Visual Perception Deficits Associated with the Magnocellular Pathway in Schizophrenia

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Although much has been written about the role of higher-order cognitive functions, such as memory, attention and executive control, relatively little is known about perceptual abnormalities in schizophrenia. Visual perception has reciprocal functional connections with higher cognitive functions and can affect behavioral outcome. Therefore, understanding mechanisms of visual deficits in schizophrenia will be helpful in elucidating the etiology of the illness, thereby contributing to the development of strategies for further assessments, efficient treatments and social rehabilitation. In this review, we surveyed representative psychophysical, electrophysiological, and neuroimaging studies that define characteristics of visual deficits in schizophrenia and elucidate underlying neural bases. Specifically, abnormalities associated with functions of the dorsal visual stream (e.g., prolonged visual masking effect, reduced EEG amplitude in visual areas, and impaired motion perception and eye movement) were summarized. After describing the visual deficits, we discussed the potential consequences of visual deficits in social outcome. Vision plays a key role in social cognition because precise and rapid processing of visual information is critical for survival and adaptive functioning in society. We examined the role of early visual deficits in social functioning with a particular focus on the processing of ‘socially-relevant’ visual stimuli (i.e. “biological motion”) in schizophrenia. Lastly, we discussed the possible influence of psychotropic medication on perception and the relationship between visual deficits and clinical symptoms. (Korean J Schizophr Res 2011;14:61-75)

Key Words: Perception · Visual pathways · Motion perception · Biological motion · fMRI · Social functioning · Schizophrenia.

Schizophrenia: Cognitive Deficits and Perceptual Deficits

Schizophrenia is a complex and severe mental disorder that affects about 1% of the population, clinically characterized by positive, negative, and disorganized symptoms. It is widely accepted that a combination of genetic and environmental factors lead to the onset of schizophrenia.20

The past two decades have witnessed the increasingly important role of cognitive deficits in schizophrenia, such as attentional problems, impaired working memory, and abnormal executive functioning.61 Indeed, cognitive deficits are better at predicting the prognosis of schizophrenia than clinical symptoms.7-9 Although perceptual processes play a crucial role in cognition, very little is known about how abnormal perception may lead to cognitive deficits. But there is evidence suggesting that impaired perceptual processing may interact with or mediate cognitive deficits,10-12 although degraded perceptual processing is not necessarily associated with cognitive deficits.13

Perceptual abnormalities in schizophrenia have been well documented in the visual system.14-27 Clinically, a considerable portion of schizophrenia patients (up to 60%) report distorted visual experience such as perception of motion, color, size, and facial expression.28-30 Visual deficits include poor performance on visual detection and/or discrimination task, altered visual backward masking (VBM) effect,17,30 decreased contrast sensitivity,18-20,24,25,27 impaired motion perception, and poor discrimination of biological motion.36,37

Since high-quality, accurate input to the sensory cortices would determine subsequent processing by heteromodal association cortices, elucidating the extent of perceptual deficits in schizophrenia is a fundamentally important task.
Visual Deficits in Schizophrenia

There are multiple ways in which perceptual problems impact on schizophrenia. Visual perceptual deficit may contribute to ‘upstream’ cognitive impairment and/or exist by itself.\(^{16,38,39}\) But perceptual deficit is not necessarily associated with clinical symptoms. Although experience of visual distortion by ‘positive’ symptoms is often reported, actual visual deficits is likely to last even after clinical treatment, therefore important for understanding the etiology of schizophrenia.\(^{40,41}\)

One very important way in which perceptual problems may affect outcome in schizophrenia is via social cognition and social dysfunction.\(^{42}\) Indeed, visual stimuli carry rich social information.\(^{36}\) Considered together, deficits in visual perceptual processing could lead to core problems in schizophrenia. Therefore, this review aims to summarize what we know about the visual system in schizophrenia. Specifically, 1) impaired visual perception associated with the functions of the dorsal (transient/magnocellular) and/or the ventral (sustained/parvocellular) visual pathways, 2) implications of visual deficits to other cognitive and social dysfunctions, and 3) possible influence of medication and clinical symptoms on visual deficits.

Deficits in Early Visual Processing in Schizophrenia

Visual system basics

The visual system consists of several different pathways, including the magnocellular (M, or transient) and parvocellular (P, or sustained) pathways. These pathways begin in the retina, via the lateral geniculate nucleus (LGN), and project to different layers of primary visual cortex (V1). Transient and sustained pathways are psychophysically defined concepts and are thought to be the functional equivalent of M and P pathways.\(^{43,44}\) In general, the neurons in the M system are sensitive to low spatial frequencies (e.g. low resolution images), have transient responses and have faster conduction. The P system neurons are selective for high spatial frequencies (e.g. crisp images) and have slow, sustained responses. The subsequent visual pathways from the M and P systems are often referred as the dorsal (“where”) stream (projected toward parietal area) and the ventral (“what”) stream (projected toward temporal area, respectively (Fig. 1). Functions of the dorsal pathway include eye-movement control, motion perception, and action guidance while the main function of the ventral pathway is object recognition. Note that these two pathways are not completely discrete, but as shown in Fig. 1, considerable functional interaction occurs during information processing.

Dysfunction in the transient visual pathways in schizophrenia

A number of past and present studies indicate that impaired visual perception in schizophrenia is mainly associated with dysfunctions of the transient (magnocellular) visual pathways.\(^{14,34,45-47}\) Much of the evidence comes from VBM studies.
The VBM effect refers to the phenomenon in which the visibility of a briefly presented target is reduced by a mask that is presented very shortly after the target (Fig. 2). As the interval between the target and the mask increases (~120 ms in healthy people), the VBM effect becomes weakened and disappears.

According to Breitmeyer and Ganz’s comprehensive model of the neural basis of backward masking, a visual stimulus initiates activity in the transient visual channel first and then activate the sustained channel. Furthermore, the VBM is closely related to the activities of the two visual channels and their interactions. This model also proposes different manifestation patterns of the VBM depending on the “energy” (i.e., duration and intensity) of the mask. When the mask has high energy, masking by “integration” (i.e., fusion of the two images) mediated by sustained visual channel is dominant. ‘Interruption’ by the transient activity of the mask to the sustained activity of the target is also effective but is obscured by integration (Fig. 3A). If the mask has low energy, fusion of visual images does not occur, but the sustained activity of the target is interrupted by a transient activity triggered by the onset of the mask (Fig. 3B), generating a non-monotonic U shaped masking function (in a target identification task).

with schizophrenia exhibit poor performance in VBM tasks compared to healthy controls. In general, schizophrenia patients require longer interval (~300 ms) between the target and the mask for correct identification of the target. Although schizophrenia patients show VBM deficits regardless of energy of the mask, Green and colleague’s studies strongly suggest that the VBM deficit in schizophrenia is mainly due to dysfunction of the transient visual channels. They used both high- and low-energy masks to explore the role of integration (mediated by sustained visual channel) and interruption (by transient channel) mechanisms. In the high-energy masking condition (Fig. 4A), both patients and healthy controls showed approximately monotonic masking functions, but patients’ accuracy over time was significantly lower compared to healthy controls. Furthermore, at 40 ms after the mask onset, the interruption effect (as represented by a dip, see Fig. 4A) was observed. The interruption effect became more prominent when this mechanism was further isolated by a low-energy mask. As seen in Fig. 4B, schizophrenia patients’ negative peak of the U-shaped masking function came up at longer ISI (30 ms~) and stayed at low accuracy while healthy controls showed a rebound in masking function. In a follow-up study, the authors further reduced reliance on sustained visual channels in masking procedures, by 1) blurring the target in the identification task, and 2) by using a location task (Note that the transient visual channels are sensitive to low spatial frequency and location). The finding was, regardless of the tasks, that schizophrenia patients exhibited significantly worse performance compared to control subjects. A limitation of these studies is the fact that the effect from sustained activity was not measured independently. Since the sustained activity always follows transient activity, its complete isolation is almost impossible. Furthermore, regardless of the involvement of the sustained visual channels, schizophrenia patients consistently show VBM deficits, which suggests that the VBM deficits is primarily associated with the dysfunction within the transient visual channel. Subsequent studies by other groups have also provided confirmative evidence supporting the hypothesis of abnormal transient visual activity in schizophrenia by changing the spatial frequency and luminance contrast of the mask.

However, underlying mechanisms for increased VBM in schizophrenia is still controversial. It has been suggested that a “hyperactive” transient activity for mask may interrupt the sustained activity for target therefore increase the masking effect in schizophrenia. However, as described in the next section, physiological evidence contradicts this hypothesis: schizophrenia patients exhibit “hypoactive” transient activities in many cases. “Hyperactive” transient activity hypothesis suggests abnormally strong interruption by greater transient activity (by mask) on sustained activity (by target). Although the VBM studies strongly suggest an abnormality of the transient visual channel, this does not eliminate the possibility of dysfunctional sustained visual channel (Note that the transient and sustained visual channels interact each other, as shown in Fig. 1). If the sustained visual channel is also dysfunctional, sustained activity by the target would be
Fig. 3. A: Integration in visual masking with high-energy mask, represented by transient/sustained channel activities and resulting hypothetical monotonic masking function. Low accuracy means a strong visual masking effect. B: Interruption in visual masking with low-energy mask, represented by transient/sustained channel activities and resulting hypothetical non-monotonic, U-shaped masking function. Y-axis in each plot indicates accuracy in the target identification task (Adapted from Breitmeyer and Ganz, 1976).
vulnerable to the transient activity by the mask, even if the activity is relatively weak hypo-, not strong. Still, this discrepancy between the hypothesis of hyper transient activity and physiological evidence needs to be further examined.

Physiological evidence of abnormal transient channel activity in schizophrenia

Physiological studies using the method of visual evoked potential (VEP) also suggest altered transient channel-related activities in schizophrenia. Physiological studies using the method of visual evoked potential (VEP) also suggest altered transient channel-related activities in schizophrenia.

The reliable finding across these studies is that schizophrenia patients exhibit decreased amplitude of VEP component P1, which peaks at ~100 ms following the onset of visual stimuli, especially under the condition emphasizing the function of the transient visual channel. For example, Butler et al. collected the steady-state visual evoked potentials (ssVEP) from schizophrenia patients under luminance contrast and “number of squares” conditions. By reducing the number of squares or luminance contrast, the transient visual activities could be emphasized, whereas by increasing the number of squares or luminance contrast, the sustained visual channel could be emphasized. As shown in Fig. 5A, schizophrenia patients’ signal-to-noise ratio for VEP was significantly lower (i.e. reduced P1 amplitude) than those of healthy controls in the magnocellular condition while negligible difference was observed in the parvocellular condition.

Another study by Foxe and colleagues examined the VEP component of N1 (peaking negatively at ~160 ms), which is mainly measured over ventral stream structures as well as the component P1. On the object identification task in which the fragmented image becomes less and less fragmented until the subject successfully identify the object, the authors observed a significant reduction in component P1 in schizophrenia patients while N1 amplitude was not different between groups. Furthermore, a reduction of the P1 amplitude was larger over the parieto-occipital scalp site that generally corresponds to the dorsal visual pathways, which receive input mostly from the transient visual channels (Fig. 1).

More recent studies using the functional magnetic resonance imaging (fMRI) technique also provide converging evidence: for example, the hemodynamic response elicited by moving gratings with low, but not high, spatial frequency is reduced in schizophrenia patients, compared with healthy subjects.

Interestingly, findings from VEP and fMRI studies suggest that the dysfunction of the transients visual channels is associated with attenuated ‘gain control’ (a process allowing sensory systems to adapt and optimize responses to stimuli within a particular surrounding context) that may be caused by N-methyl-D-aspartate (NMDA) deficit. NMDA receptors amplify responses to isolated visual stimuli as well as increasing the effect of lateral inhibition, thereby plays a central role in gain control. Thus, blockade of NMDA transmission produces shallow gain and decreased neural amplitude to stimuli, which may provide a possible cause of decreased VEP.
amplitude in schizophrenia.

**Motion perception in schizophrenia**

While the visual stimuli used in the VBM tasks and VEP studies tap the earlier components (e.g. V1) in the visual pathways, the reduced VEP amplitude along the dorsal sites in schizophrenia patients suggest that these individuals would have difficulty processing more complex and dynamic visual stimuli such as motion. In fact, impaired motion perception is another well-documented abnormality in schizophrenia.

Moving visual stimuli consists of various components, including contrast, velocity, orientation and direction. Among these, the core component for motion perception is, needless to say, velocity. Indeed, past studies have revealed that schizophrenia patients are specifically deficient in discriminating velocity signals. For example, Chen et al. tested schizophrenia patients and healthy subjects on three different visual tasks that tap different aspects of visual functions: velocity discrimination between two moving gratings (e.g. Fig. 6A), contrast detection, and orientation discrimination between two static gratings. Only in the velocity discrimination task, schizophrenia patients required significantly higher contrast threshold for successful discrimination of velocities of the two moving gratings. This deficit was not observed when velocity was very slow or fast. However, at slow velocities, one can make use of ‘position’ cue (i.e. a traveling distance of a specific portion of the stimulus), and at fast velocities, ‘contrast’ information is available (i.e. fast motion induces lower contrast). When these position and contrast cues were minimized by randomization, patients exhibited impaired velocity discrimination in all range, confirming that impaired motion perception is exclusively due to the velocity-based components.

Motion perception deficit in schizophrenia is also manifested as specific to motion types. When velocity is fixed and the task is to detect coherent motion (global) or to discriminate motion direction (local), patients exhibit deficient perception of global, but not local motion stimuli. Several studies investigated ability to detect coherent motion in schizophrenia. For example, in a motion detection task using a random-dot-cinematograms (RDC) in which some portion of the dots move coherently while the others are moving randomly, patients generally exhibit lower accuracy and require higher motion signal strength for comparable performance to those of control subjects.

The area MT (V5) at the occipito-temporal junction is the core area for motion processing in the primate brain, and some parts within MT share similarity with V1, focusing on local signals whereas other parts are more involved in processing global motion signals. These anatomical properties...
of MT indicate that neural units at the global stage have large receptive field and integrate dispersed local motion signals. Therefore, impaired motion perception specific to global motion strongly suggests that local-to-global integration process within the dorsal visual pathways, especially including area MT, is abnormal in schizophrenia.

Indeed, neuroimaging and electrophysiological studies implicate altered activation associated with motion perception in area MT and other sensory cortical networks. In a recent fMRI study, schizophrenia patients exhibited decreased activation in MT and increased inferior prefrontal cortex (PFC) activity during the motion tasks (coherent motion detection and speed discrimination), but not during a non-motion (contrast detection) task. This result is intriguing in that schizophrenia patients may recruit alternative neural networks that compensate for deficient motion-related activation by leaning more on cognitive systems. Interestingly, such compensatory activation in PFC area is also observed in other cognitive domain (working memory).)

A recent EEG study also suggests impaired integration process in schizophrenia: During a motion perception task schizophrenia patients showed enhanced early-phase activity while diminished late-phase activity which is likely to be associated with late-stage motion processing (i.e. integration) over parietal areas. Although several psychophysical, neuroimaging and electrophysiological reports strongly suggest dysfunction of motion-related brain networks as a potential neural substrate, its specific mechanisms are yet to be elucidated.

In this sense, a widely known center-surround interaction that mediates visual information processing provides a useful clue for investigating specific neural abnormality in schizophrenia. The center-surround interaction refers to the neural response to a visual stimulus and is not entirely dependent upon its impact on the classical receptive field; if the same stimulus (e.g. motion) hits inside and outside of the receptive field simultaneously, ‘suppression’ occurs due to center-surround antagonism disturbing precise perception. In MT, this phenomenon is more prominent when the stimuli have high-contrast while ‘summation’ (facilitation) occurs with low-contrast stimuli.

One study found a significantly weakened center-surround antagonistic mechanism in schizophrenia using high-contrast moving gratings (Fig. 7). Since the center-surround interactions are associated with the segmentation of moving objects in the background, slow visual pursuit of moving objects, and perception of three-dimensional shape, abnormal center-surround suppression may affect these important perceptual functions in schizophrenia. Indeed, schizophrenia patients do have trouble segmenting moving forms from the background. Another study using a random dot pattern (global motion), however, reported enhanced, not weakened, center-surround suppression in schizophrenia, suggesting that the abnormal center-surround mechanism in schizophrenia may be ‘imbalanced’ rather than simply deficient.

These conflicting reports, however, should be carefully interpreted in the context of psychopharmacological effects and/or clinical symptoms. Interestingly, elderly subjects also show reduced center-surround suppression, thereby outperforming young subjects in motion perception of large high-contrast patterns. Age-related decrease in GABA-mediated inhibition has been associated with perceptual deficits in non-human primates. Therefore, a decreased cortical inhibition by deficient GABAergic system is thought to be responsible for the weakening of inhibitory center-surround interactions, and indeed, abnormal GABAergic system is associated with schizophrenia. In this context, Chen et al.’s results impli-
cate an excessive inhibitory control of motion processing, mediated by abnormally strong GABAergic effect. Since elderly subjects show “enhanced” motion perception of motion due to reduced center-surround suppression, testing them on the center-surround motion stimuli consisting of coherent/random dot patterns as used in Chen et al. \(^{64}\) may be helpful for understanding abnormal mechanisms within the MT area.

Tadin et al. \(^{27}\) reported that the weakened center-surround mechanism was significantly correlated with the negative symptom severity in schizophrenic patients. However, no correlation was observed between enhanced center-surround suppression and clinical symptoms in Chen et al. \(^{64}\) Interestingly, negative symptoms seem to be more frequently correlated with perceptual deficits in schizophrenia. \(^{26}\) It is not clear how perceptual problems are related to negative symptoms. This will be discussed further later in this paper.

**Motion perception and smooth-pursuit eye movement**

Smooth-pursuit eye movement (SPEM) is a slow and continuous eye movement that allows us to track moving objects such as a bird or a fly. It has been reliably reported that schizophrenia patients show deficient SPEM while other subtypes of eye movement such as saccadic eye movement are relatively spared. \(^{62,81-86}\) Several brain regions were implicated to explain impaired SPEM, including MT, the medial superior temporal region (MST), the frontal eye fields (FEF), and more. Since MT and MST are also involved in motion perception, one may ask whether dysfunction of MT and MST would explain both motion perception deficit and impaired SPEM, and whether impaired motion perception and SPEM would be associated with each other. Stuve et al. \(^{13}\) investigated this question by observing correlation between motion perception threshold and smooth-pursuit gain. The results indicate significant negative correlation between gain and motion perception threshold in schizophrenic observers, suggesting impaired ability to match eye and target velocities due to MT dysfunction. Indeed, imaging studies provided supporting evidence that SPEM velocity is correlated with activation strength in MT. \(^{83,86}\)

**Visual Deficits And Social Outcome in Schizophrenia**

Investigation of the relationship between perceptual ability and social functioning in schizophrenia is relatively new but very important in that it can provide clues for the way basic perceptual abilities affect higher-level social cognitive functions and behavioral outcome. Furthermore, it could contribute towards developing behavioral strategies for effective remediation.

**Social consequences of visual perception deficits in schizophrenia**

Perceptual and cognitive abilities interact with social behavior. For example, deficits in vigilance/sustained attention and working memory reliably observed in schizophrenia may result in difficulties in distinguishing relevant social cues from irrelevant ones (e.g., facial expression, body gestures) over an extended period of time (i.e., vigilance, attention), and forgetting of recent information during a conversation (i.e., working memory). Similarly, the influence of visual processing on social cognition is also important when one considers the speed with which social cues are emitted: social cues often appear and disappear abruptly and rapidly. Thus, those with impairments in visual processing may not be able to perceive appropriate social cues. Indeed, there is evidence to suggest that visual deficits are associated with social dysfunction in schizophrenia. For example, visual processing measured by the Span of Apprehension Test (SPAN), and the Continuous Performance Test (CPT) are correlated with emotion recognition performance. \(^{39,87,88}\)

Early visual processing and social functioning

Experimental studies provide some evidence of the relationship between visual processing and social functioning. Sergi and Green \(^{89}\) measured social perception with the Half-Profile of Nonverbal Sensitivity (Half-PONS), which requires subjects to assign situational labels to brief videotaped scenes of facial expressions, gestures, and/or voice intonation, \(^{88}\) and conducted a target identification task in a VBM paradigm with a low-energy mask (i.e., transient visual channel emphasized). Their results indicate that schizophrenia patients with better Half-PONS score were also showed better backward masking performance, supporting the hypothesis that social perception is related to very early aspects of visual processing. Kelemen et al. \(^{91}\) compared the theory-of-mind (ToM) scores, with performance on a global motion perception task and found that the threshold for global motion detection was correlated with the ToM scores in schizophrenia patients.

These studies suggest that rapid capture of briefly presented or moving visual signals, depending more on the dorsal visual pathway is critical for social cognition as mentioned earlier in this section. But how specifically do they interact with each other? According to Premack’s theory, \(^{92}\) motion per-
ception is critical for developing ToM and related social-cognitive abilities in children. Even very young infants are sensitive to moving stimuli and are able to divide them into self-propelled and non self-propelled signals, which suggest the roots of the concepts of causality, intention and so on. In this context, investigation of another unique type of motion that taps both visual system and social cognition (biological motion) could enhance our understanding of the intersection of visual and social domains and its underlying neural mechanisms.

Perception of biological motion in schizophrenia

Biological motion (BM) is defined as motion generated by living things. We are acutely sensitive to biological motion signals. BM perception has its primary role in survival, but is also instrumental for developing social skills (note how much of our time is devoted to interacting with others). Indeed, people can readily recognize drastically simplified human movements portrayed by point-light (PL) animations that depicts familiar human activities with only a couple of markers on the head and joints of the body (Fig. 8). PL animations are particularly advantageous in terms of their lack of explicit representation of body shape, only providing activity information by the kinematic information in the spatiotemporal pattern of the markers. Studies using PL animations demonstrated that perception of BM is rapid, specific to orientation, easily recognized even under masking conditions, size and position invariant, appears to be three-dimensionally processed, and extends to perception of gender and of social signals such as mood and intention.

Therefore, BM perception is a particularly important aspect of visual perception that is socially meaningful. Indeed, infants of 4 to 6 months of age exhibit preference for BM patterns to scrambled motion. It has been suggested that a visual system has a specialized network for effortless and efficient processing of BM signals. Brain lesion case studies and neurophysiological and neuroimaging studies indicating that the posterior portion of the superior temporal sulcus (STSp) (Fig. 9) is crucial for BM processing. STSp shows selectively stronger activations to BM than other areas.

It is well documented that schizophrenia patients show social deficits, including impairments in social perception and social cognition. For example, schizophrenia patients show deficient face perception, emotional processing, ToM, and judging the direction of eye-gaze. Structural and functional imaging studies on social perception/cognition and social functioning have explored brain areas involved in these functions: they include the anterior cingulated cortex, the superior temporal cortex, and the amygdala. Therefore, the STS region is thought to be a relay station between the visual system and the social system: This area receives input from the two (dorsal/ventral) pathways and is reciprocally connected with frontal cortices, implicating possible influence of top-down cognitive functions on visual perception. Furthermore, a structural imaging study reported partial volumetric reduction in the anterior portion of the STS in

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**Fig. 8.** Examples of stimuli used in the biological motion task. Frames on the top show normal biological activity (walking) from quasi-successive point-light animation sequences. Scrambled (non-biological) motion frames (bottom) are the corresponding counterparts of the biological sequences on the top (Adapted from Kim et al., 2005).

**Fig. 9.** Inflated whole-brain images (right hemisphere) showing regions of the middle temporal area (MT, Left) and the posterior region of the superior temporal sulcus (STSp, Right) (Adapted from Kim et al., 2011).
schizophrenia.

All of the findings from psychophysical, neuroimaging, and social function studies point to impaired perception of biological motion in schizophrenia. Indeed, schizophrenia patients have difficulty discriminating BM from non-BM.\(^{36,37}\) In Kim et al.,\(^{36}\) schizophrenia patients were asked to judge whether the given motion in each trial depicts a human motion or not. A series of biological PL animations and phase-scrambled (spatially and temporally) motions that disorganize the global figure but maintain local motion of each dot consisting PL animation (Fig. 8) were presented in random order. Results indicated that schizophrenia patients are significantly less sensitive in distinguishing BM from scrambled motion. Interestingly, schizophrenia patients’ lower sensitivity (d’) could not be attributed to poor recognition of BM, rather, they tended to perceive scrambled motion as BM in higher frequency (i.e. higher false-alarm rate); this finding was confirmed in the subsequent study.\(^{37}\)

Another important finding from Kim et al’s study\(^{36}\) was that the discrimination sensitivity (d’) was significantly correlated with general social functioning measured with the Zigler social-competence scale,\(^{126}\) but not correlated with clinical symptoms. Note that impaired BM perception is not restricted to schizophrenic population: it is impaired in those with poor social functioning, because the high-level visual stimuli such as biological motion may tap in to social cognitive processes and therefore inflate the apparent association between visual perception and functional outcome mediated by social cognition.\(^{127}\) Autistic children and obsessive-compulsive disorder (OCD) patients who have social problems also show poor discrimination and/or detection of BM.\(^{128,129}\) These findings support the role of visual perception in social functioning. Consistent with the poor performance on the biological motion discrimination, Kim et al.\(^{37}\) reported abnormal pattern of the STSp activation in schizophrenia. In healthy subjects, STSp was significantly more activated to BM (specifically, when the subjects correctly perceived BM as ‘biological’ or ‘hits’) than to scrambled motion (correct perception of scrambled motion as ‘scrambled’ or ‘correct rejections’). Interestingly, STSp was also strongly activated when subject misperceived scrambled motion as biological (i.e. “false alarms”), suggesting the role of top-down influence. On the other hand, STSp in schizophrenia patients did not show differential activation according to stimulus-response categories; overall STSp activation was as strong as that of healthy subjects, thus, activation to scrambled motion was greater than healthy group. These results indicate that there is a higher incidence of false alarms in behavioral performance and suggest that schizophrenia patients tend to “see” living things in randomness, correlated with increased activity in the STSp. These findings imply that schizophrenia patients tend to see meaning where there is none,\(^{130}\) perhaps because they adapt a more lenient criterion for distinguishing perception and imagination owing to abnormal up-regulation of dopamine.\(^{113}\) In the case of BM perception, these self-generated, false impressions of meaning (i.e. higher false alarm rate and strong STSp activation to non-BM) may have negative social consequences, in that schizophrenia patients may misconstrue the actions or intentions of other people.

Lastly, an interesting, but not very surprising, point is that the magnitude of the correlation between perception and social functioning appears to be systematically dependent on the level of visual processing.\(^{127}\) For example, Kim et al.\(^{36}\) observed a strong correlation (r=0.71) between social functioning and biological motion perception. But Butler et al.\(^{34}\) focused on the transient and sustained visual channels and found a moderate correlation (r=0.37 to r=0.50). Lastly, Sergi et al.\(^{130}\) reported lower correlation (r=0.03 to r=0.33) between social function and visual forward/backward masking performance that mainly taps V1. Precise mechanism how visual information (related with social functioning) is accumulated along the visual pathways is not clear yet, but the findings so far suggest a systematic relationship.

Clinical Symptoms and Medication Effects

Medication effect on deficits in visual perception

Patients are usually medicated in most studies of schizophrenia (and many other mental disorders). The potential effects of antipsychotic medication on visual perception, particularly if these drugs affect the GABAergic and NMDA systems,\(^ {59,360}\) cannot be ignored. Reporting correlation between performance on tasks and daily dose of drugs is the most common way to address the possibility of medication effect. General observation of these correlations indicates that there is no specific or known pattern of interaction between medication and perception. For instance, VBM deficits were still observed in schizophrenia patients who were unmedicated or in remission.\(^ {133}\) Likewise, unmedicated, healthy first-degree relatives of schizophrenic patients often exhibit VBM deficits, however, some researchers have reported that performance depends on the type of antipsychotic drugs (i.e. typical and atypical medications).\(^ {134,135}\) As shown in Table 1, medication effect appears negligible in most cases, but still unpredictable exceptions have been observed. Finding medication-free pa-
Table 1. Medication effect and correlation with symptom severity

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Task</th>
<th>Correlation with Symptoms</th>
<th>Correlation with Medication (typical, and/or atypical)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green et al.</td>
<td>1994</td>
<td>VBM</td>
<td>Negative Symptom</td>
<td>Trend, not significant</td>
</tr>
<tr>
<td>O'Donnell et al.</td>
<td>1996</td>
<td>SF</td>
<td>No correlation</td>
<td></td>
</tr>
<tr>
<td>Cadenhead et al.</td>
<td>1998</td>
<td>VBM</td>
<td>No correlation</td>
<td></td>
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<tr>
<td>Thaker et al.</td>
<td>1999</td>
<td>SPEM</td>
<td>No correlation</td>
<td></td>
</tr>
<tr>
<td>Slaghuis and Curran</td>
<td>1999</td>
<td>SF masking</td>
<td>Negative symptom</td>
<td></td>
</tr>
<tr>
<td>Keri et al.</td>
<td>2000</td>
<td>VBM</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Butler et al.</td>
<td>2001</td>
<td>VEP</td>
<td>Unpredictable</td>
<td></td>
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<td>2002</td>
<td>VBM</td>
<td>Negative, Positive</td>
<td>No correlation</td>
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<tr>
<td>Keri et al.</td>
<td>2002</td>
<td>CS</td>
<td>No correlation</td>
<td>Negative correlation</td>
</tr>
<tr>
<td>Li et al.</td>
<td>2002</td>
<td>Motion</td>
<td>Overall symptom</td>
<td>No correlation</td>
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<td>Schechter et al.</td>
<td>2003</td>
<td>VBM</td>
<td>Negative symptom</td>
<td>No correlation</td>
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<td>2003</td>
<td>Motion CS</td>
<td>Negative symptom</td>
<td></td>
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<td>Chen et al.</td>
<td>2003</td>
<td>Motion</td>
<td>Overall symptom</td>
<td>No correlation</td>
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<tr>
<td>Slaghuis</td>
<td>2004</td>
<td>VBM</td>
<td>Negative symptom</td>
<td></td>
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<td>Malaspina et al.</td>
<td>2004</td>
<td>FGP</td>
<td>Negative symptom</td>
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<tr>
<td>Chen et al.</td>
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<td>CS, Velocity</td>
<td>No correlation</td>
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<td>VEP</td>
<td>No correlation</td>
<td>No correlation</td>
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<td>SPEM, Motion CS</td>
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<td>Tadin et al.</td>
<td>2006</td>
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<tr>
<td>Chen et al.</td>
<td>2008</td>
<td>Motion</td>
<td>No correlation</td>
<td>No correlation</td>
</tr>
<tr>
<td>Martinez et al.</td>
<td>2008</td>
<td>SF (fMRI)</td>
<td>Not mentioned</td>
<td>No correlation</td>
</tr>
<tr>
<td>Brittain et al.</td>
<td>2010</td>
<td>VFM, Motion, Form</td>
<td>Positive symptom</td>
<td>No correlation</td>
</tr>
<tr>
<td>Laprévote et al.</td>
<td>2010</td>
<td>Face decoding</td>
<td>No correlation</td>
<td>No correlation</td>
</tr>
</tbody>
</table>

VBM: Visual Backward Masking, VFM: Visual Forward Masking, CS: Contrast Sensitivity, SPEM: Smooth Pursuit Eye Movement, VEP: Visual evoked potential, SF: spatial frequency, FGP: Figure-Ground Perception

The relationship between perceptual deficits and positive symptoms is little known, even though positive symptoms include “perceptual” aspects, such as hallucinations. But nevertheless, correlations between positive symptoms and visual function have been rarely observed. This does not mean that impaired visual perception is unrelated to positive symptoms at all. One possibility is that schizophrenic participants tend to be chronic in a majority of these studies and are medicated to reduce delusions and hallucinations. However, there are studies suggesting indirect influence of hallucinations on visual perception. For example, schizophrenia patients with severe hallucination tend to attribute events to external sources based on processes of mental imagery, and top-down information processing. Higher rate of misperceiving non-biological motion as biological motion in schizophrenia is another good example. Whatever the underlying mechanism is, visual deficits exist in schizophrenia patients with its underlying neural bases, interacting with clinical symptoms but not simply modulated by them.
Visual perception has been extensively investigated in healthy population. However, vision research has not been the focus of intense activity in schizophrenia and other psychiatric disorders such as autism and obsessive-compulsive disorder, compared with the interest in cognitive deficits. As reviewed in this paper, deficits in visual processing play a very important role in schizophrenia, and these impairments are even more significant in terms of interaction with higher-order cognition and social functioning which eventually affects the functional outcome. Investigation of visual deficit in schizophrenia also has methodological advantages: 1) visual system is well understood through numerous behavioral and brain imaging studies in healthy population, 2) Structure and function of each brain area in the visual system are clear and specified well, and 3) recent development of brain imaging and computational techniques allows us to understand functional connectivity between the early perceptual brain areas and frontoparietal regions involved in higher cognitive functions. All of these can be easily applied for understanding the perceptual experience and underlying neural mechanisms in schizophrenia, which eventually contribute to developing additional diagnostic tools and strategies for treatment and rehabilitation.

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