

Vision Science and Schizophrenia Research: Toward a Re-view of the Disorder Editors' Introduction to Special Section

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This theme section on vision science and schizophrenia research demonstrates that our understanding of the disorder could be significantly accelerated by a greater adoption of the methods of *vision science*. In this introduction, we briefly describe what vision science is, how it has advanced our understanding of schizophrenia, and what challenges and opportunities lay ahead regarding schizophrenia research. We then summarize the articles that follow. These include reviews of abnormal form perception (perceptual organization and backward masking) and motion processing, and an article on reduced size contrast illusions experienced by hearing but not deaf persons with schizophrenia. These articles reveal that the methods of basic vision research can provide insights into a number of aspects of the disorder, including pathophysiology, development, cognition, social cognition, and phenomenology. Importantly, studies of visual processing in schizophrenia make it clear that there are impairments in the functioning of basic neural mechanisms (eg, center-surround modulation, contextual modulation of feedforward processing, reentrant processing) that are found throughout the cortex and that are operative in multiple forms of cognitive dysfunction in the illness. Such evidence allows for an updated view of schizophrenia as a condition involving generalized failures in neural network formation and maintenance, as opposed to a primary failure in a higher level factor (eg, cognitive control) that accounts for all other types of perceptual and cognitive dysfunction. Finally, studies of vision in schizophrenia can identify sensitive probes of neural functioning that can be used as biomarkers of treatment response.

Key words: schizophrenia/perception/vision/cognition/
CNTRICS/RDoC

Cognitive impairment is now recognized as a core aspect of schizophrenia. It accounts for a significant portion of functional disability, and consequently, finding methods

to improve cognition is seen as among the most urgent research priorities regarding the disorder.¹ This is reflected in several major initiatives over the past decade, including Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS), Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia (CNTRICS), and Research Domain Criteria (RDoC). Goals of MATRICS and CNTRICS included identifying the most relevant domains of cognitive impairment in schizophrenia and then developing reliable and valid measures of these processes to assist in the development and evaluation of novel procognitive interventions. Similarly, RDoC includes a focus on domains of cognition as a means of identifying the core mechanisms underlying psychopathology. We wish to demonstrate in this special theme section of *Schizophrenia Bulletin* that progress toward the goals of these important initiatives—better understanding of both cognitive dysfunction in schizophrenia and the mechanisms involved in the disorder as a whole—could be significantly accelerated by a greater adoption of the methods of vision science into the field of schizophrenia research. This is important because, to date, most efforts to understand cognitive function in schizophrenia have focused on the frontal lobe, with far less work done on other brain regions and their associated functions (see figures 1 and 2). We believe a more balanced approach would be beneficial. As the neuropsychologist Weiskrantz pointed out, “there is an extremely rich neuropsychological harvest to be gathered in the human visual system.”² Aside from telling us about the visual and associated neural abnormalities associated with the disorder and its subtypes, understanding vision in schizophrenia can also elucidate the widespread abnormalities in brain circuitry and function, where visual disturbances constitute replicable, low-level, and concrete examples.

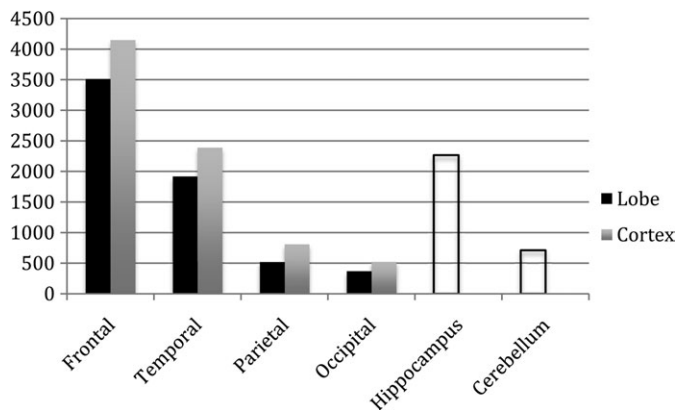


Fig. 1. PubMed citations by brain region, for regions commonly studied in schizophrenia research, as of December 1, 2010. All items are searched in conjunction with the term “schizophrenia.”

In this Introduction to the theme section, we begin by providing a historical context for the recent increased focus on studies of visual processing in schizophrenia. This is followed by a brief introduction to vision science and the potential of this approach for schizophrenia researchers. We then provide descriptions of the articles in this section and end by discussing future challenges and opportunities.

Historical Perspective

In 1903, Kraepelin³ reported incomplete perception of very briefly exposed stimuli among dementia praecox patients. This might have been the beginning of many continuous years of research on visual disturbances in schizophrenia. However, in 1911, Bleuler⁴ noted that he was unable to replicate the finding. He also noted that he was not aware of any evidence of perceptual impairment that could not be accounted for by failures in attention, affective splitting, negativism, poor motivation, or conceptual disturbance. Therefore, Bleuler^{4(p9)} concluded that both sensory and perceptual functioning is normal in schizophrenia and that primary disturbances of perception are “not demonstrable.” For the most part, this put an end to research on visual processing in schizophrenia until the cognitive revolution in the 1950s and 1960s, when the number of studies in this area began to increase slowly.

Since the time of Bleuler,⁴ other factors have hindered progress. First, visual processing disturbances are subtle and typically are not apparent to the untrained observer. Whereas impaired memory or attention, or disorganized speech, for example, may be very easy to notice, problems in low spatial frequency processing or contour processing may be much harder to pinpoint without the appropriate tools. The functional consequences of visual problems, such as difficulty reading,⁵ may also be misattributed to higher level problems such as attentional disturbance. Moreover, visual deficits may be harder for patients to accurately report. Whereas higher level cognitive prob-

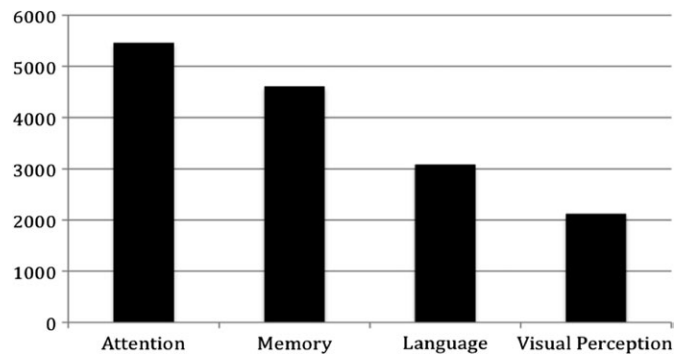


Fig. 2. PubMed citations by cognitive function (searched in conjunction with the term “schizophrenia”) as of December 1, 2010. Note that the search for “vision and schizophrenia” returned only 253 articles. The general term “perception” was not used because it generated articles on nonvisual perception (eg, audition, olfaction), in addition to articles on topics such “perception of smoking risk”, etc. A similar problem was noted for a number of components of executive functioning, such as “planning”, “problem solving,” and “reasoning,” although it should be noted that the search for the single aspect of executive function known as “cognitive control” by itself retrieved 2030 items (when searched in conjunction with the term “schizophrenia”), nearly as many as the search on “visual perception and schizophrenia.”

lems are—almost by definition—more accessible to the conscious grasp of the patient, many kinds of perceptual processes do not require awareness,⁶ let alone attention.⁷ It would not be surprising, therefore, for problems with perception to be reported with less frequency and accuracy in the clinic and at home.

Yet another factor that may explain the relative neglect of visual disturbances in schizophrenia research is the dominance of certain theoretical models, which emphasize a critical role for the prefrontal cortex and abnormal dopamine regulation (eg, ref. ^{8,9}). Support for these models may have caused the relatively dopamine-poor visual processing regions of the brain¹⁰ to be viewed as less relevant.

Practical considerations may have also retarded the progress of vision research in schizophrenia. For example, many visual perception paradigms with demonstrated construct validity have unknown psychometric properties, including test-retest reliability, or lack validation on large and diverse subject samples. In addition, certain tasks cannot yet plausibly be implemented in clinical trials because, for example, they are too lengthy, and it is unclear how difficult to make the task or how much practice to include so that valid data can be obtained from schizophrenia patients.

Nevertheless, the reason we are writing this article and the reason why there is a special theme section is because the study of vision has provided—and continues to provide—important insights about the illness. Clinical reports of abnormal visual perception (including in newly diagnosed patients) have been published for over 50 years (see Silverstein and Keane,¹¹ this issue, and Arieti¹²), experimental studies of vision in schizophrenia date back

over 50 years,¹³ perceptual disturbances in prodromal and first-episode cases have been evidenced for at least 20 years,¹⁴ and visual disturbances in children at risk for schizophrenia predict later development of the disorder.¹⁵ The occipital lobe, although still not as commonly studied, is increasingly viewed as relevant, especially with an increased understanding of the role of *N*-Methyl-D-aspartate (NMDA) and γ -aminobutyric acid (GABA) receptors in vision and in schizophrenia.^{16,17} Correspondingly, perception is included as a core domain in the ongoing CNTRICS and RDoC initiatives mentioned above. In short, the study of vision in schizophrenia is evolving from being a secondary and esoteric interest in the field to one that is expected to play a more central role in illuminating the nature of the disorder.

In the next section, we briefly introduce the vision science approach both in terms of the questions that it aims to answer and the methods it can use for doing so. We then go on to summarize the articles in this special section. This introductory article concludes with a discussion of important but underexplored issues on the topic of vision and neuroscience that relate to schizophrenia research.

Vision Science and its Relevance to Schizophrenia Research

Vision science is an interdisciplinary field that integrates contributions from cognitive psychology, neuropsychology, neuroscience, statistics, engineering, philosophy, and computer science to promote an understanding of how patterns of retinal activation are transformed into meaningful visual experiences. It has been called the “single most coherent, integrated, and successful branch of cognitive science”^{18(pxviii)}, and it is generally accepted that, within the field of basic cognitive neuroscience, far more work has been done on vision than on any other domain. It has generated a number of behavioral methods that are efficient, well established, and well-grounded in neuroscience and that can therefore be useful to schizophrenia researchers. Vision has been of such interest partly because it delivers more information about the world than any other sense—up to 90% according to some estimates.¹⁹ Moreover, approximately 30% of the human neocortex is involved in visual processing.²⁰ The import of vision for normal cognition and the intense focus on vision within cognitive neuroscience has not resulted in a similar focus in the field of schizophrenia research, however (see figures 1 and 2). It is therefore relevant to ask: In what ways can vision science reveal unique information about schizophrenia?

Broadly speaking, vision research tools can help clinically minded researchers accomplish at least 6 goals: (1) Describe schizophrenia-related impairment on perceptual tasks; (2) connect these behavioral differences to neural mechanisms and thus demonstrate how patients differ from controls in terms of brain structure and function; (3) identify how these neural mechanisms develop

abnormally by examining differences in trajectories of change relative to control subjects; (4) examine how medication or training alters the neural mechanisms by seeing how behavior resulting from these mechanisms changes; (5) examine whether symptom changes correlate with—and possibly take place after—psychophysical changes, to potentially validate aspects of perceptual dysfunction as biomarkers; and (6) examine whether certain subgroups of schizophrenia patients or certain symptoms or traits are associated with more pronounced visual deficits so as to potentially distinguish subtypes of the disorder.

But there are deeper reasons to be interested in vision. Vision, like other types of cognition, can be considered a form of computation used to construct a model of the environment,¹⁸ and its processes can be seen as involving hypothesis generation and testing, just as with other cognitive functions.^{21,22} It has been hypothesized that the computational algorithms (ie, the sequences of steps that transform representations) used to process visual data are identical to the ones used by the brain in other domains of cognition^{19,23}—with the important proviso that these operations are perhaps more readily comprehended in the domain of vision. This is because visual processing, or “visual thinking,” is based on concrete and physical properties of stimuli, whereas in other cognitive domains (eg, language) relationships between different components of the mental representation are typically more abstract (eg, metaphor or simile).¹⁹ Examining the brain’s computational mechanisms, as involved in vision, may therefore provide the clearest examples of these mechanisms and their associated neurobiological bases. As an example, context-processing disturbances have been demonstrated in schizophrenia in several domains of cognition, including working memory, language, social cognition, and cognitive control. Contextual modulation can be studied more concretely, however, by examining center-surround modulations in neurons in primary visual cortex, where the influence of stimuli outside of the classical receptive field is now well established (eg ref. Lamme²⁴). These contextual influences at the synaptic level are relevant not only to gain control²⁵ but also to contour integration and other aspects of perceptual organization (PO),²⁶ and to motion processing²⁷ as well, all of which are impaired in schizophrenia (see Silverstein and Keane¹¹ and Chen²⁸ in this section). Moreover, neurophysiological and computational studies have further demonstrated the role of contextual modulation in selective attention, working memory, learning, and disambiguation in language, among others,²³ all of which are, again, impaired in schizophrenia. Other basic cortical functions, such as reentry, or feedback from higher to lower cortical regions, have also been well-characterized in vision, and these mechanisms are increasingly being incorporated into theories of other cognitive functions and of schizophrenia²⁹ (see also Green et al.³⁰ in this section). In short, visual disturbances do not only tell us about

vision; they also tell us about how the brain functions and how it may malfunction in schizophrenia.

The foregoing evidence bolsters that view that schizophrenia involves widespread failures in the formation and maintenance of neural networks. More specifically, converging evidence suggests a primary impairment in rapidly modulating sensory or activated, stored information to generate (spatial and temporal) context-sensitive, coherent representations from novel patterns of input (see Silverstein and Keane, this theme section). This view contrasts sharply with the hypothesis that most perceptual and cognitive impairment in schizophrenia results from a failure in a higher level process (eg, cognitive control) that imposes order on well-formed representations deriving from perceptual and cognitive processes.^{16,22,23} There are 2 major problems with the latter view, however. First, evidence suggests that functions as apparently different as vision and cognitive control are subserved by similar neurobiological circuitry and computations. In this view, the primary structured representations of the occipital lobe involve groupings of basic units of visual information, whereas the primary “gestalts” of the prefrontal cortex involve representations of action sequences, anticipated behavior-consequence links, and binding of temporal context with ongoing and anticipated behavior (see supplement to Silverstein and Keane¹¹ for references). In support of this is a recent study on cognitive control in schizophrenia that identified these types of binding failures in the frontal cortex.³¹ Second, there is much evidence that (1) perception does not require cognitive control and (2) there are disturbances in perceptual processing in schizophrenia that cannot be explained in terms of higher level deficits.

Regarding (1), for example, intact contour integration has been observed in the neglected visual field in patients with hemispatial neglect,³² and in healthy subjects, contour integration happens automatically even when participants do not want it to or are not attending to the contour-containing stimuli.³³ Moreover, visual processes such as spatial frequency processing, PO, form perception, and motion perception are found throughout the animal kingdom in species with far less frontal cortex development than humans. Regarding (2), involvement of the occipital lobe in contour integration has been found in anesthetized monkeys,³⁴ with the same regions showing hypoactivation in studies with schizophrenia patients,³⁵ suggesting that the basic binding process that is impaired does not normally require cognitive control. Similarly, contour integration deficits have been repeatedly demonstrated in people with amblyopia, a condition involving reduced integration of information in early visual cortex regions, associated with suppressed input from one eye, and these patients are not characterized by impairments in frontal cortex functioning. Further, in collinear facilitation tasks, when both patients and controls attend to flankers to the same degree (as verified by a secondary

task), only patients show impaired ability at integrating the flanker elements (see Silverstein and Keane,¹¹ this section). Patients are also less susceptible to certain illusions and it is doubtful that deficits in cognitive control help subjects recover correct shape information. In addition, there is abundant evidence for magnocellular deficits, based on studies of motion, spatial frequency, and contrast sensitivity processing. These deficits have well-known origins in early sensory processing centers. Finally, findings of increased occipital lobe gray matter loss in poor outcome patients,³⁶ the subgroup that typically shows the most severe perceptual impairments, suggests a primary role for occipital lobe dysfunction in visual stimulus assembly failures in schizophrenia. In short, the evidence from vision research highlights that much coordination of perceptual and cognitive activity emerges via self-organization in local populations of neurons, which is a general property of circuitry throughout the brain. This view does not negate the importance of different brain regions for specialized processing, such as that the occipital lobe is a visual information processor, whereas the prefrontal cortex is heavily involved in strategic planning and goal maintenance. Nor does it negate the possibility that there are abnormalities in schizophrenia that are due to faulty interregional interactions. Rather, this view highlights the primary importance of coordinating processes for diverse mental functions, the likelihood that at least some perceptual phenomena and their abnormalities in schizophrenia are best accounted for by failures in this process within visual pathways, and the relative simplicity of viewing and comprehending coordinating processes, and their impairments in schizophrenia, through the lens of vision research (see Silverstein and Keane, this issue, for further discussion of cognitive coordination and schizophrenia).

Given the potential yield of vision research for understanding schizophrenia, an important question is: how can the tools of vision science be used to both reveal dysfunction while at the same time circumventing generalized deficit confounds (eg, poor performance due to impaired attention, low motivation, sedation from medication, etc.)? First, and perhaps most obviously, a task can be designed so that abnormal perception provides a task advantage (eg, ref. Place and Gilmore³⁷). For example, if a visual illusion makes a task harder and if the mechanisms generating the illusion are impaired in schizophrenia, then patients will in some cases outperform controls on the task.³⁸ A visual deficit may also be identified as an abnormal within-subject difference between a test and control condition, where only the former depends on a target visual process (eg, ref. Keri et al³⁹). In other cases, tasks can be designed so that the predicted pattern of performance for patients across multiple conditions is different from that of controls and also different from what would be expected by a generalized deficit (eg, patients perform differently than controls across

conditions in a hypothesis-consistent manner, but not more poorly overall) (eg, ref. Knight et al⁴⁰). In still other cases, when the lifetime developmental trajectory of performance on certain tasks is known for patients and healthy controls and when the neural mechanisms underlying this development are known, then the differential development of the visual pathways⁴¹ and neural network properties⁴² in schizophrenia can be inferred.

Summary of Articles in the Special Section on Vision Science and Schizophrenia

The articles in this series provide representative, but far from exhaustive, examples of work being done in the area of vision science and schizophrenia. For the most part, they focus on intermediate-level vision (eg, PO, object processing) within the dorsal stream (motion processing) and within the ventral stream (processing of high spatial frequency forms) and they make reference to psychophysical, electrophysiological, and imaging data. We wish to acknowledge here the excellent special section on sensory processing in schizophrenia, edited by Dan Javitt, in the 2009 volume of *Schizophrenia Bulletin* (volume 35, issue 6). This series of articles also highlighted disturbances in visual processing in schizophrenia, although it generally focused on earlier processes than those covered in the current section. Taken together with the series in this issue, a broader picture emerges both of how vision can be studied in schizophrenia and of what those methods can reveal.

Silverstein and Keane¹¹ review the literature on PO in schizophrenia from 2005 to present. At the outset, the article describes PO impairment and its relation to symptomatology, illness progression, and treatment outcome. A major conclusion is that PO impairment has both trait and state-like aspects. For example, greater PO impairment may characterize a more severely ill patient subtype, namely those with poor premorbid social functioning and poor prognosis; at the same time, extent of PO dysfunction is correlated with level of disorganized symptoms, and normalization of PO during treatment for an acute psychotic episode correlates with a reduction in disorganized symptoms. The article next reviews imaging data. An important outcome is that the neural mechanisms underlying normal PO are differentially active among persons with schizophrenia. For example, impaired integration of spatially separated contour elements is associated with reduced BOLD response during functional magnetic resonance imaging (fMRI) in traditional visual integration areas (eg, V2, V3, and V4); at the same time, there is increased response (compensatory activity) in higher regions such as the fusiform gyrus. Electroencephalography (EEG) studies also indicate neural signatures of impaired PO, such as reduced amplitude of an event-related potential called “closure negativity” and reduced synchrony of oscillations within the beta and gamma

bands. The article then goes on to describe the cognitive/behavioral consequences of PO impairment. Problems in organizing visual information plausibly contribute to difficulties in selective attention, working memory, face processing, social cognition, scene perception, and action segmentation, with the latter 4 potentially having a role in delusion formation. The article concludes with discussions of the specificity of PO impairment to schizophrenia and the implications of the impairment for processing outside of vision.

The article by Horton and Silverstein⁴³ provides an example of how a task can be designed so that a perceptual “deficit” can produce superior task performance. The authors employed the Ebbinghaus illusion, in which the perceived size of a central shape can be modulated by changing the size of surrounding shapes. This study reveals 2 important findings. First, it replicates past data showing that schizophrenia patients with hearing demonstrate a reduced illusion effect (more accurate size judgments), presumably owing to a reduced ability to represent and integrate visual contextual information. Second, the performance of deaf schizophrenia patients differed significantly from that of hearing patients and was more normal (ie, they demonstrated strong illusion effects). Thus, one or more factors associated with deafness reversed the schizophrenia-related spatial context integration deficit. As the authors discuss, the most likely candidate mechanisms are post-deafness cortical reorganization involving a larger area of the brain being devoted to visual processing and/or an increased sensitivity to peripheral visual cues as a result of many years of using sign language. This article, therefore, highlights the plasticity of PO impairments in schizophrenia.

Green and colleagues have done pioneering work in the area of backward masking in schizophrenia for many years. This work built on earlier psychological studies of backward masking in schizophrenia, has incorporated refinements of masking as a psychophysical technique, and has integrated this technique with EEG and fMRI methods. A review of their work is long overdue and their article in this issue³⁰ provides a concise but comprehensive summary of how studies of visual masking have implicated specific brain regions (eg, magnocellular pathway, lateral occipital complex) in the perceptual abnormality. Recent work from this group has also highlighted failures of reentrant processing, which has implications for nonvisual processes as well, as noted above. Finally, they discuss how the findings from visual masking studies can be viewed in terms of problems in visual tuning. Overall, this article provides important examples of how the well-established methods of vision science can shed light on a range of neural mechanisms involved in schizophrenia.

Chen²⁸ reviews the research progress on visual motion processing in schizophrenia. The processing of visual motion signals is essential not only for the perception of

movement but also for motion-related cognitive and motor functions. In the past decade, a series of seminal studies have been conducted in this important area. These studies have found that abnormal motion processing in schizophrenia ranges from discrimination of basic motion features to integration of spatially distributed motion signals. By synthesizing the findings from basic psychophysical studies, the article first illustrates that 2 types of motion processing deficits—those of speed discrimination and coherent motion detection—exist in this mental disorder. The surveyed neuroimaging studies suggest that the motion perception deficits involve: (1) areas subserving basic motion processing, such as middle temporal visual area (MT) in the extrastriate cortex and (2) regions of the parietal cortex and the inferior convexity of the prefrontal cortex that may be recruited as part of efforts to compensate for the faulty motion-related information generated by MT. The article then focuses on studies of the role of center-surround interaction in motion processing. These studies converge in identifying a schizophrenia-related inhibitory impairment affecting the distributed cortical processing required to integrate visual information across space. This impairment appears to be involved in mediating different levels of abnormal motion processing in schizophrenia. The article also highlights the tentative relationships between deficient motion processing and putative functional consequences involving eye tracking and social perception. Finally, potential applications of motion processing tasks in treatment development studies are noted.

Challenges for the Future

Despite progress in understanding visual processing disturbances in schizophrenia, many challenges remain. One is simply to conduct research with more life-like stimuli to see if the same sort of perceptual disturbances are exhibited in those cases. Over the last 100 years, perceptual research has made many important contributions using extremely simplistic forms such as dots, lines, geometric shapes, and Gabor patches. The usage of these stimuli is entirely understandable because it constrains complex processing problems and allows a relatively direct way to manipulate and observe the mechanisms of interest. Nevertheless, the approach has its limitations.^{44,45} For example, when subjects witness a real 3D object, they may attend to it differently or they may rely more on action-oriented representations, which, in turn, may alter the processes under consideration (eg, grouping, motion perception). Alternatively, a stimulus displayed in all its details may involve unknown or unexpected interactions between different aspects of the visual input that are not present with more simplistic stimuli. In addition, real-world stimuli are more meaningful to patients and may therefore activate affective or semantic information, which are known to affect visual processing.^{40,46,47} Overlooking these sorts of

effects may not be a problem—and indeed may be preferable—for the basic researcher, but if we are to understand how patients differentially view and interact with the world, then it seems worthwhile to develop stimuli that approximate the objects and situations encountered in daily life. As a specific example, PO task stimuli often involve fragmented objects or separated oriented patches of luminance contrast (ie, Gabor patches) and patients are known to be rather poor at integrating these elements over space. But how might patients handle integration in more ecologically valid contexts such as when perceiving partially occluded objects in a crowded scene or in degraded contexts such as in the dark or rain or snow or fog? Similarly, do motion processing deficits lead to problems such as an inability to judge the speed of moving objects (eg, cars) or to a reduced ability to judge the distance between oneself when moving and other objects such as traffic lights or other cars? Do the abnormalities involved in altered backward masking performance reveal themselves as a reduced ability to comprehend briefly displayed visual stimuli that are replaced by others (eg, as encountered when watching television)? Data from laboratory studies and anecdotal reports by our patients (eg, altered sense of motion as a car passenger) suggest that the answer to these questions is “yes,” but for reasons specified above there can be no sure answers until the appropriate studies are conducted. Answering such questions will begin the process of translating basic psychophysical research into real-world understanding and treatment.

It will also be important to study perception during interaction with objects, especially in the context of grasping and reaching. It has been proposed that the visual system consists of 2 basic subsystems reflecting “vision for perception” (the ventral stream) and “vision for action” (the dorsal stream).⁴⁸ The former primarily processes objects in an allocentric fashion that is invariant to minor changes in rotation, size and illumination. The latter, being action oriented, is mostly involved in generating egocentric representations that depend on the distance between the observer and the object. To date, while distinctions between dorsal and ventral stream processing have been made in studies of schizophrenia, these have typically been done within the context of the “what” and “where” systems (which also can be distinguished along the ventral and dorsal streams). To our knowledge, there is only a single published study examining grasping behavior in schizophrenia.⁴⁹ The study found that patients have a normal size contrast illusion (ie, to the same extent as controls) when using their fingers to indicate size without grasping and an increased illusion when reaching toward the stimulus (a condition under which controls normally do not demonstrate illusion effects). These 2 results along with those of Horton and Silverstein⁴³—who found a reduced illusion effect on a task that tapped the “vision for perception” pathway—suggest that the study of visual illusions in schizophrenia patients can reveal highly specific information about the integrity of neurophysiological

mechanisms, including their differential impairment (see also ref. Kantowitz⁵⁰).

The quality of our results will only be as good as are our measurement instruments, and therefore continued task development is critical. This is one issue that, in general, studies of vision in schizophrenia have addressed very well, by continually incorporating advances from vision research. As can be seen even in the small sample of research reviewed in this special section, progress has occurred in the study of PO, backward masking, and motion perception in schizophrenia by incorporating paradigms that more specifically and more efficiently probe the neurobiological and functional mechanisms of interest. This bodes well for use of these measures in genetic studies and in early phase clinical trials, where rapid assessment of a medication's effects on specific neural systems is required. Although each task has its limitations, those imported from basic vision research typically are well validated, have been tested with multiple control conditions, and are known to tap into the functioning of a relatively narrow range of mechanisms. Moreover, the sophisticated curve fitting and staircase techniques that can be used for modeling perceptual data (eg, ref. ^{51,52}) allow for rapid assessment of various aspects of performance ability (and variability). These methods can, for example, utilize Bayesian statistics to simultaneously estimate threshold and slope of a fitted curve while also taking into account "lapsing" errors (eg, errors due to failures of attention⁵³). In short, the field of vision science of schizophrenia is poised to continue to make meaningful contributions to a number of areas of schizophrenia research (eg, cognition, genetics, treatment, etc.).

An additional issue for future work involves treatment of visual disturbances in schizophrenia. Two questions are (1) Can impaired visual processing be improved? and (2) what are the benefits? Regarding the former, people with schizophrenia can in certain instances exhibit approximately normal learning during PO tasks (see ref. Silverstein and Keane⁵⁴ for review); they can also improve on such tasks during treatment. So it seems that perceptual dysfunction can in principle be improved to relatively normal levels. It remains an open question, however, as to which specific pharmacological or psychological methods best promote improvement or what further developments in these methods would look like. Regarding the second question, very little is known about the consequences of improved perceptual performance. Would it, for example, improve the abilities to read, drive, understand nonverbal facial cues, or operate machinery? Would it reduce certain sorts of symptoms? Given the hypothesized links between abnormal perception, altered experience of the self and world, and delusion formation, we at least have an idea of what relevant endpoints might be for treatment studies. Importantly, however, even if the impairments did not seriously affect complex, everyday behaviors, and even if the impairments could not be reduced through treatment, the

topic would still very much be valuable for further investigation. This is because, as described above, identifying visual deficits in schizophrenia can reveal which neural mechanisms are impaired; it can reveal how the impairment of these mechanisms unfolds over time; it can help taxonomize the illness by differentiating patients who are and are not characterized by perceptual dysfunction; and it can reveal more general brain differences in the disorder, among other things.

In conclusion, incorporating vision science methods into schizophrenia research has benefitted the field and holds the promise of significant further benefit. A number of specific visual processing impairments have been identified and demonstrated in the illness. In some cases, these are associated with specific developmental pathways to illness (eg, poor premorbid functioning) as well as with specific symptom clusters. Moreover, the links between these impairments and specific neurobiological and neurophysiological changes are becoming increasingly well understood. This growing body of evidence is leading to a re-vision of how cognitive impairment is seen in the disorder—from being due primarily to frontal lobe impairments to involving other regions as well, including the occipital lobe. Conversely, evidence from studies of vision also reveals that these impairments are not solely due to occipital lobe dysfunction. It is now clear that many (but not all) aspects of visual processing can interact with attention, involve feedback from temporal, parietal, and frontal areas and can be (depending on how the task is designed) affected by memory, expectations, and strategy. Finally, studies of visual processing have accelerated our understanding of cortical processing algorithms that are common to multiple forms of cognition and that are rooted in the general cyto-architectural properties of the cortex. This work has also highlighted the roles of NMDA and GABA receptors in both visual processing and schizophrenia. Based on these considerations, we believe vision science provides a number of reliable, valid, brief, well-tolerated, and state-sensitive measures that can serve as probes of the integrity of widespread computational processes that are operative, albeit in less concrete form than found in vision, outside of the occipital lobe (ie, tools that may be useful to researchers and/or clinicians). In short, applying methods developed within the vision science community to the study of schizophrenia can both clarify the nature of visual processing impairments and assist with the whole brain approach that appears to be necessary to understand more global failures of computation that may underlie the phenomenology and symptomatology of the disorder(s).

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