2 = .05$	.82	66.7%	63.6%	$\chi^2 = .18$	.92
Ethnicity			$\chi^2 = .87$	.83			$\chi^2 = 5.62$	.47
American Indian	2.3%	.0%			4.8%	.0%		
African-American	36.4%	38.9%			47.6%	27.3%		
Mixed race	2.3%	2.8%			.0%	4.5%		
Caucasian	59.1%	58.3%			47.6%	68.2%		
Medication								
Haloperidol equivalent	11.7 (7.4)	—	—	—	11.8 (7.1)	11.7 (8.0)	$F = .01$	.94
Symptoms								
BNSS total	21.3 (17.8)	—	—	—	36.3 (12.8)	7.0 (6.3)	$F = 91.9$	<.001
BPRS total	34.7 (8.2)	—	—	—	36.2 (8.0)	33.8 (8.1)	$F = .99$	.33
BPRS psychosis	2.2 (1.1)	—	—	—	2.09 (1.0)	2.40 (1.3)	$F = .77$	.39
BPRS disorganized	1.4 (.4)	—	—	—	1.29 (.3)	1.43 (.4)	$F = 2.03$	.16
BPRS negative	1.7 (.6)	—	—	—	2.06 (.6)	1.40 (.5)	$F = 14.95$	<.001

All patients were receiving antipsychotic medication: 11 were receiving first-generation antipsychotics, 21 were receiving clozapine, 19 were receiving a second-generation antipsychotic other than clozapine, 8 were receiving more than one second-generation antipsychotic, 25 were receiving an antidepressant, 14 were receiving an anti-anxiety medication, 7 were receiving an anticholinergic, and 8 were receiving a mood stabilizer.

BPRS, Brief Psychiatric Rating Scale; SZ, schizophrenia.

<sup>a</sup>Test statistics and  $p$  values reflect three group analyses, conducted on high (HI-NEG) and low negative symptom (LOW-NEG), and healthy control (CN) groups. Note that one patient was missing Brief Negative Symptom Scale (BNSS) ratings and was only included in the overall SZ versus CN analyses.



**Figure 1.** Effort-cost task trial sequence. Participants initially select which balloon they want to pop. The easy selection always offers \$1 for 20 button presses. The hard selection offers \$3–\$7 for 100 presses. After each press the size of the balloon increases in proportion to how many presses are needed to reach the pin at the top of screen.

Once the subject selected an alternative, each button press resulted in a fan-like motion by an object resembling a fireplace bellow that visually inflated the balloon and produced a “pumping” sound. The balloon expanded with each press until it reached the pin at the top of the screen where it popped, making a popping sound. After it popped, a message appeared where the balloons had been indicating the amount of money that resulted from that trial (ranging from \$0 to \$7). A running tally of total earnings was displayed in the lower right corner of the screen.

On each trial, the easy alternative required 20 button presses to pop the balloon, whereas the difficult alternative required 100 button presses. The easy alternative offered a payoff of \$1. The effortful alternative offered \$3, \$4, \$5, \$6 or \$7 payoffs, in equal proportions of trials. On half of all trials, the payoff was certain (100%), whereas on the other half the payoff was uncertain (50% payoff). Both the payoff probability and payoff amounts were presented on the screen throughout the trial. Trials were presented in a pseudo-random order, with certain- and uncertain-payoff trials mixed in the same block. A total of 60 trials were administered (30 uncertain, 30 certain), with 6 trials of each type (1 vs. 3, 1 vs. 4, and so forth) administered in each condition.

Effort-cost decision-making was quantified as the percentage of difficult and easy item selections, examined in relation to potential payoff value and probability. Note that the payoff in the easy condition, at \$1/20 presses, corresponds to 5 cents/press. Participants who base their effort allocation purely on the ratio of rewards to presses should never select the difficult alternative when the

reward is \$3 or \$4, should be equally likely to pick the \$1 as the \$5 alternatives, and should always pick the effortful alternative when the reward is \$6 or \$7. Alternatively, participants seeking to maximize total reward should always choose the effortful response.

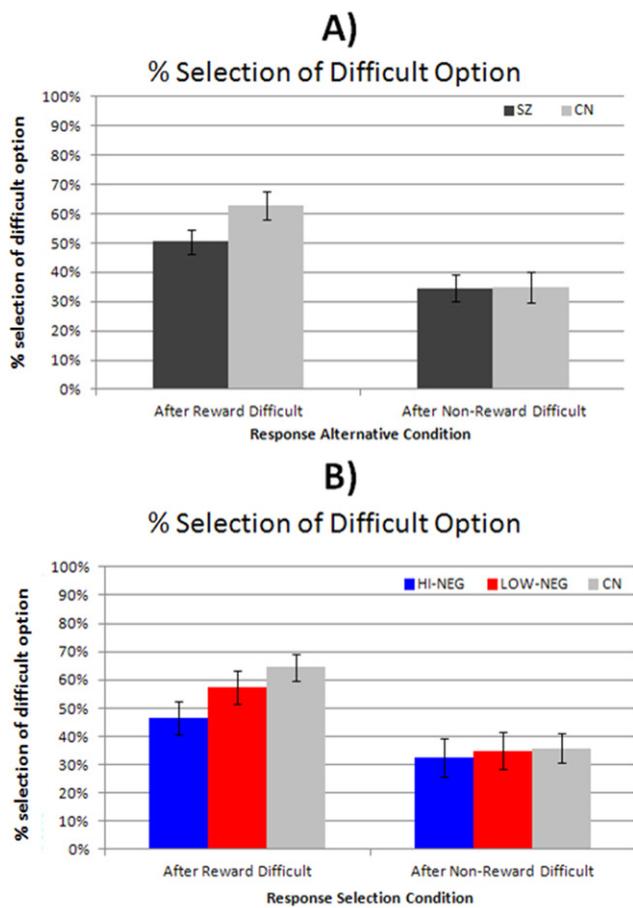
## Results

### Selection of Effortful Alternative in Relation to Value

Panels A and B of Figure 2 present the proportion of effortful response alternative selections as a function of potential gain value (\$3–\$7). A 2 Group (SZ vs. CN)  $\times$  2 Probability (50% vs. 100%)  $\times$  5 Value (\$3, \$4, \$5, \$6, \$7) repeated-measures analysis of variance (ANOVA) indicated significant within-subjects effects of probability [ $F_{1,78} = 120.6, p < .01$ ] and value [ $F_{4,78} = 61.90, p < .001$ ]. However, the between-subjects effect was nonsignificant [ $F_{1,78} = 1.12, p = .29$ ]. These analyses indicate that, overall, participants rationally traded off effort with expected utility reflected by probability and magnitude of the prospective payoff. The Probability  $\times$  Value [ $F_{4,78} = 7.20, p < .001$ ] and Probability  $\times$  Group [ $F_{1,78} = 16.34, p < .001$ ] interactions were significant, and there was marginally significant Value  $\times$  Group interaction [ $F_{2,5,78} = 2.71, p = .058$ ]. The Probability  $\times$  Value  $\times$  Group interaction was nonsignificant [ $F_{2,96,78} = .96, p = .43$ ].

To follow-up the significant interactions, a series of one-way ANOVAs were conducted. Results indicated significant group differences for the \$5 condition [ $F_{1,78} = 5.28, p = .024$ ], \$6 condition





**Figure 3.** Probability of selecting the difficult effort alternative after prior reward or nonreward in the 50% probability condition. (A) Both SZ and CN are more likely to select the more difficult response alternative after receiving a reward on the prior trial. (B) The patient data are split into HI-NEG and LOW-NEG symptom groups. Abbreviations as in Figure 2.

With regard to the role of negative symptoms, a repeated-measures ANOVA indicated a significant Group × Condition interaction [ $F_{2,69} = 3.78, p < .03$ ]. Follow-up one-way ANOVAs indicated a trend toward a group difference in the probability of selecting the effortful option after reward in the 50% probability condition [ $F_{2,69} = 2.82, p = .07$ ]. There were no differences after nonreward [ $F_{2,69} = .07, p = .93$ ]. Independent-samples *t* tests indicated that the HI-NEG selected a significantly lower proportion of effortful choices after reward than CN ( $p < .02$ ); however, there were no differences between HI-NEG and LOW-NEG or LOW-NEG and CN.

We found no significant differences in SZ vs. CN or three-group analyses when we examined the tendency to repeat prior decisions, make effortful choices on trials after reward across

probabilities, or repeat decisions specifically in the 100% probability condition. Thus, prior rewards have less influence on subsequent allocation of effortful behavior in HI-NEG patients only when these rewards are uncertain (Figure 3B).

**Total Task Completion Time and Response Vigor**

As shown in Table 2, patients took significantly longer to complete the task than CN. Additionally, HI-NEG patients had higher total task completion time than CN ( $p < .001$ ) but did not differ from LOW-NEG ( $p = .16$ ). The CN and LOW-NEG did not differ in total task completion time ( $p = .08$ ).

Response vigor was examined by calculating the average number of presses/sec for high and low-effort options. The SZ had less response vigor than CN in both the high- and low-effort conditions, and this difference was most pronounced in HI-NEG patients who made fewer clicks/sec than CN in the low ( $p < .001$ ) and high-effort conditions ( $p < .001$ ) and showed a trend toward less clicks/sec than LOW-NEG patients in low-effort ( $p = .051$ ) and high-effort conditions (.061). The LOW-NEG patients did not differ from CN in the high-effort condition ( $p = .12$ ) but had fewer clicks/sec than CN in the low-effort condition ( $p < .001$ ) (Table 2). Such reductions in response vigor, across effort conditions, likely reflect the motor slowing typical of SZ.

**Role of Specific Symptoms and Antipsychotics**

Effort-based decision making would seem to be most relevant for clinical ratings of avolition and anhedonia. We examined Spearman correlations between these subscales from the BNSS and selection of the high-effort option in relation to value, and although they were in the expected direction, none of the correlations approached significance. Median splits on the basis of these same symptom ratings produced the same pattern of results as observed with the BNSS total score but fell short of significance. Similarly, Spearman correlations between BNSS total score and selection of the high-effort option in relation to value were nonsignificant, whereas the use of a categorical approach, as presented in the preceding text [and in Gold et al. (11) and Strauss et al. (18)], did yield significant effects (Figures 2 and 3). Higher avolition ( $r = -.32, p < .04$ ) and total negative symptoms ( $r = -.33, p < .04$ ) on the BNSS were associated with less response vigor in the low-effort condition, and there were trends for these scores in the high-effort condition: avolition:  $r = -.30, p = .06$ ; total:  $r = -.26, p = .10$ . There were no significant correlations between task variables and BPRS positive, disorganized, negative, or total symptom scores.

We also examined the role of antipsychotic medication dose through the use of the Andreasen et al. (32) haloperidol equivalent dosage conversion tables. There were two important results: 1) as shown in Table 1, the HI-NEG and LOW-NEG groups did not differ in total antipsychotic dose burden; and 2) there were no significant Pearson or Spearman correlations between willingness to choose the effortful response alternative, total completion time, or response vigor and total antipsychotic dose. Thus, it does not seem that our findings are related to amount of antipsychotic

**Table 2.** Total Task Completion Time and Response Vigor Estimates of Effortful Behavior

	SZ	CN	<i>F, p</i>	HI-NEG	LOW-NEG	<i>F, p</i> (3-group comparison)
Total Task Completion Time	31.4 min (14.9)	22.9 min (8.9)	$F = 8.80, <.01$	34.5 min (17.5)	29.0 min (11.9)	$F = 5.72, <.01$
Response Vigor						
Low-effort	2.6 (.67)	3.8 (.75)	$F = 53.51, <.001$	2.4 (.65)	2.8 (.65)	$F = 28.9, <.001$
High-effort	2.9 (.80)	3.48 (.70)	$F = 10.24, <.01$	2.71 (.79)	3.16 (.79)	$F = 6.80, <.01$

Abbreviations as in Table 1.

medication that patients were receiving, and that the LOW-NEG group did not differ reliably from the CN on effort-based decision making suggests that the presence of antipsychotic medication, by itself, does not reliably alter these processes.

### Role of General Neuropsychological Impairment

To examine the contributions of neuropsychological functioning to effort-based decision-making, we calculated correlations between the MATRICS Consensus Cognitive Battery total score and percentage selection of the high-effort option at \$6, \$7 values, response vigor, and total task completion time. In CN, better general cognition was associated with greater likelihood of selecting the difficult option at \$6 ( $r = .52, p < .001$ ) and \$7 ( $r = .53, p < .001$ ) values; however, relationships with response vigor and task completion time were nonsignificant. In SZ, better general cognition was associated with greater likelihood of selecting the difficult option at \$6 ( $r = .41, p < .01$ ) and \$7 ( $r = .32, p < .04$ ) values, more response vigor ( $r = .60, p < .001$ ), and shorter task completion time ( $r = -.40, p < .01$ ). In SZ, significant correlations between effortful decision making indices were observed with the processing speed, verbal and visual memory, and reasoning/problem solving domain scores (all  $p < .05$ ) with more robust correlations observed with the composite score. Thus, across groups, better cognitive performance was associated with willingness to exert more effort for high value choices.

### Discussion

These data suggest that negative symptoms are associated with abnormalities in effort-cost calculations. Patients with higher levels of negative symptoms were less willing to increase effort for higher levels of reward and were also less responsive to the receipt of an uncertain reward in motivating subsequent effortful behavior. This alteration in decision making was accompanied by more general evidence of reduced behavioral activation as seen in decreased response vigor in both high- and low-effort conditions and increased time needed to complete the task despite selecting more low-effort choices. These abnormalities were largely shared across the HI- and LOW-NEG groups.

One reason the HI-NEG group might have worked less for higher reward values is that they did not value them as highly as did CN. Therefore, the HI-NEG patients could have chosen the higher effort response less frequently because they found the increased level of effort involved to be aversive or because the reward that was available was not “worth” the amount of added effort or both.

That the HI-NEG patients did not differ from CN in the \$3–\$5 trials and did not differ from CN on the 50% probability trials might be evidence that it is not purely effort aversion at work. That is, if one is effort-averse, it would be most sensible to avoid that effort when the payoff and probability of payoff is the lowest. This suggests that the HI-NEG patients might fail to value higher levels of reward. Although HI-NEG SZ patients did increase their numbers of high-effort responses as reward value increased, this increase was less pronounced than in the other groups. That is, HI-NEG patients are not simply unwilling to make high-effort responses, but they are less likely to do so, depending on a rougher cost/benefit calculation.

In prior work, we have shown that patients have difficulty representing the expected value of response alternatives (11) in reinforcement learning paradigms, and demonstrated inconsistent preferences in simple decision-making tasks (19). Such

degradation in the representation of value could undermine effort-based decision-making. Simply put, it is hard for the benefits to outweigh the costs if benefits are not represented precisely, particularly if the costs are salient. This would seem to be the situation with the 100% probability trials: the effort cost might be more salient (100 presses vs. 20) than the differences in relative reward values. In the 50% probability trials, the risk of nonreward was so salient that it drove down effort expenditure in all groups. Thus, it seems that the 100% trials were most sensitive to the effort-cost computations associated with negative symptom severity. Thus, both altered effort computations and altered representations of value are likely implicated in motivational deficits. These “cognitive” abnormalities are accompanied by evidence of reduced response vigor and task engagement.

That this effect was found with the total negative symptom score and not when using the avolition or anhedonia items is somewhat surprising, given our theoretical framework. The link between increased effort-cost computations and avolition/anhedonia is clear, whereas that is less true of decreased emotional expressivity and alolia. Although negative symptom rating scales typically yield two factors (one expressive, one experiential) (33), these factors are typically moderately correlated, suggesting that they co-vary within patients. Thus, that we observed the expected effects with the total score might reflect the greater sensitivity derived from the increased number of items. It is also noteworthy that the predicted effects were not observed with correlations between task behavior and either total or individual negative symptom domain scores, but significant effects were detected with a categorical approach. This is a violation of the general rule that continuous data offer greater power than categorical approaches. However, categorical approaches would offer greater power if low levels of negative symptoms were, to some extent, secondary consequences of factors such as extra-pyramidal side effects, depression, and the impact of positive symptoms, whereas higher levels of severity were more often a part of the primary psychopathology, as suggested by Kirkpatrick *et al.* (34).

Treadway *et al.* (35) recently reported very similar alterations of effort-based decision making in depressed patients. This is striking because anhedonia is one of the diagnostic criteria for depression. Nonetheless, the results raise the possibility that there might be different paths to the same behavioral outcome in different clinical populations.

Patients with low levels of negative symptoms did not show reliably altered effort-cost computation, suggesting that the impairment is primarily related to negative symptom severity rather than the diagnosis of SZ. Interestingly, willingness to expend effort was associated with cognitive performance in CN and patients—more cognitively able participants chose to work for payoffs that rewarded their effort expenditure most advantageously, a very practical form of intelligence. Results also suggest that altered effort-cost computations in SZ do not seem to be a consequence of antipsychotic treatment-induced dopaminergic blockade. We found neither correlation with total antipsychotic burden nor differences in dose between the HI-NEG and LOW-NEG groups. This finding, in a clinical population, does not in any way challenge the basic neuroscience evidence linking dopamine function and effort computation (21). Note that a tonic effect of dopamine blockade would be expected to increase the overall cost of effort, perhaps especially for low-value choices. Instead, the present results are consistent with a mechanism by which the higher expected values of rewarding options are discounted. We speculate that this might result from degraded orbitofrontal and/or anterior cingulate function, given the literature linking these

areas to expected value computations and our previous evidence linking negative symptoms to orbitofrontal dysfunction (11). Moreover, it is possible that prefrontal expected value computations are necessary in the healthy state to drive phasic increases in subcortical dopamine when the reward benefit is high and that these increases drive motivated responding in high-effort conditions. Indeed, Gan *et al.* (36) showed evidence in rodents for phasic DA elevations for high-value options. Thus, given the lack of relationship with antipsychotic dose and the lack of effect at lower values, it seems likely that the patient deficit is not related to tonic dopamine blockade but rather to dysfunction in upstream computations of reward values.

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