Abstract

Laterization of brain function was established on the basis of clinical-pathological correlations over a century ago. In the past two decades, this line of research has attempted to link the complex behaviors evident in schizophrenia to the failure to develop and maintain a normal pattern of hemispheric activity. This issue of Schizophrenia Bulletin reviews and presents data from multiple perspectives of methods applied to the study of laterality in schizophrenia. Brain disorders affecting systems that modulate complex behavior are commonly related to laterality. Therefore, this dimension of brain function merits further investigation in schizophrenia.

Key words: Laterality, hemispheric activity, functional imaging.


This issue of Schizophrenia Bulletin is devoted to an overview of laterality. Hemispheric asymmetry of brain function has been of interest to neurologists ever since Broca (1863), Dax (1865), and Hughlings-Jackson (1876) demonstrated the profound differences between the effects of unilateral lesions on language and on other cognitive functions. For psychiatrists and psychologists, the phenomena of laterality have not presented in such a compelling fashion in the clinic. Perhaps as a consequence, the concept of laterality has been slow to influence the mainstream of psychiatric thinking, even within neurobiological theory. Nonetheless, laterality hypotheses of schizophrenia were proposed more than two decades ago (Gruzelier and Venables 1974; Flor-Henry 1976; Gur 1977, 1978) and have since been tested using increasingly powerful neurobehavioral, neuroanatomic, and neurophysiologic methods.

As this issue will show, the hypothesis has not been consistently examined, even in studies that were in a position to do so. Yet, almost surprisingly, this dimension has fared quite well in the turbulence of empirical testing. It has been reformulated and modified, to be sure, but the evidence continues to grow that schizophrenia, like many other brain disorders, is related to lateralized brain dysfunction. On the other hand, it is also becoming clear that the question of whether schizophrenia is characterized by dysfunction of one or the other hemisphere is simplistic and needs to be reformulated. Some authors have tried such formulations, and common to all of them is the belief that complex behavior requires the participation of neural networks. In this context, laterality can explain only a limited fashion one gradient or dimension that modulates such networks.

Understanding lateralization of brain function in health and disease, however, provides a heuristic hypothesis for building a neuropsychiatric perspective of schizophrenia (Crow 1990). The neuropsychiatric dimension needs to converge with careful dissection of the neurobehavioral dysfunction evident in schizophrenia and pursuit of the underlying mechanism that regulates it. By examining schizophrenia within the context of other brain disorders, we will be able to assess the nature and extent of aberrant behavior and the brain systems affected that stimulate or may control such behavior. For example, the recognition that memory impairment is prominent in schizophrenia has led to productive lines of research attempting to tease apart the specific memory systems involved. This research has applied structural and functional imaging methods to investigate memory-related neural tissue and processes, and conducted animal work to advance the understanding of the molecular basis for memory. Likewise, comparing the memory deficit in schizophrenia to other brain disorders, such as epilepsy (see Hyde and Weinberger 1997), can give a perspective.
and stimulate hypotheses on the pathophysiology of schizophrenia. The study of laterality of brain function provides an opportunity to apply both research strategies.

The review by Harris (1999, this issue) details some of the history of the theory and research on hemispheric specialization and how pathological behavior, or "madness," has received some cursory notation. Early and careful documentation of neurobehavioral dysfunction following brain lesions is the foundation for experimental paradigms applied in cognitive neuroscience and in functional imaging studies today. Reading some of the theoretical arguments of our predecessors can be a humbling experience. With all the advanced tools at our disposal now, has our understanding increased commensurately?

Lateralization of brain structure and function, initially considered unique to humans, is evident in other species. Cowell et al. (1999, this issue) examine the evidence for cerebral lateralization in animals. They point out the lack of integration between animal and human work. Animal studies strongly support the critical role of early development for achieving healthy adjustment and accounting for dysfunctional states. This line of investigation is pivotal as we advance translational research.

Manual preference, or handedness, has considered an index of lateralization with the majority of the population being right-handed. For most right-handers the left hemisphere specializes in language and the right hemisphere in spatial abilities. Satz and Green (1999, this issue) review the evidence for a leftward shift, or mixed-handedness, in schizophrenia and consider neurodevelopmental factors that may underlie the shift. Features of schizophrenia in the symptomatic, neurocognitive, neuroanatomic, and genetic domains are examined in relation to the possibility of a neurodevelopmental insult affecting lateralized brain organization.

Ragland et al. (1999, this issue) examine laterality indices in a range of neurobehavioral parameters including motor and sensory measures, as well as the neurocognitive domains of language and spatial abilities, and verbal and spatial memory. Patients with schizophrenia from a large prospective sample show meager indication of lateralized disturbances in sensory processing and motor speed. They do, however, have more language than spatial deficits, implicating relative left hemispheric dysfunction in regions needed for complex cognitive behavior. Laterality effects in performance were mediated by sex differences, and the results underscore the importance of examining sex differences in laterality research.

Multiple psychophysiological measures have been applied in the study of brain lateralization in schizophrenia. Gruzelier (1999, this issue) examines the evidence for the association between laterality imbalance and disease-related variables, including clinical syndromes and medication. The hemispheric basis for positive and negative syndromes in schizophrenia and personality dimensions in schizotypy is evaluated across diverse measures, including eye movements, lateral inattention, cardiac vagal tone, motoneuron excitability, the P300, and other evoked potential components. It is proposed that syndrome differences may relate to hemispheric function, interhemispheric connectivity, and neurotransmitters.

Neuroanatomic investigations permit examination of structural asymmetries of the brain that may underlie neurobehavioral parameters. A recent issue of Schizophrenia Bulletin examined the neuropathology of schizophrenia (Buchanan and Carpenter 1997). Neuroimaging methods have provided in vivo measures of brain anatomy. Petty (1999, this issue) presents an overview of neuroanatomic asymmetries from an evolutionary outlook and describes findings in healthy people and schizophrenia patients. This provides a multilevel vista from gross anatomy to cellular and neurochemical studies.

Functional imaging has been applied in the study of schizophrenia more than in any other neuropsychiatric disorder. A range of methods for evaluating cerebral metabolism and blood flow as well as neuroreceptor functioning, is reviewed by Gur and Chin (1999, this issue). Laterality has not been tested directly in the majority of studies; however, the laterality dimension seems to interact with specific brain systems that modulate neurobehavioral domains that are dysfunctional in schizophrenia.

One may vacillate, after reading this diverse set of contributions, between being overwhelmed by the amount of data that have converged on the issue of laterality in schizophrenia and feeling some exasperation at the paucity of solid answers for questions that seem quite rudimentary. Our hope is that these seven articles will induce investigators of schizophrenia to include laterality as a focus of inquiry. As a guiding hypothesis, laterality can facilitate the design of studies and data analysis plans around a dimension with established neural substrates. As an angle on the symptoms and pathophysiology of schizophrenia, laterality can assist researchers, clinicians, and patients in efforts to conceptualize facets of the manifestations of this disabling and complex disorder.

References


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