



Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Neuroleptic-free youth at ultrahigh risk for psychosis evidence diminished emotion reactivity that is predicted by depression and anxiety

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ARTICLE INFO

Article history:

Received 23 November 2016

Received in revised form 9 August 2017

Accepted 10 August 2017

Available online xxxx

Keywords:

Emotion

Emotion regulation

Psychosis

Anhedonia

Social functioning

ABSTRACT

Although abnormalities in emotional response have long been considered a core feature of the chronic phase of schizophrenia, few investigations have examined emotional response in individuals at ultrahigh-risk (UHR) for psychosis. We investigated whether neuroleptic-free UHR ($n = 29$) and healthy control ($n = 32$) participants differed in emotional reactivity and emotion regulation on a laboratory-based task that required reporting levels of positive and negative affect to pleasant, unpleasant, and neutral stimuli. Results indicated that the UHR group evidenced reduced emotional reactivity, including decreased positive emotion to pleasant stimuli and decreased negative emotion to unpleasant stimuli. Furthermore, within the UHR group, attenuated positive emotion to pleasant stimuli was associated with greater severity of depression and anxiety. There were no group differences in self-reported emotion regulation effectiveness to unpleasant or pleasant stimuli. Findings suggest that UHR youth display a profile of emotional experience abnormalities that differs from the chronic phase of illness, which can be characterized as reduced positive emotion reactivity to pleasant stimuli (i.e., anhedonia) that may be driven by mood and anxiety symptoms.

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1. Introduction

Anhedonia has long been considered a core feature of schizophrenia (Bleuler, 1950; Kraepelin, 1919). However, modern empirical research calls into question whether the traditional definition of anhedonia as a diminished capacity to experience pleasure accurately characterizes the nature of emotional experience abnormalities in the chronic phase of illness (see Kring and Moran, 2008 and Strauss and Gold, 2012 for reviews). For example, recent meta-analyses of laboratory-based studies that present participants with evocative stimuli indicate that individuals diagnosed with schizophrenia report experiencing levels of positive emotion (i.e., valence) (Cohen and Minor, 2010) and arousal (Llerena et al., 2012) that are comparable to healthy controls when exposed to pleasant stimuli. Some ecological momentary assessment (EMA) studies also indicate that persons with schizophrenia report increases in positive emotion that are comparable to healthy controls when engaged in real-world activities (Gard et al., 2007; Oorschot et al., 2013; Kimhy et al., 2016). Such findings have led some to propose that anhedonia

should be re-conceptualized in schizophrenia and no longer considered a diminished *capacity* for pleasure (Strauss and Gold, 2012).

However, not all aspects of emotional experience are fully intact in individuals with schizophrenia. Laboratory-based studies indicate that individuals with schizophrenia report experiencing greater intensity of negative emotion than controls in response to unpleasant, pleasant, and neutral stimuli (Cohen and Minor, 2010). EMA studies also indicate increased intensity, frequency, and duration of negative emotion reactivity (Myin-Germeys et al., 2000). These findings may suggest that negative, rather than positive emotion reactivity abnormalities are central to schizophrenia (Horan et al., 2006; Cohen et al., 2011; Strauss and Gold, 2012). Despite the well-replicated finding of increased negative emotion reactivity in schizophrenia and evidence that these abnormalities predict poor clinical outcome (e.g., community-based functional outcome, symptoms), few studies have examined factors underlying increased negative emotion reactivity in this critical population. Several recent studies point to a role for emotion regulation abnormalities (i.e., impairments in using strategies to decrease the intensity, duration, or frequency of negative emotion), such that individuals with schizophrenia fail to effectively implement strategies to control emotional response. The magnitude of self-reported and neurophysiological emotion regulation abnormalities also predicts abnormal negative emotion reactivity and a range of clinical outcomes (e.g., social functioning,

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psychosis, negative symptoms) (Horan et al., 2013; Strauss et al., 2013a, 2013b, 2015; Morris et al., 2012; van der Meer et al., 2014).

Although the affective landscape associated with the chronic phase of schizophrenia is becoming increasingly well mapped, few studies have examined emotional reactivity or regulation in the prodromal phase of illness. This represents a significant gap in the literature given the critical etiological relevance of the period immediately preceding onset (Haroun et al., 2006) and the presumed role of anhedonia in the transition from ultrahigh risk (UHR) state to diagnosable psychotic disorder (Meehl, 2001). The prodromal phase also offers an opportunity to examine emotional reactivity and regulation independent of the effects of antipsychotic medications that often confound interpretation in studies of the chronic phase of schizophrenia.

To our knowledge, only one published study has examined emotional reactivity in UHR youth. Yee et al. (2010) examined a small group of UHR ($n = 13$) participants, as well as groups of first-episode schizophrenia patients ($n = 40$), chronic schizophrenia patients ($n = 37$), and healthy controls ($n = 74$), who viewed emotion-eliciting static images (e.g., threat, mutilation, contamination, illness, population, erotica, families, food, nature) while self-reported valence and arousal were reported separately. Relevant to the present study, the UHR group self-reported attenuated positive emotion to the pleasant pictures compared to the chronic schizophrenia group, and self-reported attenuated positive emotion to the neutral images compared to both the chronic and first-episode schizophrenia groups. Participants in the UHR group also reported attenuated negative emotion to unpleasant images compared to the chronic schizophrenia group.

Similarly, we are aware of only one published study that investigated emotion regulation in UHR youth. Kimhy et al. (2016) assessed UHR, control, and chronic schizophrenia participants with self-report questionnaires and interviews that measured habitual emotion regulation strategy use, emotional awareness, functional outcome, and symptoms. Findings indicated that UHR and chronic schizophrenia patients reported less frequent use of reappraisal than controls, and less use of reappraisal predicted poor community-based functional outcome (Kimhy et al., 2016). Thus, two initial studies provide preliminary evidence for diminished emotional reactivity and abnormal emotion regulation processes in UHR youth that predict poor community-based functional outcome; however, there is need for additional studies that replicate and extend these findings using adequately sized samples of neuroleptic-free UHR youth and laboratory-based emotional reactivity and regulation paradigms.

The current study presented UHR and control groups with pleasant, unpleasant, and neutral stimuli and asked them to make separate reports of positive and negative emotion in the context of emotional reactivity or regulation instructions. Three hypotheses were evaluated: 1) Based on initial evidence suggesting potential attenuation of emotional experience (Yee et al., 2010), we predicted that the UHR group would report less positive emotion to pleasant stimuli (i.e., a true anhedonia) and less negative emotion to unpleasant stimuli compared to controls. 2) Based on evidence for an emotion regulation abnormality in chronic schizophrenia (Horan et al., 2013; Strauss et al., 2013a, 2013b, 2015; Morris et al., 2012; van der Meer et al., 2014) and UHR youth (Kimhy et al., 2016), we hypothesized that UHR youth would fail to decrease negative emotion effectively using a distancing reappraisal strategy. 3) Based on evidence linking emotional reactivity and regulation abnormalities to poor community-based functional outcome in schizophrenia and UHR youth (Kimhy et al., 2016; Yee et al., 2010), we also predicted that emotional reactivity and regulation would be associated with poorer real-world social function in the UHR group.

2. Method

2.1. Participants

Participants in this IRB approved study included 61 adolescents/young adults (29 UHR and 32 controls) between the ages of 12–

21 years ($M = 18.76$, $SD = 2.14$). Control participants were recruited via email, newspaper advertisements, and Craigslist. Recruitment of UHR participants utilized these sources as well, but also included an in-depth effort that targeted clinical (psychologist and psychiatrist), college counseling, psychiatric hospital and community-mental health center referrals (this involved recruitment presentations from ADAPT lab personnel, phone calls, as well as regular mailers). In addition, recruitment utilized a bus advertisement campaign spanning the Boulder, Aurora, and Denver Metropolitan areas, as well as presentations for community mental health events. Exclusion criteria for both groups included history of head injury, neurological disorder, DSM-IV-TR Axis I psychotic disorder or substance dependence, and being prescribed antipsychotic medication. The study also screened for recent cannabis use (in an effort to devise a representative sample, this was not treated as an exclusionary criteria). A urine sample was screened for the presence of tetrahydrocannabinol (THC cutoff 50 ng/mL) utilizing Instant Technologies iCup (Norfolk, VA). The rapid drug screen has detection times up to one month and is commonly used in drug research (McRae-Clark et al., 2013). We also administered a self-report instrument, the Alcohol/Drug Use Scale (AUS/DUS) (Drake et al., 1996). Urine Panel data was unavailable for 6 controls and 4 UHR participants while self-report data was available for each participant. Results from the urine panel indicated that 4 controls (~13%), 13 (~45%) of UHR screened positive. Self-report results indicated at least some use in the past month or more frequent for 11 controls (~34%) and 17 UHR (~59%) participants. We did not include participants who endorsed using cannabis on the day of testing. Other comorbid Axis I disorders were not exclusion criteria for UHR participants. Rates of the most elevated current comorbid Axis I conditions in the UHR participants included anxiety disorders 10 (34.3%) and mood disorders 8 (27.6%). Comorbid Axis I disorders are typical of UHR individuals and the present rates are comparable to other studies (Fusar-Poli et al., 2014). The presence of any psychotic disorder in a first-degree relative or any Axis I disorder in the participant was exclusionary criteria for controls.

2.2. Measures

2.2.1. UHR categorization

The Structured Interview for Prodromal Syndromes (SIPS) (Miller et al., 1999) was administered to detect the presence of a prodromal syndrome in three possible ways: 1) the presence of attenuated positive symptoms and/or 2) decline in global functioning accompanying the presence of schizotypal personality disorder and age <19 and/or 3) a family history of schizophrenia with decline in functioning (Miller et al., 1999). In the present study 89.7% met for category 1 alone, 3.4% met for category 3 alone, and 6.9% met for both categories 1 and 3 (no participants met for category 2). The SIPS contains an instrument, the Scale of Prodromal Symptoms (SOPS), which rates the severity of relevant symptoms along a 7-point scale ranging from absent to severe and psychotic. Ratings in the range of 3 to 5 are required for designation as “prodromal”. This measure gauges several distinct categories of prodromal symptom domains including positive (unusual thoughts, suspiciousness, grandiosity, perceptual abnormalities, disorganized communication) and negative dimensions (social anhedonia, avolition, expression of emotion, experience of emotions and self, ideational richness, occupational functioning). The Structured Clinical Interview for the Diagnostic and Statistical Manual was administered to determine the presence of psychosis and substance dependence exclusionary criteria (SCID-I) (First et al., 1995). Clinical interviews were conducted in person by advanced doctoral students, trained over a two-month period. All interviewers had inter-rater reliabilities that exceeded the minimum study criterion of Kappa ≥ 80 . The clinical interviews were completed on both UHR and Control groups (see Table 1).

2.2.2. Global social functioning

Social functioning was assessed with the Global Functioning Scale: Social (GFS-S) (Auther et al., 2006). This inventory provides ratings of

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