# Visual Perception and Its Impairment in Schizophrenia

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Much work in the cognitive neuroscience of schizophrenia has focused on attention, memory, and executive functioning. To date, less work has focused on perceptual processing. However, perceptual functions are frequently disrupted in schizophrenia, and thus this domain has been included in the CNTRICS (Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia) project. In this article, we describe the basic science presentation and the breakout group discussion on the topic of perception from the first CNTRICS meeting, held in Bethesda, Maryland on February 26 and 27, 2007. The importance of perceptual dysfunction in schizophrenia, the nature of perceptual abnormalities in this disorder, and the critical need to develop perceptual tests appropriate for future clinical trials were discussed. Although deficits are also seen in auditory, olfactory, and somatosensory processing in schizophrenia, the first CNTRICS meeting focused on visual processing deficits. Key concepts of gain control and integration in visual perception were introduced. Definitions and examples of these concepts are provided in this article. Use of visual gain control and integration fit a number of the criteria suggested by the CNTRICS committee, provide fundamental constructs for understanding the visual system in schizophrenia, and are inclusive of both lower-level and higher-level perceptual deficits.

**Key Words:** Contrast, form, gain control, magnocellular, motion, visual integration

Much work in the cognitive neuroscience of schizophrenia has focused on attention, memory, and executive functioning. Less work has focused on perceptual processing. Indeed, during the National Institute of Mental Health MATRICS (Measurement and Treatment Research to Improve Cognition in Schizophrenia) consensus process, perception was not identified as one of the core cognitive domains relevant to schizophrenia or its treatment (1). This omission is in one sense appropriate, because a goal of MATRICS was to identify existing neuropsychological tests that are useful for clinical trials of schizophrenia, and tests of perception are not widely used by neuropsychologists. In contrast, as we demonstrate in the following text, the omission of assessment of perceptual function from the MATRICS battery means that a set of functions that are frequently disrupted in schizophrenia are not being routinely assessed in clinical trials. This situation is likely to be remedied through the CNTRICS (Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia) project. In the following sections, we describe the outcome of presentations and breakout groups on the topic of perception from the first CNTRICS meeting. These recognize the importance of perceptual dysfunction in schizophrenia, the nature of perceptual abnormalities associated with this disorder, and the critical need to develop perceptual tests for future clinical trials. Although there are also auditory, olfactory, and somatosensory deficits in schizophrenia, the CNTRICS meeting focused on visual processing. A great deal of work has been done on visual processing in schizophrenia, and the visual system is well-characterized from a physiological point of view in normal subjects and is a useful system for evaluating basic concepts of perceptual dysfunction in schizophrenia.

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## Basic Science of Perceptual Processing

### Visual System Basics

Our current view of the architecture of the early visual system and cortical processing streams is given in Figure 1. The visual system consists of several different pathways, including the magnocellular (M) and parvocellular (P) pathways beginning in the retina and projecting, via the lateral geniculate nucleus (LGN) of the thalamus, to different layers of primary visual cortex (V1).

The M system is driven by neurons in the LGN with large cell bodies and, in general, conducts low-resolution visual information rapidly to cortex and is involved in initial attentional capture (typically by stimulus onset/offset and/or movement) and processing of overall stimulus organization (2–5). The P system originates with LGN neurons with smaller cell bodies and, in contrast, conducts high-resolution visual information to cortex and is involved in processing of fine-grained stimulus details and object identification (2,6). Specific properties of the M and P pathways give rise to these functions. For instance, the M pathway has low spatial resolution, detects low contrast and motion, is color-blind, and has a fast response (7,8). The P pathway has high spatial resolution, does not respond to low contrast, is color tuned, and has a slow response[1].

The M and P pathways project mainly to the dorsal ("where," parieto-occipital) and ventral ("what," tempero-occipital) streams, respectively, although there is significant interaction between these streams. Functions of the dorsal stream include eye movement control, action guidance, initial attention modulation, motion perception, and visual/somatosensory integration. In the parietal/occipital region, the dorsal stream incorporates areas V3 and middle temporal/medial superior temporal area (MT/MST). As information moves up the hierarchy, more complex processing is achieved. For instance, while V1 is involved with measuring local motion (of small objects), as signals move to higher cortical areas, processing of greater areas of visual space become possible such that V3 is involved in global motion (of larger, more complex objects), and MT/MST mediate global

[1]There is also evidence (reviewed in Hendry and Reid [86]) for a third class of "koniocellular" neurons in LGN with very small cell bodies. These cells are thought to drive a third visual pathway that remains poorly understood but is thought to be involved in integration of somatosensory-proprioceptive information.

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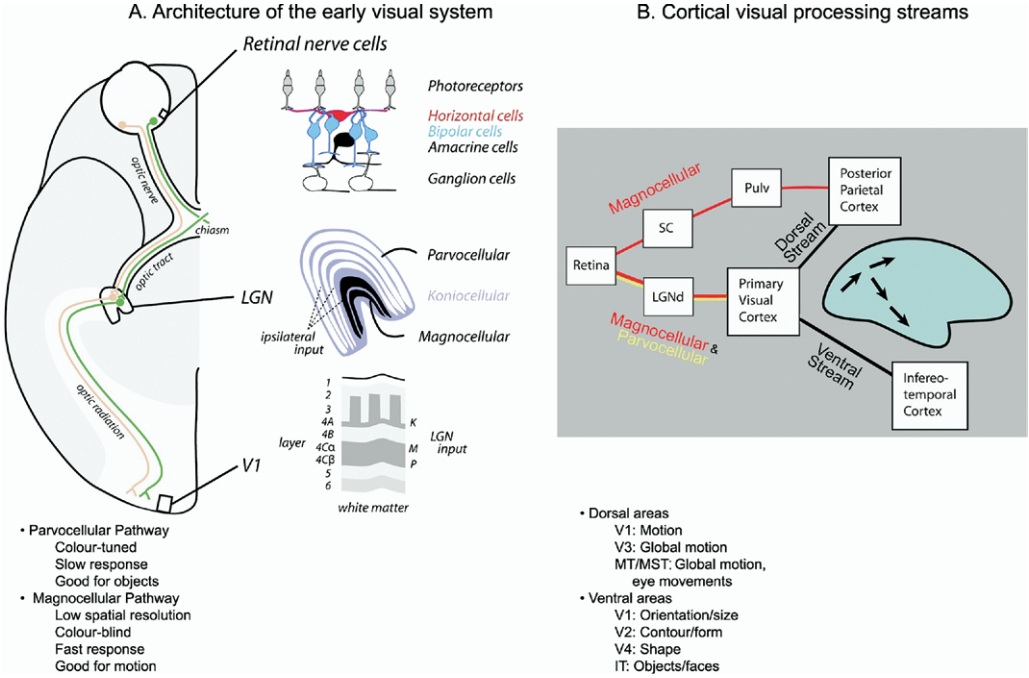


**Figure 1. (A)** Architecture of the early visual system [left part adapted by permission from Macmillan Publishers Ltd: *Nat Rev Neurosci* 8:276–286, copyright 2007 (87); **(B)** Visual cortical processing streams. LGN, lateral geniculate nucleus; Pulv, pulvinar; SC, superior colliculus.

motion and eye movements. The function of the ventral stream is object recognition. It is also modulated by attention due to inputs from frontal cortex and dorsal stream. Again, as information moves up the hierarchy, more complex processing is achieved. The ventral stream processes orientation and size (V1), contour and form (V2), then shape (V4), and finally objects and faces (IT) (9,10).

A central concept in understanding how neurons respond to visual information is that, when stimuli fall in a region of space known as the receptive field, they induce neurons to fire. For example, ganglion cells in the retina do not respond well to uniform fields of light but do respond to spots of light (11). Some neurons in the LGN respond to larger spots of light (i.e., have larger receptive fields), and others respond to smaller spots of light (i.e., have smaller receptive fields). Light around the spot, such as occurs when a uniform field of light is presented, will inhibit neurons from firing. This confers on the neuron the ability to signal change in luminance. The size and complexity of receptive fields increases as one progresses through the visual hierarchy: in the retina/LGN receptive fields respond preferentially to spots of light, in V1 they are tuned for orientation (preferring lines or bars) (12), and in area V2 they respond preferentially to corners or junctions (13), whereas in V4 they prefer more complex feature arrangements (14).

## Functional Concepts: Definitions of Gain Control and Integration

Visual processing involves several types of neural interactions, including lateral excitatory facilitation, inhibition, and top-down feedback. We divide these interactions into two classes, on the basis of their effects: the first is concerned with optimization of response levels (gain control), and the second is concerned with grouping of neural responses through enhanced neural co-activation (integration).

**Gain Control.** Gain control refers to processes that allow sensory systems to adapt and optimize their responses to stimuli within a particular surrounding context. Gain control is primarily concerned with controlling the dynamic range of neural response and can in that sense be considered a lower-level class of process than other modulatory processes (such as integration), even though it is likely that it operates at all levels of the visual system. Gain control mechanisms might reflect both intrinsic neuronal properties and lateral interactions between neurons. These processes permit sensory subsystems to modulate their response levels to take into account spatial and temporal context. Gain control processes also assist sensory subsystems in optimizing overall response levels within a limited dynamic signaling range and in increasing contrast between adjacent and successive stimuli. These interactions amplify or attenuate the signal and thus affect integrity of sensory registration.

Gain control in the visual system has been largely studied in early stages of processing such as at the level of the LGN or primary visual cortex. There are a number of ways in which neurons can be influenced by their neighbors in order to control the signaling range and/or indicate salience. These include intracellular mechanisms, direct excitatory and inhibitory connections between neurons, and feedback.

One example in which gain control likely plays a role is in the signaling of salience within a "pop-out" phenomenon (Figure 2). Let us suppose we are interested in signaling the presence of the orientation discrepancy in the lower right corner of the texture. We further suppose the visual system achieves this by pooling responses across a population of orientation-tuned neurons in V1. The top row shows the "raw" neural response where gain control is not operating; the pooled response is uniform—all neurons are responding equally. In the bottom row, divisive gain control is operating. Now the large number of neighboring neurons that receive the same horizontal stimulation inhibit each other and decrease signaling, allowing the response arising from the small diagonally textured patch to "pop out."

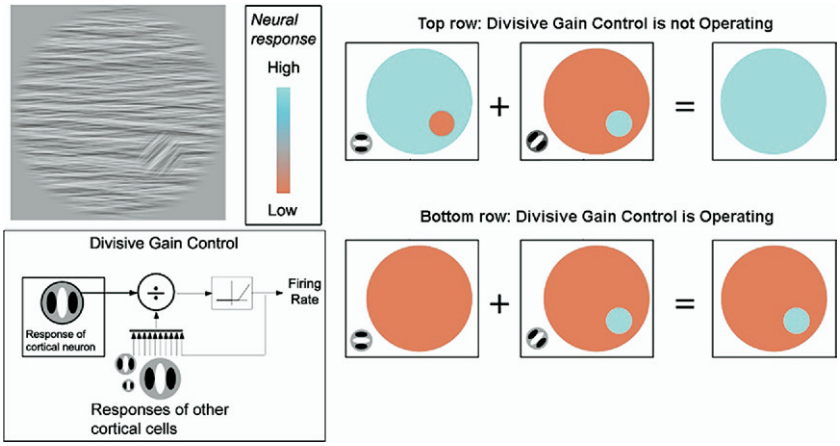


**Figure 2.** Gain control can contribute to orientation "pop-out." In this example, the top row of the right side of the figure shows the "raw" neural response where gain control is not operating. In the bottom row, divisive gain control is operating and the large number of neighboring neurons that receive the same horizontal stimulus inhibit each other and decrease signaling, allowing the response from the small diagonally textured patch to "pop out." Under this view the visual system operates as a cascaded gain-control/integration system, deriving increasingly complex types of salience.

Another example of gain control involves the M pathway where neurons show a steeply rising increase in response to low-contrast stimuli, which reaches a saturation-level once luminance contrast reaches approximately 16% (7). This leads to a characteristic S-shaped, nonlinear contrast gain control curve (Figure 3A). The initial steeply rising part of the curve reflects substantial amplification of low-contrast stimuli, permitting M-pathway neurons to respond robustly even at low contrasts. The nonlinear gain control mechanisms, however, result in saturating responses at higher contrasts. Neurons in the P-pathway exhibit less gain control than M-pathway neurons. Thus, they are less responsive at lower contrasts, but their responses do not saturate at higher contrasts. In construction of future tasks to study gain control, including behavioral tasks, it is important to include both low- and high-contrast stimuli to demonstrate how perceptual responses change in patients when stimulus contrast changes from low to high levels.

Visual pathways within the brain use glutamate as their primary neurotransmitter, and N-methyl d-aspartate (NMDA) seems to have a central role in gain control. For instance, NMDA receptors amplify responses to isolated stimuli as well as amplifying the effects of lateral inhibition (e.g., increase surround antagonism of center receptive field responses) (15). Thus, an NMDA deficit would result in decreased amplification and less lateral inhibition. Indeed, NMDA antagonists produce shallower gain at low contrast and a much lower plateau indicating decreased signal amplification (16,17) (Figure 3A).

**Integration.** Integration refers to processing one step beyond the registration of brightness, color, orientation, motion, and depth cues. Integration is the process linking the output of neurons that individually code local (often small) attributes of a scene into global (typically larger) complex structure, more suitable for the guidance of behavior. Recurrent innervation of primary cortex by higher levels leads to recurrent interaction between regions that can further increase the salience of grouped stimuli. Integration underpins Gestalt grouping phenomena and object recognition. Cells in later visual areas code more global/complex properties by integrating the response of neurons with smaller receptive fields that code, for example, (local) form and motion. Mechanisms of integration include direct connectivity between neurons (e.g., excitation/inhibition and synchronization) as well as feedback (18). In V1, there are contextual influences on local processing, and at higher levels, possibly as early as V2, integration occurs in terms of global grouping of contextual structure (e.g., contours) (Figure 4).

**Implications.** Gain control and integration are both involved in the perception of complex stimuli. Sensory systems use gain control to adapt and optimize responses so that they can then be successfully integrated at higher levels of the visual system via recurrent interactions between areas.

## Gain Control in Schizophrenia

Gain control plays an important role in our perception of contrast and motion in that it allows sensory subsystems to maximize the response-difference arising from different stimuli. Several methods have been used for assessing contrast detection in schizophrenia. First, patients with schizophrenia show decreased contrast sensitivity (i.e., need more contrast to detect a grating) across a range of grating-sizes in behavioral studies (19,20). Second, patients show reduced amplitude responses to simple visual stimuli with steady-state or transient electrophysiological techniques (21,22), indicating deficits in contrast gain control within the early visual system.

Stimulus response properties of M- and P-neurons overlap significantly, making differentiation difficult, particularly in be-

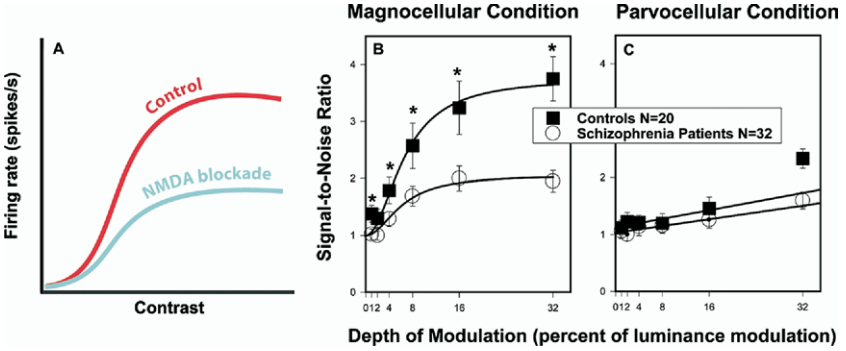


**Figure 3.** Contrast response functions and N-methyl d-aspartate (NMDA) effects (**[A]**. Adapted from Kwon *et al.* [16], used with permission; **[B and C]** adapted from Butler *et al. Arch Gen Psychiatry*, May 2005, 62, 495–504, copyright © 2005, American Medical Association, all rights reserved [22]). The NMDA antagonists produce shallower gain at low contrast and a much lower plateau in visual evoked potential responses indicating decreased signal amplification. The patient visual evoked potential contrast response curve in the magnocellular condition shows similar decreased gain at low luminance contrast and a lower plateau, indicating decreased signal amplification.

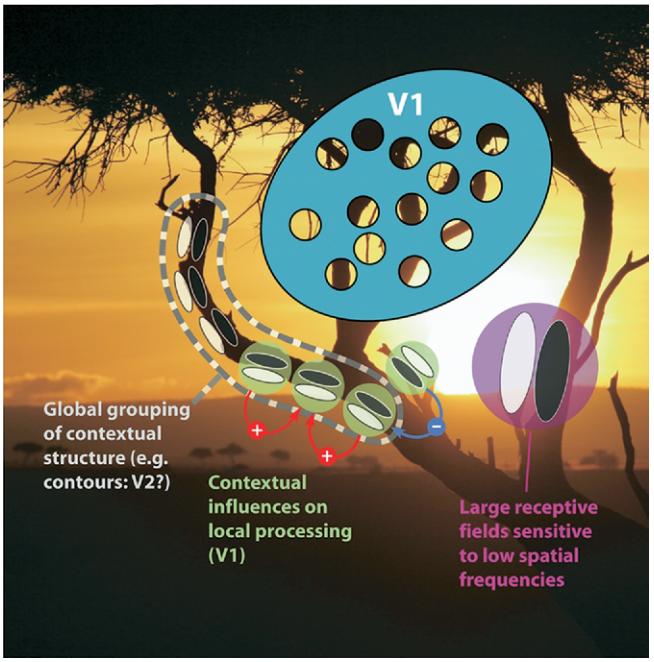


**Figure 4.** Contextual effects on orientation (reprinted from *Neuron*, 48, Dakin S and Frith U, Vagaries of visual perception in autism, 497–507, copyright 2005, with permission from Elsevier [88]). Oriented structure within our complex visual environment leads to various types of interactions between detectors in V1 (blue region), including integration ("+" connections) and gain control ("−" connections).

havioral studies. Nevertheless, features that bias stimuli toward the M-pathway include high temporal frequency, low spatial frequency, low absolute luminance, and low contrast. Although behavioral studies have found contrast sensitivity deficits across spatial frequencies, often thresholds are relatively low (e.g., < 10% contrast; [20]), limiting P-pathway involvement. In one study in which thresholds were higher (e.g., > 16% contrast), relative preservation at high spatial frequencies was observed (22). Similarly, larger contrast sensitivity deficits were found when stimuli were presented dynamically rather than statically, also suggesting greater M-pathway, than P-pathway, impairment (19).

In steady-state evoked potential studies, stimuli have been biased toward M- versus P-pathways with different standing levels of luminance contrast ("pedestals"). Under such conditions, differential M- versus P-pathway biased responses have been observed (22) (Figure 3B and 3C). To the extent that P-pathway dysfunction occurs, patient curves show decreased gain at low luminance contrast and a lower plateau, indicating decreased signal amplification, as in the M-pathway. The decreased slope at low contrast and decreased plateau in patients closely resembles results seen after microinfusion of an NDMA antagonist into cat LGN and visual cortex (16,17) (Figure 3A and 3B), consistent with glutamatergic theories of schizophrenia (23–25).

A third approach uses an illusion in which the contrast of a small textured disk appears reduced when presented within a high-contrast surround compared with when it is presented in isolation (26) (Figure 5). Note that stimuli used in this study were presented greatly above their contrast detection threshold. Patients with schizophrenia were much less susceptible to the illusion, with 12 of 15 patients being more accurate (less biased) than the most accurate control (27). These results are consistent with decreased center-surround antagonism and hence decreased contrast gain control in schizophrenia patients. Gain control in this illusion might be due to short-range lateral interactions (e.g., γ-aminobutyric acid [GABA]-ergic projections).

A large number of studies have reported motion processing deficits in schizophrenia (28–32). Motion is signaled by direction-sensitive cells in V1 and then pooled by MT neurons with: 1) larger receptive fields, and 2) center-surround antagonism (as a likely substrate for gain control). A recent study (33) provides evidence for decreased gain control in schizophrenia in a motion discrimination task. Whereas center-surround antagonism in control subjects resulted in reduced ability to perceive motion of a high-contrast stimulus as its size increased, patients with schizophrenia did not show this reduction in motion perception. Importantly, like Dakin *et al.* (27), these authors find that a disruptive context has less influence on patients than on controls, arguing against nonspecific deficits or lack of attention as an underlying cause of differences. Increased center-surround antagonism, indicative of increased gain control, has also been found in motion studies in schizophrenia (34).

Significant correlations between impaired motion perception and M-pathway dysfunction also point to motion processing deficits in schizophrenia resulting from impaired gain control (28). Patients with schizophrenia show preferential M-pathway dysfunction (21,22,28,35–38), although deficits have also been observed in parvocellular processing (19,20). The M-pathway has several properties (speed of processing, low spatial resolution) that make it a suitable physiological substrate for gain control (39). The P-pathway also exhibits nonlinear gain characteristics, although less so than the M-pathway. Mechanisms of

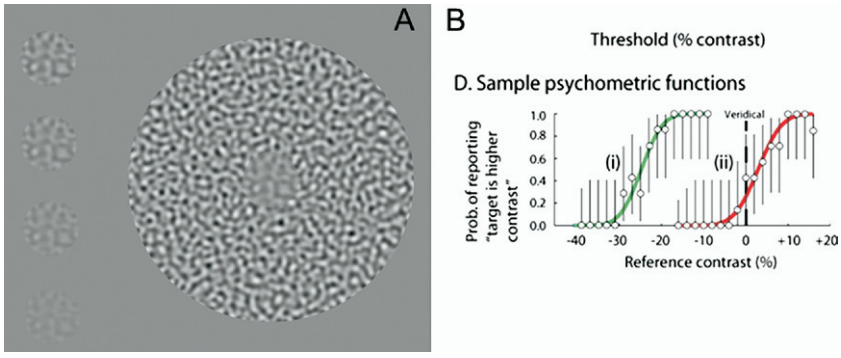


**Figure 5.** The "contrast-contrast" illusion reveals contrast gain control deficits in schizophrenia (reprinted from *Curr Biol*, 15, Dakin S, Carlin P, Hemsley D, Weak suppression of visual context in chronic schizophrenia, R822–824, copyright 2005, with permission from Elsevier [27]). **(A)** The small region at the center of the large circular patch is physically identical to the small patch at the top left but generally seems to be of much lower contrast as a consequence of contrast gain control. **(B)** One can quantify this effect by plotting the probability that subjects said the central patch was higher contrast than a matching variable contrast reference patch. A typical control subject (green line) indicated that the central patch had a substantially lower contrast than it actually did (indicated by the shift in the green curve to lower reference contrasts). Data from a representative patient with schizophrenia (red line) indicated that they were not susceptible to the illusion and matched the contrast largely correctly.

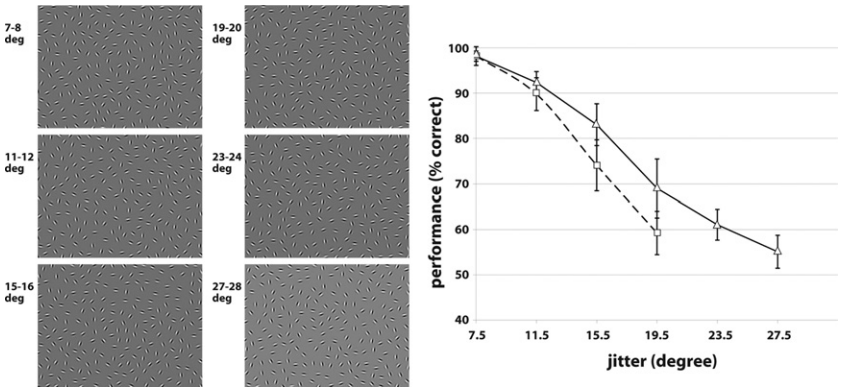


**Figure 6.** Performance of the schizophrenia group (dashed line) and healthy control group (solid line) across six conditions of contour element jitter manipulation. The subject's task was to indicate, with a two-button response device, on each trial, whether the narrow part of the egg-shaped contour is pointing to the left or the right. With increasing element jitter (± the number of degrees noted on the x axis), the correlations between adjacent contour elements decrease, and perception of the contour amidst dense background noise becomes more difficult. The left-hand side shows the increasing element jitter of the adjacent contours amidst the background noise. Schizophrenia patients were not able to perform at above chance levels in the two most difficult conditions (reprinted from *Computers in Human Behavior*, 22, Kozma-Wiebe P, *et al.*, Development of a world-wide web based contour integration test, 971–980, 2006, with permission from Elsevier [65]).

gain control dysfunction include NMDA and GABA-ergic dysfunction. Indeed, NMDA dysfunction seems to be linked to gain control in the M-pathway. Other neurotransmitters (e.g., 40), which are also implicated in schizophrenia, also modulate visual processing. For example, dopamine deficiency has been linked to impaired perceptual and electrophysiological response to contrast signals including those presented in a center surround paradigm (41,42). A recent neurophysiological study suggests that nicotine increases gain control in the visual cortex (43). This might be important in understanding "self-medication" with smoking and strengthens the hypothesis of weak gain control in schizophrenia. It is a challenge to understand and reconcile the involvement of different types of neurotransmitters in visual perception. It is also unclear whether perceptual deficits exhibited by people with schizophrenia for the processing of transient (moving/flickering) stimuli arise from intrinsic dorsal stream dysfunction or from aberrant M-pathway input (21,44).

In summary, gain control studies in schizophrenia clearly show that patients have difficulty modulating neuronal responses to take advantage of the surrounding context. There is also evidence that gain control deficits, seen in contrast detection and M-pathway deficits, are important in predicting outcome (22,45), and are related to higher-level problems in perceptual organization (28,46) and to symptomatology (20,47–51).

## Integration in Schizophrenia

Visual integration deficits are seen in contrast, contour, form, and motion processing in schizophrenia. For example, in the last 10 years the connectivity supporting the integration of orientation across space (into extended visual contours) has been studied psychophysically with so-called "flank facilitation" paradigms (52). Here one measures the detectability of a low-contrast oriented target in the presence of two similar higher-contrast flanking patches arranged so the triplet forms an elongated contour. With some target-flank separations control subjects find it easier to detect the central element when the flanks are present than when they are absent (facilitation). Patients with schizophrenia do not exhibit such a difference, suggesting a failure in ability to integrate the collinear flankers (53). This would seem to implicate weaker interactions between orientation detectors possibly mediated by abnormal long-range horizontal connectivity in V1.

There are numerous examples of poor form processing in schizophrenia that would seem to directly implicate integration deficits. These include deficits in object recognition, grouping, perceptual closure, face processing, and reading (54–62). Classic studies show that there is less influence of global on local processing (54,58). Indeed, patients perform better than control subjects under conditions when global integration would normally interfere with responses to individual elements (54,56,58). A number of studies have used a psychophysically rigorous contour integration paradigm (63). This task examines the ability to perceive a contour made up of separate elements within a background of noise elements. Both the contour segments, and background noise elements are small oriented Gabor elements, which are designed to be well-matched to the spatial frequency processing characteristics of orientation-selective simple cells in primary visual cortex (V1); therefore they are ideal for the examination of these features and their integration. Embedded contours constructed from such elements cannot be detected by purely local feature detectors or by the known types of orientation-tuned neurons with large receptive fields (e.g., 64); their detection requires the integration of local orientation measurements (Figure 6). Deficits in contour integration have been extensively documented in schizophrenia (57,65–67). This is thought to result from decreased NMDA-modulated lateral excitation among the spatial filters signaling these elements and the consequent reduction in synchronization of this neural activity ([68]; see also for reviews [69,70]). Simpler Gestalt tasks, involving perception of basic shapes with nonfragmented contours, are not affected in schizophrenia, however (71).

Interactions between dorsal and ventral streams and frontal cortex provide one model for how form integration deficits might arise in schizophrenia. Processing is substantially faster via the dorsal stream, which would permit it to prime ventral stream areas (72–74). A fundamental role of the M system/dorsal stream might be to produce a low-resolution template of the visual scene that influences perceptual processes, such as categorization of natural images, object recognition, and perceptual grouping in the ventral occipito-temporal cortex, by allowing P pathway fine-detailed input to be used more effectively (3,75–80). With a perceptual closure paradigm Doniger *et al.* (59) found that patients had impaired ability to recognize fragmented pictures. Patients also had decreased amplitude of the dorsal stream-generated P100-evoked potential component, which occurred earlier in time than impairment in the ventral stream-generated closure negativity ($N_{cl}$) component associated with object recognition. Initial P input to the ventral stream was normal as indicated by an intact N1 component. Thus, the impaired behavioral closure and decreased $N_{cl}$ seem to be due to lack of interactions between dorsal and ventral stream areas leading to decreased priming of ventral stream. This provides an

example of integration deficits due to lack of recurrent interactions in schizophrenia.

As discussed in the preceding text, numerous studies have shown motion processing deficits in schizophrenia (28,30–32,81). Whereas gain control is involved in motion deficits (e.g., 33), processing of motion also clearly involves integration, because motion is signaled by direction-sensitive cells in V1 whose responses are then pooled by MT neurons with larger receptive fields to signal complex motion.

In summary, there are numerous examples of integration deficits in schizophrenia. Impairments in visual integration have been linked to increases in disorganized symptoms (57,66,67), poorer premorbid social functioning (82), presence of childhood trauma in schizophrenia (83), and illness severity and chronicity (84).

## How the Constructs Fit the Criteria

### Gain Control

First, this construct is readily measured in humans with such tasks as contrast sensitivity, contrast illusions, visual evoked potential contrast paradigms activating the M pathway, and pop-out stimuli. Second, there is strong evidence of impairment in schizophrenia. Third, there is relatively strong clarity of the link to neural circuitry. In vision, gain control is generally related to mechanisms in the LGN and visual cortex, and deficits have been found in these areas in diffusion tensor imaging, functional magnetic resonance imaging, and post-mortem anatomical studies. Fourth, there is a moderate amount of clarity of the understanding of the mechanisms. Use of the construct of gain control with the concomitant emphasis on short-term lateral interactions, center-surround mechanisms, and intrinsic neuronal properties specified in the definition provide mechanisms known to be involved and that need further testing. Fifth, there are explicit animal models that include recording of evoked potentials in cats and monkeys, particularly after NMDA antagonist infusion. Further models need to be developed. Sixth, there are strong links to neural systems through neuropsychopharmacology. Links have been found to NMDA, GABA-ergic, and nicotine function. Seventh, measures are highly amenable for use in human imaging studies. Finally, there are moderate links to functional outcome, and more work is needed in this area.

### Integration

First, integration is readily measured in humans with grouping, perceptual closure, face processing, and contour integration tasks. Second, there is strong evidence of impairment in schizophrenia. Third, there is moderate evidence of a link to neural circuitry. Integration involves V2 and higher areas. There is much evidence for this in healthy subjects, but less evidence for actual disturbance in these specific circuits in schizophrenia, because most studies have been behavioral. Fourth, there is a relatively strong amount of clarity of the mechanisms. Mechanisms include long-range lateral interactions and recurrent processing. Deficits in paradigms such as contour integration are thought to be related to NMDA-modulated lateral excitation among the spatial filters signaling these elements as well as GABA-related inhibition of noise. Fifth, animal models of integration deficits have not been developed. Sixth, link to neural systems through neuropsychopharmacology is not well developed. Giersch *et al.* (85) have demonstrated effects of lorazepam and other benzodiazepines on GABA inhibitory activity on a visual closure task, but further work needs to be done. Seventh, measures are highly amenable for use in human imaging studies. Eighth, there is a moderately strong link to functional outcome in schizophrenia. For instance, there is high face validity regarding functional outcome for deficits in gestalt processing, perceptual closure, face processing, reading, and contour integration. In addition, there is evidence that perceptual organization deficits are linked to poorer premorbid social functioning (which is associated with poor outcome) and at least one study linking these deficits with longer stays in state hospitals.

## Other Perceptual Constructs Discussed at the Meeting

In addition to visual gain control and integration, a number of other constructs were discussed during the Perceptual Breakout Session at the meeting and were also felt to be potential candidates for consideration. These included: 1) early auditory processing that can be assessed with tone matching and auditory event-related potential paradigms; 2) auditory integration that can be assessed with phonemic/linguistic processing, prosody, auditory object processing, streaming/cocktail party, and reafferentation paradigms; 3) olfactory processing; 4) somatosensory processing/reafferentation; and 5) cross-modal integration.

## Conclusions

Gain control and integration are readily measured in humans, and there is strong evidence of their impairment in schizophrenia. A strength of both constructs is that they are grounded in both computational and cognitive theory and known brain function in humans and animals. Both constructs have been reliably measured with a range of paradigms. Both constructs are essential for perceptual function. Further study of these constructs in schizophrenia will be helpful in understanding the substrates of perceptual deficits in schizophrenia and the contribution of perceptual deficits to higher-level dysfunction. However, it is important to note that both gain control and integration are complicated constructs.

There are a number of practical advantages of these constructs: 1) testing is straightforward (cards/computers); 2) behavioral tests can elicit superior performance in schizophrenia, ruling out attentional/top down effects; 3) the underlying neural circuitry is becoming clearer; 4) imaging visual areas is straightforward, because they are large and many of them are located near the cortical surface; and 5) drug models (e.g., ketamine) and animal models (macaque) are established.

In conclusion, consistent deficits in visual processing are observed in schizophrenia. Reductions in gain control and integration can account for findings from a number of experimental paradigms (including contrast detection, gestalt processing, motion perception, and eye-movement control). The neurophysiology of both processes is likely to involve effects of glutamatergic activity at NMDA receptors and interactions between M- and P-pathways. Moreover, some tasks have been designed so that reduced gain control or integration leads to superior performance compared with control subjects, ruling out the possibility that the impairment reflects a generalized deficit.

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