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Negative Symptoms are Associated with an Increased Subjective Cost of Cognitive Effort

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Abstract

Motivational deficits in schizophrenia are proposed to be due in part to abnormal effort-cost computations. Inflated subjective cognitive effort costs may explain diminished functioning in schizophrenia to the extent that they drive avoidance of complex decision-making and planning. While previous data support inflated subjective physical effort costs for individuals with schizophrenia, evidence on cognitive effort is mixed. We exploited the methodological advantages of a recently developed cognitive effort-discounting paradigm (Westbrook, Kester, & Braver, 2013) to examine effort-cost computations in schizophrenia. The paradigm quantifies subjective costs in terms of explicit, continuous discounting of monetary rewards based on parametrically varied demands (levels N of the N-back working memory task), holding objective features of task duration and reward likelihood constant. Both healthy participants (N=25) and schizophrenia patients (N=25) showed systematic influences of reward and task demands on choice patterns. Critically, however, participants with schizophrenia discounted rewards more steeply as a function of effort, indicating that effort was more costly for this group. Moreover, discounting varied robustly with symptomatology, such that schizophrenia patients with greater clinically-rated negative symptom severity discounted rewards more steeply. These findings extend the current literature on abnormal-effort cost computations in schizophrenia by establishing a clear relationship between the costliness of cognitive effort and negative symptoms.

Summary: Reductions in motivational drive and goal-directed behavior are widely reported in schizophrenia. In the current manuscript we provide novel evidence for the role of subjectively inflated effort costs in these deficits.

Keywords: Schizophrenia, Avolition, Effort, Negative Symptoms, Decision-Making

Introduction

Deficits in goal pursuit, labeled “avolition”, have long been considered a cardinal symptom of schizophrenia (SZ) (Bleuler, 1950). Such symptoms are both debilitating and resistant to current interventions (Milev, Ho, Arndt, & Andreasen, 2005). Recent work has shown intact hedonics in SZ, such that patients rate “liking” enjoyable experiences similarly to controls; however, despite intact hedonics, patients demonstrate reductions in their “drive” to pursue rewards (for review see (Kring & Barch, 2014; Strauss & Gold, 2014). A growing body of research suggests that SZ patients might have reduced motivational drive because of subjectively inflated effort costs (for review see (Fervaha, Foussias, Agid, & Remington, 2013; Gold, Waltz, & Frank, 2015; Michael F Green, Horan, Barch, & Gold, 2015). Indeed, recent studies support that SZ patients with greater negative symptom severity find physical effort especially costly (Barch, Treadway, & Schoen, 2014; Fervaha, Graff-Guerrero, et al., 2013; Gold et al., 2015; Hartmann et al., 2015; Reddy et al., 2015; Treadway, Peterman, Zald, & Park, 2015).

Cognitive effort, however, may be even more important for adaptive functioning in modern society, as it is necessary for complex planning and decision-making. For example, individuals with stronger negative symptoms may have defeatist attitudes about consumer decisions that moreover may relate to diminished effort allocation (Granholm, Ruiz, Gallegos-Rodriguez, Holden, & Link, 2015). More generally, diminished social and occupational functioning are related to deficits in executive functioning in schizophrenia (Michael Foster Green, Kern, Braff, & Mintz, 2000; Michael F Green, Kern, & Heaton, 2004). However, evidence for inflated cognitive effort costs in schizophrenia is mixed (Gold et al., 2014; Michael F Green et al., 2015; Reddy et al., 2015; Wolf et al., 2014). Moreover, no studies to date have linked the subjective cost of cognitive effort with clinically relevant dimensions of avolition.

There are multiple reasons to suspect abnormal cognitive effort cost computations in SZ. First, dopaminergic innervation of the striatum, which mediates motivational influences on effortful action (Assadi, Yücel, & Pantelis, 2009; Kurniawan, Guitart-Masip, & Dolan, 2011; Salamone, Correa, Farrar, & Mingote, 2007), is significantly altered in SZ, including both increased presynaptic dopamine availability and altered D2 receptor expression (Howes & Kapur, 2009). Further, indirect but consistent evidence was found by Wolf and colleagues showing that a putative marker of dopaminergic function in the ventral striatum (BOLD response to reward cues) predicted decreased persistence with a taxing cognitive task (Wolf et al., 2014). Also, mice models of a phenotype which over-expresses striatal D2 receptors, similar to what is found in schizophrenia, display reduced effort expenditure despite intact hedonics (Ward et al., 2012). Second, recent evidence suggests that physical and cognitive effort may share a common motivational hub in the striatum (Schmidt, Lebreton, Cléry-Melin, Daunizeau, & Pessiglione, 2012), thus the robust deficits in physical effort seen in previous SZ studies may imply cognitive effort deficits as well. Third, the anterior cingulate cortex, which is central to selecting and maintaining effortful action (Cowen, Davis, & Nitz, 2012; Holroyd & Yeung, 2012) and effortful cognitive control in particular (Hosking, Cocker, & Winstanley, 2014; Shenhav, Botvinick, & Cohen, 2013) can show abnormal function in SZ (Carter, MacDonald III, Ross, & Stenger, 2001; Dolan et al., 1995).

Despite clear evidence for exaggerated physical effort costs in SZ, evidence on cognitive effort costs and their relationship to symptomatology is mixed. For example, Wolf and colleagues found that persistence with an effortful task was related to negative symptoms (Wolf et al., 2014), but other measures of cognitive effort expenditure have not shown relationships to clinician-rated negative symptoms (Gold et al., 2014; Horan et al., 2015). The lack of clarity may

stem, in part, from methodological limitations. Previous studies, for example, have examined binary choice tasks measuring whether decision-makers tend to avoid higher cognitive demands, but not *how much* they wish to avoid higher demands, limiting the kinds of inferences that can be drawn. Moreover, individuals with SZ may not be consciously aware of subtle differences in demand, and this awareness appears critical for demand avoidance in binary choice tasks (Gold et al., 2014). In the current study, we address these limitations by using a recent paradigm (cognitive effort discounting, or COGED;(Westbrook et al., 2013)) in which demands are fully explicit, and with which we can quantify not only the tendency to avoid high demands, but also the strength of the desire to avoid demands, in terms of the subjective cost of cognitive effort.

In COGED, participants first practice variously demanding levels of a working memory task (N-back: levels N=1-4). Next, participants make a series of two-alternative forced choices between repeating a more difficult level for a larger reward or the relatively easy 1-back for a smaller reward that is titrated until participants are indifferent between the two offers for each higher level (see Figure 1). The indifference offer for each level then quantifies subjective effort costs in terms of discounted reward value. COGED has several desirable features. 1. Time-on-task is identical across all load levels and options are not probabilistic so choices are based on subjective effort rather than differential task duration or reward probability. 2. Subjective costs can be measured as a function of cognitive load, since load is parametrically varied (by N). 3. Objective demands are explicit, controlling for the confound that demand avoidance varies as a function of conscious awareness. 4. Perhaps most importantly, discounted reward is a continuous measure and, as such, quantifies not just whether a participant wishes to avoid high demands, but by how much they wish to avoid them. This last feature affords the opportunity to investigate

whether the subjective cost of cognitive effort, as a continuous measure, relates to clinical dimensions like avolition.

We hypothesized that individuals with SZ would show higher subjective costs of cognitive effort compared to controls. Specifically, we predict that SZ patients would require greater monetary incentive to choose to repeat more cognitively demanding tasks. Further, we hypothesized that cognitive effort avoidance would be correlated with clinician-rated negative symptoms such that individuals with greater negative symptom severity would show increased cognitive effort avoidance. Finally, we predicted that these effects would be obtained independently of N-back task performance and medication status.

Methods

Participants

Participants were 25 individuals meeting DSM-IV criteria for SZ or schizoaffective disorder (SZA; N=7), and 25 controls (CN), with no personal or family history of psychosis, from the Saint Louis Community. Five SZ patients were unmedicated. Exclusion criteria included 1) DSM-IV diagnosis of substance abuse or dependence in the past six months; 2) DSM-IV diagnosis of major depressive disorder or dysthymia in the past year; 3) changes in medication dosage two weeks prior to consent; 4) past head injury with documented neurological sequelae and/or loss of consciousness; 5) mental retardation. The Washington University Institutional Review Board approved the study. Participants provided written, informed consent in accordance with Washington University's Human Subject Committee's criteria.

Clinical/Individual Difference Assessments

Diagnoses were determined by the Structured Clinical Interview for DSM-IV-TR (First, Spitzer, Gibbon, & Williams, 2001). Negative Symptoms were assessed using the Brief Negative Symptom Scale (BNSS) (Kirkpatrick et al., 2011). Trait desire to engage in cognitively demanding activity was assessed using the Need for Cognition Scale (NCS) (Cacioppo & Petty, 1982). Pre-morbid IQ was assessed using the Wechsler Test of Adult Reading (Wechsler, 2001). All participants were required to pass a urine drug screen and a Breathalyzer test.

Cognitive Effort Assessment

To measure cognitive effort costs, we used the recently developed cognitive effort-discounting task, COGED (Westbrook et al., 2013), in which participants make a series of self-timed, two-alternative choices between receiving greater monetary rewards for higher demands (higher N-back level), or lesser monetary rewards for lower demands (1-back). First, participants

practice two runs of N-back (64 items each; 16 targets each run) for each level, in order of increasing difficulty. Interstimulus intervals were two seconds, thus runs were 128 seconds each, regardless of N-back level. After experiencing each N-back level, participants completed the NASA Task Load Index (Hart & Staveland, 1988) giving Likert self-report ratings of mental demand, physical demand, temporal demand, performance, effort, and frustration.

----Insert Figure 1 Here----

After experiencing all levels of the N-back, participants made a series of choices about repeating a level up to 10 more times for cash rewards. Prior to decision-making, participants are told that in order to receive reward they must exert as much effort as they did when they first performed each level. Critically, after each choice, the 1-back offer (i.e., reward amount) is titrated until participants are indifferent between a base reward offer for the harder level, and a lesser reward amount for the 1-back (Figure 1). The point of indifference is critical because it quantifies how much more subjectively costly the high-demand level is relative to a low-demand level. In our study, three high-demand N-back levels ($N = 2-4$) were used for SZ patients and four were used for HC ($N = 2-5$), two base reward amounts were used (\$2 and \$5), and each level-amount pair was titrated over a series of five decision trials. Hence, there were a total of 30 decision trials for SZ and 40 decision trials for HC, yielding six and eight indifference points, respectively. Finally, one of the participant's choices is selected at random, determining both what level they must repeat and the amount they are paid for repeating it. Participants were paid for task completion regardless of task performance; however, this was not known to participants during discounting.

Data Analysis

N-back Performance

The sensitivity index, d' , was used to quantify N-back performance, controlling for target or non-target response biases. Raw d' values were adjusted by the “log linear” transformation to address extreme false-alarm and hit proportions (Hautus, 1995).

Effort-Based Decision-Making Performance

Subjective effort costs were quantified as the subjective value of discounted rewards. Namely, the indifference point for a given level-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 was $\$1.43 / \$2 = 0.715$ (cf. Figure 1).

A multi-level model was used to test for group differences in discounting, accounting for hierarchical nesting of indifference points within participants. The model best describing the data, accounting for model complexity was one in which subjective values were predicted by task level N , and intercept and level effects were allowed to vary by participant. As described below, there were no reward amount effects, and moreover, a larger model in which reward amount was included as a predictor did not explain sufficient variance to justify the added complexity, as determined by a nested model comparison ($\chi^2_{df=4} = 7.29; p = 0.20$). Hence, the simpler model was used in this and all subsequent analyses. Note that diagnostic group membership G is a participant-level variable, yielding a group x level interaction ($G \times N$), captured by the term γ_{11} and a main effect captured by γ_{01} . Multi-level models were fit in R using the lme4 package, version 1.1-7 (Bates & Sarkar, 2007).

$$SV = \beta_0 + \beta_1 N + \epsilon$$

$$\beta_0 = \gamma_{00} + \gamma_{01} G + \eta_0$$

$$\beta_1 = \gamma_{10} + \gamma_{11} G + \eta_1$$

Relationship between N-back performance and effort expenditure

A second multilevel model was fit to determine whether group effects could be explained by group differences in N-back performance. For this model, performance d' was included such that subjective value was given by:

$$SV = \beta_0 + \beta_1 N + \beta_2 d' + \epsilon.$$

A larger model in which the relationship between d' and SV varied by participant did not explain sufficient additional variance to justify the added complexity, as determined by a nested model comparison ($\chi^2_{df=4} = 5.41; p = 0.25$). Thus, we used a model in which the effect of performance was fixed across participants; we note that the significance of other parameters was the same either way.

Analysis of External Correlates

The subjective cost of effort on the N-back, for a given participant, can be estimated for each level of the N-back, or, as a summary measure for that participant, across all levels. Area Under the discounting Curve (AUC) connecting subjective values across all levels provides a desirably atheoretical (Myerson, Green, & Warusawitharana, 2001) summary measure of effort costliness for that participant, with smaller values indicating more steeply discounted values and more subjectively costly effort. AUC was calculated from the subjective values for levels $N = 2-4$, and then tested for correlation with BNSS (the Avolition Subscale and total score), Need for Cognition, IQ, and olanzapine equivalent antipsychotic dosage (Gardner, Murphy, O'Donnell, Centorrino, & Baldessarini, 2014). We also included a summary N-back performance measure to determine whether the relationship between BNSS variables and AUC was mediated by task performance.

Results

----Insert Table 1 Here----

Demographics

Groups did not differ significantly in age, gender, ethnicity, parental education, or IQ (Table 1). Personal education of the SZ group was lower than the HC group. Interestingly, and supporting our hypothesis that cognitive effort costs are inflated in SZ, the SZ group self-reported decreased desire to engage in cognitively demanding activities in their daily lives as measured by the Need for Cognition Scale (Table 1).

----Insert Table 2 Here----

N-back Performance

N-back performance (d') decreased with load, and was lower for SZ relative to HC (Table 2). Nevertheless, performance was acceptably reasonable and above chance for all levels for both HC and SZ groups.

Table 2: N-back Performance by Group

Effort Discounting

----Insert Figure 2 Here----

Both SZ and HC participants discounted reward offers for higher levels of the N-back task, and did so in a mostly monotonic fashion, with mean subjective value (SV) declining for every level except between $N = 4$ and $N = 5$ (for HC; Figure 2). Thus, discounting for individuals in both groups was sensitive to task load, and subjective costs increased with objective demands, as expected. There was no effect of reward offer amount on SV in either group, nor at any level (all p 's ≥ 0.129). SV's are averaged across amounts for Figure 2.

Mean SV was numerically lower for the SZ group for every level of the N-back. To test whether there was a group difference in SV's, taking into account the hierarchical structure of the data, where each participant has six indifferent points, including both amounts (\$2 and \$5) and three demand levels ($N = 2-4$), and each is a member of a group, we used a multi-level multiple regression. Fixed effects (Table 3) reveal a reliable effect of group such that individuals with SZ ($G = 1$) discount rewards more steeply than HC ($G = 0$).

----Insert Table 3 Here----

Analysis of Self-Reported Effort Expenditure

For further evidence that Groups differ in subjective cognitive effort on the N-back, we also examined self-report data. Using the exact same model structure as Equation 1, we asked whether Group and task level predicted each of the self-reported NASA Task Load Index ratings (ranging from 1-21). Supporting our hypothesis that individuals with SZ find cognitive effort more costly, the Group effect was significant such that individuals with SZ reported higher “mental demand” ($\gamma_{01} = 6.87; t = 4.17; p < 0.001$) and “effort” ($\gamma_{01} = 5.68; t = 3.71; p < 0.001$). Self-report ratings were only somewhat specific to cognitive effort, however. While individuals with SZ did not report any differences in terms of “physical demand” ($\gamma_{01} = 2.54; t = 1.50; p = 0.139$), they did report greater “temporal demand” ($\gamma_{01} = 5.50; t = 3.05; p = 0.004$), “frustration” ($\gamma_{01} = 6.86; t = 4.20; p < 0.001$), and lower “performance” ($\gamma_{01} = 8.30; t = 5.19; p < 0.001$). Finally, zero-order correlations between NASA “effort” and clinician-rated negative symptoms were not significant.

Relationship between N-back performance and effort expenditure

Performance, indexed by d' , was not a reliable predictor of SV ($\beta_2 = 0.041$; $t = 1.34$; $p = 0.183$). Moreover, like amount, including a performance predictor increases complexity of the model unjustifiably according to a nested model comparison ($\chi^2_{df=1} = 1.68$; $p = 0.195$). Nevertheless, including a Performance predictor increases the p -value of the Group predictor of SV to trend-level ($p = 0.089$). Since our ability to reject a null Group effect was attenuated by the addition of an (albeit null) Performance predictor, we cannot rule out that group differences in discounting have some contribution from N-back performance.

Effort Expenditure and External Correlates

The subjective costliness of cognitive effort can be summarized for an individual by AUC, the Area Under the discounting Curve: effectively, the average discounting rate across levels ($N = 2-4$). Importantly, a summary measure allows us to ask whether individual differences in effort costliness, as quantified by AUC, relate to negative symptoms, and avolition in particular. In fact, BNSS Total ($\beta = -0.008$; $p \leq 0.01$), and also BNSS Avolition ($\beta = -0.010$; $p = 0.01$) subscale scores were both strong and reliable predictors of AUC in our SZ sample (Figure 3). Inconsistent with our hypotheses, the BNSS Blunted Affect/Expressivity subscale significantly correlated with AUC ($r = -0.401$; $p = 0.044$). However, when both BNSS Blunted Affect/Expressivity and Avolition subscale scales were entered simultaneously to predict AUC, only the Avolition subscale was significant (Avolition, $p = 0.03$; Blunted Affect, $p = 0.22$), suggesting that shared variance between the BNSS Avolition and Blunted Affect/Expressivity subscales may be driving the relationship between blunted affect and AUC.

----Insert Figure 3 Here----

Reliable relationships support our hypothesis that individuals with stronger negative symptoms find cognitive effort more costly. Other explanations are possible, however. For

instance, individuals with greater negative symptoms may also find monetary rewards less desirable and thus discount more, regardless of subjective effort costs. To test this, we asked participants to self-report factors guiding their decision-making, on a scale of 1 (“Not at all”) to 10 (“A lot”). Among other questions, we asked “To what degree were your choices based on the offer amount (\$) of each task?”. We included participants’ response ratings in separate multiple regressions with BNSS Total and BNSS Avolition. Critically, though higher participant scores on this question predicted higher AUC, both total BNSS ($\beta = -0.008$; $p \leq 0.01$) and the Avolition subscale ($\beta = -0.009$; $p = 0.02$) predict AUC over and above self-report ratings of interest in monetary offer amounts.

We were also concerned that individual difference relationships might reflect poorer N-back performance by those with greater negative symptoms. To test this, we included participants’ cross-level average d' , in separate multiple regressions. We again found that, both total BNSS ($\beta = -0.007$; $p \leq 0.01$) and the Avolition subscale ($\beta = -0.010$; $p = 0.01$) remained reliable predictors of AUC, controlling for performance.

We further examined separate multiple regressions, including olanzapine equivalents, IQ, or Need for Cognition to test whether the relationships between negative symptoms and AUC were explained by medication, general cognitive capacity, or self-reported desire to engage in cognitively demanding activities, respectively. In all cases we found that, both total BNSS and the Avolition scores remained reliable predictors of AUC, (all p 's ≤ 0.01).

Finally, we wanted to examine whether our effort discounting metric, AUC, accounted for variance in negative symptoms over and above self-reported experience with the task (i.e., NASA Task Load Index ratings). To test this, we averaged self-report ratings across levels for each participant, and entered the average score (for Mental Demand, Effort, etc.) into separate

multiple regressions with AUC as predictors of BNSS total and avolition. In all models, AUC reliably predicted negative symptoms and avolition (all p 's ≤ 0.02), controlling for each of the self-report items. Conversely, none of the self-report measures predicted BNSS total or avolition, controlling for AUC, except that higher self-reported "physical demand" predicted higher BNSS total scores ($p = 0.03$). Self-reported "effort" was trend-level ($p = 0.05$ and 0.07 for total and avolition scores, respectively); all other scores, including "mental demand," "temporal demand," and "frustration" were non-significant (all p 's ≥ 0.15). Thus, discounting robustly predicted negative symptoms, controlling for self-reported experience with the N-back, on all dimensions.

Discussion

The goal of the current study was to test for subjectively inflated effort costs in SZ, and examine relationships between symptoms of avolition and subjective effort, using a recently developed cognitive effort discounting paradigm (COGED). First, we found discounting at all reward amounts and task demand levels, for both HC and SZ participants, and moreover that both groups discount rewards more with increasing load. This pattern of results supports that the N-back working memory task is subjectively costly and that both HC and SZ participants are sensitive to objective load. Second, we found evidence of steeper effort discounting among SZ relative to HC, supporting the hypothesis that cognitive effort is more subjectively costly in SZ at the group level (though group discounting differences might relate to group N-back performance differences). Third, we found a robust relationship between steeper discounting and stronger negative symptoms, supporting the hypothesis that patients with greater negative symptom severity, and stronger avolition in particular, find cognitive effort more costly. Alternatively, it shows that those with stronger negative symptoms are less willing to perform cognitively demanding tasks. Importantly, the relationship between negative symptoms and effort

expenditure could not be accounted for by task performance, IQ, self-reported interest in money, or medication status. Finally, higher self-reported “effort” and “mental demand” on the N-back, as measured by the NASA Task Load Index, also supported the hypothesis that cognitive effort is more costly in SZ, this finding was less specific as multiple task demand characteristics (e.g., temporal demand, perceived accuracy) differed between groups. Moreover, COGED appears to have greater diagnostic sensitivity to clinician-rated negative symptoms than self-report measures. These findings and their relation to previous reports are discussed below.

Our results provide the most direct evidence to date that cognitive effort costs are subjectively inflated for individuals with SZ, particularly those patients with more severe negative symptoms. Our group discounting effect converges with previous reports by Wolf et al. and Reddy et al. of diminished persistence with and greater avoidance of demanding tasks, respectively (Reddy et al., 2015; Wolf et al., 2014). However, our result extends these data in important ways. First, COGED measures sensitivity to effort costs independent of task duration, unlike progressive ratio tasks in which persistence is strictly correlated with time-on-task. In contrast, in COGED, high and low demand (N-back) levels have identical duration. Hence our result supports that individuals with SZ find the N-back more costly, not simply that they prefer shorter duration tasks.

Another key difference is that, in COGED, choices are fully explicit: high demand options are always paired with a larger, explicit reward, making clear the dimensions on which participants are to choose. Namely, participants should choose based on their own preferences for more or less demanding tasks for larger and smaller rewards. Recently, Gold et al., with various implicit designs, found either no difference in the degree to which HC and SZ participants avoid higher demands, or even that SZ participants avoid demands *less* (Gold et al.,

2014). However, they also provided evidence that demand awareness was critical and thus implicit paradigms may not yield reliable decision biases. Reddy et al., on the other hand, used a similar, but explicit demand avoidance paradigm and *did* observe greater demand avoidance among SZ relative to HC (Reddy et al., 2015). Our results thus confirm the utility of explicit designs by revealing greater effort costs among SZ participants when choices are fully explicit. Relatedly, explicit incentives for the high demand option are offered in both COGED and by Reddy et al. (but not Gold et al.), and incentives may be necessary for revealing effort cost functions (Gold et al., 2014; Reddy et al., 2015). In particular, incentives may be necessary for 1) orienting participants to value-based decision-making and 2) motivating the recruitment of costly decision-making mechanisms. Multi-attribute decision-making (e.g. choices with both cost and benefits) is effortful (Payne, Bettman, & Johnson, 1988), and enhanced by larger incentives (Smith & Walker, 1993). Hence, incentive differentials in COGED promote precisely the kind of value-based decision-making necessary to reveal underlying differences in subjective cost functions.

Another key difference of our approach and the demand avoidance paradigms used by Reddy et al. and Gold et al. is that COGED quantifies subjective costs on a continuous dimension (of subject values) and thus offers potentially greater sensitivity than binary choice outcomes measured in demand avoidance (Gold et al., 2014; Reddy et al., 2015). Greater sensitivity could explain why we found a robust relationship with clinically-rated negative symptoms where neither Horan et al. nor Gold et al. found one (Gold et al., 2014; Horan et al., 2015). Our result converges with patterns of diminished persistence observed by Wolf et al., and support the interpretation that diminished persistence was related to stronger negative symptoms specifically because of inflated effort costs (Wolf et al., 2014).

The current results are also consistent with studies showing that individuals with SZ are also less willing to expend *physical* effort for reward and the effect is stronger with increasing negative symptoms (Barch et al., 2014; Fervaha, Graff-Guerrero, et al., 2013; Gold et al., 2013; Reddy et al., 2015; Treadway et al., 2015). A parsimonious account unifies physical and cognitive effort, yet there are reasons to make a distinction. Fundamentally different behavioral economic and metabolic considerations govern physical and cognitive effort along with the neural systems mediating them (Westbrook & Braver, 2015). On one hand, both forms of effort may share common motivational mechanisms. Incentive cue reactivity of the ventral striatum, putatively trained by dopamine, encodes motivation for both physical and cognitive effort (Schmidt et al., 2012). Indeed, diminished persistence on a cognitive progressive ratio task predicted both hypoactivation of the ventral striatum, and clinician-rated avolition in SZ patients (Wolf et al., 2014). On the other hand, systemic antagonism of dopamine has a robust effect on decision-making about physical, but not cognitive effort in rats (Hosking, Floresco, & Winstanley, 2014). These apparently discrepant results are resolved by the fact that evidence for a common motivational hub for physical and cognitive effort addresses only one link in a processing chain of cost-tracking mechanisms and cognitive and motor effectors relevant to different forms of effort expenditure. Future studies will need to be conducted to discern how the neural correlates of effort expenditure are distinct throughout up- and downstream processes and regions, and ultimately how this circuitry may be disrupted in SZ. Moreover, dissociations imply that interventions may have dramatically different therapeutic consequences for physical and cognitive effort.

Applications Outside of Schizophrenia

The current study provides novel evidence for increased cognitive effort costs in SZ patients compared to healthy controls. While this group-level difference is informative, the relationship between avolition/anhedonia and effort allocation was far more robust in the current study suggesting a critical link between the subjective cost of cognitive effort and motivational impairments. Importantly, motivational impairments are linked to multiple forms of psychopathology. Thus, while the focus of the current work has been in SZ, it will be important for future studies to address how abnormal cognitive effort cost computations may manifest across diagnostic boundaries. Indeed, evidence for abnormal physical effort-cost computations have been seen in other disorders, most notably depression (Treadway, Bossaller, Shelton, & Zald, 2012; Yang et al., 2014). However, the role of aberrant cognitive effort allocation to the severity of motivational impairments in depression has not yet been tested. Further, a recent review has hypothesized that aberrant effort-cost computations in SZ and depression may be mediated by similar neural systems, involving prefrontal/anterior cingulate and striatal circuits (Salamone, Koychev, Correa, & McGuire, 2015). However, studies still need to be conducted to test such proposals of overlapping circuitry. Thus, future studies may benefit from using COGED across diagnostic boundaries in order to identify shared/distinct etiology of motivational deficits between SZ and depression. One important question will be whether effort deficits are more generally linked to severity of psychopathology, instead of a particular disorder per se.

It will also be important for future work to understand how aberrant effort allocation is related to other components of reward processing known to be disturbed in psychiatric disorders (Barch, Pagliaccio, & Luking, 2015). For example, both SZ (Grimm, Vollstädt-Klein, Krebs, Zink, & Smolka, 2012; Juckel, Schlagenhauf, Koslowski, Filonov, et al., 2006; Juckel, Schlagenhauf, Koslowski, Wüstenberg, et al., 2006; Nielsen et al., 2012; Radua et al., 2015) and

depression (Forbes et al., 2009; Pizzagalli et al., 2009; Zhang, Chang, Guo, Zhang, & Wang, 2013) have been associated with hypoactivation of ventral striatal signaling during reward anticipation. However, work has yet to be conducted to discern whether such deficits in mentally representing reward extend to cost.

In summary, understanding how cognitive effort costs manifest across clinical populations and interact with other aspects of reward processing represents a ripe topic for future studies. The current study demonstrates that COGED is sensitive to motivational impairment for cognitive effort making it an intriguing paradigm for such transdiagnostic exploration.

Limitations

Although the current study reports an intriguing relationship between cognitive effort expenditure and negative symptoms, the results are limited by a number of factors. 1. The sample size of the current study was relatively small (N=25 per group). Thus, as stated above, future studies will need to be conducted in order to determine if our results generalize to larger samples. 2. The current study was limited in its inclusion of external correlates. For example, we did not include measures of positive symptoms nor depression in our experimental design. While positive symptoms have not been related to effort expenditure in previous studies, the exclusion of these measures limits our ability to make claims about the specificity of the relationship we observed between negative symptoms and our novel effort discounting task, COGED (Fervaha, Graff-Guerrero, et al., 2013; Gold et al., 2014; Gold et al., 2013; Hartmann et al., 2015; Horan et al., 2015; Treadway et al., 2015; Wolf et al., 2014). Future studies examining the role of cognitive effort in SZ would benefit from utilizing such measures to establish whether the relationship between cognitive effort and symptomatology is unique to the negative symptom domain. 3. The majority of our SZ sample was prescribed anti-psychotic medication. Given

dopamine's critical role in effort allocation and the impact that anti-psychotics have on D2 receptors, our results must be interpreted with caution. While we did not find relationships between olanzapine equivalent anti-psychotic dose and effort allocation, more data is needed on medication naïve patients to conclusively determine the role of anti-psychotics in effort avoidance in SZ.

Summary

The current study provides the most direct evidence to date of subjectively inflated cognitive effort costs in SZ. This finding provides converging evidence with multiple reports suggesting that cognitive (Reddy et al., 2015; Wolf et al., 2014) and physical (Barch et al., 2014; Gold et al., 2013; Reddy et al., 2015; Treadway et al., 2015) effort allocation are reduced for individuals with SZ compared to controls. Our study extends such reports, by directly analyzing the subjective costliness of cognitive effort rather than patterns of persistence, or binary demand avoidance, and showing that this cost has a robust relationship to negative symptoms. Beyond supporting the hypothesis of abnormal cognitive effort cost computations in SZ, we have also shown the methodological advantages of a recent COGED paradigm for quantifying effort costs. Future studies are needed to better delineate the role of effort allocation in motivational impairment across diagnostic categories (e.g., depression), and to understand how abnormal effort cost computations might interact with other aberrant components of reward processing to produce motivational impairments. .

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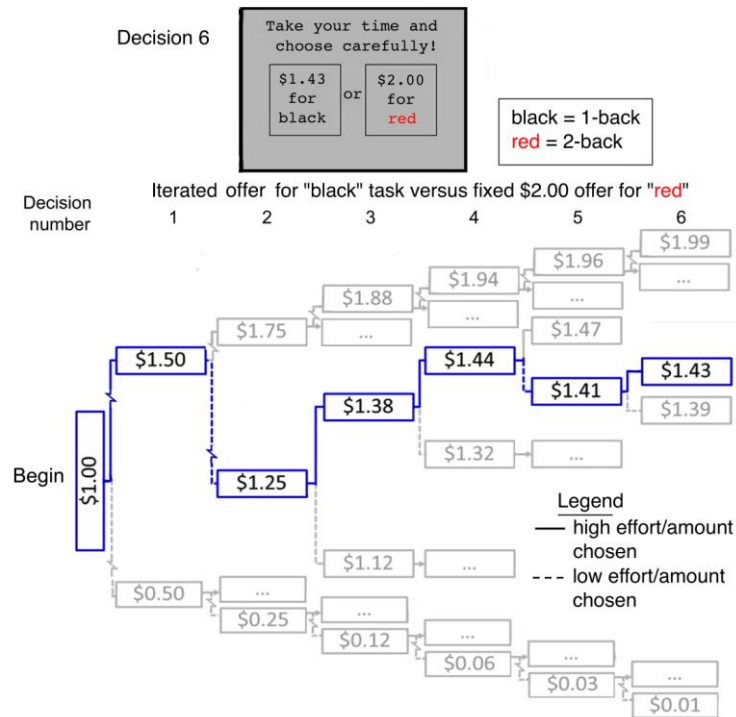


Figure 1. Schematic of offer adjustments for the smaller reward for smaller cognitive load, pursuant to decisions in the COGED paradigm. If a participant chooses the harder option, the offer for the easier amount is increased, if they choose the easier option, the offer is decreased until participants are approximately indifferent between offers (after 5 choices).

Table 1: Participant Characteristics

Characteristics	Healthy Controls (N=25)		Individuals with Schizophrenia (N=25)		p-value
	Mean	SD	Mean	SD	
Demographics					
Age (years)	36	7.0	35	10.3	0.65
Sex (% male)	52%		48%		0.78
Ethnicity (% non-Caucasian)	44%		44%		1.00
Personal Education (years)	16	2.6	12	2.2	<0.01
Parental Education (years)	15	1.9	14	2.9	0.74
Medication status					
Atypical antipsychotics (%)	76%				
Medicated (no antipsychotics)	4%				
Not Medicated (%)	20%				
Clinical ratings					
Brief Negative Symptom Scale					
Total Score	NA	NA	25	16	
Avolition/Anhedonia Subscale	NA	NA	16	10.4	
Self-Report					
Need for Cognition	67	13	59	8.7	0.01
Neurocognitive Measures					
Wechsler Test of Adult Reading (FSIQ)	102	13	99	11	0.42

Table 2. Mean d' by N-back Level N (SD)

Group	1	2	3	4	5
HC	3.6 (0.70)	2.4 (0.85)	1.6 (0.42)	1.2 (0.52)	1.1 (0.49)
SZ	3.2 (0.62)	1.7 (0.70)	1.3 (0.49)	0.87 (0.52)	NA
Wilcox p	0.04	0.02	0.06	0.04	NA
Cohen's d	4.9	2.2	1.9	1.0	NA

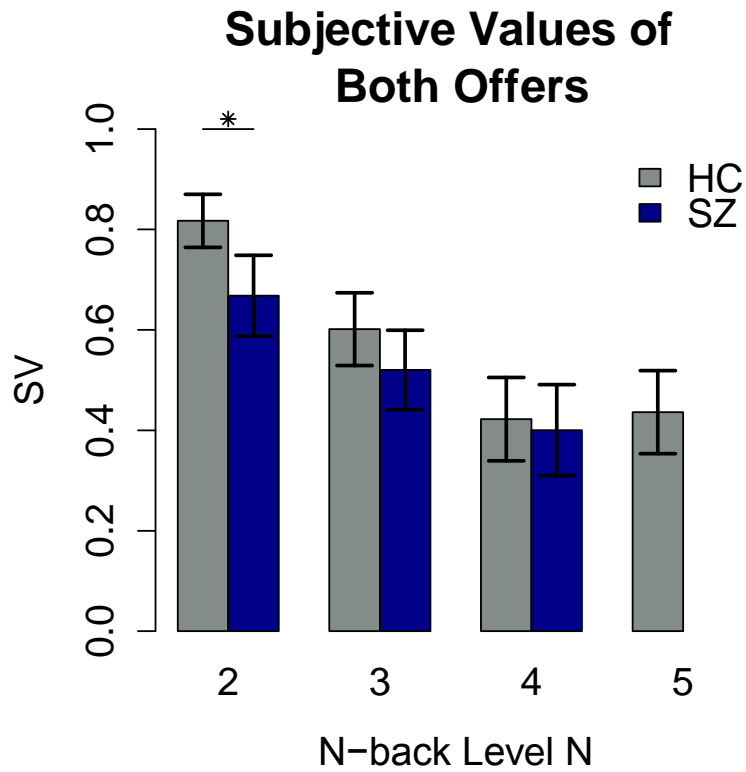


Figure 2. Declining subjective values by N-back load level and by participant group suggest that the subjective costs of engagement rise with objective load and that individuals with schizophrenia find the N-back more costly.

Table 3. Parameter Estimates, Equations 1—4

	Estimate	Std. Error	<i>t</i>	<i>p</i>
Intercept, γ_{00}	1.21	0.095	12.7	< 0.001
Task, γ_{10}	-0.20	0.033	-5.96	< 0.001
Group, γ_{01}	-0.27	0.134	-2.04	0.047
Task x Group, γ_{11}	0.06	0.047	1.36	0.182

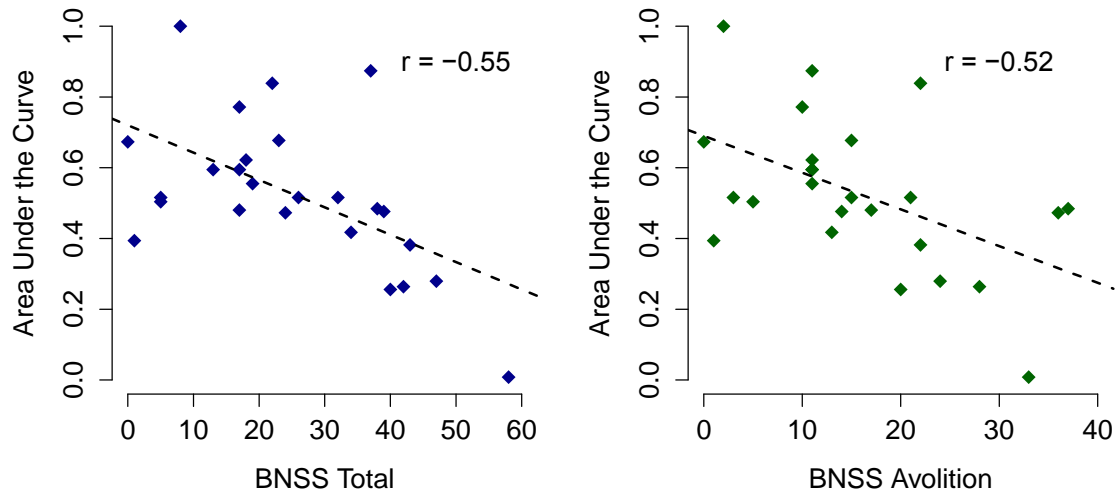


Figure 3. A) Increasing BNSS Total negative symptoms predict lower Area Under the Discounting Curve – or greater subjective costs across N-back levels. B) Increasing BNSS Avolition subscores predict lower Area Under the Discounting Curve.