

The brain and mind as a network: can neuroimaging and connectomics help us to better understand psychiatric disorders?

Maria I. López-Ibor Alcocer

Department of Psychiatry, Faculty of Medicine,
Complutense University Madrid, Madrid, Spain

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Correspondence to Maria I. López-Ibor Alcocer, MD,
Department of Psychiatry, Faculty of Medicine,
Complutense University Madrid, 28040 Madrid, Spain
Tel: +34 913 162 740; fax: +34 913 162 749
e-mail: mariaines@lopezibor.com

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The conceptualization of the brain as a network and associating mental disorders with disruptions in brain connectivity is not new and was suggested in the first decades of the 20th century. Both Kraepelin and Bleuler [1,2] considered mental disorders as the loss of links: ‘Dementia praecox is considered as a result of the destruction of the internal links of personality and loss of the inner unity of the activities of intellect, emotion and volition in themselves and between each other’.

However, in the past two decades, the evolution of brain imaging techniques overcame this view with a simpler and more locationist and reductionist approach. Still, mental disorders have to be considered as the reflection of various pathobiological processes that interact in a complex network.

When neuroimaging techniques started to be available for psychiatric patients, research projects were designed to try to identify brain areas that could be affected in these disorders. This approach of dividing the brain according to its anatomical structure and its functioning has provided some insight into the neurobiological basis of many psychiatric disorders, but this approach may come to an end.

It is clear today that segmenting the brain and studying its parts is insufficient to account for the complexity of brain alterations associated with mental disorders. Research data over the last years of the 20th century reveal an important matter: mental disorders have to be considered as functional disorders, and if we want to apply these techniques we have to consider the symptoms patients have at the precise moment of registering and while performing some tasks; otherwise the results would be inconclusive.

We now know that neuroanatomy has not been very receptive to the importance of brain circuits even though brain circuits were described more than hundred years ago. The first description of corticosubcortical circuits and even of a visceral brain was given by Christfried Jakob [3] in studies carried out between 1908 and 1911. These circuits are not mentioned again until 1937; James

Papez [4] described the emotions circuit that bears his name (called by many as the Papez–Jakob circuit), and in 1949 Paul McLean described the limbic system or emotional brain.

Ten years ago, almost simultaneously, Olaf Sporns and Patric Hagmann [5,6] provided two new and equivalent terms – connectome and connectomics – names that have given rise to a new perspective of neuroscience that opens up new possibilities.

Connectomics is based on the increasing evidence that these individual differences in brain connectivity are associated with variability in important cognitive and behavioral functions. The connectome is being studied through a combination of histological (dissection and staining of white matter fibers, axonal degeneration studies), neuroinformatic (database management), and functional imaging (diffusion tensor imaging, tractography) techniques [7]. The connectome is a dynamic map, which varies with the sensory input, the overall state of the brain, with learning, development, and tasks to be performed.

Van Horn *et al.* [8] have reconsidered the famous hypothetical brain damage case of Phineas Gage previously analyzed by Damasio *et al.* [9], who came to the conclusion that the rod that penetrated the skull destroyed about 4% of gray and 11% of white matter of the railroad worker’s brain, and was able to identify lost connections whose psychopathological effects would be felt later; that is, the consequences of loss of connections would affect different processes like memory, attention, emotions, etc. later.

Twenty years ago, when our group started to apply neuroimaging techniques, we first chose obsessive-compulsive disorders (OCD) patients for two reasons: first because it is the most ‘organic’ mental disorder, as psychosurgery techniques were being applied for more severe patients with successful results since many years, and the second because these patients were able to collaborate and willing to accept brain scans, MRI, or PET. First research projects were designed to try to identify neuroanatomical areas

affected in OCD patients, but from the beginning results indicated that in this disorder ventrocorticostriatal circuits were largely described as being affected in OCD: to establish correlations between symptoms and neurofunctional basis, studies were designed to identify alterations while patients were performing a task or when they were having active symptoms, and more recently research data have shown intrinsic alterations in the architecture of a network supporting cognitive control in OCD patients and critical deregulations in functional connectivity within the paralimbic network when OCD patients were engaged in a cognitive task.

This knowledge may be instrumental in the discovery of new neurobiological markers of psychiatric disorders, as well as in the definition of specific targets for psychopharmacological interventions, for measuring behavior patterns; in addition, the mapping of these structural and functional networks in our participants provided an important set of data that can be used to help understand variations in 'typical' brain function.

Limitations of clinical research can be overcome if emphasis is placed on psychopathology and on the adaptive value of symptoms and dysfunctions. Localizationism can be overcome. Progressing as we have done, suddenly we have become aware that the crisis of psychiatry is not unique. The whole of modern medicine is running away from its deepest tradition. Diseases are not to be investigated *per anatomen* nor the *sedes causae* looked for in organs. Connectomics is the new discipline that encompasses neuroscience with social being in the process of giving rise to a new language. Curiously enough, the main descriptions of Kraepelin, Bleuler, and many others of the great masters insist, once again, on the breakdown of links between the functions that shape personality.

Network medicine and network psychiatry open new avenues for research by identifying connectivity profiles associated with different clinical outcomes, providing a great opportunity and a greater challenge [10,11].

Acknowledgements

Conflicts of interest

There is no conflicts of interest.

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