



## Impaired effort allocation in patients with schizophrenia

Michael T. Treadway<sup>a,\*</sup>, Joel S. Peterman<sup>b</sup>, David H. Zald<sup>b,c</sup>, Sohee Park<sup>b,c</sup>

<sup>a</sup> Department of Psychology, Emory University, Atlanta, GA 30322, United States

<sup>b</sup> Department of Psychology, Vanderbilt University, Nashville, TN 37240, United States

<sup>c</sup> Department of Psychiatry, Vanderbilt University, Nashville, TN 37240, United States



### ARTICLE INFO

#### Article history:

Received 3 September 2014

Received in revised form 16 November 2014

Accepted 19 November 2014

Available online 5 December 2014

#### Keywords:

Negative symptoms

Motivation

Effort-based decision-making

Schizophrenia

EEfRT

### ABSTRACT

A hallmark of negative symptoms in schizophrenia is reduced motivation and goal directed behavior. While preclinical models suggest that blunted striatal dopamine levels can produce such reductions, this mechanism is inconsistent with evidence for enhanced striatal dopamine levels in schizophrenia. In seeking to reconcile this discrepancy, one possibility is that negative symptoms reflect a failure of striatal motivational systems to mobilize appropriately in response to reward-related information. In the present study, we used a laboratory effort-based decision-making task in a sample of patients with schizophrenia and healthy controls to examine allocation of effort in exchange for varying levels of monetary reward. We found that patients and controls did not differ in the overall amount of effort expenditure, but patients made significantly less optimal choices in terms of maximizing rewards. These results provide further evidence for a selective deficit in the ability of schizophrenia patients to utilize environmental cues to guide reward-seeking behavior.

© 2014 Elsevier B.V. All rights reserved.

### 1. Introduction

A growing body of evidence suggests that reduced motivation and goal-directed behavior may occur in schizophrenia without concomitant alterations of hedonic responsivity (Gard et al., 2007; Gold et al., 2008; Barch and Dowd, 2010; Folley and Park, 2010). In preclinical models, effort-based decision-making paradigms that assess the willingness to invest greater effort in order to obtain larger or preferred rewards have repeatedly implicated disruption of corticostriatal dopamine (DA) as a possible substrate for motivational impairments (Salamone and Correa, 2012; Treadway and Zald, 2013); indeed, potentiation or attenuation of DA signaling can increase or decrease effort expenditure for rewards in both rodents (Salamone et al., 2007; Floresco et al., 2008; Bardgett et al., 2009) and humans (Venugopalan et al., 2011; Wardle et al., 2011).

In the context of schizophrenia, however, it appears unlikely that negative symptoms are mediated by a global reduction in striatal DA given robust evidence for striatal DA elevations as a mechanism underlying symptoms of psychosis (Fusar-Poli and Meyer-Lindenberg, 2012; Howes et al., 2013). An alternative explanation is that both positive and negative symptoms result from irregular (as opposed to simply enhanced or reduced) striatal DA release that may not respond appropriately to meaningful reward incentives. Consistent with this model, several recent studies of effort-based decision-making in patients with schizophrenia have found no evidence for a global reduction of effort

expenditure, but rather an apparent failure to mobilize effort in response to maximally rewarding cues (Fervaha et al., 2013; Gold et al., 2013; Barch et al., 2014). In the present study, we adopted a similar methodology in an attempt to replicate these prior findings and extend them with a more direct investigation into the utilization of reward magnitude and probability information in guiding effort-based choice in schizophrenia patients.

### 2. Methods

#### 2.1. Participants and procedure

All subjects provided written informed consent, and all study procedures were approved by the Vanderbilt Institutional Review Board. 13 outpatients with schizophrenia (SZ) participated in the study, and data from 15 healthy control subjects (HC) were drawn from a prior published study (Treadway et al., 2012). All patients were recruited from private-care facilities in Nashville, TN, and completed the Structured Clinical Interview for DSM-IV (First et al., 2005) to confirm diagnosis. Exclusion criteria for the SZ were: IQ lower than 85, a prior history of head trauma/neurological disorder, or a history of drug use in the previous year. The severity of symptoms was evaluated with SANS and SAPS interviews (Zigler and Levine, 1981; Andreasen, 1984a,b). Subjects were then instructed to complete the Effort-Expenditure for Rewards Task (EEfRT). One patient failed to comply with task instructions, and was excluded from the study. A summary of demographics and symptom scores are reported in Table 1. The two groups differed in years of education, which was included as a covariate

\* Corresponding author.

E-mail address: [mtreadway@emory.edu](mailto:mtreadway@emory.edu) (M.T. Treadway).

**Table 1**  
Demographic characteristics.

	SZ (n = 12)		HC (n = 15)		p-Value
	Mean	SD	Mean	SD	
Sex	5/12 female		9/15 female		0.34
Age	38.5	10.1	39.7	8.2	0.72
Years of education	13.7	1.9	16.3	1.8	0.008
SAPS (Andreasen, 1984a)	19.2	11.2	–	–	
SANS (Andreasen, 1984b)	25.8	12.7	–	–	
Chlorpromazine Equivalent Dose (CPZ) (Woods, 2003)	428.5	362.3	–	–	

in subsequent group analyses. However, note that SZ had intact IQ (mean = 100; S.D. = 10.4).

**2.2. Effort Expenditure for Rewards Task (EEfRT)**

The effort Expenditure for Rewards Task (EEfRT) is a computerized effort-based decision-making task (Treadway et al., 2009) (Fig. 1). On each trial the participant must choose between, a ‘high effort’ option and a ‘low effort’ option, which require varying amounts of speeded manual button pressing. For low-effort choices, participants are eligible to win \$1.00, while eligible amounts for selecting the high effort option ranged between \$1.24 and \$4.30 (“reward magnitude”). Additionally, probability of reward receipt (regardless of choice) varied across trials. Participants were provided with accurate probability cues at the beginning of each trial indicating that they had a “high” (88%), “medium” (50%) or “low” (12%) probability of receiving money for the choice made on that trial. The inclusion of probability and reward magnitude manipulations in the EEfRT facilitates the evaluation of two constructs: overall willingness to expend effort for rewards (since the high effort option is always associated with a greater expected value), and the utilization of reinforcement parameters in the allocation of effort resources (i.e. is effort allocated when reward values and probabilities are most favorable).

**2.3. Statistical analyses**

Statistical analyses were consistent with prior studies using the EEfRT in samples with schizophrenia patients (Barch et al., 2014). Participant choice data was entered into a 2 (group) × 3 (probability level) × 4 (reward value) Repeated-measures ANOVA, with reward magnitude values for the high effort option binned into four groups: <\$1.96; \$1.96–\$2.77; \$2.77–\$3.58; and ≥\$3.58. A Huynh–Feldt correction was applied in cases where the assumption of sphericity was not met.

To further evaluate group differences in the utilization for both probability and reward value information when making effort allocations, individual logistic regression analyses were performed for each subject with expected value (defined as per-trial reward value \* probability) as a single regressor predicting effort choice.

**3. Results**

**3.1. Main effects of the EEfRT**

Consistent with prior studies using the EEfRT, there were significant main effects of probability (Huynh–Feldt  $F_{(2, 39.7)} = 9.69, p = 0.001$ ) and reward value (Huynh–Feldt  $F_{(3, 64.9)} = 15.31, p < 0.00001$ ), such that all subjects were more likely to choose the high effort option when the reward value and probability of receiving reward were higher. There were no group differences in average reaction time between HC (M = 1.32, SD = 0.44) and SZ (M = 1.10 SD = 0.71) ( $t_{25} = 1.02, p = 0.319$ ), and no differences in successful completion of high and low effort options ( $t_{25} = -0.75, p = 0.458$ ), with both groups completing over 95% of trials on average.

**3.2. Group effects**

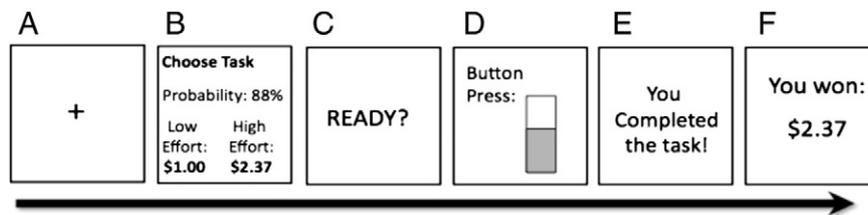
There was no main effect of group in terms of the total number of high-effort options made ( $F_{(1, 25)} = 0.62, p = 0.440$ ). This was true even when controlling for years of education. However, there were significant interactions of group-by-probability (Huynh–Feldt  $F_{(2, 39.8)} = 5.42, p = 0.012$ ) (Cohen's  $d = 0.90$ ) and group-by-reward value (Huynh–Feldt  $F_{(3, 62.2)} = 7.50, p < 0.0004$ ) (Cohen's  $d = 1.06$ ), such that HC were significantly more likely to choose the high effort option when the probability and reward magnitudes were higher, while choice behavior among SZ remained relatively constant across different levels of probability and reward (Fig. 2). There was no three-way interaction (Huynh–Feldt  $F_{(6, 5.9)} = 1.35, p = 0.24$ ). These interaction effects remained significant even when controlling for chlorpromazine equivalent medication doses (CPZ), and when 2 patients who chose no high effort options were excluded. There were no interactions between education level and either probability or reward magnitude, though there was a trend-level main effect of years of education such that higher education levels predicted a larger number of high effort choices.

**3.3. Sensitivity to reinforcement parameters**

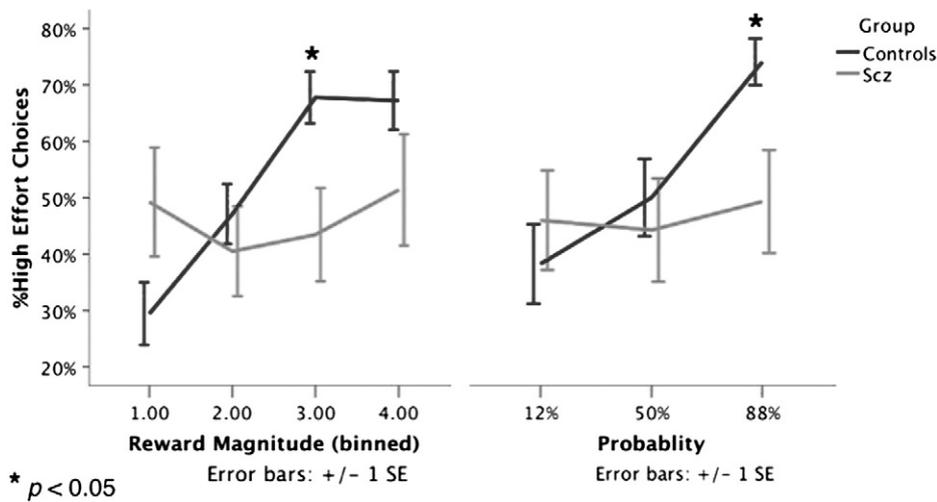
The pattern of interactions suggested that HC relied much more on the probability and reward magnitude information to guide their allocation of effort than did SZ. To further test this hypothesis, per-subject expected value (EV) beta weights were compared across groups; higher beta weights indicate EV was a stronger predictor of choice behavior. EV beta weights were significantly larger for HC than SZ ( $t_{25} = 3.59, p = 0.002$ ) and follow-up one-sample t-tests confirmed that EV beta weights were significantly greater than 0 for HC ( $t_{14} = 4.40, p = 0.001$ ) but not for SZ ( $t_{11} = 0.86, p = 0.410$ ), suggesting that HC, but not SZ were relying on EV information to guide effort decisions (Fig. 3).

**3.4. Associations with negative symptoms**

Given the theoretical link between effort-based decision-making and negative symptoms, we tested for an association between EV beta



**Fig. 1.** Schematic diagram of a single trial of the Effort-Expenditure for Rewards Task. A. 1 s fixation cue. B. 5 s choice period where subjects are presented with information regarding the reward magnitude of the High Effort option, and the probability of receiving a reward. C. A 1 s “ready” screen. D. Subjects must make rapid button presses to complete the chosen task while a virtual “bar” fills up to indicate their progress. E. Subjects receive feedback on task completion. F. Subjects receive feedback about any money received for that trial.



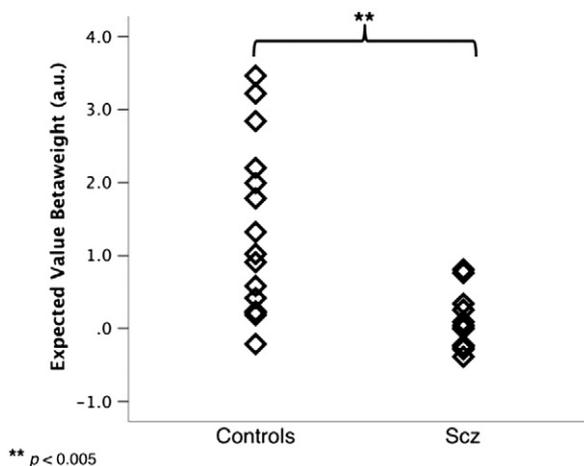
**Fig. 2.** High effort choices made by controls and patients with schizophrenia across differing levels of probability and reward magnitude. We observed significant interactions for both group-by-probability and group-by-reward value such that control participants increased the proportion of high effort choices made during trials with high probability and reward magnitude to a much a greater extent than did schizophrenia patients.

weights and negative symptom severity assessed by the SANS. Using a regression analysis with CPZ as a nuisance covariate, we observed a trend-level association between SANS and EV beta weights ( $b = -0.60$ ,  $p = 0.051$ ), such that individuals with higher negative symptoms had more difficulty incorporating reward and probability information when making effort-related decisions.

#### 4. Discussion

In this study, we replicated prior findings suggesting that SZ patients show significant impairment in the ability to allocate physical effort resources in pursuit of rewards. This is in keeping with three prior independent effort-based decision-making studies, all of which found that SZ did not make fewer high effort choices than HC on average, but generally failed to select the high effort option for the most rewarded trials (Fervaha et al., 2013; Gold et al., 2013; Barch et al., 2014).

Our study extended this finding through an examination of the use of expected value information in predicting choice behavior; whereas controls appeared to rely heavily on expected value to guide allocation of effort, this information had little effect on choices made by SZ, with EV being a significant predictor of choice behavior for only two patients.



**Fig. 3.** Utilization of expected value (EV) when making effort-allocation choices. Single-subject logistic regression analyses revealed that betaweights for EV were significantly higher for controls than patients with schizophrenia, indicating that controls utilized EV information when making effort-allocation decisions, while schizophrenia patients did not. au = arbitrary units.

Moreover, we observed a trend-level association between negative symptoms and magnitude of EV betaweights. The inability to translate reward-relevant information into goal-directed behavior has emerged as a key deficit in daily functioning of individuals with schizophrenia, with recent ecological momentary assessment data highlighting the difficulty that patients experience in completing effortful actions, even when they expect to enjoy them (Gard et al., 2014). These deficits may reflect a parallel to the aberrant salience model of schizophrenia (Winton-Brown et al., 2014), although in this case the problem arises in discriminating between different incentives rather than attentional cues.

This study has several caveats. First, our sample size was small, though we note that prior studies with patient samples ranging from 16 to 59 all found significant group-by-probability and group-by-value interactions with effect sizes ranging from  $d = 0.31$  to  $1.06$  and  $d = 0.37$  to  $1.35$ , consistent with the current report. A second limitation is that all patients were receiving antipsychotic drugs, which can produce side effects of apathy and lethargy. That said, there were no group differences in completion rates, reaction times, or overall number of high effort options, and our main effects were unchanged by controlling for the medication dose. Lastly, given the persistent working memory deficit in schizophrenia, it is possible that failure to maintain the task goal or the mental representation of the reward value may have played a role in EEfRT performance. Future studies should examine the impact of working memory deficits in optimal allocation of effort.

In sum, this paper replicates and extends prior work suggesting that schizophrenia is associated with selective deficits in reward-maximizing allocation of effort during goal-directed activity.

#### Role of funding source

This study was supported by the National Institute of Mental Health (NIMH) grants F31MH087015, K99MH102355 (MTT), and T32 MH018921-21A1 (JSP), and a Brain & Behavior Research Foundation NARSAD grant (SP).

#### Contributors

MTT, DHZ and SP designed the study, MTT and JSP collected and analyzed the data, MTT, JSP, DHZ, and SP wrote the paper.

#### Conflict of interest

The authors report no conflict of interest related to this work, financial or otherwise.

#### Acknowledgments

The authors report no conflict of interest related to this work, financial or otherwise. This study was supported by the National Institute of Mental Health (NIMH) grants F31MH087015, K99MH102355 (MTT), and T32 MH018921-21A1 (JSP), and a Brain &

Behavior Research Foundation NARSAD grant (SP). The authors wish to thank Lindsey McIntosh and Heath Nichols for help with recruitment and symptom assessment.

## References

- Andreasen, N.C., 1984a. The Scale for the Assessment of Positive Symptoms (SAPS). University of Iowa, Iowa City.
- Andreasen, N.C., 1984b. Scale for the Assessment of Negative Symptoms. University of Iowa, Iowa City.
- Barch, D.M., Dowd, E.C., 2010. Goal representations and motivational drive in schizophrenia: the role of prefrontal–striatal interactions. *Schizophr. Bull.* 36 (5), 919–934.
- Barch, D.M., Treadway, M.T., Schoen, N., 2014. Effort, anhedonia, and function in schizophrenia: reduced effort allocation predicts amotivation and functional impairment. *J. Abnorm. Psychol.* 123 (2), 387.
- Bardgett, M.E., Depenbrock, M., Downs, N., Points, M., Green, L., 2009. Dopamine modulates effort-based decision making in rats. *Behav. Neurosci.* 123 (2), 242–251.
- Fervaha, G., Graff-Guerrero, A., Zakzanis, K.K., Foussias, G., Agid, O., Remington, G., 2013. Incentive motivation deficits in schizophrenia reflect effort computation impairments during cost–benefit decision-making. *J. Psychiatr. Res.* 47 (11), 1590–1596.
- First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 2005. Structured Clinical Interview for DSM-IV-TR Axis I Disorders – Patient Edition (with Psychotic Screen). Biometrics Research Department.
- Floresco, S.B., Tse, M.T., Ghods-Sharifi, S., 2008. Dopaminergic and glutamatergic regulation of effort- and delay-based decision making. *Neuropsychopharmacology* 33 (8), 1966–1979.
- Folley, B.S., Park, S., 2010. Relative food preference and hedonic judgments in schizophrenia. *Psychiatry Res.* 175 (1), 33–37.
- Fusar-Poli, P., Meyer-Lindenberg, A., 2012. Striatal presynaptic dopamine in schizophrenia, part II: meta-analysis of [18F/11C]-DOPA PET studies. *Schizophr. Bull.* sbr180.
- Gard, D.E., Kring, A.M., Gard, M.G., Horan, W.P., Green, M.F., 2007. Anhedonia in schizophrenia: distinctions between anticipatory and consummatory pleasure. *Schizophr. Res.* 93 (1–3), 253–260.
- Gard, D.E., Sanchez, A.H., Cooper, K., Fisher, M., Garrett, C., Vinogradov, S., 2014. Do People With Schizophrenia Have Difficulty Anticipating Pleasure, Engaging in Effortful Behavior, or Both?
- Gold, J.M., Waltz, J.A., Prentice, K.J., Morris, S.E., Heerey, E.A., 2008. Reward processing in schizophrenia: a deficit in the representation of value. *Schizophr. Bull.* 34 (5), 835–847.
- Gold, J.M., Strauss, G.P., Waltz, J.A., Robinson, B.M., Brown, J.K., Frank, M.J., 2013. Negative symptoms of schizophrenia are associated with abnormal effort–cost computations. *Biol. Psychiatry* 74 (2), 130–136.
- Howes, O.D., Shotbolt, P., Bloomfield, M., Daalman, K., Demjaha, A., Dieren, K.M.J., Ibrahim, K., Kim, E., McGuire, P., Kahn, R.S., 2013. Dopaminergic function in the psychosis spectrum: an [18F]-DOPA imaging study in healthy individuals with auditory hallucinations. *Schizophr. Bull.* 39 (4), 807–814.
- Salamone, J.D., Correa, M., 2012. The mysterious motivational functions of mesolimbic dopamine. *Neuron* 76 (3), 470–485.
- Salamone, J.D., Correa, M., Farrar, A., Mingote, S.M., 2007. Effort-related functions of nucleus accumbens dopamine and associated forebrain circuits. *Psychopharmacology (Berlin)* 191 (3), 461–482.
- Treadway, M.T., Zald, D.H., 2013. Parsing anhedonia translational models of reward-processing deficits in psychopathology. *Curr. Dir. Psychol. Sci.* 22 (3), 244–249.
- Treadway, M.T., Buckholtz, J.W., Schwartzman, A.N., Lambert, W.E., Zald, D.H., 2009. Worth the 'EFFORT'? The Effort Expenditure for Rewards Task as an objective measure of motivation and anhedonia. *PLoS One* 4 (8), e6598.
- Treadway, M.T., Bossaller, N.A., Shelton, R.C., Zald, D.H., 2012. Effort-based decision-making in major depressive disorder: a translational model of motivational anhedonia. *J. Abnorm. Psychol.* 121 (3), 553.
- Venugopalan, V.V., Casey, K.F., O'Hara, C., O'Loughlin, J., Benkelfat, C., Fellows, L.K., Leyton, M., 2011. Acute phenylalanine/tyrosine depletion reduces motivation to smoke cigarettes across stages of addiction. *Neuropsychopharmacology* 36, 2469–2476.
- Wardle, M.C., Treadway, M.T., Mayo, L.M., Zald, D.H., de Wit, H., 2011. Amping up effort: effects of d-amphetamine on human effort-based decision-making. *J. Neurosci.* 31 (46), 16597–16602.
- Winton-Brown, T.T., Fusar-Poli, P., Ungless, M.A., Howes, O.D., 2014. Dopaminergic basis of salience dysregulation in psychosis. *Trends Neurosci.* 37 (2), 85–94.
- Woods, S.W., 2003. Chlorpromazine equivalent doses for the newer atypical antipsychotics. *J. Clin. Psychiatry* 64 (6), 663–667.
- Zigler, E., Levine, J., 1981. Premorbid competence in schizophrenia: what is being measured? *J. Consult. Clin. Psychol.* 49 (1), 96.