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Motivational deficits in individuals at-risk for psychosis and across the course of schizophrenia

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ABSTRACT

Motivational impairment is a critical factor that contributes to functional disability in schizophrenia and undermines an individual's ability to engage in and adhere to effective treatment. However, little is known about the developmental trajectory of deficits in motivation and whether these deficits are present prior to the onset of psychosis. We assessed several components of motivation including anticipatory versus consummatory pleasure (using the Temporal Experience of Pleasure Scale (TEPS)), and behavioral drive, behavioral inhibition, and reward responsivity (using the Behavioral Inhibition Scale/Behavioral Activation Scale (BIS/BAS)). A total of 234 participants completed study measures, including 60 clinical high risk (CHR) participants, 60 recent-onset schizophrenia participants (RO), 78 chronic schizophrenia participants (SZ) and 29 healthy controls (HC) age matched to the CHR group. CHR participants endorsed greater deficits in anticipatory pleasure and reward responsivity, relative to HC comparison participants and individuals diagnosed with schizophrenia. Motivational deficits were not more pronounced over the course of illness. Depressed mood was uniquely associated with impairments in motivation in the CHR sample, but not the schizophrenia participants. The results suggest that CHR individuals experience multiple contributors to impaired motivation, and thus multiple leverage points for treatment.

1. Introduction

Dating back to the earliest descriptions of schizophrenia by Kraepelin and Bleuler, amotivation/avolition was observed to be central to the phenomenology and course of schizophrenia (McGlashan, 2011). Amotivation and negative symptoms more broadly are resistant to current treatment options and often lead to substantial functional impairment(Foussias and Remington, 2010; Foussias et al., 2011). Motivation, or goal-directed behavior, is reliant on several component processes, such as the anticipation of reward (e.g., *wanting*), the hedonic experience of rewards (e.g., *liking*), the ability to develop and sustain a representation of reward, and guiding and planning behavior towards that future reward (in the face of competing stimuli; e.g., *learning* (Gold et al., 2008, 2012). In schizophrenia, patients have demonstrated deficits in anticipatory pleasure despite intact in-the-moment hedonic experiences (e.g., *wanting* vs. *liking* discrepancy) (Gard et al., 2007; Cohen and Minor, 2010; Foussias and Remington, 2010), as well as difficulty maintaining cognitive representation of rewarding experiences and redirecting behavior back to rewarding experiences (Barch and Dowd, 2010).

While much of the research on motivation in schizophrenia has focused heavily on *wanting* vs. *liking*, and on the use of rewards to guide behavior, there is also a large literature on underlying traits linked to the likelihood to pursue rewards—behavioral approach (driven by appetitive motives) and behavioral avoidance (driven by aversive motives). Individuals with a high degree of approach motivation are more likely to pursue new and potentially rewarding experiences, while those with behavioral avoidance are more likely to anticipate punishment and as such avoid such experiences. The behavioral inhibition system is hypothesized to be sensitive to threat cues and to activate responses of avoidance via noradrenergic and serotonergic activity (Depue and Iacono, 1989; Harre and Parrott, 1996; Cools et al., 2005), while the behavioral activation system controls reward sensitivity via dopaminergic activity (Sutton and Davidson, 1997). Only two studies to date have examined the behavioral inhibition and behavioral activation systems (BIS/BAS) in schizophrenia, despite important implications

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for negative symptoms and motivation specifically. In the first study, Scholten et al. (2006) found that individuals with schizophrenia were more sensitive to threat than healthy controls, but no differences were detected between patients and controls in the behavioral activation system. In a more recent study (Engel et al., 2013), the BAS system was found to be negatively associated with more severe negative symptoms, suggesting heterogeneity within schizophrenia samples. Thus far, most studies on motivation and reward processing in schizophrenia have been conducted on individuals who have been persistently ill for most of their adult lives. It is therefore unknown whether motivational deficits worsen over the course of schizophrenia. The stability of negative symptoms generally, however, has been examined and while it appears they might be stable in severity across the course of psychosis, some studies suggest that as the duration of *untreated* psychosis increases, individuals with schizophrenia experience worsening negative symptoms over time (Chang et al., 2013). Although motivational deficits are often considered within the context of negative symptoms and reward processing, the presence of mood and anxiety symptoms is also linked to motivational capacity in schizophrenia. In particular, depressed mood is associated with decreased hedonic capacity while anxiety symptom severity is associated with greater threat sensitivity/avoidance behavior (Barch et al., 2008). These studies raise questions about the degree of behavioral activation and avoidance within schizophrenia samples that vary in the degree of negative symptom severity, as well as other factors, such as the duration of illness, and the presence of comorbid depressive and anxiety symptoms. In the current study, we examined negative symptom severity, mood and anxiety symptoms, and motivational deficits across the course of schizophrenia, using a cross-sectional design.

The primary aim of this study was to examine several behavioral components of motivation (wanting, liking, approach and avoidance) in individuals at various stages of experiencing psychosis: those at clinical high risk (CHR) of developing a psychotic disorder, those within the first 5 years of onset of schizophrenia (Recent Onset; RO), and those with persistent schizophrenia or schizoaffective disorder (SZ). We tested the following hypotheses: 1) Individuals with persistent schizophrenia will demonstrate greater motivational impairments than those at-risk or with a recent onset of schizophrenia, and 2) mood and anxiety symptoms will influence the degree of motivational impairments at all stages of illness, such that more severe anxiety and depression will be positively correlated with avoidance and negatively correlated with wanting, liking, and approach motivation in all participant groups.

2. Methods

2.1. Participants

The study included 234 participants:, 60 clinical high risk (CHR), 60 recent-onset schizophrenia (RO), 78 persistent schizophrenia (SZ) participants and 29 healthy controls (HC) who were recruited for randomized controlled trials of cognitive training (ClinicalTrials.gov NCT00655239, NCT00694889, and NCT00312962). The HC participants were age-matched to the CHR participants. Participants in the HC, CHR and RO groups were drawn from two research programs at the University of California, San Francisco (UCSF) and University of California at Davis (UCD) and persistent SZ participants from a research program at the San Francisco VA Medical Center (SFVAMC). Patient participants were recruited from community mental health centers, outpatient clinics, local schools and universities, and HC participants were recruited via advertisement. CHR status was ascertained using the Structured Interview for Prodromal Syndromes (SIPS version 4.0 (Miller et al., 2002). All CHR participants met one of the following prodromal syndromes on the SIPS/SOPS,: 1) the presence of attenuated positive, psychotic symptoms, occurring at least weekly with onset or worsening in the past year, 2) brief intermittent psychotic symptoms, which must have begun in the past three months, or 3) a 30% decline in GAF score over the past year, plus either a diagnosis of schizotypal personality disorder or a first-degree relative with a psychotic disorder. Recent onset participants were included based on a diagnosis of schizophrenia, schizophreniform, or schizoaffective disorder with an onset within the past five years as determined by the Structured Clinical Interview for the DSM-IV TR Axis I disorder interview (SCIP-I; First, 1996). Onset of illness was defined by the date diagnostic criteria were first met, as assessed by the SCID. Persistent schizophrenia participants were diagnosed using the SCID-I. Healthy controls did not meet DSM-IV criteria for an Axis I psychiatric disorder as determined by the SCID-I or meet criteria for a prodromal syndrome, and had no first-degree relatives with psychosis, based on participant and collateral informant reports during the SIPS interview. CHR, RO and SZ participants were clinically stable at the time of testing (no hospitalization within the past 3 months and stable dose of medication over the past month), as per the requirements for the parent cognitive training study. Other inclusion criteria included: 1) good general physical health; 2) fluent and proficient in English; 3) IQ > 70 (WASI, 1st edition, 2-subtest version: Vocabulary and Matric Reasoning); 4) no neurological disorder; and 5) no substance dependence or significant use that would interfere with study participation.

2.2. Procedure

Advanced graduate students, predoctoral interns, postdoctoral fellows, and trained bachelor-level research assistants administered the measures described below in the context of a larger battery of cognitive and clinical assessments. All participants gave written informed consent or assent for the study and were compensated for their participation in all assessments. Parental informed consent for minors was also obtained. After an intake evaluation that determined study eligibility, participants underwent a structured diagnostic clinical interview and completed self-report measures of motivation and clinician ratings of symptom severity. Only baseline, cross-sectional data were included in this study.

2.3. Measures

We assessed several components of motivation including negative symptom severity and mood and anxiety using the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987), anticipatory (*wanting*) versus consummatory (*liking*) pleasure using the Temporal Experience of Pleasure Scale (TEPS; Gard et al., 2006), and behavioral drive, behavioral inhibition, and reward responsivity using the Behavioral Inhibition Scale/Behavioral Activation Scale (BIS/BAS; Carver and White, 1994). The TEPS includes eighteen items and are rated on a scale of 1 (very flase for me) to 6 (very true for me). The BIS/BAS measure is comprised of twenty-four items rated on scale of 1 (very true for me) to 4 (very false for me), of which seven items represent the BIS. The BAS scales were designed to measure approach motivation traits while the BIS scale was designed to measure aversive motivation traits. Examples of TEPS and BIS/BAS items are in Table 1. The PANSS is clinician-administered, while the TEPS and BIS/BAS are self-report measures.

2.4. Data analytic plan

First, data were inspected for normality and outliers were windsorized at a level of 95%. Less than 5% of the data on these measures, within each group, were adjusted. One-way ANOVAs and chi-square tests were conducted to test for demographic differences. To better understand the relationship between the TEPS and BIS/BAS scales, we used Pearson correlation analyses. BIS/BAS scores were reverse coded, such that higher ratings represented greater degrees of approach motivation. To test hypothesis 1, a series of one-way ANOVAs were used to compare the mean differences in anticipatory and consummatory pleasure and approach and aversive motivation between groups. In order to test Hypothesis 2, mood and anxiety symptoms were examined