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A Bayesian model comparison approach to test the specificity of visual integration impairment in schizophrenia or psychosis

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ABSTRACT

Impaired visual integration is well documented in schizophrenia and related to functional outcomes. However, it is unclear if this deficit is specific to schizophrenia, or characteristic of psychosis more broadly. To address this question, this study used a Bayesian model comparison approach to examine the evidence of three grouping models of visual integration performance in 116 individuals with schizophrenia (SZ), schizoaffective disorder (SA), bipolar disorder (BD) with or without a history of prominent psychosis (BDP + and BDP-, respectively), or no psychiatric diagnosis (healthy controls; HC). We compared: (1) Psychosis Model (psychosis, non-psychosis), where the psychosis group included SZ, SA, and BDP +, and the non-psychosis group included BDP- and HC; (2) Schizophrenia Model (SZ, non-SZ); and (3) DSM Model (SZ, SA, BD, HC). The relationship between visual integration and general cognition was also explored. The Psychosis Model showed the strongest evidence, and visual integration was associated with general cognition in participants with psychosis. The results were consistent with the Research Domain Criteria (RDoC) framework, indicating that visual integration impairment is characteristic of psychosis and not specific to SZ or DSM categories, and may share similar disease pathways with observed neurocognitive deficits in psychotic disorders.

1. Introduction

Visual integration, the ability to combine discrete elements to form a holistic representation, underlies critical perceptual functions such as Gestalt grouping and is critical to cognitive processes within the environment (e.g., object identification, face processing; Butler et al., 2008). Deficits in visual integration are well-documented in schizophrenia (SZ) and have been shown to be related to clinical symptoms, cognition, and functional outcomes (Silverstein et al., 2006,1996,2000; Tso et al., 2014,2012; Uhlhaas et al., 2006a,2005). Some evidence suggests that disruption in early perceptual processing may be one mechanism through which social functioning is compromised in SZ (Butler, 2009; Silverstein and Keane, 2011a). Recent data show that visual integration impairment is evident in first-episode psychosis and worsens with illness chronicity (Keane et al., 2016), suggesting that it may be a characteristic of psychosis or a function of illness severity rather than specific to the diagnostic category of schizophrenia. Given the functional and etiological relevance of visual integration in SZ and psychotic disorders, this question would have important implications for our understanding of the pathophysiology and treatment of severe mental illnesses. To this end, the current study aimed to test the diagnostic specificity of visual integration impairment in schizophrenia or psychosis.

Visual integration is an interactive process linking the bottom-up sensory data output of neurons that code local features of a scene to cells within downstream visual areas that code global and typically larger complex formations modulated by context and prior experiences. Within healthy individuals, effective visual integration relies on long-range connections in V2 or higher areas to produce grouping (Silverstein and Keane, 2011b). Successful visual integration has been shown to be related to the N_{cl} (closure negativity) event-related potentials (ERP) wave, localized in the lateral occipital complex (LOC; Butler et al., 2013). However, proper functioning of the visual system also depends on top-down modulation of the visual cortex (Engel et al., 2001; Freeman et al., 2003; Gilbert and Li, 2013) and a balance in neuronal excitation/ inhibition, supported by NMDA receptor functions

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(e.g., to modulate lateral excitation) and GABAergic functions (e.g., to inhibit noise; Butler et al., 2008). In fact, neural oscillations and synchronization, particularly at the beta and gamma frequency bands, are often implicated in visual processing and integration (Castelhano et al., 2015; Kloosterman et al., 2015; Uhlhaas et al., 2006).

Visual integration can be psychophysically assessed with perceptual closure tasks, grouping paradigms, and, most commonly, a contour integration task that requires participants to identify a contour comprised of elements within a background of similar noise elements (Butler et al., 2008). Individuals with SZ and psychosis typically perform worse than healthy controls on these tasks, suggesting impaired visual integration (review by Butler, 2009). The exact origin of visual integration deficits in psychosis is unclear. Distributed dysfunctions across the visual system, beginning from the retina (Adams and Nasrallah, 2017), to primary visual cortex V1 (Anderson et al., 2017), to extrastriate visual cortex V2-V4 (Butler et al., 2013; Silverstein et al., 2009), and to associated visual areas in the dorsal and ventral processing streams (Butler et al., 2013; Green et al., 2015; Silverstein et al., 2015b), have been reported. Regardless of the origin, visual integration impairment has been shown to be related to poorer social cognition and functional outcome in SZ (Silverstein and Keane, 2011b; Tso et al., 2014), suggesting that visual abnormalities may have downstream effects on higher-level cognition and social functioning in SZ. Given the scientific rigor of its measurement and functional relevance in SZ, visual integration offers a unique window to examine and understand the pathophysiology of psychotic disorders.

One question that needs clarification in the literature is whether visual integration impairment is specific to schizophrenia or common to other psychiatric disorders. This question arises as the field is moving toward a dimensional understanding of psychopathologies, led by the National Institute of Mental Health Research Domain Criteria (RDoC) initiative. This shift away from diagnostic categories (e.g., Diagnostic and Statistical Manual for Mental Disorders; DSM) to functional dimensions linked with pathophysiology (e.g., visual perception; Insel et al., 2010; Insel, 2014) may improve our understanding of psychopathology through a data-driven approach. In line with this effort, visual integration has been examined in other psychiatric disorders with clinical manifestations suggesting abnormal visual perception, including body dysmorphic disorder and obsessive-compulsive disorder; however, no impairment was found in these disorders when compared with healthy controls and schizophrenia (Silverstein et al., 2015a). It remains unclear, nevertheless, whether visual integration is affected in disorders in which psychosis is always present or highly prevalent, particularly those considered to be on the "schizophrenia-bipolar psychosis spectrum" (Keshavan et al., 2011). Bipolar disorder (BD) is a disorder frequently (>50%) affected by psychosis (Keck et al., 2003) and has substantial clinical, cognitive, neurobiological, and genetic overlap with schizophrenia (Brown, 2015; Hall et al., 2015; Pearlson, 2015; Pearlson and Ford, 2014; Tondo et al., 2015). Yet, no studies thus far have examined visual integration in BD. Additionally, there is evidence that BD patients with a history of psychosis (BDP+), compared with those without (BDP-), exhibit cognitive deficits (Hill et al., 2013; Ruocco et al., 2014) and neurobiological abnormalities (Ivleva et al., 2013; Mathew et al., 2014) similar in extent and severity to those observed in SZ. This suggests that the presence of psychosis, regardless of diagnostic category, might represent a distinct psychopathology that differentially impacts cognitive functions (including visual integration). Indeed, research studies often combine participants with SZ and schizoaffective disorder (SA) into one patient group, with the assumption that psychosis, rather than the DSM categories, is the underlying illness dimension causing the observed abnormalities of interest. This assumption is rarely explicitly tested in the schizophrenia literature, and visual integration is a well-researched topic in which the "schizophrenia" samples often comprise both SZ and SA (Butler et al., 2013; Chen et al., 2003; Silverstein et al., 2006). This makes it difficult to determine if the two diagnostic groups do indeed exhibit similar deficits to support the schizophrenia or psychosis hypothesis of visual integration deficits. Taken together, to address the question of specificity of visual integration impairment to schizophrenia or psychosis, it is necessary to include BD and stratify it by history of psychosis, as well as separate SA from SZ.

The current study aims to address the question whether visual integration impairment is characteristic of psychosis in general, specific to schizophrenia, or a function of DSM diagnosis. We assessed visual integration using a contour integration task in 116 participants: three patient groups along the "schizophrenia-bipolar psychosis spectrum" (SZ, SA, BDP+), BDP-, and HC. Participants were grouped according to three distinct models: 1) The Psychosis Model (psychosis, non-psychosis), where the psychosis group included SZ, SA, and BDP+, and the non-psychosis group included BDP- and HC; 2) The Schizophrenia Model (SZ, non-SZ); and 3) The DSM Model (SZ, SA, BD, and HC). We then used Bayesian model comparison to determine which model was a more likely generative model of the observed visual integration performance data. We hypothesized that visual integration in the psychosis group would be worse than the non-psychosis group, and the Psychosis Model would be the winning model among the three competing models. Additionally, we examined the relationship between visual integration and cognitive measures within the psychosis group and hypothesized that poorer visual integration would be associated with worse cognitive functions.

2. Method

2.1. Participants

A total of 116 participants completed the study: 25 SZ, 22 SA, 31 BD, and 38 HC. Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition (DSM-IV; American Psychiatric Association, 2000) diagnoses were established using the Structured Clinical Interview for the DSM-IV (SCID-IV; First et al., 1997) for SZ, SA, and HC participants. BD participants were originally recruited via a separate study, which characterized participants using the Diagnostic Interview for Genetic Studies (DIGS Version 4.0; Nurnberger et al., 1994). BD participants were divided into two groups by history of prominent psychosis, defined as having had at least two mood episodes with psychotic features. Subsequently, 11 BD participants were assigned to the BDP+ group and 20 to the BDP- group. The clinical and HC groups were matched for age, sex, and parental education (Table 1). Fifty-two participants of this study (29 SZ/SA and 23 HC) were part of a previous report (Tso et al., 2014). Eighty-seven participants of this study (37 SZ/SA, 27 BD, and 23 HC) participated in another study focusing on eye gaze perception, reported elsewhere (Yao et al., 2018).

Participants were recruited via a university research registry, mental health clinics, other research studies, and advertisements. All participants were 18–65 years of age with at least 20/30 vision according to a Snellen chart. Participants who were unable to provide informed consent or had a history of substance dependence/abuse in the past 12 months were excluded. HC with a history of a DSM-IV Axis I diagnosis, significant medical conditions that affect brain functions, or family history of psychosis or mania among first-degree relatives were excluded. The study was conducted in accordance with the World Medical Association Declaration of Helsinki and the research protocol was approved by the Institutional Review Board of the University of Michigan Medical School. Written informed consent was obtained from each participant prior to data collection.

2.2. Visual integration

A Contour Integration task was used to measure visual integration. The task was presented on a Windows PC using MATLAB (MathWorks, Inc.). A chin-rest was used to maintain a distance of 16 inches between the computer screen and the participant. The stimulus was presented on