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Incentive motivation deficits in schizophrenia reflect effort computation impairments during cost-benefit decision-making

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ABSTRACT

Background: Motivational impairments are a core feature of schizophrenia and although there are numerous reports studying this feature using clinical rating scales, objective behavioural assessments are lacking. Here, we use a translational paradigm to measure incentive motivation in individuals with schizophrenia.

Methods: Sixteen stable outpatients with schizophrenia and sixteen matched healthy controls completed a modified version of the Effort Expenditure for Rewards Task that accounts for differences in motoric ability. Briefly, subjects were presented with a series of trials where they may choose to expend a greater amount of effort for a larger monetary reward versus less effort for a smaller reward. Additionally, the probability of receiving money for a given trial was varied at 12%, 50% and 88%. Clinical and other reward-related variables were also evaluated.

Results: Patients opted to expend greater effort significantly less than controls for trials of high, but uncertain (i.e. 50% and 88% probability) incentive value, which was related to amotivation and neurocognitive deficits. Other abnormalities were also noted but were related to different clinical variables such as impulsivity (low reward and 12% probability). These motivational deficits were not due to group differences in reward learning, reward valuation or hedonic capacity.

Conclusions: Our findings offer novel support for incentive motivation deficits in schizophrenia. Clinical amotivation is associated with impairments in the computation of effort during cost-benefit decision-making. This objective translational paradigm may guide future investigations of the neural circuitry underlying these motivational impairments.

1. Introduction

Amotivation, or apathy, is a well-documented clinical feature of schizophrenia (SCZ) and a key determinant of longitudinal functioning (Faerden et al., 2010; Foussias et al., 2011). It has even been argued that amotivation is at the core of the schizophrenic syndrome (Foussias and Remington, 2010). Consistent with these clinical observations are behavioural findings of reduced goal-directed behaviour based on observed movement (Farrow et al., 2005; Tremeau et al., 2012). However, studies employing objective task-based assessments of these deficits in individuals with SCZ are scarce in the literature.

In the behavioural neuroscience literature, motivation is typically evaluated by measuring the amount of effort an organism expends for a given reward (Salamone et al., 2007). Working within such a framework, pre-clinical studies have implicated a neural network subserving the computation of effort costs that involves the mesolimbic dopaminergic system (Salamone et al., 2007) and the anterior cingulate cortex (Rudebeck et al., 2006; Walton et al., 2002). Specifically, increases in dopaminergic transmission are associated with increases in motivated behaviour (e.g. greater number of lever presses for a given reward) (Bardgett et al., 2009), whereas disruption of dopaminergic functioning, through focal lesions or pharmacologically induced receptor antagonism/depletion, reduces motivated behaviour (Cousins and Salamone, 1994; Salamone et al., 1991). There is also evidence that pharmacological manipulations of

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the dopaminergic system in healthy human subjects affect motivation (Wardle et al., 2011). Moreover, and consistent with the pre-clinical literature, activity within the human anterior cingulate cortex tracks decisions to expend effort (Croxson et al., 2009; Prevost et al., 2010). Given that functioning within these neural regions have been previously shown to be abnormal in SCZ (Juckel et al., 2006b; Minzenberg et al., 2009; Simon et al., 2010), such neural dysfunctions may translate to altered computations of effort cost and, therefore, bias cost-benefit decision-making. Impairment of this sort would surface behaviourally as a reduction in motivated behaviour, and clinically as apathy.

It is of note that multiple deficits have been found under the umbrella constructs of reward and motivation processing in SCZ (Barch and Dowd, 2010). These include deficits in reward learning (Waltz et al., 2007), neural responses to reward (Waltz et al., 2010), and value representations (Gold et al., 2012), to name a few. All of these inter-related, yet distinct, processes can theoretically undermine motivated behaviour. As a result, assessment of incentive motivation, or the willingness to expend effort for a reward, remains elusive. In the present study, we sought to behaviourally demonstrate incentive motivation deficits in SCZ, while accounting for other reward-related variables. We hypothesised that individuals with SCZ would demonstrate deficits in their willingness to expend effort for reward, which would not be accounted for by reward learning capacity or valuation of the reward, consistent with the notion of impairment in the computation of effort cost.

2. Methods

2.1. Participants

Sixteen outpatients with SCZ and sixteen demographically matched healthy control subjects (HC) participated in the present study. All patients were tested while on a stable dose of antipsychotic medication, with no changes for at least 4 weeks. Patients were relatively early in their disease course (i.e. age between 18 and 35 years) and had a DSM-IV-TR diagnosis of SCZ confirmed through medical records and the Mini International Neuropsychiatric Interview – Plus edition (MINI-Plus) (Sheehan et al., 1998). Patients were excluded from the study if they met diagnostic criteria for a current mood disorder or substance use disorder within the past 3 months; had a history of neurological or major medical disease; were experiencing significant akathisia (global rating of >2 on the Barnes Akathisia Rating Scale) (Barnes, 1989) or extrapyramidal symptoms (3 or more ratings of >2 on the Simpson–Angus Rating Scale) (Simpson & Angus, 1970).

HC subjects had similar inclusion and exclusion criteria as the patients, but did not meet criteria for any current or previous Axis I disorders as per the MINI-Plus, or any Cluster A personality disorder as per the Structured Clinical Interview for DSM-IV Disorders – Axis II (SCID-II) (First and Gibbon, 1997). Furthermore, control subjects reported no family history of a psychotic disorder.

All participants were right handed as determined using the Edinburgh Handedness Inventory (Oldfield, 1971). The study protocol was approved by the Institutional Research Ethics Board and all participants provided written informed consent. All SCZ subjects were deemed competent to provide consent as per the MacArthur Competence Assessment Tool (Appelbaum and Grisso, 2001).

2.2. Clinical ratings

All participants were administered a battery of measures to assess psychopathology including: the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984); Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1982); Calgary Depression Scale for Schizophrenia (CDSS) (Addington et al., 1990); Apathy Evaluation Scale – Clinician version (AES-C) (Marin et al., 1991); Quality of Life Scale – Abbreviated version (QLS-A) (Fervaha and Remington, 2012; Heinrichs et al., 1984); Barrett Impulsiveness Scale (BIS-11) (Patton et al., 1995); and the Snaith et al., 1995 Pleasure Scale (SHAPS). Neurocognition was assessed using the MATRICS Consensus Cognitive Battery (MCCB) (Nuechterlein et al., 2008).

2.3. Effort-based decision-making task

The task used in the present study was a modified version of the Effort Expenditure for Rewards Task (Treadway et al., 2009). Briefly, this is a multi-trial game that assesses participants' willingness to expend effort for a monetary reward (Fig. 1). On each trial, subjects choose to complete an "easy" button press trial or a "hard" trial. For the easy trials, subjects must press the L-key (on a standard keyboard) with their right (dominant) hand index finger a set

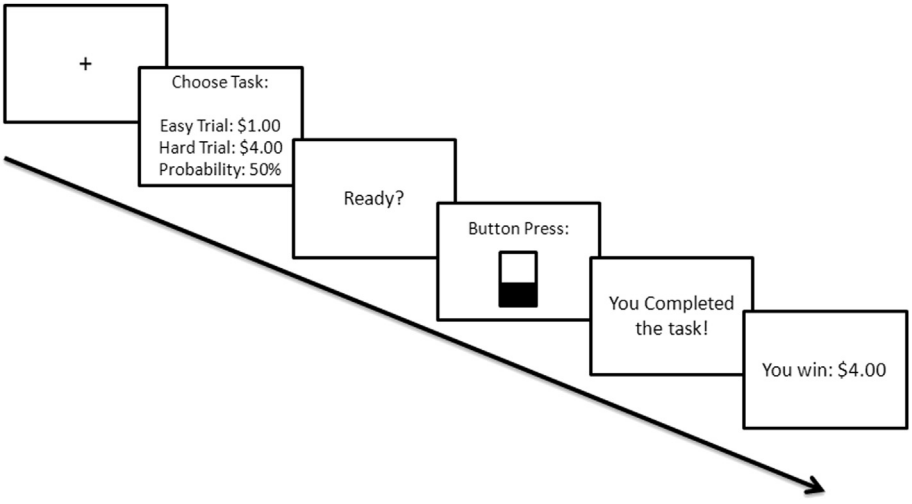

Fig. 1. Diagram depicting the sequence of a single trial of the effort-based decision-making task. Trials begin with a fixation cue. Then, during the decision-phase, subjects are presented with information regarding the reward magnitudes of the easy and hard trial options and the probability of receiving a reward. Once subjects make a decision, they then proceed to the actual effort trial where they make button presses for an individually determined number of times in order to complete the task. Of note, subjects are able to track their progress through an illustrative bar which is progressively filled after each button press, with the top indicating completion of the task. Participants are then shown feedback as to whether they completed the task and subsequently receive information of the monetary winnings for that trial.