## Redefining schizophrenia

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## Reconceptualización de la esquizofrenia

Nowadays, psychiatry is facing important challenges that begin in the lack of definition of diseases. The concept of schizophrenia has a provisionality which has determined that it has been suffering a crisis since its origin. For Colodron1, this will go into the history of Psychiatry as one of the greatest conflicts waged to discover what exists after so many constructs which were, at one time, necessary but which later became an obstacle for the progress of psychiatric and scientific knowledge.

The meeting point of the data from different areas of neurosciences from neuroimaging, neuropsychology, neuropharmacology and neurogenetics, tends towards a psychopathology that is re-expressed in its classical principles for the sake of better compatibility with the basic sciences<sup>2,3,4</sup>. All of these leads us to new ways of reconsidering the schizophrenic illness.

One of these present models defines schizophrenia as a cognitive disorder that would be present in all the patients beyond the different clinical forms. This dysfunction, called cognitive dysmetria by Andreasen<sup>5</sup>, would be the consequence of a disorder of the connections between the cerebral regions responsible for the coordination and synchronization of the cognitive functions (cortico-thalamic-cerebellar-cortical circuit).

The frontal lobe and especially the prefrontal cortex, together with the temporal-limbic structures and the basal ganglia are three widely interconnected cerebral systems that have been involved in the pathophysiology of schizophrenia since the time of Emil Kraepelin, up to the point of having considered schizophrenia as a frontal-temporal-limbic disease.

The evidence that many of these patients have structural abnormalities, that vary in degree more than in type of lesion, could suggest that the schizophrenic condition is homogeneous. However, there is an absolute conviction among the clinicians that the different subgroups or subtypes of schizophrenia respond to different etiological principles. Thus, it is an idea that is based on a multifactorial etiological model that would involve a genetic factor (polygenic) and environmental factors that would affect both early as well as late neurodevelopment<sup>6</sup>.

Within the hypothesis of neurodevelopment, the changes in the cytoarchitecture suggest that the process originates in the last quarter of pregnancy. The involvement occurs equally in both hemispheres, altering the development of the temporal cortex, especially the parahippo-

campal gyrus, an essential structure in the affective and intellectual integration next to the temporal cortex and amygdala. The 100% absence of concordance in monozygotic twins, increase of births in winter, greater incidence of perinatal factors and presence of symptoms of schizophrenic type in neurological diseases support the involvement of environmental factors.

On the other hand, metabolism and cerebral perfusion studies show that there is a hypofrontality that is manifested when faced with certain mental tasks but not with others, suggesting a dependency on the context<sup>7</sup>. These data are consistent with the hypothesis of a neuronal deorganization in the areas involved more than the presence of a destructive process (neurodegenerative model). The pathophysiology mechanism can be based on a distortion of the neural processing, above all, in the frontal and temporal limbic networks with early interference in the cerebral integrative processes.

Thus, the progress of neurosciences, and among them, more outstandingly neuroimaging and genetics, is leading to a re-consideration of psychological disorders and especially of schizophrenia.

Extensive development of cognitive neurosciences has given rise to better knowledge of the neural correlates of the psychopathological symptoms.

One of the possibilities of an alternative phenotype to schizophrenia is to focus on the investigation of a single symptom. We believe that the auditory hallucinations are a good candidate for different reasons.

It is one of the most frequent symptoms of the disease (it appears in about 80% of the patients).

It is possibly the most qualitatively defined, categorial and easy to measure symptom and it is the only symptom in which we find clear neurobiological correlates with functional neuroimaging techniques.

In our country, we are beginning to investigate in this sense, trying to combine efforts with different strategies. We are studying the forms of clinical analysis of hallucinations more deeply and we have translated and validated the PSYRATS scale to Spanish (González et al., 2002). We are investigating on the correlation of auditory hallucinations with functional neuroimaging (see Font in this same volume).

Finally, we are trying to search for possible genes that could be involved in the vulnerability of the hallucinations (Toirac et al., 2002) by studies of association and links.

The hope of this confluence of efforts is to reduce the heterogeneity of a disorder exclusively defined with descriptive criteria in the search for a more integrating taxonomy, more clinically significant and with better reliability and validity.

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