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Effort-based decision making as an objective paradigm for the assessment of motivational deficits in schizophrenia

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ABSTRACT

Background: Negative symptoms and motivational deficits are prevalent features of schizophrenia, and represent robust predictors of real-world functional outcomes. The standard for assessment of these symptoms is clinical interview and severity ratings on standardized rating scales. In the present study we examined the psychometric properties of a performance-based measure of motivational deficits in patients with schizophrenia.
Methods: Ninety-seven patients with schizophrenia were included in this investigation. Patients' willingness to expend effort for reward (i.e., motivation) was evaluated using an effort-based decision making paradigm where participants chose over a series of trials whether to expend a greater amount of effort for a larger monetary reward versus less effort for a smaller reward. Effort performance was evaluated twice, separated by a two-week interval.
Results: Patients with schizophrenia opted to expend greater effort for trials with higher reward value and greater likelihood of reward receipt. Patients did not find the task overly difficult and reported being motivated to perform well, underscoring the tolerability of the task for patients. Test–retest consistency was good and there was only minimal change in scores over time. Effort performance was not related to sociodemographic or clinical variables (e.g., positive symptoms); however, deficit syndrome patients exerted effort for reward at a significantly lower rate than nondeficit patients.
Conclusions: The effort-based decision making task used in the present study represents an objective paradigm that can be used to evaluate motivational impairments in patients with schizophrenia. Such performance-based measures of motivation may also serve as viable endpoints in clinical trials.

1. Introduction

Negative symptoms are a prevalent feature of schizophrenia (Bobes et al., 2010), for which there are no currently effective treatments (Fusar-Poli et al., 2015). The importance of negative symptoms is underscored by consistent findings across studies suggesting that they represent a critical barrier to patients' ability to achieve functional recovery (Ventura et al., 2009; Hunter and Barry, 2012; Rabinowitz et al., 2012; Fervaha et al., 2014b). Of the broad array of negative symptoms observed among patients with schizophrenia, symptoms related to amotivation have emerged as particularly important predictors of poor functional outcome (Foussias et al., 2011; Konstantakopoulos et al., 2011; Green et al., 2012; Fervaha et al., 2013a; Strauss et al., 2013; Galderisi et al., 2014).

Despite the functional burden of these symptoms, our understanding of the mechanisms underlying amotivation remains incomplete. Further, current "gold standard" methods of evaluating motivational deficits rely on clinical ratings usually based on patient self-report (Strauss et al., 2012; Kring et al., 2013). Recently, several studies have employed performance-based tasks to objectively demonstrate effort-related motivational deficits in patients with schizophrenia (Fervaha et al., 2013c; Gold et al., 2013; Barch et al., 2014; Wolf et al., 2014; Docx et al., 2015; Hartmann et al., 2015; Treadway et al., 2015). Specifically, these studies demonstrate that within a controlled laboratory setting patients are generally less willing to expend effort in pursuit of reward compared to matched healthy volunteers. The use of performance-based assessment tools to capture motivational deficits offers several advantages, such as the ability to evaluate these symptoms relatively free of external biases that can potentially undermine community functioning (e.g., availability of resources) (Patterson and Mausbach, 2010). Importantly, performance on these tasks has been associated with severity of motivational impairment and functional status (Fervaha et al., 2013c; Barch et al., 2014; Hartmann et al., 2015).

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Another potential advantage of certain performance-based assessments of amotivation is the existence of analogous paradigms for use pre-clinically, effectively setting the stage for translational investigations (Salamone and Correa, 2012; Fervaha et al., 2013b). Future studies may evaluate potential pro-motivation interventions both in humans and other species using such paradigms. It may well be the case that these laboratory-based assessments of motivation, which have been linked to specific neural circuits (Fervaha et al., 2013b), are more sensitive to treatment response. This may be the case as real-world impairments are typically multifactorial, being (putatively) caused by impairments in neural processes as well as situational factors. For instance, patients may lack engagement within the community due to their impaired ability to process environmental cues (i.e., neural processing), but also because of stigma, lack of opportunity, or lack of support (i.e., situational factors). Utilizing a translational objective paradigm akin to those used pre-clinically may represent a strategy with stronger links between circuit functioning and behavior, as situational factors are minimized in this context. There are several lines of investigation to support this position; for example, single doses of amphetamine have been found to increase effort expenditure in pursuit of reward among healthy controls (Wardle et al., 2011), a finding that mirrors pre-clinical work in rodents (Bardgett et al., 2009). However, amphetamine has not produced substantial effects on clinically rated negative symptoms in patients with schizophrenia (Barch and Carter, 2005; Pietrzak et al., 2010).

In the present study we sought to examine the psychometrics of an effort-based decision making task, including metrics to evaluate the utility of such an assessment in the context of repeated measurements. We focus on effort-based decision making as a novel translational paradigm evaluating effort-related motivational deficits (Fervaha et al., 2013b). Establishing the psychometrics of an objective performance-based assessment of motivational deficits in patients with schizophrenia serves as an important first step in determining whether such a paradigm might have utility in the context of clinical trials evaluating the efficacy of potential treatments. In order to serve this purpose, a task should be sensitive to manipulation effects, have high test-retest consistency, and demonstrate minimal practice effects, among other desirable characteristics (Carter et al., 2011).

2. Methods

2.1. Participants

Patients with schizophrenia were recruited from outpatient clinics at the Centre for Addiction and Mental Health in Toronto, Ontario, Canada. Selection criteria for participants included: (1) diagnosis of a schizophrenia spectrum disorder, confirmed using the Mini International Neuropsychiatric Interview (Sheehan et al., 1998), (2) age 18–65 years, (3) competence to provide informed consent, evaluated using the MacArthur Competence Assessment Tool (Appelbaum and Grisso, 2001), (4) no serious or unstable medical condition, and (5) ability to communicate in English. The study was approved by the institutional research ethics board, and all participants provided written informed consent prior to study participation.

2.2. Instruments and procedure

This study involved three visits on different days within one month. The first visit included clinical assessments, and during the next two visits participants completed the effort-based decision making task. These latter two visits were conducted 2 weeks apart. Participants received a fixed amount of monetary compensation at the end of each study visit for their participation in the present study. During the first visit, psychopathology was evaluated using the 18-item Brief Psychiatric Rating Scale (BPRS) (Guy, 1976), and the self-report version of the Apathy Evaluation Scale (AES) (Marin et al., 1991). Neurocognition was evaluated using the Brief Neurocognitive Assessment for Schizophrenia (Fervaha et al., 2014a, 2015).

The effort-based decision making task used in the present study represents a modified version of the Effort Expenditure for Rewards Task (Treadway et al., 2009). Briefly, this represents a multi-trial game that assesses participants' willingness to expend effort for monetary reward. On each trial, subjects choose to complete an “easy” or “hard” trial (Fig. 1). For an easy trial, subjects must use the index finger of their dominant hand to press the L-key (on a standard keyboard; S-key for left-handed individuals) a set number of times within 10 s to win $1.00. For hard trials, participants must use the pinky finger of their non-dominant hand to press the S-key (L-key for left-handed individuals) a set number of times also within 10 s to win $1.50–6.00. The easy trial was always worth $1.00, whereas there were 10 possible values for the hard trial option ranging from $1.50 to $6.00 in $0.50 increments. Probability of receiving reward was also varied at 3 levels, and each reward magnitude for the hard trial option was presented once for each probability level, resulting in a total number of 30 trials. The version of the task used in the present study includes several modifications compared with the original paradigm (Treadway et al., 2009). These modifications include: (1) equalization of the duration of each trial, thus nullifying decision costs related to temporal delay; (2) fixed number of 30 trials, with a brief break mid-way through the task; (3) use of rounded values for probability (i.e., 10%, 50%, and 90%) and monetary reward (e.g., $3.00, $3.50, $4.00); and (4) calibration of the requisite number of button presses. To this last point, before beginning the task, participants' maximum button pressing rate for their non-dominant hand was evaluated across 3 trials where they were instructed to press the respective key as many times as possible (Fervaha et al., 2013c). The highest value across the 3 trials was used as the maximum rate, and the button press criterion for easy and hard trials was based on this personalized value. Specifically, the hard task required 80% of the subject's calculated maximum rate, whereas the easy task required half this number. Before the actual task, participants completed 4 practice trials to ensure familiarity and comprehension of the task. The primary outcome variable was proportion of trials where participants selected the hard trial option. Participants were instructed to perform as if they were playing for “real” rewards, however the monetary rewards were fictional, meaning that participants did not actually receive performance-contingent payments; that the rewards were hypothetical was described to participants before they completed the task. In the instructions, the task was described as a button-pressing game, and participants were not explicitly told that the task was evaluating motivation. The task was executed in MATLAB R2009b (Mathworks Inc., Natick, MA) using PsychToolbox (Brainard, 1997) running in Windows.

Directly following task administration, participants completed another calibration run with their non-dominant pinky finger to evaluate potential fatigue effects. Participants next completed a questionnaire regarding the task and testing procedures. Participants were asked to rate the level effort/difficulty of the easy and hard trials on an 11-point Likert scale with scores ranging from 0 (not at all difficult) to 10 (extremely difficult). As an index of tolerability, participants were also asked to rate how difficult they found the task overall using the same Likert scale. In addition, participants were also asked whether they were driven to perform well and win money during the task.

2.3. Statistical analyses

Whether the task was effective in having participants expend effort for reward was evaluated by examining incentive effects. Specifically, we evaluated whether participants were more likely to select hard trials for the higher value trials (indexed by the 90% probability condition) versus lower value trials (indexed by the 10% probability condition). We also examined the effect of probability and reward level on effort expenditure using a 3-by-2 repeated-measures analysis of variance (ANOVA) model. Reward values were binned into large and small

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