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EDITORIAL

How can connectomics advance our knowledge of psychiatric disorders?

Connectomics defines a new field in neuroscience, which aims to map the structural and functional networks through which the brain is interconnected by using cutting-edge imaging techniques, and to characterise the systems-level properties of these networks using graph theoretical approaches. The motivating hypothesis behind studying the brain as a network, or a set of sub-networks, is that the pattern of connectivity between regions specialised in specific functions poses specific limits on brain dynamics and may therefore inform brain processing abilities.[1]

The conceptualization of the brain as a network is not new and was suggested in the first decades of the 20th century.[1] There is a long history of associating brain and mind disorders with disruptions in brain connectivity (e.g., Lichtheim's classical characterization of the aphasias). However, in the past two decades, the evolution of brain imaging techniques that allow the study of brain structure and function *in vivo* has obscured this view in favour of a simpler and reductionist approach. The reductionist approach of segregating the brain according to its function and anatomical structure has provided important insight into the neurobiological underpinnings of many psychiatric disorders, but this approach may have reached its limit. It is clear today that segmenting the brain and studying its parts in isolation is insufficient to account for the complexity of brain alterations associated with mental disorders. This points to the need for a shift in how scientists interrogate the biological basis of mental illness, highlighted by the absence of recent fundamental advancement in understanding core brain deficits associated with some of the most debilitating psychiatric disorders such as schizophrenia. This lack of new basic knowledge has important implications for the development of new treatments, as recently discussed in a special issue of the Journal *Nature* (http://www.nature.com/news/2010/101110/full/468158a.html).

In the past few years, a number of studies have started conceptualizing mental disorders in terms of alterations in large-scale functional and structural brain networks.[2,3] Regarding functional alterations, scientists have used functional magnetic resonance imaging to map brain networks when patients are not engaged in goal-directed actions, a condition called the resting-state [e.g., Zalesky et al.[4] and Zhang et al.[5]], as well as when patients are instructed to perform a specific task [e.g., Cocchi et al.[6]]. Harrison et al.[7], for one, showed the relevance of ventral corticostriatal networks in characterizing the symptoms of obsessive-compulsive disorder (OCD) in the resting-state. More recently, using a sophisticated graph theoretical approach to map resting-state brain functional connectivity, Zhang et al.[5] showed intrinsic alterations in the architecture of a network supporting cognitive control in OCD patients. On the other hand, Cocchi et al.[6] showed critical deregulations in functional connectivity within the paralimbic network, a network encompassing the insular and the anterior cingulate cortices, when OCD patients engaged a cognitive task. This task-induced deregulation was correlated with symptoms of state anxiety, suggesting that functional alterations in the paralimbic network may be a marker of difficulty in engaging in goal-directed behaviour due to symptoms. Together, these studies provide an illustration of how the mapping of brain connectivity - performed while patients are at rest or while they are engaging a task - can reveal different aspects of aberrantly synchronised neural activity in OCD. Combined with the investigation of structural networks inferred from diffusion tensor imaging (DTI) and cortical thickness measurements,[8] findings from studies like those mentioned above have improved our understanding of the biological underpinnings of psychiatric disorders. 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 psycho-pharmacological interventions.

In summary, connectomics has been touted as a potential breakthrough in providing novel and more meaningful insights into the neurobiological underpinnings associated with psychiatric diagnoses and symptoms.[9] Connectomics may help elucidate the genetic basis of brain alterations in psychiatric disorders.[10] Moreover, task-based studies may advance our knowledge of environmentally-driven brain dysfunctions emerging in a specific context, such as when

cognitive control is required.[6,11] Future utilization of connectomics in psychiatry research requires the development of statistical methods to compare the connectome (i.e., connectional map of the human brain) between groups of patients and healthy controls as well as computational approaches to identify faulty circuits in the connectome that can serve as biological markers of disease.[12] While the field of connectomics is nascent and further methodological advancements are needed to refine the characterization of brain dynamics, progress towards understanding the human connectome in health and disease will inevitably depend on the development, and use, of such novel methods.

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Disclosures

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