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Transdiagnostic psychiatric symptoms related to visual evoked potential abnormalities

Jeffrey S. Bedwell [a,*], Pamela D. Butler [b], Chi C. Chan [a], Benjamin J. Trachik [a]

[a] Department of Psychology, University of Central Florida, Orlando, FL, USA
[b] Nathan S. Kline Institute for Psychiatric Research, Orangeburg, NY, USA

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ABSTRACT

Visual processing abnormalities have been reported across a range of psychotic and mood disorders, but are typically examined within a particular disorder. The current study used a novel transdiagnostic approach to examine diagnostic classes, clinician-rated current symptoms, and self-reported personality traits in relation to visual processing abnormalities. We examined transient visual-evoked potentials (VEPs) from 48 adults (56% female), representing a wide range of psychotic and mood disorders, as well as individuals with no history of psychiatric disorder. Stimuli were low contrast check arrays presented on green and red backgrounds. Pairwise comparisons between individuals with schizophrenia-spectrum disorders (SSD), chronic mood disorders (CMD), and nonpsychiatric controls (NC) revealed no overall differences for either P1 or N1 amplitude. However, there was a significant interaction with the color background in which the NC group showed a significant increase in P1 amplitude to the red, vs. green, background, while the SSD group showed no change. This was related to an increase in social anhedonia and general negative symptoms. Stepwise regressions across the entire sample revealed that individuals with greater apathy and/or eccentric behavior had a reduced P1 amplitude. These relationships provide clues for uncovering the underlying causal pathology for these transdiagnostic symptoms.

1. Introduction

There is considerable evidence that at least a subset of individuals with schizophrenia have abnormalities in visual processing (Butler et al., 2008; Yoon et al., 2013). As many of these abnormalities have been replicated in samples of first-degree relatives of individuals with schizophrenia (Bedwell et al., 2003; Green et al., 2006; Bakanidze et al., 2013; Sponheim et al., 2013) and nonpsychiatric schizotypy (Aichert et al., 2012; Bedwell et al., 2013), they may reflect underlying vulnerability for schizophrenia and serve as useful biomarkers. However, visual processing deficits have also been reported in other psychiatric disorders, including autism (Marco et al., 2011), bipolar disorder (Yeap et al., 2009), and unipolar depression (Normann et al., 2007), and therefore may not be specific to the diagnostic category of schizophrenia. Existing studies on these relationships have primarily examined visual processing deficits within a single diagnostic category or construct, as compared to nonpsychiatric controls. This strategy limits our understanding of how such endophenotypes may reflect vulnerability factors that do not respect the divisions in current psychiatric classification system. To address these limitations, the current study uses a broad transdiagnostic approach, consistent with the Research Domain Criteria (RDoC) initiative from the National Institute of Mental Health (Cuthbert and Insel, 2013), to examine how past and present psychiatric symptoms relate to visual processing. Visual processing is a subconstruct in the RDoC matrix (under Perception: Cognitive Systems).

Over the past decade, much of the research in this area has assessed visual-evoked potentials (VEPs), obtained from electroencephalography. The current study will focus on the P1 and N1 VEP components. P1 represents a positive voltage peak approximately 90–160 ms following stimulus onset, which is thought to originate from the dorsal and ventral extrastriate cortex (Di Russo et al., 2002). N1 is a negative voltage deflection that often shows multiple peaks in the range of 140–220 ms following stimulus onset and is thought to reflect primarily a ventral stream generator (Di Russo et al., 2002).

Within psychiatric research, the majority of transient VEP studies have assessed schizophrenia-spectrum conditions. The most consistent and replicated finding is that the P1 component shows a reduced amplitude in individuals with schizophrenia (Schechter et al., 2005; Yeap et al., 2008b; Butler et al., 2013; Verleger et al., 2013) or psychometrically-defined schizotypy (Koychev et al., 2010; Bedwell et al., 2013) as compared to nonpsychiatric controls. While the majority of studies

* Corresponding author.
E-mail address: Jeffrey.bedwell@ucf.edu (J.S. Bedwell).

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that have examined N1 in schizophrenia/schizotypy have found no significant difference from nonpsychiatric controls (Foxe et al., 2005; Butler et al., 2013; Verleger et al., 2013), some have reported that the N1 amplitude was also reduced in schizophrenia (Butler and Javitt, 2005; Martinez et al., 2012).

Transient VEPs to basic visual stimuli have also been examined in other diagnostic groups. Two studies reported a reduced P1 amplitude in bipolar I disorder (Yeap et al., 2009; Verleger et al., 2013), and that bipolar I disorder did not differ from schizophrenia on P1 amplitude (Verleger et al., 2013). However, a study on bipolar II disorder found no difference from controls on P1 amplitude (Elvsashagen et al., 2012). Two studies on unipolar depression found a reduction in both P1 and N1 amplitude (Normann et al., 2007), which may be particularly true for the subtype of "anxious-agitated" depression (Pierson et al., 1996).

Diffuse red light is known to suppress the magnocellular/dorsal pathway (de Monasterio, 1978; Livingstone and Hubel, 1984). A recent study found that while control participants showed the expected reduction in P1 amplitude in response to a high-contrast stimulus on a red background, individuals with high-schizotypy showed no change (Bedwell et al., 2013). Consistent with this finding, a different pattern of behavioral accuracy change to a red background on visual backward masking tasks has been previously reported in individuals with schizophrenia (Bedwell et al., 2011b) and their first degree relatives (Bedwell et al., 2003).

Given the findings of VEP abnormalities across multiple psychiatric disorders, it is possible that a shared phenomenological characteristic and/or underlying vulnerability factor accounts for particular VEP abnormalities. Therefore, the current study uses a novel approach of recruiting a wide range of psychiatric disorders and focusing on particular symptoms that relate to the VEP abnormalities. Most existing studies have either not reported symptom relationships, or only reported VEP relationships with broad categories of current symptoms such as current total positive or negative symptom ratings in schizophrenia, which have generally shown no relationship to P1 amplitude (Schechter et al., 2005; Obayashi et al., 2009). Based on previous findings within samples of a single diagnosis, the current study examined the diagnostic classes of schizophrenia-spectrum disorders and chronic mood disorders in order to assess the relationship of these broad diagnostic relationships with VEP amplitudes. We complemented this methodology with clinician ratings of particular current symptoms, and self-reported psychometric trait measures of specific schizotypy features and subtypes of anhedonia. We expected that this novel combination of lifetime vs. current symptoms and self-reported vs. clinician-rated symptoms would optimize our ability to examine symptom correlates of VEP abnormalities across diagnoses. We also included red and comparison (green) backgrounds to examine the previously reported red light effect for the first time in a transdiagnostic sample.

As this approach has not been previously published in the VEP literature to our knowledge, analyses of transdiagnostic symptom relationships with VEP amplitudes was exploratory. In terms of diagnostic class differences, we hypothesized that, across stimuli conditions, the schizophrenia-spectrum group and chronic mood disorder groups would have a smaller P1, but not N1, mean amplitude when compared to nonpsychiatric controls, but would not differ from each other on either P1 or N1 amplitude (e.g., Verleger et al., 2013). We additionally hypothesized that the schizophrenia-spectrum group in particular would show a group by color interaction on the P1 amplitude when compared to the nonpsychiatric controls, such that controls would show a reduction in P1 amplitude to the red background, while the schizophrenia-spectrum group would show no change.

2. Methods

2.1. Participants

Participants were recruited with attempts to include a wide range of psychiatric disorders, ranging from psychotic disorders, nonpsychotic mood and anxiety disorders, to no diagnosis. Attempts were made to recruit a sufficient number of individuals with schizophrenia-spectrum disorders and chronic mood disorders (e.g., bipolar disorder), given the existing findings of P1 amplitude abnormalities. This broad diagnostic inclusion was chosen to be consistent with the NIMH RDoC aim of examining dimensional symptom relationships that cut across multiple disorders, and to help ensure a wide range of severity across the symptoms measured. Participants were recruited from the local community using advertisements such as flyers in psychiatric clinics, newspaper advertisements, and online advertisements (e.g., Craigslist). Some of these advertisements mentioned that we are looking for individuals with "schizophrenia, schizoaffective disorder, or bipolar disorder" in order to recruit a sufficient number of these individuals. All participants completed informed consent prior to data collection and were paid a cash stipend for time spent participating in this study. Exclusionary criteria included self-reported history of significant neurological injury or symptoms (e.g., seizures), substance abuse in the past month or dependence in the past 6 months, medical conditions that may affect brain functioning, or English not being the native language. In addition, we administered the Reading subtest from the Wide Range Achievement Test 3rd edition (WRAT-3; Wilkinson, 1993) and excluded those with estimated IQ < 70, as well as those who showed indication of color blindness using the Ischihara Color Blindness Test, or an estimated corrected visual acuity worse than 20/40 using a Snellen wall chart.

Following exclusions, including exclusions for poor accuracy on the task of interest (described below), the final sample used in the data analyses consisted of 48 individuals (see Table 1 for demographics and descriptive statistics). Based on the Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID-I) and the Avoidant, Paranoid, and Schizotypal sections of the Structured Clinical Interview for DSM-IV Axis-II Disorders (SCID-II), the sample consisted of the following primary diagnoses: 14 (29.2%) no diagnosis, 10 (20.8%) bipolar I (7 of which had history of psychosis), 6 (12.5%) schizoaffective disorder, 4 (8.3%) major depressive disorder (MDD), 3 (6.3%) schizophrenia, 2 (4.2%) delusional disorder, 2 (4.2%) social phobia, 1 (2%) posttraumatic stress disorder, 1 (2%) generalized anxiety disorder, 1 (2%) dysthymic disorder, 1 (2%) bipolar II (nonpsychotic), 1 (2%) schizotypal and avoidant personality disorders and MDD, 1 (2%) paranoid personality disorder and MDD, 1 (2%) avoidant personality disorder and MDD.

2.2. Procedures

Following informed consent and administration of the structured interviews and visual/cognitive screens, participants then completed the Structured Clinical Interview for Positive and Negative Syndrome Scale (SCI-PANSS; Kay et al., 1987), the Schizotypal Personality Questionnaire-Brief Revised (SPQ-BR; Cohen et al., 2010; Callaway et al., 2014), the Temporal Experience of Pleasure Scale (TEPS; Gard et al., 2007), and the Anticipatory and Consummatory Interpersonal Pleasure Scale (ACIPS; Gooding et al., 2014; Gooding and Pflum, 2014). Participants then completed the VEP task.

2.2.1. VEP "Check" task

Stimuli were 8×8 arrays of isolated checks, similar to those used in transient VEP studies by others (Butler et al., 2007; Yeap