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AVOLITION IN SCHIZOPHRENIA IS ASSOCIATED WITH REDUCED WILLINGNESS TO EXPEND EFFORT FOR REWARD ON A PROGRESSIVE RATIO TASK

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Abstract

The current study examined whether effort-cost computation was associated with negative symptoms of schizophrenia (SZ). Participants included outpatients diagnosed with SZ ($n = 27$) and demographically matched healthy controls ($n = 32$) who completed a Progressive Ratio Task that required incrementally greater amounts of physical effort to obtain monetary reward. Breakpoint, the point at which participants were no longer willing to exert effort for a certain reward value, was examined as an index of effort-cost computation. There were no group differences in breakpoint for low, medium, or high value rewards on the Progressive Ratio Task. However, lower breakpoint scores were associated with greater severity of avolition and anhedonia symptoms in SZ patients. Findings provide further evidence that impaired effort-cost computation is linked to motivational abnormalities in SZ.

Keywords

Psychosis; Reward; Negative Symptoms; Effort; Motivation

1.0. Introduction

Negative symptoms have long been considered a core component of the schizophrenia (SZ) diagnosis (Kraepelin, 1919). Two distinct negative symptom dimensions have been

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Contributors

Gregory Strauss designed the study. Statistical analyses and writing of the first draft of the manuscript were performed by Gregory Strauss and Kayla Whearty. All authors contributed to and approved the final manuscript.

Conflict of Interest

Dr. Strauss receives royalties and consultation fees from ProPhase LLC in connection with commercial use of the Brief Negative Symptom Scale and other professional activities. Kayla Whearty, Lindsay Morra, Kathryn Ossenfort, Sara Sullivan, and Katherine Frost have no conflicts to report.

identified, one reflecting reduced motivation (avolition, anhedonia, and asociality) and the other diminished expressivity (alogia, restricted affect) (Blanchard and Cohen, 2006; Horan et al., 2011; Strauss et al., 2012b). There is growing evidence that motivational symptoms play a greater role than expressivity symptoms in determining a range of clinical outcomes (e.g., work and social function, recovery, subjective well-being) (Foussias and Remington, 2010; Strauss et al., 2010; Strauss et al., 2013; Strauss et al., 2012c). Unfortunately, attempts to remediate motivational symptoms via pharmacological treatment have proven ineffective (Fusar-Poli et al., 2015).

Given limited progress in treating motivational symptoms, there has been increased interest in identifying mechanisms leading to reduced goal-directed behavior in SZ (Barch and Dowd, 2010; Strauss et al., 2014). The most straightforward explanation of avolition is that patients do not engage in activities because they do not find them enjoyable. However, experience sampling and laboratory-based studies do not support this hypothesis, indicating that SZ patients have a normal hedonic capacity (Cohen and Minor, 2010; Gard et al., 2007; Kring and Moran, 2008; Llerena et al., 2012; Oorschot et al., 2013; Strauss and Gold, 2012). Rather, motivational symptoms appear to be more closely tied to a range of reward processing abnormalities, such as impaired reward anticipation (Juckel et al., 2006; Waltz et al., 2010), reinforcement learning (Culbreth et al., 2015; Gold et al., 2012; Strauss et al., 2011a; Waltz et al., 2007), and difficulty generating, updating, or maintaining mental representations of value (Gard et al., 2011; Heerey et al., 2007; Kring et al., 2011; Strauss et al., 2011b; Ursu et al., 2011) (for reviews see Barch and Dowd, 2010; Kring and Barch, 2014; Strauss et al., 2014).

Fewer studies have examined the association between motivational symptoms and another aspect of reward processing, effort-cost computation (i.e., determining whether the benefits of an action outweigh the costs needed to obtain them). Pre-clinical studies indicate that dopamine plays a key role in determining the amount of effort an animal will expend to obtain rewards of differing value, with evidence that focal dopamine depletion in the accumbens reduces willingness to exert high effort for higher value rewards and that effort can be increased via the administration of amphetamine (Hodos, 1961; Salamone et al., 1994). Human studies mirror these effects, indicating that individual differences in dopamine release predict willingness to expend effort for high value rewards and that amphetamine administration increases effortful behavior (Treadway et al., 2012; Wardle et al., 2011). Anterior cingulate cortex (ACC) structure and function also predicts effort-cost computation in animal and human studies, potentially via interactions with the dopamine system (Croxson et al., 2009; Endepols et al., 2010; Prevost et al., 2010; Walton et al., 2002; Walton et al., 2009).

There are several reasons to expect that SZ patients would display abnormalities in effort-cost computation, including structural and functional ACC abnormalities and over-expression of postsynaptic D2 receptors that influence dopamine function (see Fervaha et al., 2013a; Green et al., 2015 for reviews). Prior studies have primarily examined effort-cost computation in SZ using decision-making tasks that examine the rate of selecting between high effort/high value and low effort/low value options (e.g., Effort Expenditure for Reward Task: Treadway et al., 2009). Results have provided mostly consistent evidence that SZ

patients are less willing to select high-effort/high-value options, and that reduced willingness to expend effort for high value rewards predicts greater negative symptom severity or poor functional outcome (Barch et al., 2014; Fervaha et al., 2015; Fervaha et al., 2013b; Gold et al., 2013; Hartmann et al., 2015; Horan et al., 2015; Reddy et al., 2015; Treadway et al., 2015; Wolf et al., 2014); however, Docx et al. (2015) did not find differences between patients and controls. Only one published study has administered a different kind of effort-cost task, the Progressive Ratio paradigm, which is well-validated in the animal literature. In Progressive Ratio tasks, subjects (animal or human) are required to perform an effortful task (e.g., button pressing or climbing a barrier) for certain reward values. Critically, the level of effort needed to obtain the reward is parametrically increased from trial to trial to find the subject's "breakpoint", i.e., the point at which the subject is no longer willing to put forth effort to obtain the reward offered. Wolf et al. (2014) administered a cognitive Progressive Ratio task to SZ patients that required completing incrementally greater numbers of mathematical operations (e.g., 6, 12, 26, 45, 100, 167, 500 trials) to obtain monetary rewards. They found that SZ had lower breakpoint scores than controls, and that lower breakpoint was significantly associated with greater severity of motivational, but not expressivity negative symptoms. Additionally, lower breakpoint scores were predicted by reduced activation of the ventral striatum on a separate reinforcement-learning task. Thus, findings in the literature to date provide relatively consistent evidence for impaired effort-cost computation in SZ and that this deficit is associated with greater severity of negative symptoms and neural mechanisms associated with approach motivation.

In the current study, we aimed to extend the literature on effort-cost computation by administering a physical effort variant of the Progressive Ratio task to evaluate differential associations with motivational and expressivity negative symptom dimensions. Consistent with prior studies (Barch et al., 2014; Fervaha et al., 2013b; Gold et al., 2013; Hartmann et al., 2015; Horan et al., 2015; Reddy et al., 2015; Treadway et al., 2015; Wolf et al., 2014), we hypothesized that SZ would have a lower breakpoint than healthy controls (CN) and that lower break point would predict greater severity of motivational, but not expressivity symptoms on the Brief Negative Symptom Scale (BNSS: Kirkpatrick et al., 2011; Strauss et al., 2012a; Strauss et al., 2012b).

2.0. Method

2.1. Participants

Participants included 27 outpatients meeting Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) criteria for schizophrenia or schizoaffective disorder (SZ) and 32 healthy controls (CN). Participants with SZ were recruited from outpatient mental health clinics in upstate New York and advertisements presented on television or the Internet. Patients were evaluated during periods of clinical stability as indicated by no change in medication type or dose within the past 6 weeks. Diagnosis was established via a best-estimate approach based on psychiatric history and the Structured Clinical Interview for DSM-IV (SCID: First et al., 2001). A total of 20 patients were prescribed second-generation antipsychotics, 2 were on first-generation antipsychotics,

and 1 was on both first and second generation antipsychotics. Four patients were stably unmedicated and not receiving antipsychotics at the time of testing.

Healthy control participants (CN) were recruited through printed and online advertisements and word of mouth among enrolled participants. All CN underwent a diagnostic interview, including the SCID-I and SCID-II (Pfohl et al., 1997) and did not meet criteria for any current Axis I or Axis II schizophrenia-spectrum personality disorder. CN also had no family history of psychosis and did not meet lifetime criteria for psychotic disorders. No participants met criteria for substance dependence in the last 6 months and all denied lifetime history of neurological disorders associated with cognitive impairment (e.g., Traumatic Brain Injury, Epilepsy).

Individuals with SZ and CN did not significantly differ in age, parental education, sex, or ethnicity; however, SZ had lower personal education than CN (see Table 1).

2.2. Procedures

Participants completed a standard clinical interview that was performed by a clinical psychologist (GPS) or a Master's level clinical psychology doctoral student (SKS) trained to reliability standards (>0.80) using gold standard training videos developed by the first author (GPS). After this interview, patients were rated on the BNSS (Kirkpatrick et al., 2011; Strauss et al., 2012a; Strauss et al., 2012b), Brief Psychiatric Rating Scale (BPRS: Overall and Gorham, 1962), and Level of Function Scale (LOF: Hawk, 1975). After the interview, the MATRICS Consensus Cognitive Battery (MCCB: Nuechterlein et al., 2008) was administered and participants completed the Progressive Ratio task.

2.3. Progressive Ratio Task

Participants completed a Progressive Ratio task that examined the effects of reward value on willingness to expend physical effort. The task structure, trial sequencing, and reward/effort ratios were modeled after Wolf et al. (2014) (see Table 2). Similar to our earlier paper that used a 2 forced-choice effort-cost paradigm (Gold et al., 2013), the effortful task involved using a videogame controller to make rapid left-right alternating button presses to inflate a single balloon presented on the computer screen until it popped (see Figure 1). Participants were told that they could choose to play each trial, skip that trial altogether, or quit the trial once it was started if they no longer wished to complete it.

At the start of each trial, the amount of reward that could be received on that trial and the amount of effort (i.e., button presses) required to obtain the reward was displayed on the screen (see Figure 1). To skip a trial or abort a trial once initiated, participants were instructed to press a specific button. On trials that participants initiated, each alternating button press caused the balloon to expand and make a corresponding inflation sound that was accompanied by a fan-like motion of a fireplace bellow located beneath the balloon. The balloon expanded until it reached a pin located at the top of the computer screen, and a popping sound occurred. After the balloon popped, a screen appeared indicating the amount of reward that had been obtained on that trial (range \$0.10 to \$0.50). A running tally of total earnings was presented continuously in the bottom right corner of the screen.

Four practice trials were administered to familiarize participants with the task setup and game controller. During practice, they were instructed to inflate 1 balloon until it popped, skip a trial without initiating it, abort a trial that had been started, and complete a trial while pressing buttons as rapidly as possible. Experimental trials consisted of 2 blocks of 7 sets of trials at 3 monetary reward levels (\$0.10, \$0.25, \$0.50) (see Table 2). Critically, the level of effort required to obtain the reward in that particular block of trials (e.g., \$0.10) parametrically increased from one trial to the next (e.g., 6, 12, 26, 45, 100, 167, 500 button presses) (see Table 2). This allowed us to identify each participant's "breakpoint", i.e., the maximum level of physical effort they were willing to exert to obtain rewards of certain value. The sequence of reward blocks was always consistent, at \$0.50, 0.25, 0.10, as is common in Progressive Ratio tasks. Once the 3 sets of reward blocks were completed, a second set of 3 blocks (\$0.50, 0.25, 0.10) was administered. A break occurred between the 2 blocks and as needed after trials to reduce physical fatigue. Participants were told that they could keep a portion of the money they earned during the task. In actuality, all participants received a \$10 bonus payment, in addition to the regular hourly compensation rate (\$20 per hour).

3.0. Results

3.1. Behavioral Progressive Ratio Results

There were no group differences in total breakpoint across all blocks, $F(1, 58) = 0.01$, $p = 0.96$, or when breakpoint was evaluated separately at the \$0.10 ($F[1, 58] = 0.02$, $p = 0.89$), \$0.25, ($F[1, 58] = 0.15$, $p = 0.70$), or \$0.50 ($F[1, 58] = 0.01$, $p = 0.93$) blocks (see Figure 2 A). There were no participants who completed all trials.

SZ displayed significantly slower total response vigor (average milliseconds per press) across all blocks ($F[1, 58] = 12.64$, $p < 0.001$), and during the \$0.50 ($F[1, 58] = 10.03$, $p < 0.01$), and \$0.25 ($F[1, 58] = 9.59$, $p < 0.01$) blocks. There was a trend toward SZ being slower than CN on the \$0.10 block ($F[1, 58] = 3.23$, $p < 0.08$) (see Figure 2B).

There were also no group differences in the percentage of trials completed ($F[1, 58] = 0.06$, $p = 0.80$), the number of trials attempted and aborted ($F[1, 58] = 1.96$, $p = 0.17$), or the number of trials not attempted ($F[1, 58] = 0.40$, $p = 0.53$).

3.2. Correlations

In SZ, lower average breakpoint scores across all conditions were significantly correlated with greater severity of BNSS anhedonia and avolition subscales, as well as the volitional dimension score (anhedonia, asociality, avolition items) (see Figures 3A-C). These correlations remained significant after excluding the 3 SZ prescribed first generation antipsychotics. Average breakpoint across all conditions was not significantly associated with the BNSS expressivity dimension. The Fisher r -to- Z test for significant differences in magnitude of correlation between BNSS MAP and EE dimensions was nonsignificant, $Z = -0.88$, $p = 0.37$.

BPRS positive, disorganized, negative, and total symptoms were not significantly correlated with breakpoint. Poorer work and total functional outcome on the LOF was associated with

lower average breakpoint values across all conditions; however, breakpoint was not significantly associated with LOF social outcome. Breakpoint was not associated with MCCB global scores, MCCB working memory, or chlorpromazine equivalent dosage (Woods, 2003). Table 3 presents a full list of the observed correlations.

4.0. Discussion

Contrary to hypotheses and most prior studies, there was no main effect of group on breakpoint for the high, medium, or low value conditions. However, as predicted, lower total breakpoint was associated with greater severity of BNSS volitional symptoms and poorer LOF work outcomes. Breakpoint was not significantly correlated with BNSS expressivity scores (restricted affect and alogia), BNSS asociality, or LOF social functioning. These findings are consistent with past studies using 2-choice decision-making effort paradigms, which found that greater severity of negative symptoms and poorer functional outcome were associated with reduced willingness to work for high-value rewards (Barch et al., 2014; Fervaha et al., 2013b; Gold et al., 2013; Hartmann et al., 2015). Results are also consistent with findings from a cognitive Progressive Ratio paradigm, which indicated that lower breakpoint was associated with greater severity of motivational symptoms and reduced activation of the ventral striatum during a separate reinforcement learning task (Wolf et al., 2014). Thus, the literature to date provides strong support for a link between greater severity of motivational symptoms and effort-cost computation abnormalities in SZ (Green et al., 2015).

Certain limitations should be considered. First, reward value was not tailored to each participant's annual income. Given that most people with SZ have significantly lower annual income than CN, lack of calibrating reward level to each participant's income may have made monetary incentives more valuable in SZ than CN. We suspect this to be true since fewer of our SZ patients held competitive jobs compared to CN. Second, the task did not impose a time constraint to perform each trial. SZ patients had slower response vigor than CN, and on average took longer to complete individual trials. The lack of time constraint may have made the task less effortful for patients, who appear to have adopted a strategy of completing a high number of trials but taking more time to do so. In future studies, implementing time restrictions based on a percentage of maximum individual motor performance may increase the difficulty of the task and therefore make effort demands more salient. Third, although we did not find a significant correlation between chlorpromazine equivalent dosage and breakpoint, we cannot rule out the possibility that antipsychotics influenced results. Chlorpromazine equivalent dosage is a crude estimate of antipsychotic burden and future studies comparing performance in unmedicated first episode patients who are tested again after being stably medicated are needed. Finally, we did not measure extrapyramidal symptoms (EPS). It is unclear whether EPS influenced the impairments in response vigor that were observed.

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Figure 1. Sample Trial Sequence

Note. Participants saw the number of button presses (e.g., \$100) required to achieve a certain monetary reward (e.g., \$0.50) at the start of each trial (top left), if they initiated the trial (top right) the balloon inflated with each press, increasing in size until it hit a pin at the top of the screen (bottom left), and popped to display the amount of reward earned (bottom right). On trials that were aborted or not started, the balloon disappeared and the next set was brought up and the first trial within that set appeared (back to top right) displaying the amount of button presses and reward value available on that trial.

Figure 2. Progressive Ratio Task Performance

Note. SZ = Schizophrenia; CN = Control; A = Mean Breakpoint; B = Mean Response Vigor (ms per press)

Figure 3.
Scatter Plots Depicting the Association Between Negative Symptoms and Breakpoint

Table 1**Participant Demographic and Clinical Characteristics**

	SZ (n = 27)	CN (n =32)	Test Statistic, p-value
Age	40.30(12.90)	38.06(11.15)	F= 0.51, p= 0.48
Participant Education	12.39(2.14)	14.61(2.16)	F= 15.65, p<0.001
Parental Education	13.28(2.05)	13.65(2.26)	F= 0.40, p= 0.53
% Male	66.7%	65.6%	$\chi^2= 0.01$, p=1.00
Race %			$\chi^2= 1.61$, p=0.66
Caucasian	70.4%	75.0%	
African-American	18.5%	12.5%	
Hispanic	3.7%	9.4%	
Mixed-Race	7.4%	3.1%	
BNSS			
Total	22.04(18.94)	--	--
Volition Dimension	2.05(1.72)	--	--
Expressivity Dimension	1.45(1.67)	--	--
BPRS			
Positive	3.33(1.27)	--	--
Negative	2.18(1.25)	--	--
Disorganized	2.08(0.86)	--	--
Total	46.62 (8.90)		
LOF			
Social	5.92(2.90)	--	--
Work	1.00(2.02)	--	--
Total	16.83(7.19)	--	--

Note. SZ = schizophrenia; CN = control; BNSS = Brief Negative Symptom Scale; BPRS = Brief Psychiatric Rating Scale; LOF = Level of Function Scale

Table 2

Progressive Ratio Task Trial Structure

Set	Cents	Trials	Cents/Press (CPT)	Presses/Cent (TPC)	log10(TPC)	Breakpoint TPC	Breakpoint log10 (TPC)
1	50	6	8.33	0.12	-0.92	0.12	-0.92
2	50	12	4.17	0.24	-0.62	0.17	-0.77
3	50	26	1.92	0.52	-0.28	0.35	-0.45
4	50	45	1.11	0.90	-0.05	0.68	-0.16
5	50	100	0.50	2.00	0.30	1.34	0.13
6	50	167	0.30	3.34	0.52	2.58	0.41
7	50	500	0.10	10.00	1.00	5.78	0.76
Complete 1-7						10.00	1.00
8	25	3	8.33	0.12	-0.92	0.12	-0.92
9	25	6	4.17	0.24	-0.62	0.17	-0.77
10	25	13	1.92	0.52	-0.28	0.35	-0.45
11	25	23	1.09	0.92	-0.04	0.69	-0.16
12	25	50	0.50	2.00	0.30	1.36	0.13
13	25	83	0.30	3.32	0.52	2.58	0.41
14	25	250	0.10	10.00	1.00	5.76	0.76
Complete 8-14						10.00	1.00
15	10	1	10.0	0.10	-1.00	0.10	-1.00
16	10	2	5.00	0.20	-0.70	0.14	-0.85
17	10	5	2.00	0.50	-0.30	0.32	-0.50
18	10	9	1.11	0.90	-0.05	0.67	-0.17
19	10	20	0.50	2.00	0.30	1.34	0.13
20	10	33	0.30	3.30	0.52	2.57	0.41
21	10	100	0.10	10.00	1.00	5.74	0.76
Complete 15-21						10.00	1.00

Note. Trial structure adopted from Wolf et al. (2014).

Table 3

Correlations Between Breakpoint and Clinical Variables in Schizophrenia Patients

	r, p-value
Negative Symptoms	
BNSS Anhedonia	-.45*
BNSS Avolition	-.43*
BNSS Asociality	-.26
BNSS MAP Dimension	-.42*
Restricted Affect	-.21
Alogia	-.12
BNSS Expressivity Dimension	-.19
BNSS Total	-.37
BPRS Negative Factor	-.23
Psychosis and General Symptoms	
BPRS Psychosis	-.09
BPRS Disorganization	-.24
BPRS Depression	.01
BPRS Total	-.32
Functional Outcome	
LOF Social	.47*
LOF Work	.19
LOF Total Outcome	.59**
MCCB	
Global	-.02
Working Memory	-.20
CPZ Equivalent Dosage	-.21

Note.

BNSS = Brief Negative Symptom Scale; MAP = Motivation and Pleasure; BPRS = Brief Psychiatric Rating Scale; LOF = Level of Function Scale; MCCB = MATRICS Consensus Cognitive Battery; CPZ = Chlorpromazine Equivalent Dosage

*
p < 0.05;

**
p < 0.01;