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Effort, Avolition, and Motivational Experience in Schizophrenia: Analysis of Behavioral and Neuroimaging Data With Relationships to Daily Motivational Experience

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Abstract

Recent research suggests that schizophrenia is associated with reduced effort allocation. We examined the willingness to expend effort, neural correlates of effort allocation, and the relationship of effort to daily motivational experience in individuals with schizophrenia. We recruited 28 individuals with schizophrenia and 30 control participants to perform an effort task during functional MRI. Individuals with schizophrenia also completed a protocol involving ecological momentary assessment (EMA). Individuals with schizophrenia with severe negative symptoms were less willing to expend effort for rewards. Daily EMAs of motivation were positively associated with effort allocation on a trend level. Individuals with schizophrenia and control participants displayed similar increases in blood-oxygen-level-dependent (BOLD) activation in frontal, cingulate, parietal, and insular regions during effort-based decision making. However, negative symptoms were associated with reduced BOLD activation in the bilateral ventral striatum. These results replicate previous reports of reduced effort allocation in patients with severe negative symptoms and provide evidence for the role of the ventral striatum in effort impairments.

Keywords

affective neuroscience, cognitive neuroscience, decision making, neuroimaging, schizophrenia

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Many individuals with schizophrenia experience prominent negative symptoms, such as reductions in motivation and decreased initiation and pursuit of goals. Such symptoms are associated with worse social and occupational functioning in individuals with schizophrenia, and thus motivational impairment represents an important target for treatment (Milev, Ho, Arndt, & Andreasen, 2005). However, current intervention strategies are marginally effective at best in treating these symptoms. Poor treatment efficacy may stem from an inadequate mechanistic understanding of factors that give rise to motivational impairment in schizophrenia. Although many potential contributory mechanisms have been proposed (Barch & Dowd, 2010; Gold, Waltz, Prentice, Morris, & Heerey, 2008; Kring & Moran, 2008), recent work has examined the possibility that motivational impairment in schizophrenia might arise from aberrant effort-based decision making (Barch, Treadway, &

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Schoen, 2014; Culbreth, Westbrook, & Barch, 2016; Docx et al., 2015; Fervaha et al., 2013, 2015; Gold et al., 2013, 2014; Hartmann et al., 2015; Horan et al., 2015; Huang et al., 2016; McCarthy, Treadway, Bennett, & Blanchard, 2016; Moran, Culbreth, & Barch, 2017; Park, Lee, Kim, Kim, & Koo, 2017; Reddy et al., 2015; Serper, Payne, Dill, Portillo, & Taliercio, 2017; Strauss et al., 2016; Treadway, Peterman, Zald, & Park, 2015; Wang et al., 2015; Wolf et al., 2014).

Effort-based decision making refers to mental calculations that individuals perform to estimate the costs and benefits of engaging in a particular action. For example, a student might estimate the subjective cost of studying an additional hour in hopes of achieving a better grade on an upcoming exam. There are important individual differences in effort estimates (e.g., some students might find the extra study time worth the prospect of a higher grade and thus expend the effort whereas others may not). Recent clinical research has found that individuals with schizophrenia are less willing than control participants to exert effort to obtain monetary rewards on experimental tasks (Barch et al., 2014; Culbreth et al., 2016; Fervaha et al., 2013; Gold et al., 2013; Huang et al., 2016; McCarthy et al., 2016; Reddy et al., 2015; Treadway et al., 2015; Wang et al., 2015; Wolf et al., 2014). Many studies have also shown that this deficit in effort exertion is linked to clinician-rated (Barch et al., 2014; Culbreth et al., 2016; Gold et al., 2013; Hartmann et al., 2015; Horan et al., 2015; Moran et al., 2017; Strauss et al., 2016; Treadway, Bossaller, Shelton, & Zald, 2012; Wang et al., 2015; Wolf et al., 2014) and ambulatory (Moran et al., 2017) assessments of motivational impairment in individuals with schizophrenia, such that schizophrenia patients with prominent motivational impairment demonstrate the least willingness to exert effort.

Alongside clinical research, work in basic neuroscience has begun to delineate the neural circuits associated with effort-based decision making. There is consistent evidence from animal studies that striatal dopamine is critically linked to effort allocation (Salamone, Koychev, Correa, & McGuire, 2015; Salamone, Wisniecki, Carlson, & Correa, 2001); for example, rodents depleted of striatal dopamine show reduced willingness to perform effortful tasks for rewards. The anterior cingulate cortex (ACC) has also been implicated in the integration of reward and cost information in the context of decision making (Floresco & Ghods-Sharifi, 2007; Floresco, Onge, Ghods-Sharifi, & Winstanley, 2008; Hosking, Cocker, & Winstanley, 2014), and specifically ablation of the ACC in rodents has been shown to reduce the choice of high-effort options. In humans, neuroimaging studies have found that blood-oxygenation-level-dependent (BOLD) activation in the ventral striatum (a region highly innervated by dopaminergic signals) varies as a function of effort (Croxson, Walton, O'Reilly, Behrens, & Rushworth, 2009; Kurniawan et al., 2010; Westbrook, Lamichhane, & Braver, 2019). Further, the dorsal ACC has been shown to integrate reward and cost information of potential actions (Croxson et al., 2009; Leotti & Delgado, 2011), suggesting a central role for this region in selecting and maintaining effortful action. Finally, the ventral medial prefrontal cortex has been shown to be critical to the valuation of actions (Treadway, Buckholtz, et al., 2012). Taken together, cortico-limbic-striatal circuits appear to be critical to effective effort-based decision making.

A limited number of studies have examined the neural correlates of effort-based decision-making deficits in individuals with schizophrenia. Huang et al. (2016) used a button-press paradigm in which individuals decided between performing an easy button-pressing task for a small reward or a hard button-pressing task for large reward during neuroimaging. They found that individuals with schizophrenia showed lower BOLD activation of the cingulate cortex, ventral striatum, and medial frontal gyrus compared with control participants during decision making. Likewise, although they did not directly examine the neural correlates of effort-based decision making, Wolf et al. (2014) demonstrated that BOLD activation in the ventral striatum and dorsolateral prefrontal cortex during reward processing positively correlated with behavioral measures of increased willingness to exert effort in individuals with schizophrenia. Thus, plausible regions of interest (ROIs) for the neural correlates of effort-based decision-making deficits in schizophrenia may be the lateral frontal cortex, cingulate cortex, and ventral striatum.

Although studies have consistently demonstrated reduced willingness of individuals with schizophrenia to exert effort for monetary rewards (for exceptions, see Docx et al., 2015; Strauss et al., 2016), several open questions remain. First, although diagnostic group differences are consistently reported, relationships between negative symptom severity in individuals with schizophrenia and effort allocation are less consistent. Thus, it is important to conduct additional studies to examine relationships between symptoms to replicate previous results. Second, although some work has been conducted examining cognitive effort in schizophrenia (Culbreth et al., 2016; Gold et al., 2014; Reddy et al., 2015), most studies have used physical effort-based decision-making tasks, and it is not currently known whether physical and cognitive effort-based decision making are associated with similar or disparate psychological processes and neural circuits (Schmidt, Lebreton, Cléry-Melin, Daunizeau, & Pessiglione, 2012). Thus, it is important to examine nonphysical tasks to observe

whether symptom and diagnostic group effects generalize across effort modality. Third, only one study to date has examined whether effort deficits measured in the lab show relationships to more ecologically valid assessments of motivation and emotionality (Moran et al., 2017), and tying experimental findings to daily motivational experience remains an important avenue for future research. Finally, although preliminary evidence suggests that patient deficits on effort-based decision-making tasks may be related to the hypoactivation of the striatum, cingulate cortex, and lateral prefrontal cortex (Huang et al., 2016; Wolf et al., 2014), more research is needed to examine the neural correlates of effort-based decision making in individuals with schizophrenia.

In the current study, we collected neuroimaging data from both control participants and individuals with schizophrenia during a well-validated cognitive effort-based decision-making task, the cognitive-effort-discounting (COGED) task (Westbrook, Kester, & Braver, 2013; Westbrook et al., 2019). Further, we collected ambulatory assessments of enjoyment and interest in daily activities of individuals with schizophrenia to observe whether willingness to expend effort and the neural correlates of effort-based decision making were associated with interest and enjoyment measured outside the lab. First, we examined whether individuals with schizophrenia were less willing than control participants to exert effort for monetary rewards. Given previous studies on aberrant effort-based decision making in individuals with psychosis (Culbreth, Moran, & Barch, 2018; Gold, Waltz, & Frank, 2015; Green, Horan, Barch, & Gold, 2015), we hypothesized that individuals with schizophrenia would be less willing than control participants to exert cognitive effort for monetary rewards, even after controlling for task performance (Culbreth et al., 2016). Further, we proposed an individual-differences relationship consistent with previous work, such that individuals with schizophrenia with the greatest negative symptom severity would be the least willing to exert effort (Culbreth et al., 2018; Gold et al., 2015b; Green et al., 2015). In addition, we proposed that this reduced willingness to expend effort would be associated with measures of enjoyment and interest collected in daily life, such that individuals with schizophrenia who were least willing to exert effort on experimental paradigms would also show the least interest and enjoyment in daily activities (Moran et al., 2017).

As a second aim, we also sought to gain preliminary evidence of the neural correlates of effort-based decision-making impairments in individuals with schizophrenia using functional MRI (fMRI). We hypothesized on the basis of previous studies (Croxson et al., 2009; Leotti & Delgado, 2011; Treadway et al., 2012) that BOLD activation in the cingulate cortex and frontal cortex would be enhanced across both control participants and those with schizophrenia during putatively difficult effort-based decision-making trials compared with putatively easy trials. However, we hypothesized that individuals with schizophrenia would show less robust recruitment of the striatum, cingulate cortex, and frontal cortex during putatively difficult compared with putatively easy effort-based decision-making trials and that activation in these regions would negatively correlate with motivational impairment.

Method

Participants

Study participants included 28 individuals meeting the criteria for schizophrenia or schizoaffective disorder given in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM–IV*; American Psychiatric Association, 1994) and 30 demographically matched control participants with no personal or family history of psychosis (First, Spitzer, Gibbon, & Williams, 2002). Participants were recruited from the St. Louis community. Exclusion criteria for individuals with schizophrenia included the following: (a) *DSM–IV* diagnosis of substance abuse or dependence in the past year, (b) *DSM–IV* diagnosis of a current major depressive episode or bipolar disorder, (c) changes in medication dosage 2 weeks before consent, (d) past head injury with documented neurological sequelae and/or loss of consciousness, (e) *Wechsler Test of Adult Reading* (WTAR) estimated full-scale IQ < 70 (Wechsler, 2001), and (f) fMRI contraindications. Exclusion criteria for control participants included the following: (a) *DSM–IV* diagnosis of substance abuse or dependence in the past year, (b) *DSM–IV* diagnosis of a current major depressive episode or bipolar disorder, (c) changes in medication dosage 2 weeks before consent, (d) past head injury with documented neurological sequelae and/or loss of consciousness, (e) WTAR estimated full-scale IQ < 70 (Wechsler, 2001), (f) fMRI contraindications, (g) personal or family history of psychosis, and (h) a current prescription for psychotropic medications. All participants were required to pass a urine drug screen before study participation. The Washington University Institutional Review Board approved the study, and participants provided written, informed consent in accordance with Washington University's Human Subjects Division criteria.

Clinical ratings

Diagnoses were determined by the Structured Clinical Interview for *DSM–IV-TR* (First et al., 2002). Negative symptoms were assessed using the Clinical Assessment

Interview for Negative Symptoms (CAINS; Kring, Gur, Blanchard, Horan, & Reise, 2013) conducted by either a master's- or doctoral-level clinician. Converging structural analyses of the CAINS have identified two moderately correlated factors, one reflecting experiential impairments (anhedonia, asociality, avolition) and the other reflecting expressive impairments (alogia, blunted affect; Horan, Kring, Gur, Reise, & Blanchard, 2011; Kring et al., 2013). These factors are now reflected in two subscales of the CAINS: the Motivation and Pleasure Subscale (MAP) and Expressive Subscale (Horan et al., 2011; Kring et al., 2013). Given the hypothesized relationship between effort allocation and motivational impairment, CAINS-MAP was the focus of the current report.

Ecological-momentary-assessment protocol

Participants with schizophrenia were provided an Android-enabled smartphone during the portion of the study involving ecological momentary assessment (EMA). During the 7-day protocol, participants received four text messages per day between 10:00 a.m. and 8:00 p.m., approximately every 2 to 3 hr. Text messages contained hyperlinks to a Qualtrics online survey (Snow, 2012). After the receipt of each text message, participants were given 15 min to begin each survey. Participants were paid $1.75 for each survey they completed within this 15-min window. The protocol was identical to that used in a previous study by our group (Moran et al., 2017).

For each survey, participants were asked to indicate their current activities from a predetermined list of options (i.e., eating/drinking, TV/radio/computer/reading, entertainment away from home, socializing, exercising, work/school, sleeping, running an errand, cleaning/hygiene/chores, cooking, therapy/doctor's appointment, in transit, nothing in particular). Next, they indicated the level of interest and level of enjoyment they experienced from these activities on a 5-point scale ranging from 1 (*not at all*) to 5 (*extremely*). Participants were also asked to indicate their activities, level of interest, and level of enjoyment since the last text message (i.e., in the last 2–3 hr) as well as for what they expected to do in the upcoming 2 to 3 hr. Current, past, and future self-reports were averaged for each survey for interest and enjoyment for all analyses, creating a single EMA enjoyment and interest (EMA-EI) measure per time point (e.g., 28 potential data points per participant). Responses to the EMA survey questions were averaged to closely mirror current experiential subscales of negative symptom interviews (e.g., CAINS-MAP), which assess interest and enjoyment with current, previous, and future activities. Overall, the EMA protocol was well tolerated (mean completion rate = 78%). All participants completed at least 33% of the surveys and thus were included in the current analyses, consistent with previous EMA research (Myin-Germeys, van Os, Schwartz, Stone, & Delespaul, 2001). EMA adherence was not significantly related to the CAINS-MAP ($r = .04$; $p = .83$).

Behavioral COGED task

Participants completed a modified version of the COGED task (Culbreth et al., 2016) that was originally developed by Westbrook et al. (2013). In this task, participants first practiced increasingly difficult versions of the cognitively demanding *N*-back task. Participants completed two 64-trial runs of each *N*-back level (1- to 4-back); each run consisted of 16 target trials and 48 nontarget trials. Next, individuals made a series of choices about repeating one task up to 10 more times for cash rewards. Specifically, each decision trial involved a two-alternative forced choice between completing a more demanding level of the *N*-back task (2- to 4-back) for a greater reward or a less demanding level (1-back) for a smaller reward. After each choice, the reward amount for the 1-back was titrated until participants were putatively indifferent between the base offer for the harder task and the offer for the 1-back (see Fig. S1 in the Supplemental Material available online). This indifference point was then divided by the base-offer amount for the hard task to quantify a subjective value for each hard-task–base-offer amount pair. Greater subjective values suggest a greater willingness to exert effort. Note that participants are instructed that they need to perform only as well on the *N*-back tasks as they performed during the practice phase to receive payment, helping to reduce any confounds associated with group or individual differences in performance levels. In the current study, three high-demand *N*-back levels ($N = 2$–4) and two base-reward amounts ($2 and $4) were used. Each task amount pair was titrated over a series of 5 decision trials, yielding a total of 30 decision-making trials and 6 indifference points across the task. After the scanning trials, one of the participant's choices was selected at random to determine the task that they were required to repeat and the amount they were paid.

Neuroimaging cognitive effort-discounting task

During fMRI scanning, participants made similar decisions between repeating a more cognitively demanding level of the *N*-back (2- to 4-back) for a greater reward ($2 or $4) or a less cognitively demanding (1-back) level for a smaller reward (Fig. S2 in the Supplemental

Material). First, the hard task-amount pair was presented in the center of the screen for 3 s (valuation phase). Participants were told to consider how they felt about performing the task for the amount offered. After a jittered interstimulus interval (0, 2, or 4 s), the easy task amount pair appeared on the screen, and participants chose which task they would rather perform for the amounts provided using a button box (decision-making phase). Finally, a jittered intertrial interval (2, 4, or 6 s) occurred before the onset of the next trial. Note that offers for the easy task were given at various degrees above and below participant -specific indifference points (100% below, 20% below, 10% below, 40% above, 60% above, and 100% above) calculated before scanning. This allowed for the manipulation of choice difficulty, given that trials that are presented closer to indifference points are putatively more difficult decisions. In total, the fMRI protocol consisted of 72 trials. These trials varied by hard-task amount offer ($2 or $4), hard-task *N*-back level (2- to 4-back), and the degree that the easy offer was presented above/below the subject-specific indifference point (100% below, 20% below, 10% below, 40% above, 60% above, 100% above). Specifically, two hard-task-load-level trials were presented for each proximity level. Hard-task amount offers were split such that $2 offers were presented during 10% below, 40% above, and 100% above indifference point levels, and $4 offers were presented during 100% below, 20% below, and 60% above load levels. Thus, the design was not completely balanced across load level, proximity, and hard-task amount. The main contrast of interest was between trials offered either 100% above or below indifference points, which are thought to be putatively easy trials, and trials offered in between (e.g., 20% below, 10% below, 40% above, 60% above), which are thought to be more difficult (Fig. S2 in the Supplemental Material).

Neuroimaging preprocessing

Images were acquired on a 3T MRI system (Magnetom Skyra; Siemens, Munich, Germany) with a 32-channel head coil, which was customized and used for the Human Connectome Project (HCP). Structural scans (0.8 mm isotropic) as well as three functional runs using a multiband echo-planar sequence (repetition time = 720 ms, echo time = 33.1 ms, flip angle = 52°, 2.4-mm isotropic voxels, and a multiband acceleration factor of 8). Each run lasted approximately 5 min.

Imaging data were run through HCP minimal preprocessing pipelines (Glasser et al., 2013). Data were then analyzed using the Analysis of Functional NeuroImages (AFNI) software package (Cox, Chen, Glen, Reynolds, & Taylor, 2017). Binary masking was applied to each image to remove voxels outside of the brain. The echo-planar imaging data sets for each participant were smoothed using an 8-mm full width at half-maximum Gaussian kernel to improve the signal-to-noise ratio. Six rigid body-motion parameters were used as regressors to correct for motion.

Data analysis

COGED behavior. Subjective effort costs were quantified as the subjective value of discounted rewards. Specifically, the indifference point for a given task amount pair was divided by the base amount to yield a subjective value. If, for example, a participant was indifferent between $1.43 for the 1-back and $2 for the 2-back, then the subjective value for the $2, 2-back pair would be $1.43/$2 = 0.715. Thus, greater subjective value estimates equal a greater willingness to choose the high-effort option. A hierarchical linear model was used to test for group differences in discounting, accounting for the hierarchical nesting of indifference points within participants. Specifically, the subjective value was predicted by the *N*-back level, diagnostic group, and their interaction. The hard-task reward amount was not found to significantly predict subjective value and did not explain additional variance to justify adding complexity to the hierarchical linear model (HLM). Thus, it was removed as a predictor in all analyses. To examine whether negative symptoms varied as a function of effort allocation, we implemented a second HLM using only the data from individuals with schizophrenia. In this model, subjective values were predicted by task level, the CAINS-MAP, and their interaction.

Supplemental analyses were conducted to quantify whether task performance influenced diagnostic and negative symptom effects on effort allocation. In short, we wanted to assess whether individuals were less willing to engage in demanding task levels simply because they were worse at the task. Thus, we conducted two additional analyses that included average *N*-back performance across task levels (d') as an additional predictor of subjective value in the models described above.

Finally, we conducted analyses to determine whether effort allocation was related to interest and enjoyment in daily activities measured via the EMA. For these analyses, subjective value estimates for each participant were averaged to create a summary score, or area under the curve (AUC), of COGED decision making. The AUC connecting subjective values across all levels provides a summary measure of mean willingness to expend cognitive effort for a reward. We conducted one HLM predicting the EMA-EI by the AUC. Further, given the strong evidence of group differences for the 2-back subjective value (Fig. 1), we conducted a supplemental analysis in which the EMA-EI was predicted by the 2-back subjective value.

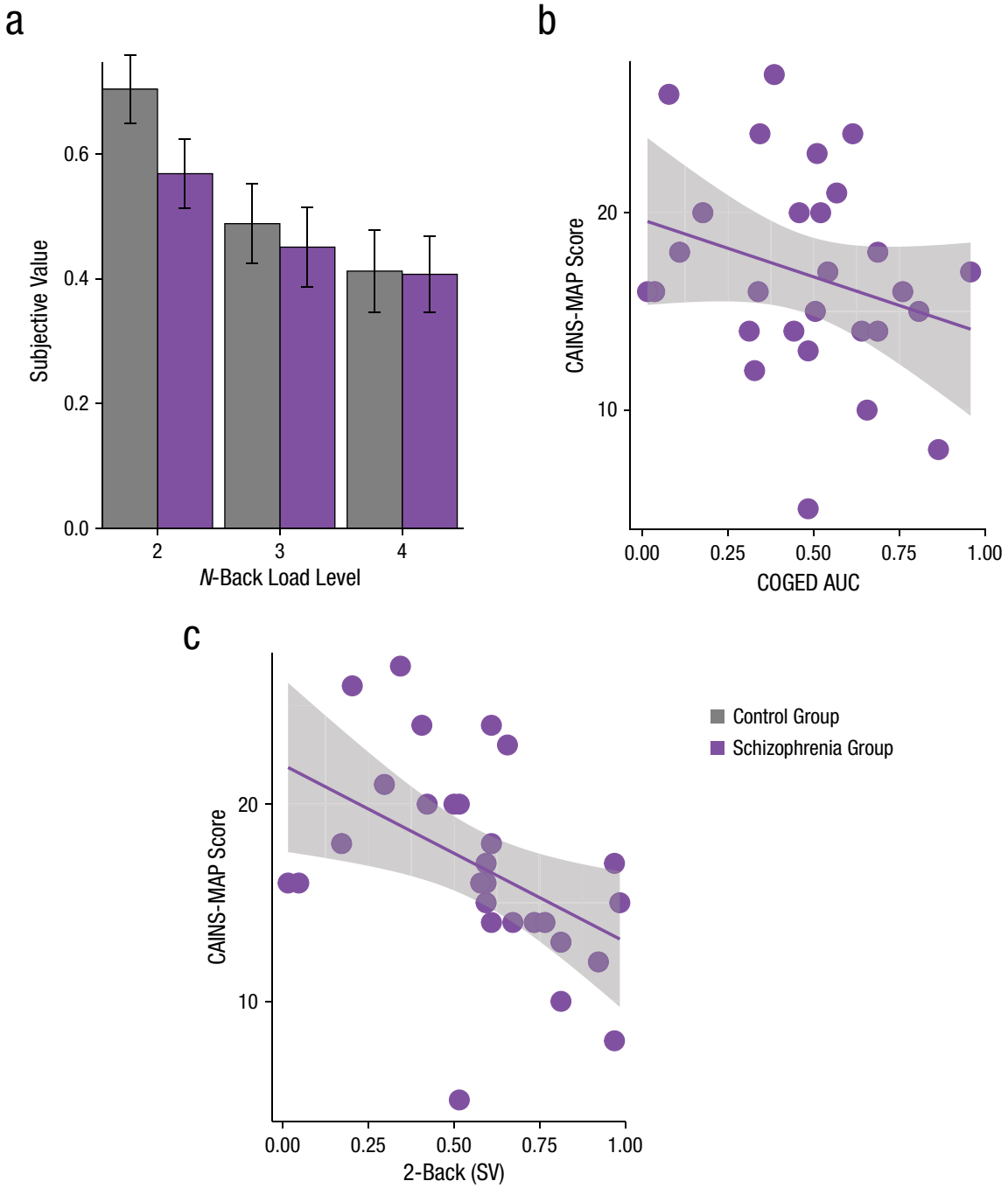

Fig. 1. Behavioral results. In (a), the graph shows subjective values at different levels of cognitive demand (*N*-back level). In (b), the scatterplot (with best-fitting regression line) shows the relationship between negative symptoms (CAINS-MAP scores) and willingness to expend effort (COGED-AUC). In (c), the scatterplot (with best-fitting regression line) shows the relationship between negative symptoms (CAINS-MAP scores) and cognitive demand on the 2-back test. The shaded areas represent the 95% confidence intervals. AUC = area under the curve; CAINS = Clinical Assessment Interview for Negative Symptoms; MAP = Motivation and Pleasure Subscale of CAINS; COGED = cognitive effort discounting; AUC = area under the curve; SV = subjective value.

COGED imaging. Each participant's fMRI data were analyzed with a general linear model (GLM) using AFNI software. Separate regressors, including a single regressor for BOLD activity during the evaluation phase as well as separate regressors for each trial type (easy vs. hard) during the decision-making phase, were modeled using an assumed hemodynamic response (GLM function). Six absolute motion parameters were also included. A contrast comparing hard with easy decision trials was created. For this GLM, we conducted an ROI analysis in

Table 1. Demographic Information and Symptom Characterization

Characteristic	Control group (n = 30)	Schizophrenia group (n = 28)	Test statistic	p
Age (years)	35.2 (10.63)	37.18 (12.25)	$t(56) = -0.66$	.51
Sex (% female)	23%	29%	$\chi^2(1) = 0.207$	.65
Ethnicity (n)			$\chi^2(2) = 1.95$	.38
African American	16	15		
Asian	4	1		
White	10	12		
Education (years)	15.47 (2.43)	12.75 (2.95)	$t(56) = 3.84$	< .001
Parental education (years)	13.92 (2.34)	14.48 (3.76)	$t(56) = 0.69$	.49
WTAR	95.58 (18.06)	93.25 (20.48)	$t(56) = 0.69$	.64
CAINS-MAP	—	16.89 (5.17)		—
CAINS-EXP	—	5.39 (4.04)		—
Medications (n)				
Unmedicated	—	5	—	—
Atypical antipsychotics	—	18	—	—
Typical antipsychotics	—	5	—	—
CPZ equivalent	—	311.81 (151.45)	—	—

Note: Values are means with standard deviations in parentheses unless otherwise indicated. CAINS = Clinical Assessment Interview for Negative Symptoms; CPZ = chlorpromazine equivalents; EXP = Expressive Subscale; MAP = Motivation and Pleasure Subscale; WTAR = Wechsler Test of Adult Reading.

AFNI using an a priori mask that included regions from a previous analysis of an identical contrast (Westbrook et al., 2019; Fig. S3 in the Supplemental Material). Further, we included the bilateral dorsal striatum defined from AFNI atlases, and bilateral ventral striatum ROIs were created using an 8-mm sphere placed at peak coordinates ($x = \pm 10$, $y = 8$, $z = -4$) on the basis of a previous study that examined the neural correlates of reward learning in schizophrenia patients (Schlagenhauf et al., 2014). The mean percentage signal change for each participant for each ROI and condition (easy vs. hard decision-making trial conditions) was extracted using the AFNI *3dmaskave* program. In addition to the primary ROI analyses, we conducted exploratory whole-brain analyses to examine task effects and group differences in the hard versus easy decision-making trials. Whole-brain statistical maps were corrected for multiple comparisons using the AFNI ClustSim program to determine cluster and activation thresholds (Cox et al., 2017; Table S1 in the Supplemental Material).

To examine whether negative symptoms or discounting behavior (AUC) varied as a function of BOLD activation, we conducted bivariate correlations between the AUC and CAINS-MAP and BOLD activation in ROIs for the hard versus easy contrast only in the schizophrenia group. A false-discovery-rate (FDR) correction was used to control for multiple comparisons (Benjamini & Hochberg, 2000).

Power analysis. For within-group correlations between symptoms, BOLD activation, and effort-based decision-making-task performance, we had approximately 75% power to detect an effect of $r \geq .4$ at an a level of .05. For t tests assessing group differences, we had approximately 73% power to detect a medium-sized effect (Cohen's d = 0.6) at an a level of .05. Finally, HLM analyses are most accurately calculated using simulations. The simulations we used revealed approximately 75% power to detect an effect size of $r \geq .4$ at an a level of .05 when testing whether a single variable (e.g., BOLD activation in a particular ROI or COGED choice behavior) predicted EMA self-report.

Results

The groups did not significantly differ in age, gender, ethnicity, or parental education. Individuals with schizophrenia reported significantly less personal education than the control participants (Table 1). Medication information and negative symptom severity of participants with schizophrenia is also listed in Table 1.

COGED behavioral results

Both participants with schizophrenia and control participants discounted reward offers for higher levels of the *N*-back task and did so in a mostly monotonic fashion (Fig. 1a). Thus, participant discounting was sensitive to task load, and subjective costs increased with objective demands, as expected. Participants with schizophrenia discounted rewards more than did control participants (Table 2, all participants), suggesting greater effort aversion in those with schizophrenia (Fig. 1a). Diagnostic group differences appeared to be largely driven by steep discounting of rewards by individuals with schizophrenia compared with control participants at the 2-back (Fig. 1a), although the interaction between

Table 2. Hierarchical Linear Models Predicting Subjective Value

Parameter	Estimate	*SE*	*p*
All participants			
N-back level	−0.21	0.07	.002
Group	−0.19	0.09	.04
N-Back Level × Group	0.07	0.04	.12
Schizophrenia only			
N-back level	−0.25	0.1	.01
CAINS-MAP	−0.03	0.01	.007
N-Back Level × CAINS-MAP	0.01	0.01	.70
All participants including *d*′			
N-back level	−0.21	0.07	> .002
Group	−0.16	0.09	.09
d′	0.04	0.04	.32
N-Back Level × Group	0.07	0.04	.12
Schizophrenia only including *d*′			
N-back level	−0.25	0.1	.01
CAINS-MAP	−0.03	0.01	.01
d′	0.12	0.04	.01
N-Back Level × CAINS-MAP	0.01	0.01	.07

Note: CAINS = Clinical Assessment Interview for Negative Symptoms; HLM = hierarchical linear model; MAP = Motivation and Pleasure Subscale.

the diagnostic group and *N*-back level was not significant (Table 2, all participants).

To determine whether the severity of experiential negative symptoms (CAINS-MAP) predicted discounting behavior, we conducted a second HLM to predict the subjective value for each task amount pair from the *N*-back level, CAINS-MAP, and their interaction (Table 2, schizophrenia only). Negative symptom severity negatively predicted subjective value, suggesting that willingness to expend effort was lowest in patients with high levels of negative symptoms. Scatterplots illustrating the relationship between negative symptoms and effort can be found in Figures 1b and 1c.

We wanted to assess whether individuals with schizophrenia were less willing to engage in demanding task levels at least in part because they are worse at the task. Thus, we conducted two analyses that included average *N*-back performance across task levels (*d*′) as a predictor of subjective value in the models described above (Table 2, all participants including *d*′ and schizophrenia only including *d*′). In these models, diagnostic group was a trend-level predictor of subjective value, suggesting that cognitive impairment is likely a partial contributor to the diagnostic group differences seen in effort allocation (Table 2, all participants including *d*′). In contrast, negative symptom severity remained a significant predictor of subjective value even when controlling for task performance (Table 2, schizophrenia only including *d*′).

Finally, levels of interest and enjoyment with daily activities measured via the EMA were not significantly predicted by willingness to expend effort on the COGED task (COGED-AUC), $\beta = 0.53$, $SE = 0.45$, $p = .24$. However, the prediction of interest and enjoyment in daily activities was significant at the trend level for the 2-back subjective value, in which group differences are the most robust, $\beta = 0.75$, $SE = 0.40$, $p = .08$.

Neuroimaging results

Behavioral quality-control analyses for the correct identification of indifference points. Decision making for neuroimaging task trials generally suggested a valid identification of indifference points (Sections S1 and S2 in the Supplemental Material). Specifically, when individuals were presented with 1-back offers below their specific indifference points, they tended to choose the hard task, and when presented with 1-back offers above the indifference points, they tended to choose the easy task (Section S1). Further, the reaction time for easy trials, which putatively require less deliberation, was faster than hard trials across both groups (Section S2).

Main effect of task across groups. Neuroimaging analyses focused on a contrast of putatively hard (e.g., where participants find $2 for 3-back vs. $1 for 1-back to be close in subjective value) compared with putatively easy (e.g., $2 for 3-back vs. $0 or $2 for 1-back, in which the subjective offer values are far apart) decision-making trials. Across participants, BOLD activation in a priori ROIs located in the cerebellar, frontal, cingulate, parietal, and insular cortices was greater during decision making in difficult compared with easy trials (Table S2 in the Supplemental Material), consistent with a previous report using a similar design with an identical contrast (Westbrook et al., 2019). Striatal ROIs did not show significant effects in this contrast (Table S2).

Follow-up whole-brain analyses revealed significant effects in similar regions compared with ROI analyses. Specifically, the posterior parietal/occipital cortex, middle cingulate cortex, posterior cingulate cortex, left postcentral gyrus, and left precuneus showed increased BOLD activation during difficult compared with easy decisions (Table S3 in the Supplemental Material). Increased BOLD activation was found for the dorsal striatum during putatively difficult compared with putatively easy decision-making trials, but this effect did not survive multiple-comparison corrections.

Diagnostic group differences. Diagnostic group differences in a priori ROIs were largely not significant for

putatively difficult compared with putatively easy decision-making trials (Table S4 in the Supplemental Material). Although control participants showed greater BOLD activation on hard vs. easy trials compared with individuals with schizophrenia in the right inferior frontal gyrus, this effect was only marginally significant and did not survive multiple-comparison corrections. Follow-up whole-brain analyses did not reveal significant differences between groups in the contrast of interest (hard vs. easy) when correcting for multiple comparisons.

Individual differences. Negative symptom severity in those with schizophrenia showed robust correlations with BOLD activation in both the left ($r = -.50$, $p = .006$) and right ($r = -.54$, $p = .004$) ventral striatum during putatively difficult compared with putatively easy decisions (Fig. 2; for correlations, see Table S5 in the Supplemental Material). Correlations remained significant after applying FDR correction. Specifically, patients with high levels of negative symptoms showed decreases in BOLD activation for hard compared with easy decision trials, whereas patients with low levels of negative symptoms showed increases in BOLD activation. For the left ventral striatum, this effect was significant at the trend level after an outlier was removed ($r = -.37$, $p = .06$). No other significant correlations were found between BOLD activation in a priori ROIs and negative symptom severity.

Correlations between the COGED task (COGED-AUC) and BOLD activation for the contrast of hard versus easy trials in a priori ROIs were also examined. Here, a positive correlation was found between the left anterior insula and discounting behavior (Fig. 2c); however, this correlation did not survive multiple-comparison corrections (Table S5 in the Supplemental Material). No other significant correlations were found between BOLD activation in a priori ROIs and negative symptom severity. No significant correlations were observed between EMA variables and BOLD activation in a priori ROIs.

EMA and task variables were not significantly associated with demographic variables. Further, correlations between BOLD activation in a priori ROIs and demographic variables were largely nonsignificant. For ROIs that showed significant associations with demographic variables, the inclusion of demographic variables as a covariate did not alter the statistical significance of associations between BOLD activation and negative symptom severity (Table S6 in the Supplemental Material).

Discussion

The goal of the current study was to examine effort-based decision making in individuals with schizophrenia. We found that individuals with schizophrenia were less willing than control participants to exert effort to obtain monetary rewards. Further, we observed that willingness to expend effort was associated with negative symptom severity, such that patients with high levels of negative symptoms were the least willing to exert effort for monetary rewards, even when controlling for task performance. Regarding neural correlates, we observed increased BOLD activation of frontal, parietal, cingulate, and insular regions during hard compared with easy trials across participants. Contrary to our hypotheses, our results showed similar patterns of BOLD activation in individuals with schizophrenia and in control participants during effort-based choice. However, negative symptom severity in individuals with schizophrenia was significantly associated with reduced BOLD activation in the bilateral ventral striatum during decision making, and greater discounting was associated with greater anterior insula activity, although this effect did not survive FDR correction. These findings are discussed in further detail below.

The findings of the current study are consistent with previous studies that have demonstrated a decreased willingness of individuals with schizophrenia to expend effort for monetary rewards (Barch et al., 2014; Culbreth et al., 2016; Fervaha et al., 2013; Gold et al., 2013; Huang et al., 2016; McCarthy et al., 2016; Reddy et al., 2015; Treadway et al., 2015; Wang et al., 2015; Wolf et al., 2014). We also found that negative symptoms were associated with effort exertion, such that greater severity of negative symptoms was associated with a decreased willingness to exert effort, consistent with several previous reports (Barch et al., 2014; Culbreth et al., 2016; Gold et al., 2013; Hartmann et al., 2015; Horan et al., 2015; Moran et al., 2017; Strauss et al., 2016; Treadway, Bossaller, et al., 2012; Wang et al., 2015; Wolf et al., 2014), In addition to measuring negative symptoms with traditional clinical interviews, we also measured negative symptoms using an EMA approach, asking individuals with schizophrenia to self-report their interest and enjoyment with daily activities using a smartphone. Using a similar approach, our lab previously found that individuals with schizophrenia who demonstrated the least willingness to exert physical effort on an experimental task also reported the least interest and enjoyment with their daily activities (Moran et al., 2017). Although the associations between cognitive effort-based decision making and EMA variables in the current report were not as robust as in our prior work, we did observe a trend-level positive association. Limited power due to a lower sample size may have contributed to nonsignificant findings in the current report.

Like Westbrook et al. (2019), who used a similar design, we observed increased BOLD activation across participants in frontal, cingulate, parietal, and insular

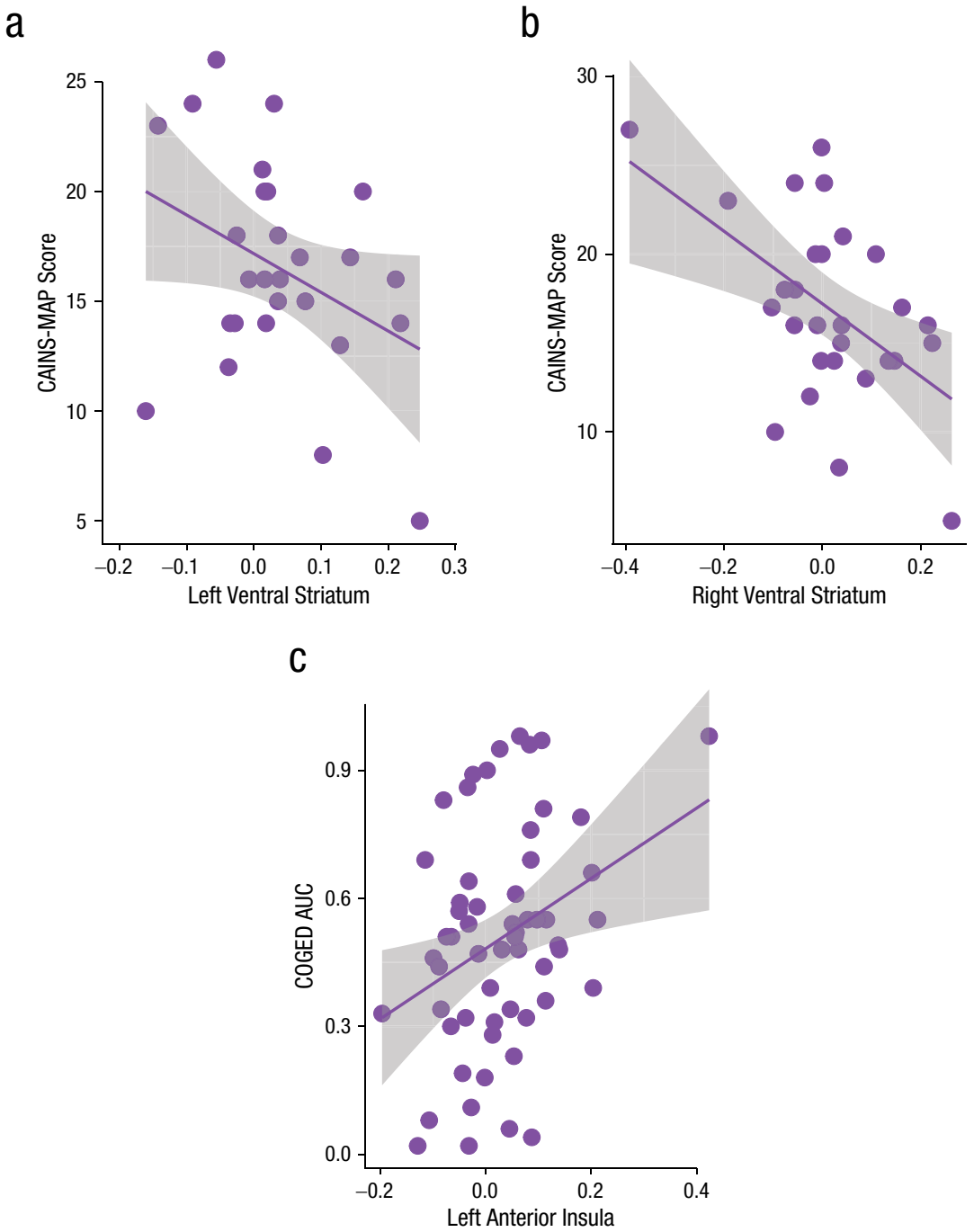

Fig. 2. The scatterplots (with best-fitting regression lines) show the relationship between brain regions of interest and negative symptoms (CAINS-MAP scores; a and b) and willingness to expend effort (COGED-AUC; c). AUC = area under the curve; CAINS, Clinical Assessment Interview for Negative Symptoms; COGED = cognitive effort-discounting task; MAP = Motivation and Pleasure Subscale of CAINS. The shaded areas represent 95% confidence intervals.

regions for hard compared with easy decision-making trials. Contrary to expectations, our results showed no significant effects in striatal regions for our overall contrast of hard compared with easy decisions. Several previous reports have found BOLD activation in the ventral and/or dorsal striatum, which varies as a function of effort during valuation and decision making (Croxson et al., 2009; Kurniawan et al., 2010; Kurniawan, Guitart-Masip, Dayan, & Dolan, 2013; Leotti & Delgado, 2011; Schmidt et al., 2012). Thus, the lack of robust BOLD

activation in the striatum for the current contrast is surprising.

Contrary to our hypotheses, similar patterns of BOLD activation for both control participants and individuals with schizophrenia were observed for our contrast of hard compared with easy trials. These results are inconsistent with a recent report (Huang et al., 2016) that found blunted reward-related BOLD activation of the dorsal and ventral striatum in participants with schizophrenia compared with control participants during effort-based decision making. However, Park et al. (2017) found largely similar patterns of BOLD activation between individuals with schizophrenia and control participants during an estimation of effortful options. Aspects of the current experimental design may have limited our ability to observe strong group differences. Specifically, decision-making trials in our neuroimaging design were administered on the basis of individual participants' indifference points derived during the behavioral portion of COGED. Thus, each participant received different trials on the basis of their own willingness to expend effort, resulting in different trial combinations in all participants. It will be important in future work to include some standard trial types across participants to determine whether more evidence of neural alterations emerge at the group level with comparisons well suited to elicit group differences.

With regard to individual differences, we observed robust correlations between negative symptom severity and BOLD activation in the bilateral ventral striatum, as well as a positive association between the willingness to expend effort and BOLD activation in the anterior insula, although at a nominal level of significance. The current striatal finding is consistent with previous work (Wolf et al., 2014) that demonstrated an association between the willingness to expend effort and ventral striatal BOLD activation on a reward-processing task in individuals with schizophrenia. Further, the correlations observed in the current report are consistent with several previous reports that examined aspects of value-based decision making and found blunting of ventral striatum BOLD activation related to increased negative symptom severity in individuals with schizophrenia (Simon et al., 2010; Waltz et al., 2010, 2013). It is noteworthy that in these studies, although associations were found between ventral striatum BOLD activation and negative symptom severity, group differences in the ventral striatum between control participants and those with schizophrenia were nonsignificant, similar to the current report.

Future work could extend the current findings in several ways. First, although multiple studies have examined effort-based decision making in schizophrenia (Culbreth et al., 2018; Gold, Waltz, & Frank, 2015a; Green et al., 2015), work has been limited to medicated patients in the chronic phase of illness. An important direction for future research remains in assessing individuals in earlier phases of illness, as well as antipsychotic naive individuals. Research that includes such patient groups will help to establish the potentially confounding role of antipsychotic medications in effort-based decision-making deficits in schizophrenia, as well as help to determine whether effort-based decision-making impairments are present across the course of illness.

Second, impairments in effort-based decision making have also been found in other psychiatric disorders (e.g., major depressive disorder; Cléry-Melin et al., 2011; Hershenberg et al., 2016; Sherdell, Waugh, & Gotlib, 2012; Treadway, Bossaller, et al., 2012; Yang et al., 2014, 2016). However, it remains unknownss whether similar behavioral effort-based decision-making impairments across these disorders involve similar or disparate psychological and neural mechanisms (Culbreth et al., 2018). Transdiagnostic samples are necessary to determine such mechanistic questions, which could have important implications for the development of novel intervention strategies to alleviate effort-based decision-making impairments.

Finally, although effort-based decision-making impairments appear to be a robust deficit in individuals with schizophrenia, little work has suggested potential treatment approaches for improving effort expenditure. Although future work is needed to better characterize the mechanisms that might give rise to aberrant effort-based decision making to guide mechanistically informed intervention, several promising interventions exist that could yield beneficial effects. For example, individuals with schizophrenia may show a decreased willingness to expend effort partly because of negative beliefs about their ability to successfully perform actions (Grant & Beck, 2008; Reddy et al., 2018), and such beliefs can be successfully targeted with cognitive behavioral therapy (Grant & Beck, 2008).

The current study has several limitations. First, the sample size was modest and included individuals with schizophrenia primarily in the chronic phase of illness. Future work will be needed to replicate and extend the current findings in a larger sample. Second, we did not collect EMA measures in our control group, which prohibits examining more typical patterns of enjoyment and interest in daily activities. However, although such typical patterns are important, they were not necessary to the aims of the current analyses. Third, many of the participants with schizophrenia were taking antipsychotic medications at the time of study completion, which may have influenced choice behavior because of their influence on dopamine systems. Fourth, given

the complexity of the EMA data, there are a multitude of potential alternatives for creating summary scores. In the current study, we averaged together self-reported interest and enjoyment for current, past, and future daily activities within each EMA time point. Such an averaged approach has the benefit of assessing general hedonic and motivational experience while limiting the number of statistical comparisons. However, it may be the case that specific questions that index particular aspects of hedonic and motivational experience show stronger associations to task and biological variables. Although we did not explore relationships between task variables and specific questions in the current study, future research may benefit from attempting to relate task variables to more specific aspects of daily motivational experience. Further, future reports may benefit from examining daily motivational experience within particular behavioral contexts (e.g., social situations, during completion of effortful behaviors) to observe whether relationships generalize across particular contexts.

Finally, negative symptoms were partially assessed using the CAINS. Converging structural analyses of the CAINS have identified two moderately correlated factors, one reflecting experiential impairments (anhedonia, asociality, avolition) and the other reflecting expressive impairments (alogia, blunted affect; Horan, Kring, Gur, Reise, & Blanchard, 2011; Kring et al., 2013). Given the hypothesized relationship between effort allocation and experiential impairment, the CAINS-MAP was the focus of the current report. A recent structural report has suggested a five-factor model of negative symptoms (i.e., anhedonia, avolition, asociality, alogia, and blunted affect; Strauss, Ahmed, Young, & Kirkpatrick, 2018). Although such a model was not used in the current report, future studies may benefit from examining relationships between the willingness to expend effort and the specific factors of this model (particularly avolition and anhedonia).

In conclusion, the current study replicates previous work suggesting a decreased willingness of individuals with schizophrenia to exert effort to obtain monetary rewards. Further, we showed that this behavioral deficit varies as a function of negative symptom severity and that negative symptom severity in patients is closely associated with the hypoactivation of the ventral striatum during effort-based choice. Future studies are needed to further examine the neural correlates of effort-based decision making in schizophrenia in larger samples, as well as to assess patients at various phases of illness. In addition, it will be important to further examine the psychological and neural mechanisms of effort-based decision making to guide the development of novel interventions.

Transparency

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Author Contributions

A. J. Culbreth, E. K. Moran, and D. M. Barch developed the initial project conceptualization; A. Westbrook provided task scripts and analytical support; S. Kandala assisted with imaging preprocessing; and A. J. Culbreth conducted statistical analyses and wrote the initial draft of the manuscript. All of the authors approved the final manuscript for submission.

Declaration of Conflicting Interests

The author(s) declared that there were no conflicts of interest with respect to the authorship or the publication of this article.

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Supplemental Material

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