BRAIN BYTES

Connectivity

Introduction

Brain function is dependent on the interactions between specialised regions of cortex that process information within local and global networks. Integration of information arising from these interactions does so in a dynamic fashion on different time scales. In order to examine the relation between structure and function, biologically informed models of neural system dynamics, which are very tightly linked to brain connectivity in its various forms, are required (1). Investigations of physical connections between neuronal structures and measurements of brain activity *in vivo* have given rise to concepts of functional, effective and anatomical connectivity, which have been useful for understanding brain mechanisms.

The Byte

Functional connectivity reduces to testing the null hypothesis that activity in two regions shares no mutual information (2). Mutual information is a statistical description of a degree to which the two regions show similar behaviour or statistical interdependence. In other words, the characterisation of brain activity in terms of functional connectivity is 'model free'. In contrast, characterising brain activity in terms of *effective connectivity* requires a causal model, in which regions and connections of interest are specified by the researcher, often constrained by a combination of neuroanatomical, neuropsychological and functional neuroimaging data. This is a crucial point, when considering the distinction between functional and effective connectivity, because it emphasises the shift from a description of what the brain does to a theory of how it does it (2). *Anatomical connectivity* refers to the anatomical layout of axons and synaptic connections and determines which neural units can directly interact with each other and thus constrains the system's functional and effective connectivity.

Currently, non-invasive neuroimaging techniques, such as functional magnetic resonance imaging (fMRI), positron emission tomography, electroencephalography (EEG), magnetoencephalography (MEG) and some optical imaging techniques, are used to study functional/effective connectivity. Since these measures vary in spatial, temporal and other features, it should be borne in mind that the term functional/effective connectivity may describe different neural substrates in different procedures (3). Most methods studying interactions between different regions of the human brain are based on the assumption that functionally related regions display coordinated blood-flow responses. Functional integration is usually assessed by examining the correlations among activity in different brain areas or by trying to explain the activity in one area with relation to the others. Functional connectivity is often referred to as being data driven whereas effective connectivity is referred as model driven. The data-driven approach uses the principal or independent component analysis to decompose neuroimaging data into a set of modes (i.e. eigenimages), which are mutually uncorrelated both spatially and temporally, and to order these modes according to the amount of variance they can explain. Then, by comparing the temporal expression of the first few modes with the variation in experimental factors, a distributed functional system associated with various factors are identified. This approach does not make any assumption about the underlying biology and is therefore of greatest practical use when it is not clear about which regions are involved in a given task. Functional connectivity provides information about the observed correlations; it does not provide any insight into how these correlations are mediated. In the SPM software package (Wellcome Department of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk/spm), functional connectivity is measured using the psycho-physiological interaction analysis where the activity in one brain region is characterised by the interaction between another region's activity and a psychological factor (4). By virtue of the integration of these physiological and experimental influences on regional responses, one is able to confer a degree of functional specificity when making inferences about functional integration or interactions between brain areas (4).

In contrast to functional connectivity, analyses of effective connectivity are based on statistical models that make anatomically based assumptions (e.g. knowledge of structural connectivity) and restrict their inferences to networks comprising a number of preselected regions (5). In general, fMRI data are modelled using the structural equation model (SEM) (6) or dynamic causal model (DCM) (4). DCM operates within a Bayesian framework where a distinction is made between the 'neuronal level' and the 'hemodynamic level'. Experimental inputs cause changes in effective connectivity expressed at the level of neurodynamics, which in turn result in changes to the observed hemodynamics. In SEM, changes in effective connectivity lead directly to changes in the covariance structure of the observed hemodynamics. Because changes in effective connectivity occur at the neuronal level, DCM is the preferred model for fMRI data (5). DCM was first introduced for the analysis of fMRI data to quantify effective connectivity between brain areas. Recently, this framework has been extended and established in the EEG and MEG domain.

Conclusions

Traditional neuroimaging studies have long painted a static picture of brain function and nowadays there is expanding interest in exploring the brain on a more dynamic level. Newer approaches such as those described within the frameworks of *connectivity* are now shedding new light on the integration within and between specialised brain regions. Sophisticated analytical approaches, such as functional and effective connectivities, allow greater inferences to be made of neuroimaging data on a network level in response to cognitive manipulation during neuroimaging experiments rather than simply static activation foci on brain maps. As an analytical approach, connectivity is still very much in its infancy; however, the various techniques are being refined by the scientific community and are rapidly becoming more powerful. This bodes well for the neuropsychiatry as most disorders in this realm do not result from well-defined structural defects but, instead, probably arise from aberrations within entire networks.

Pritha Das[1,2], Jim Lagopoulos[1,2]

[1]CADE Clinic, Royal North Shore Hospital, St Leonards, NSW Australia; and
[2]Academic Discipline of Psychological Medicine, Northern Clinical School, University of Sydney, Sydney, NSW, Australia

Dr Pritha Das
CADE Clinic, Level 5, Building 36, Royal North Shore Hospital, St Leonards, NSW 2065, Australia.
Tel: +61 2 9926 7746;
Fax: +61 2 9926 7730;
E-mail: pdas6843@usyd.edu.au

Acta Neuropsychiatrica 2009: 2:91–92

DOI: 10.1111/j.1601-5215.2009.0374.x

References

1. Stephan KE, Riera JJ, Deco G, Horwitz B. The Brain Connectivity Workshops: moving the frontiers of computational systems neuroscience. Neuroimage 2008;**42**:1–9.
2. Lee L, Harrison LM, Mechelli A. A report of the functional connectivity workshop, Dusseldorf 2002. Neuroimage 2003;**19**:457–465.
3. Horwitz B. The elusive concept of brain connectivity. Neuroimage 2003;**19**:466–470.
4. Friston KJ, Buechel C, Fink GR, Morris J, Rolls E, Dolan RJ. Psychophysiological and modulatory interactions in neuroimaging. Neuroimage 1997;**6**:218–229.
5. Penny WD, Stephan KE, Mechelli A, Friston KJ. Modelling functional integration: a comparison of structural equation and dynamic causal models. Neuroimage 2004;**23**(Suppl. 1):S264–S274.
6. Mcintosh AR, Gonzalez-Lima F. Network interactions among limbic cortices, basal forebrain, and cerebellum differentiate a tone conditioned as a Pavlovian excitor or inhibitor: fluorodeoxyglucose mapping and covariance structural modeling. J Neurophysiol 1994;**72**:1717–1733.