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Commentary

VISUAL IMPAIRMENTS IN SCHIZOPHRENIA: THEIR SIGNIFICANCE AND UNREALIZED CLINICAL POTENTIAL

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In recent years, there has been increased interest in visual abnormalities in schizophrenia. The target article by Jurišić et al. offers a concise, up-to-date review of this field, and transcends disciplinary boundaries to integrate retinal, vascular, and perceptual findings (Jurišić et al. 2019). The reviewed data unambiguously point to one of the main implications of the paper, which is that any adequate characterization of schizophrenia must take into account visual impairments. Visual impairments are important because they can be found in a majority of cases, they predict future illness onset (Hayes et al. 2019), and they can serve as endophenotype, trait or episode markers, depending on the type of anomaly (Silverstein 2016). In this brief commentary, we wish to emphasize several points that were not elaborated upon in the target article.

First, despite accumulating data on retinal structural abnormalities in schizophrenia, as revealed by optical coherence tomography (OCT), studies have not yet shown when in the course of illness retinal cell structure starts to deteriorate. Does it occur in the prodromal stage? Or at the first episode? Does retinal thinning occur in lockstep with the number of psychotic episodes or illness duration? Addressing these questions can offer new insights. It can help determine when global CNS changes (e.g., neuropil loss) begin, and whether people with schizophrenia can be subtyped in terms of extent and location of post-diagnosis CNS changes. Additionally, clarification of the sequential course of retinal thinning can help determine whether retinal thinning corresponds with gray and/or white matter loss in schizophrenia, and whether it precedes or follows such changes. Clarifying this would provide insight regarding the directionality of effects and their treatment implycations. For example, if the temporal ordering were: occipital lobe volume loss, lateral geniculate nucleus (LGN) volume loss, and then retinal thinning (due to loss of axons and possibly neurons that project to the areas of atrophy), this would suggest retrograde transynaptic degeneration (RTSD). In this case, retinal structural changes could alert clinicians to the likely presence of prior and ongoing brain volume loss and cognitive decline, with subsequent initiation of treatment as needed to slow down or prevent further tissue loss. In contrast, if atrophy occurs in the other direction (anterograde TSD), this would imply that reductions in retinal cell structure integrity are a harbinger of brain volume loss and could suggest the importance of initiation of treatments that have shown protective effects (e.g., cognitive remediation) (Eack et al. 2010). It is also possible, of course, that degree of volume loss in the brain and retina are independent, and therefore longitudinal studies to clarify the temporal relationship between brain and retinal changes are necessary.

Another unresolved issue concerns the relative contributions of the retina, subcortex, and cortex to visual distortions and hallucinations in schizophrenia. For example, open questions include the extent to which hallucinations in schizophrenia can be conceptualized within a sensory deprivation model, as a result of reduced retinal output and/or weakened input reaching the occipital lobe. It has also been hypothesized that several visual distortions in schizophrenia (e.g., visual distortions in early schizophrenia in contrast sensitivity) are due to compensatory amplifying responses (at the visual cortex level) to weak retinal signals and concurrent noise (Silverstein et al. 2017). To facilitate research in this area, it will be important to develop relatively brief self-report measures of sensory distortions found in people with schizophrenia, and to clarify relationships between visual distortions and visual hallucinations.

Jurišić et al. justifiably suggest that visual assessments hold promise for identifying endophenotypes for certain schizophrenia subtypes. However, this suggestion would be better supported were it to take into account existing literature (going back to the 1980s) showing that some basic visual impairments are more characteristic of patients with poor (rather than good) premorbid social functioning (Knight 1992). In particular, poor premorbid functioning has been linked to poor prognosis, occipital lobe atrophy, familial aggregation of schizophrenia, cognitive disorganization, and visual processing impairments, which have been found to cluster together (Dorph-Petersen et al. 2007, Keane et al. 2019, Wickham et al. 2001). Visual assessments offer opportunities to clarify the heterogeneity that characterizes the illness.

At the end of the target article, the authors mention predictive coding, which has typically been demonstrated in vision in schizophrenia using high level tasks (e.g., Keane et al. 2013). However, predictive coding has also been demonstrated in the retina in animal studies, and has been shown in the human cone flicker ERG response (McAnany & Alexander 2009). Predictive processing in the retina has been studied through evaluation of the omitted stimulus response (OSR), which represents the retinal response to the unexpected absence of a stimulus. Exploring the OSR in people with schizophrenia would provide evidence on the ubiquity of predictive coding errors in the CNS in the disorder, and on the degree of its independence from higher-level cognitive processes. The advantage of having a retinal assay of predictive coding is that it would allow researchers to explore the mechanisms which may contribute to neural prediction errors, as well as the genesis of positive symptoms, with an objective, brief, and cost-effective method.

Several issues remain that were not addressed in the target paper. For example, the prevalence of different retinal, vascular, brain, and perceptual impairments in schizophrenia is relatively unknown. It is also important to determine the extent to which specific visual impairments are related to fixed familial traits (endophenotype), clinical state (symptoms), or illness duration (stage). As discussed above, some visual impairments may be associated with illness risk (e.g., poor visual acuity; ERG anomalies), while others are characteristic of a specific subtype of schizophrenia. Identifying which visual impairments may be reliable indicators of clinical state could also prove useful in predicting (and possibly preventing) relapse and in monitoring treatment response. Relatedly, there is much to be learned regarding the extent to which these abnormalities are modifiable by rehabilitative, pharmacologic, or brain stimulation therapies. Regarding these, recent work suggests that visual training programs may be effective in remediating some visual processing impairments, but this work is in its infancy. Another question pertains to whether visual impairments span all psychotic disorders or whether they are instead more specific to schizophrenia or at least non-affective psychosis. There is evidence suggesting that the latter view is correct for at least some types of visual changes, but the issue is far from settled. Finally, there is a need for longitudinal studies of visual system and perceptual function in schizophrenia, to move beyond the largely correlational studies linking structural and functional changes on the one hand, and perceptual and symptom changes on the other. Data on each of these issues will help establish causal links and allow for a greater understanding of the roles of visual system changes (e.g., causes, effects, manifestations of generalized CNS changes) in schizophrenia spectrum disorders and the extent to which the visual system provides a useful window into illness-related pathophysiology.

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