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THE CONTRIBUTION OF RETINAL DYSFUNCTIONS TO VISUAL IMPAIRMENTS IN SCHIZOPHRENIA

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In their comprehensive review, Jurišić et al. summarized and synthesized several aspects of retinal dysfunctions in schizophrenia (Jurišić et al. 2019). There is some evidence that patients with chronic schizophrenia display a thickening of retinal nerve fiber layer, abnormalities of the vascular architecture, and reduced macular volume, which is in accordance with the electrophysiological findings (dysfunctional bipolar and Muller cells). However, it is not clear whether these anomalies are inherent features of the illness and can be detected in the initial phase of psychosis, or they are a mere consequence of non-specific deterioration during the illness. Metabolic abnormalities associated with antipsychotic medications and lifestyle factors may be especially relevant. From a functional point of view, a critical question is how retinal dysfunctions are related to higher-level visual abnormalities, including altered smooth pursuit eye movements, lowered motion perception, and attentional dysfunctions. These factors are partly trait markers of schizophrenia, but, on the other hand, some are associated with psychotic symptoms and visual illusions.

Recent results from basic sciences may shed light on these issues. It is well-known that some sensory neurons in the visual system prefer certain stimulus features (e.g., motion, orientation, or hue), although in real life vision, these features change simultaneously. It is not known how this multidimensionality of vision is altered in schizophrenia. The first step is to better understand these integrative mechanisms at the retinal level. Kühn and Gollisch (2019) recently investigated direction-selective ganglion cells that responded to a moving surface texture where direction, speed, and spatial pattern in the receptive field continuously changed. The authors found that the neurons showed the same direction preference despite the ambiguities of luminance changes during stimulation. The stability of encoding was mediated by the coordinated activity of a population of direction-selective cells (synergistic motion decoding). Importantly, the coordinated activity of cells represents more information than that obtained from single cells added together (Kühn & Gollisch 2019). Given that coordinated neuronal activity is especially vulnerable in schizophrenia, it is possible that integrated response biases at the retinal level may induce anomalous perceptual experiences in psychosis, which is a testable hypothesis for future studies.

Another important mechanism implicated in perceptual anomalies characteristic of schizophrenia is the distorted role of context: the surrounding environment has a profound effect on the perception of target stimuli. Interestingly, direction-selective ganglion cells in the retina are affected by motion context. It has recently been demonstrated that posterior-preferring direction-selective ganglion cells are modulated by cholinergic amacrine cells, which makes them sensitive to moving contours. In addition, a new type of wide field amacrine cells has been identified, which may serve as "continuity detectors" of moving contours (Huang et al. 2019). Cholinergic mechanisms are likely to interact with dopamine in the retina, which can be visualized with novel positron emission tomography (PET) techniques. Using targeted mass spectrometry, both D2 and D3 dopamine receptors, which are the main targets of antipsychotic medications, have been identified in the human retina, although D2 receptors were much more abundant than D3 receptors (Caravaggio et al. 2018). Critically, D2, but not D3 receptors were reduced in the retina of schizophrenia patients, which, together with the cholinergic mechanisms, may have an impact on contextual modulation of visual stimuli (e.g., enhancement or suppression by the surround). Altogether, these novel findings from basic visual sciences would significantly contribute to the understanding how retinal dysfunctions in schizophrenia play a role in higher level visual anomalies, abnormal perceptual experiences, and psychotic symptoms. By the identification of neurochemical mechanisms, the retina may be a real window into the psychotic brain, providing a better understanding of the mechanisms of antipsychotic medications.

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