Spatial integration in perception and cognition: An empirical approach to the pathophysiology of schizophrenia

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Abstract: Evidence for a dysfunction in cognitive coordination in schizophrenia is emerging, but it is not specific enough to prove (or disprove) this long-standing hypothesis. Many aspects of the external world are spatially mapped in the brain. A comprehensive internal representation relies on integration of information across space. Focus on spatial integration in the perceptual and cognitive processes will generate empirical data that shed light on the pathophysiology of schizophrenia.

When Bleuler (1911/1961) coined the term *schizophrenia*, few realized how difficult it would be to unravel the brain mechanisms underlying this devastating mental disorder. Bleuler's view of "split mind" as a basis of schizophrenia is sensible but nevertheless intricate for empirical assessment, at least up to now. Several theories have been developed to address issues of functional impairments of the brain associated with schizophrenia (e.g., Beaumont & Dimond 1973; Friston 1998). Because the search for a relationship between schizophrenia and observable organic loss in the brain regions does not seem very promising, the hope of using dysfunction in brain networks to understand schizophrenia has been revived. Phillips & Silverstein's (P&S's) perspective on cognitive coordination in schizophrenia represents a new endeavor in this direction.

By incorporating recent advances in neurophysiology into the study of psychotic conditions and reviewing experimental data associated with schizophrenic patients, P&S conjecture that dysfunction in cognitive coordination is implicated in schizophrenia. This perspective appears to be reasonable in that it is consistent with many clinical and laboratory observations reported for schizophrenic patients. On the other hand, some of these observations are also consistent with a different perspective – a dysfunction restricted to a specialized perceptual or cognitive process.

Does dysfunction of cognitive coordination play a major role in some, rather than in other, pathophysiological processes of schizophrenia? Or does dysfunction in cognitive coordination processes and in specialized cognitive processes co-exist in schizophrenia? To distinguish these two possibilities, current empirical evidence is not adequate. To further appreciate the cognitive coordination issue, we need empirical data that address not only abnormal functions in cognitive coordination but also normal functions in relevant specialized cognitive processes in schizophrenia.

Separating a deficit in cognitive coordination from a deficit in a specialized cognitive process has never been an easy task. This is because many cognitive functions involve both specialized and coordinated processes and, as a consequence, the two types of deficits sometime show similar characteristics in behavioral responses. One aspect of cognitive function – spatial integration – is, however, distinctive in this respect. Information from the external world is represented largely point-to-point in the perceptual and cognitive systems. Take vision as an example: Images of visual fields are retinotopically mapped to the striate cortex in primates. In order for the visual brain to form a coherent percept, information from different spatial locations must be integrated. This representation principle used by the brain presents a unique opportunity to differentiate the two types of dysfunctions – cognitive coordination versus functioning of a specialized cognitive process – that are potentially linked to schizophrenia. By assessing the processing of spatially localized information versus spatially distributed information, we can, in principle, dissociate the coordination of cognitive processes from the functioning of specialized cognitive processes in schizophrenia (Holzman 1994).

Perceptual organization, a visual process requiring cognitive coordination, has been explored in schizophrenia. The results remain inconclusive as far as whether a grouping dysfunction exists (Rief 1991). On the one hand, Place and Gilmore (1980) showed that, when asked to report the number of lines displayed heterogeneously, a task that is performed more efficiently without grouping, schizophrenic patients performed better than normal subjects, suggesting deficient perceptual organizing ability. On the other hand, Chey and Holzman (1997) showed that schizophrenic patients performed as well as normal controls did on tasks requiring the application of Gestalt principles of organization (i.e., proximity, collinearity, or similarity). A number of other studies showed results either consistent or inconsistent with a dysfunctional perceptual grouping in schizophrenia (e.g., John & Hemsley 1992; Silverstein et al. 2000). These apparent inconsistencies may be due to schizophrenic patients' reduced but not diminished ability to combine information into a coherent whole, as pointed out by P&S. Before attributing these results to a dysfunction in cognitive coordination, it is necessary to assess whether the processing of other elementary information – for example, spatially localized information – is normal in schizophrenia. This critical assessment is often missing from many studies. Without such an assessment, the demonstrated deficits in schizophrenia cannot be attributed solely to a dysfunction in perceptual grouping.

One example of incomplete separation of a specialized versus a coordination deficit can be seen in the study of global and local motion processing in schizophrenia (Chen et al. 2003; cited by P&S). This study aimed to identify the stage of motion processing, the global or the local, responsible for the deficient behavioral manifestation shown in previous studies (e.g., Chen et al. 1999a; 1999b), and found that detection of coherent motion embedded in a random-dot field, but not detection of motion embedded in gratings, was deficient in schizophrenic patients. Because only detection of coherent motion requires spatial integration of motion signals, the results were taken as evidence for a deficit in global motion processing (or dynamic grouping, as stated by P&S). The detection of coherent motion also involves rejection of noise; whether this nonintegration component contributes to the performance of the patients remains unclear. Thus, further empirical studies are needed to differentiate whether or not the deficit shown in the patients is due mainly to a failure in spatial integration, rather than in noise rejection. The same reasoning can be applied to the contour integration study in schizophrenia (Silverstein et al. 2000; also cited in the target article). That study showed that schizophrenic patients were less able to detect the contours that are composed of Gabor elements. Again, contour detection in that stimulus configuration also involves rejection of Gabor elements that do not belong to contours (distractors or noise). To be qualified as evidence for dysfunction in cognitive coordination, empirical studies need to show functional integrity of other cognitive processes, including filtering out noise and encoding spatially localized visual information (such as single dot, in the case of detection of coherent motion, or single Gabor element, in the case of contour detection).

The concept of cognitive coordination, put forward by P&S, emphasizes the importance of the interaction among different cognitive processes, rather than the integrity of individual cognitive processes. One empirical approach to address the issue of cognitive coordination is to study spatial integration in relation to spatial structure of the perceptual and cognitive systems. Take vision again as an example. One aspect of spatial interaction in the visual system can be described as the effect of visual stimulation in the surround on the responses to visual stimulation in the center. This effect has been shown at both the neuronal and the psychophysical levels (e.g., Allman et al. 1985; Born 2000; Xing & Heeger 2000). One advantage of this center-surround paradigm is that there is no involvement of noise or distractor in the visual stimuli. Application of this paradigm will allow spatial integration of visual information to be isolated from specialized sensory encoding and allow assessment of how visual information at different spatial locations interact with each other. The outcomes of this type of study

will then shed new light on cognitive coordination in schizophrenia.

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Mechanisms of disrupted language comprehension in schizophrenia

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Abstract: Mechanisms that contribute to perceptual processing dysfunction in schizophrenia were examined by Phillips & Silverstein, and formulated as involving disruptions in both local and higher-level coordination of signals. We agree that dysfunction in the coordination of cognitive functions (disconnection) is also indicated for many of the linguistic processing deficits documented for schizophrenia. We suggest, however, that it may be necessary to add a timing mechanism to the theoretical account.

The notion that aberrations in sensory-perceptual and attentional processing contribute to higher-order cognitive dysfunction in schizophrenia was apparent to the first clinicians that studied the disorder. Development of behavioral and neurophysiological methodologies in the past four decades has provided neurobiological links to those observations. Phillips & Silverstein (P&S) provide a careful and compelling integration of such studies, beginning with the experimental evidence indicating consistent difficulties in perceptual grouping and organization which cannot be explained by inattention alone.

P&S describe the interference of perceptual discriminations that is indicative of failures of Gestalt organization. We agree that similar integrative and organization failures may contribute to schizophrenia patients' deficits in language comprehension, and that the types of rhythmic activity (i.e., gamma band oscillations) that P&S emphasize as relevant for primary perceptual integration are likely to be significant for language function. We emphasize, however, the importance of a timing mechanism for any theoretical account of language dysfunction in this disorder. We will direct our comments to the relevance of both mechanisms (cognitive coordination and temporal processing) for language function in schizophrenia.

First, our data on receptive syntax processes in schizophrenia (Condray et al. 2002) are consistent with a formulation of the type advocated by P&S. Compared with controls, patients exhibited reduced accuracy (i.e., not knowing who did what to whom) about object-relative sentences ("*The senator that the reporter attacked admitted the error.*"). More important, receptive syntax and general intelligence were correlated in controls; these functions were not associated in patients. Recent additional analyses of those data illustrate P&S's argument regarding the failure of higher-order coordination of functions that may be more locally specialized. An initial multiple regression analysis determined comprehension accuracy was predicted by a model that included the variables temporal processing accuracy (intelligibility of rapid speech) and a diagnosis *x* semantic knowledge (WAIS-R Vocabulary subtest score) interaction term [Model: $R^2 = .32$, Adjusted $R^2 = .30$, $F_{2,50} = 11.88$, $p < .001$. Predictors: temporal processing (t-test = 3.21, $p = .002$); diagnosis *x* semantic knowledge (t-test = 2.94, $p < .01$)].

Table 1 presents the results of the separate regression analyses conducted for each group to increase understanding about the significant interaction. Findings show different patterns of association for the two groups: For patients, temporal processing predicted comprehension accuracy, but semantic knowledge did not; for controls, the reverse was true. Overall, the cumulative patterns obtained for patients' receptive syntax performance are generally consistent with P&S's assumption of a failure to coordinate cortical activity within and between cognitive sub-systems. These data suggest the additional importance of temporal processing for patients' language comprehension.

Table 1 (Condray & Steinhauer). *Summary of separate multiple regression analyses for variables predicting comprehension accuracy for schizophrenia patients and normal controls*

R^2 Adj.	R^2 F-ratio	df	p beta	SE beta	*t*test p
Patients (n=32)	.22	.16	4.02	2.29	.03
Variables					
Temporal Processing	.64	.25	2.63	.014	
Semantic Knowledge	.03	.02	1.06	.30	
Controls (n=21)	.59	.54	12.92	2,18	<.001
Variables					
Temporal Processing	.92	.46	1.99	.061	
Semantic Knowledge	.10	.03	4.13	.001	

As a second consideration, we suggest that inclusion of a timing mechanism in theoretical accounts is necessary to explain the full range of language dysfunction in this disorder. Deficits in time-dependent processing as a core feature of schizophrenia have been pursued as an independent line of investigation (for a review of the early literature, see Braff et al. 1991). Findings indicate that schizophrenia is associated with disturbances in the processing of sequential, rapidly presented stimuli, including the disruptions in auditory sensory gating and visual backward masking discussed in the target article. Recognizing that this disturbance may be more complex than a mere slow processing speed, Braff and colleagues suggested that more refined distinctions are necessary, such as Breitmeyer's transient/sustained neural channel model (Breitmeyer & Ganz 1976). That model is based on the parallel and complementary pathways of the visual system, with functional distinctions made on the basis of temporal latency, and temporal and spatial resolution. Backward masking effects are assumed to be a result of the interruption of the slower responding of the sustained channels to the target stimulus by the faster responding of the transient channels to the mask. One hypothesis is that the visual backward masking deficit in schizophrenia is due to an overreactive transient channel that compromises sustained channel function (Green et al. 1994).

Most of the experimental tasks described by P&S involve rapid, sequential presentation of stimuli, but it is not clear whether they subsume a dysfunction of timing under their cognitive coordination mechanism. In combination with our receptive syntax data, considerations regarding semantic memory deficit in schizophrenia include the possibility that some type of timing dysfunction is a key mechanism. In particular, compromised semantic memory, as indexed by semantic priming deficits, may be due to dysfunction in the temporal dynamics of neural channel activation and synchronization. Recent visual backward masking studies have demonstrated that disruptions to patients' perception of rapid, sequential bits of information (single letters) represent a robust phenomenon (Butler et al. 2003; Cadenhead et al. 1997; Green et al. 1999). It is not known, however, if visual backward masking deficit can account for semantic priming disturbance in schizophrenia. Alternatively, it is possible that a temporal processing disturbance alone is sufficient to explain semantic priming dysfunction in this population. This latter type of account has been advanced for theories of dyslexia ("dyschronia": Llinas 1993; cf. the "cognitive dysmetria" for schizophrenia proposed by An-