Disorders of the Isodendritic Core of the Brainstem

by Jean Lud Cadet

Abstract

The dopamine hypothesis of schizophrenia has not lived up to its explanatory potential. Other efforts have been made but have depended heavily on the limbic system in their analysis of the problem. Based on the clinical and basic research that has been conducted so far, the thesis is presented here that the group of schizophrenias is due to disorders of the isodendritic core of the brainstem. The concept of the core is described, and the data that support the contention are presented briefly.

I read the excellent review on the neuropathology of schizophrenia with great interest (Weinberger, Wagner, and Wyatt 1983). I was first introduced to the neuroanatomical approach to psychosis by the reading of Fishman's article (1975) in 1978. Later on, I became familiar with Stevens' earlier effort (1973). The article by Weinberger and his coworkers has thus appeared at a most opportune time when a consensus is developing vis à vis the need to go beyond the dopamine hypothesis in order to elucidate the schizophrenias (Haracz 1982). In their article, however, the limbic system is still regarded as the prime suspect in the etiology of the syndrome. The purpose of this correspondence is to suggest another interpretation of the neuropathological studies that have been accumulated so far. Herein is introduced the idea that the schizophrenias are disorders of the isodendritic core of the brainstem (IDCB).

Ramon-Moliner (1975), Ramon-Moliner and Nauta (1966), and Nauta and Haymaker (1969) include the following structures in the core: several medullary nuclei, the raphe nuclei, locus ceruleus, substantia nigra, superior colliculus, substantia innominata, and the hypothalamus and its surrounding structures. Characteristically, the cells found in the core are generalized, vary in size, have extensive overlapping dendritic fields, and interdigitate freely with fibers of passage. They extend from the spinal cord to the basal forebrain and, more importantly, they project widely to the allo- and the neocortex (Emson and Lindvall 1979; Cooper, Bloom, and Roth 1982). Pathological changes have been reported in many of the areas listed above (Weinberger, Wagner, and Wyatt 1983). One may thus conclude that any apparent nonspecificity of these findings is only superficial since the loci of these lesions form subsets of the IDCB. Indeed these cells might be susceptible to similar kinds of genetic or environmental injuries since they might evolve from embryologically pluripotential predecessors. Some possible examples of such damage are neurodegenerative diseases like postencephalitic parkinsonism, Parkinson's disease, ALS-Parkinson-Dementia complex of Guam, Alzheimer's disease (Appel 1981; Rossor 1981; Whitehouse et al. 1982; Mann and Yates 1983), and olivopontocerebellar atrophy in a subtype of which deficiency of glutamate dehydrogenase (GDH) has been demonstrated (Plaitakis 1982).

If the abnormalities causing schizophrenia are in these groups of cells, the course and timing of the clinical presentation will depend on the stage in development when the damage occurred, the extent of the structural changes, the virulence of the slow virus strain, or the nature of the biochemical defect, e.g., enzymatic,
neurohormonal, or immunologic. These, in turn, would be affected by host factors, thus ensuring nonuniform courses of the illness. This supposition might account for the protean presentations of the schizophrenias. Furthermore, as already mentioned, the cells project widely to the limbic system and the rest of the cortical mantle. They also receive reciprocal fibers from association areas which are modality specific in some regions but crossmodal in others (Pandya and Seltzer 1982; Van Hoesen 1982). Hence, lesions in the IDCB might influence higher cortical functions in a transsynaptic way. They might also lead to abnormal oculomotor functions by direct damage to the brainstem nuclei or by affecting the frontal eyefields or cerebellar pathways (Bender, Rudolph, and Stacy 1982), or cause autonomic dysfunction by influencing the reticular formation (Strub and Black 1981). This is consistent with the studies demonstrating that schizophrenic patients show deficits on neurotransmitter testing (Chapman 1979), hypofrontality by blood studies (Ingvar and Franzen 1974) and by positron tomography (Buchsbaum et al. 1982), eye movement abnormalities (Levin et al. 1982), and psychophysiological changes (Venables 1980). Progress of the process might lead to similar if not identical outcome in many patients: the so-called chronic undifferentiated category (Tsuang 1982).

In summary, the dopamine hypothesis, although it has generated important neurobiological research, has not elucidated the etiology of the schizophrenias. Consequently, other attempts have been made to explain this complex entity. It is generally agreed that the biochemistry needs to be better integrated with the restrictive and nonrestrictive aspects of the neuroanatomy of the interrelated aminergic systems. These efforts have centered around the limbic system. A creative postulation is that of Crow (1982), who suggests two types of schizophrenia—one with negative, the other with positive symptoms. This idea, though stimulating, might be too clinically restrictive. Herein is submitted the proposal that the schizophrenias are disorders of the isodendritic core of the brainstem. The broad projections and the feedback connections of that system via relay stations are thought to account for the clinical presentation. Different etiological factors and the progression rate of the pathoanatomic substrate might dictate its natural history. This concept is felt to be broader and yet still to allow for a systematic approach to the syndrome. Clinical neuropsychiatrists may contribute by probing possible neuropsychological impairments in neurological patients with brainstem lesions. Finally, further pathological investigation concentrating on the structures of the IDCB may be a productive area for future research endeavors.

References


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**Announcement**

The Ninth Annual Conference of the International Association of Psycho-Social Rehabilitation Services will be held May 17-19, 1984, at the Hyatt Regency Chicago, Illinois Center, Chicago, IL. The theme will be Psycho-Social Rehabilitation: The State of the Art.

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