



Research paper

Diminished Hedonic response in neuroleptic-free youth at ultra high-risk for psychosis[☆]Gregory P. Strauss^{*}, Ivan Ruiz, Katherine H. Visser, Laura P. Crespo, Elizabeth K. Dickinson

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ABSTRACT

Hedonic response is preserved in schizophrenia. However, it is unclear whether this is also true in individuals meeting criteria for “prodromal” psychosis, who are considered to be at symptomatic high risk for developing the disorder. In this study, we examined neurophysiological and self-reported response to emotional stimuli in UHR ($n = 23$) and healthy control (CN; $n = 30$) participants who passively viewed pleasant, unpleasant, and neutral images for 500 ms while the electroencephalogram was recorded and then provided self-reports of valence and arousal to the stimuli. The Late Positive Potential (LPP) event related potential (ERP) component was used as a neurophysiological marker of emotional reactivity. Results indicated that CN participants had higher LPP amplitude for pleasant and unpleasant compared to neutral stimuli; however, UHR youth displayed no differences in LPP amplitude among pleasant, unpleasant, and neutral stimuli. Self-report data mirrored neurophysiological data, as UHR youth had lower reports of positive emotion to pleasant stimuli and negative emotion to unpleasant stimuli compared to CN participants. Furthermore, the presence of a mood disorder diagnosis predicted reduced neurophysiological emotional reactivity in UHR youth.

Findings suggest that youth at UHR for psychosis display diminished subjective and neurophysiological reactivity to emotional stimuli, and that symptoms of depression may result in diminished emotional reactivity.

1. Introduction

Anhedonia, traditionally defined as a diminished capacity for positive emotion (Rado, 1953), has been considered a core feature of schizophrenia (SZ) since the earliest conceptualizations of the disorder (Bleuler, 1950; Kraepelin, 1919). However, modern laboratory-based studies of affective response call the validity of this definition into question in SZ. Specifically, recent meta-analyses indicate that SZ patients and controls evidence comparable self-reports of valence (Cohen and Minor, 2010) and arousal (Llerena et al., 2012) to pleasant stimuli. Neuroimaging findings parallel the self-report data, with similar activation of key reward structures (e.g., ventral striatum) between SZ and control groups during the receipt of reward outcomes (Radua et al., 2015). Electrophysiological studies also indicate intact hedonic response, as indicated by comparable amplitude of the Late Positive Potential (LPP) and other ERP components between SZ patients and controls when participants are viewing pleasant stimuli (Horan et al., 2012; Horan et al., 2010). These findings suggest that at both subjective and objective levels of analysis, hedonic response may be intact in SZ. However, not all aspects of emotional response are normal in SZ.

Compared to controls, SZ patients report greater intensity of negative emotion to unpleasant, neutral, and pleasant stimuli (Cohen and Minor, 2010), and display greater amygdala activation to unpleasant stimuli (Anticevic et al., 2010).

Few studies have examined whether youth at ultra-high risk (UHR) for developing a psychotic disorder also display intact hedonic response. The majority of prior studies have examined self-reported anhedonia assessed via trait questionnaires or clinical rating scales, finding that rates of self-reported anhedonia are elevated in UHR youth and that elevated reports reflect a latent vulnerability for developing schizophrenia-spectrum disorders (Meehl, 2001; Velthorst et al., 2009). Very few studies have examined anhedonia in UHR youth using laboratory-based paradigms. Of the three studies examining self-reported emotional experience in the prodromal phase of illness, UHR participants have consistently been found to report less positive emotion to pleasant stimuli and less negative emotion to unpleasant stimuli than CN participants (Gruber et al. in press; Jung et al., 2016; Yee et al., 2010). Furthermore, diminished emotional reactivity to both pleasant and unpleasant stimuli has been associated with greater severity of depression (Gruber et al. in press). This pattern of findings should be

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interpreted with the relatively low rate of conversion to a psychotic disorder among those deemed UHR in mind. Only approximately 37% of those identified as UHR will develop a psychotic disorder at four-year follow-up (Schultze-Lutter et al., 2015), with the majority going on to develop mood and anxiety disorders (Addington et al., 2011). Diminished self-reported emotional reactivity in the UHR group may therefore reflect a latent vulnerability for developing anhedonia and mood symptoms more generally, rather than schizophrenia specifically.

Although self-report data provides valuable information regarding a participant's perceived emotional experience, these reports are subject to certain reporting biases and demand characteristics (Robinson and Clore, 2002; Strauss and Gold, 2012). An important next step is therefore to determine whether objective indicators of hedonic response, such as neurophysiological measures, also indicate diminished responsiveness in UHR youth. The current study examined neurophysiological response to emotional stimuli in UHR youth and evaluated associations with clinical symptoms. Participants completed a Rapid Serial Visual Presentation task during which pleasant, unpleasant, and neutral photographs were presented while the electroencephalogram (EEG) was recorded. The LPP event related potential (ERP) component was used as an objective, neurophysiological marker of emotional reactivity. The LPP is a centroparietal midline ERP component that becomes evident at approximately 300 ms after stimulus onset and manifests as a greater relative positivity for both pleasant and unpleasant than neutral stimuli that persists throughout stimulus presentation (Hajcak et al., 2012). After the ERP task, participants made unipolar reports of positive emotion, negative emotion, and arousal to the stimuli. Based on results from prior self-report studies examining UHR youth (Gruber et al. in press; Jung et al., 2016; Yee et al., 2010), we hypothesized that the UHR group would display diminished self-reported positive emotion to pleasant stimuli and diminished negative emotion to unpleasant stimuli compared to controls. Our second hypothesis was that controls would evidence robust neurophysiological emotional reactivity, as indicated by significantly greater amplitude of the LPP for pleasant and unpleasant than neutral pictures. However, we predicted that UHR youth would evidence diminished neurophysiological emotional reactivity, as indicated by no significant differences in LPP amplitude among pleasant, unpleasant, and neutral stimulus conditions.

2. Method

2.1. Participants

Participants included 23 UHR youth and 30 healthy controls (CN). UHR participants were recruited from a psychosis risk evaluation program in New York state, which received referrals from local clinicians (e.g., Psychiatrists, Psychologists, Social Workers, School Psychiatrists) to perform diagnostic assessment and monitoring evaluations for youth displaying psychotic experiences. UHR youth were also recruited via online and print advertisements, in-person presentations to community mental health centers, and calls or in-person meetings with members of the local school system (e.g., superintendent, principals). UHR participants were included if they met criteria for a prodromal syndrome on the Structured Interview for Prodromal Syndromes (Miller et al., 1999). SIPS criteria included: 1) Attenuated Positive Symptoms (i.e., SIPS score of at least 3–5 on at least one positive symptom item, with worsening symptoms over the past year) ($n = 19$); 2) Genetic Risk and Deterioration Syndrome (i.e., 1st degree relative with a psychotic disorder and decline in global functioning over the past year) ($n = 4$). UHR youth did not meet lifetime criteria for a DSM-IV-TR psychotic disorder as determined via SCID interview (First et al., 2002) and had never been prescribed an antipsychotic.

CN participants were recruited from the local community using posted flyers, newspapers advertisements, and electronic advertisements. CN participants had no current Axis I or II DSM-IV diagnoses as

Table 1
Participant demographics.

	UHR ($n = 23$)	CN ($n = 30$)	Test statistic, p -value
Age	19.6 (1.78)	19.7 (1.37)	$F(1,51) = 0.02$, $p = 0.89$
Participant education	13.3 (1.69)	13.6 (1.43)	$F(1,51) = 0.59$, $p = 0.45$
Parental education	14.8 (2.53)	15.1 (2.36)	$F(1,50) = 0.13$, $p = 0.71$
% Male	30.4	23.3	$\chi^2(1) = 0.34$, $p = 0.56$
Ethnicity %			$\chi^2(4) = 2.79$, $p = 0.59$
Caucasian	65.2	73.3	
African-American	0.0	6.7	
Latin-American	13.0	6.7	
Asian	17.4	10.0	
Native American	0.0	0.0	
Mixed-race	4.3	3.3	
Clinical symptoms			
SIPS positive	8.95 (3.83)	–	–
SIPS negative	7.00 (5.48)	–	–
SIPS disorganized	4.00 (2.49)	–	–
SIPS mood item	1.95 (1.83)	–	–
PINS MAP	9.19 (10.21)	–	–
PINS EXP	6.00 (6.83)	–	–

Note. UHR = Ultra High-Risk for Psychosis; CN = Healthy Control. SIPS = Structured Interview for Prodromal Syndromes; PINS = Prodromal Inventory for Negative Symptoms; MAP = PINS Motivation and Pleasure Subscale; EXP = PINS Diminished Expression Subscale; PINS MAP $\alpha = 0.92$, $\alpha = \text{EXP } 0.95$. In the UHR group, comorbid conditions included: major depressive disorder (MDD) ($n = 6$), bipolar disorder ($n = 3$), dysthymic disorder ($n = 1$), panic disorder (PD) ($n = 7$), social phobia ($n = 2$), obsessive compulsive disorder (OCD) ($n = 4$), generalized anxiety disorder (GAD) ($n = 3$), post-traumatic stress disorder (PTSD) ($n = 1$), substance use disorder ($n = 2$), borderline personality disorder ($n = 1$), bulimia nervosa ($n = 1$), attention deficit/hyperactivity disorder (ADHD) ($n = 1$). In the UHR group, psychiatric medications prescribed included: Clonazepam ($n = 2$), Fluvoxamine ($n = 1$), Hydroxyzine ($n = 1$), Fluoxetine ($n = 1$), Escitalopram ($n = 2$), Adderall ($n = 2$), Lithium ($n = 1$), Bupropion ($n = 3$).

established by the SCID-I and SCID-II (First et al., 2002; Pfohl et al., 1997), no family history of psychosis, and were not taking psychotropic medications. All participants were free from lifetime neurological disease. Moreover, participants provided written informed consent for a protocol approved by the Binghamton University Institutional Review Board and received monetary compensation for their participation. Groups did not significantly differ on age, ethnicity, sex, personal education, or parental education (see Table 1).

2.2. Procedures

Prior to completing the behavioral and ERP tasks, examiners who were trained to reliability standards ($\text{ICC} > 0.80$), conducted a structured diagnostic interview with all participants to complete the SCID-I, SCID-II, and SIPS. SIPS training was provided by a clinical psychologist previously trained in SIPS assessment (GPS), using in-person and gold-standard training videos. SIPS interviews were either performed directly by the PI or by a clinical psychology doctoral student trained to reliability standards who consulted with the PI on all cases for consensus. A clinical interview was also completed to assess symptom severity in the UHR group, after which ratings were made on the Prodromal Inventory for Negative Symptoms (PINS: Pelletier-Baldelli et al., 2017).

2.3. ERP Task

Participants completed a Rapid Serial Visual Presentation (RSVP) task modeled after Hajcak and Olvet (2008) while the electroencephalogram (EEG) was recorded. Participants were told that they would be shown scenes depicting pleasant (e.g., cute puppies), unpleasant (e.g., snakes), and neutral (e.g., spoons) content, and that they were to simply view the images freely.

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