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Impaired reward responsiveness in schizophrenia

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ABSTRACT

Background: Anhedonia is a core negative symptom of schizophrenia. Schizophrenia patients report largely intact pleasure in consuming rewards, but have impairments in generating motivated behavior to pursue rewards, and show reduced fMRI activation of the reward pathway during presentation of rewarded stimuli. A computer based task measuring the development of a response bias in favor of rewarded stimuli permits assessment of reward-induced motivation. We hypothesized that subjects with schizophrenia would be impaired on this task.
Methods: 58 schizophrenia subjects (SCZ) and 52 healthy controls (CON) were studied with a signal detection task to assess reward responsiveness. In multiple trials over three blocks subjects were asked to correctly identify two stimuli that were paired with unequal chance of monetary reward. The critical outcome variable was response bias, the development of a greater percent correct identification of the stimulus that was rewarded more often.
Results: An ANOVA on response bias with Block as a repeated-measures factor and Diagnosis as a between-group factor indicated that SCZ subjects achieved a lower bias to rewarded stimuli than CON subjects ($F(1,105) = 8.82$, $p = 0.004$, $\eta^2 = 0.078$). Post hoc tests indicated that SCZ subjects had significantly impaired bias in Block 1 ($p = 0.002$) and Block 2 ($p = 0.05$), indicating that SCZ were slower to achieve normal levels of bias during the session.
Conclusions: SCZ subjects were slower to develop response bias to rewarded stimuli than CON subjects. This finding is consonant with the hypothesis that people with schizophrenia have a blunted capacity to modify behavior in response to reward.

1. Introduction

The etiology and pathophysiology of schizophrenia remains a mystery, although some primary risk factors have been identified, including environmental factors, genetic vulnerabilities, and abnormal neural function (Insel, 2010; Mueser and McGurk, 2004; Mulle, 2012). It has been recognized for many decades that schizophrenia encompasses not only what we now term positive symptoms such as hallucinations and delusions, but also negative symptoms, such as anhedonia and avolition (Bleuler, 1950; Kraepelin, 1919). Patients with prominent negative symptoms such as anhedonia, apathy, and impaired motivation have a particularly poor prognosis (Buchanan and Gold, 1996; Gard et al., 2009; Kiang et al., 2003). Thus it is important to understand the neural underpinnings of these symptoms in order to achieve more effective treatment of these symptoms in our patients.

Anhedonia, the inability to derive pleasure from positive stimuli (Gorwood, 2008), is considered one of the principal symptoms of schizophrenia. Pleasure is a multifaceted construct that includes both consummatory pleasure, the instantaneous pleasure derived from a pleasurable act and anticipatory pleasure, the pleasure derived from the expectation of pleasure in the future. This distinction has been described in the depression literature (Klein, 1984) and the schizophrenia literature (Gard et al., 2007). Since this distinction between the two components of pleasure was established, much research has been conducted on both consummatory and anticipatory pleasure, including detailed parsing of differences between SCZ and CON subjects in these two components. In previous studies, when individuals were given self-report measures, such as the Temporal Experience of Pleasure Scale (TEPS) (Gard et al., 2006), no significant difference in consummatory pleasure distinguished subjects with schizophrenia from controls (Gard et al., 2007), such that individuals with schizophrenia reported comparable experience of in-the-moment pleasure as controls. A large meta-analysis of research published between 1987 and 2007 further validated the finding that schizophrenia subjects do not report a

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decrease in hedonic pleasure when compared to a control group (Cohen and Minor, 2010). However, evidence from studies using the hedonic ratings of olfactory stimuli indicate that this aspect of consummatory reward processing is impaired in schizophrenia (Moberg et al., 2003), and particularly so in deficit syndrome schizophrenia (Strauss et al., 2010). Schizophrenia subjects exhibit impairments in generating motivation to pursue rewards, and this impaired motivation is linked to poor functional outcome (Gard et al., 2009). Furthermore, in self-report studies, individuals with schizophrenia predicted that future events would result in less pleasure than did their control counterparts (Gard et al., 2007; Chan et al., 2010). Interestingly, in a replication study using the TEPS with a new cohort of schizophrenia subjects, the opposite result was obtained: schizophrenia subjects self-reported a difference in consummatory pleasure but not anticipatory pleasure, when compared to controls (Strauss et al., 2011).

This inconsistency calls for a new measure of motivation for reward that does not rely on self-report data. Interviews and other methods that rely on self-report from subjects may be subject to self-report bias or interviewer bias (Cohen and Minor, 2010). Therefore, we opted to use a computer-based task to measure the development of response bias in favor of the more frequently rewarded stimuli. This measure, developed to assess reward processing in depressed patients, allowed for an objective laboratory measure of response bias as a measure of reward-motivated changes in behavior (Pizzagalli et al., 2005). In a previous study that utilized this paradigm, Pizzagalli et al. (2005) found that depressive patients exhibited reduced responsiveness when compared to controls. One prior study compared performance on this task between schizophrenia and control subjects and found no difference in response bias (Heerey et al., 2008). However, we speculated that a deficit in response bias would be more detectable in a schizophrenia population heavily weighted with negative symptoms such as we see in our Veterans Affairs population. We hypothesized that our schizophrenia subjects would react more slowly to the more frequently rewarded stimuli and would be slower to develop a response bias toward the more frequently rewarded stimuli than healthy psychiatric controls. Against the background of the known psychomotor and processing speed slowing previously reported in schizophrenia (Bervoets et al., 2014; Dickinson et al., 2007; Knowles et al., 2010), our secondary hypothesis was that our schizophrenia subjects would exhibit a slowing of reaction time to the stimuli than controls.

2. Experimental materials and methods

2.1. Subjects

Informed written consent was obtained from 110 subjects (58 schizophrenia subjects, SCZ, and 52 psychiatric control subjects, CON). All subjects were recruited from an urban population of generally low socioeconomic status at the Atlanta Veterans Affairs Medical Center. The SCZ group was recruited from the outpatient mental health clinics. The CON group was recruited from the primary care clinics. Additionally, both groups were recruited via flyers posted within the medical center. For the SCZ group, a diagnosis of schizophrenia or schizoaffective disorder was confirmed using the Structured Clinical Interview for DSM-IV, Axis I (SCID-I; First et al., 2001). Subjects were excluded if they failed a five-panel drug screen, had a history of head trauma resulting in sustained loss of consciousness for greater than 5 min, seizure disorder, bipolar disorder, or current unstable medical illnesses. Most SCZ subjects were taking a single second generation antipsychotic medication (n = 49). Three subjects were taking a first generation antipsychotic medication, three were taking both a first and second-generation antipsychotic medication, and three were not taking any antipsychotic medication at the time of testing. For all SCZ subjects, their antipsychotic status was stable for at least one month. Potential control subjects were screened out for the same exclusion criteria as was used for the SCZ group, with the additional exclusion for a history of a major psychiatric condition.

2.2. Subject evaluations

The Fagerstrom Tolerance Questionnaire (Fagerström, 1978) was administered to all subjects to determine smoker status. The Positive and Negative Syndrome Scale for Schizophrenia (PANSS; Kay et al., 1987) was administered to all SCZ subjects. The Schedule for the Deficit Syndrome (SDS; Kirkpatrick et al., 1989) was administered to all SCZ subjects to determine deficit syndrome category, either deficit or non-deficit, and total negative symptom scores. Additional information on the severity of current negative symptoms was assessed on the schizophrenia subjects with the Abrams and Taylor Scale for Emotional Blunting (Abrams and Taylor, 1978). We examined performance on intelligence quotient (IQ) testing using the Reynolds Intellectual Screening Test (Reynolds and Kamphaus, 2003).

2.3. Signal detection task

A reward response bias paradigm was used to measure reward responsiveness and signal detection bias (Pizzagalli et al., 2005). Each subject completed 100 trials, each divided into 3 blocks, for a total of 300 trials. Blocks were separated by a 30 s break. Before beginning the task, subjects were provided with instructions and informed that the goal of the task was to earn as much money as possible. The task was demonstrated to each subject, and two practice trials were conducted. The task was performed using a Dell laptop and a keypad that contains two keys labeled “long” and “short”. During each trial one of two possible stimuli was presented: either a cartoon drawing of a face with a mouth that is 13 mm long or a nearly identical face with a shorter mouth of 11.5 mm. At the beginning of each trial a plus sign was presented to act as a fixation point for 500 ms followed by the presentation of a mouthless cartoon face. After an interval of 500 ms one of two mouth stimuli, either the 11.5 mm mouth or the13 mm mouth, appeared on the face for 100 ms. Following the presentation of the mouth stimuli, the mouthless face remained on the screen until the subject made a choice. Subjects were asked to correctly determine which of the two stimuli was presented and make a selection on the keypad. The setup of the keypad was randomized such that either the long stimulus or the short stimulus was designated by the left or right keypad button. Subjects receive a small reward for making the correct choice on some trials. Reward feedback includes presentation of a screen stating “Correct!! You won 5 cents”. Both the long mouth and short mouth stimuli were presented with equal frequency, but the reward paradigm was systematically manipulated such that correct determination of one stimulus was rewarded more frequently than correct determination of the other stimulus. The reward feedback was displayed more frequently for correct determination of one stimulus (“rich stimulus”) when compared to the other stimulus (“lean stimulus”) according to an asymmetric reinforcement ratio of 3:1 in each block. During the course of 100 trials, correct identification of the rich stimulus was rewarded approximately 30 times compared to 10 times for correct identification of the lean stimulus. The subjects were randomized to receive either the long stimulus or the short stimulus as the rich stimulus. Subjects were able to take home the amount of money they won with a maximum payout of $18.00.

2.4. Data processing and reduction

Performance on the task was assessed based on the measures of reaction time, discriminability and response bias after the methods of Pizzagalli et al. (2005). Reaction time (RT) is the speed in milliseconds (ms) between the stimulus for each trial and the subjects' response. RT was calculated separately as the mean RT for Rich and Lean stimuli that the subject identified correctly (“hits”) and incorrectly (“misses”).

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