Functional Connectivity:

MRI Measures of Spontaneous Fluctuations in Intrinsic Networks

Diseases of connectivity

Gwenaëlle Douaud (FMRIB Centre, University of Oxford)

Abstract: Resting-state functional connectivity MRI is a powerful tool which provides information about large-scale networks in the human brain. These networks comprehensively cover the entire repertoire of functional networks utilised by the brain in "action" (as seen using task-based fMRI, Smith et al., PNAS 2009). Resting-state functional connectivity MRI (fcMRI), like any other imaging techniques, has advantages and inconvenients, that other speakers will have likely covered earlier in this educational course. Some of these advantages – such as being free from confounds related to task performance, or being able to sample broader patient populations – are very relevant in the clinical realm and make fcMRI a clear favourite amongst the clinical neuroimaging community. While methods to investigate fcMRI vary greatly across studies (seed-based, ICA, graph theory, multi-modal analysis etc.), each of them can provide better insights into the pathophysiological process at play or be a sensitive biomarker. Efforts have also been made recently towards methods development, which will likely benefit the sensitivity and interpretability of the clinical results.

In this talk, I will therefore cover the following points:

- Advantages and inconvenients of fcMRI, in particular for clinical studies

- Methodological approaches: seed-based, ICA, graph theory, multi-modal analysis: what information they provide, and what their comparative merits and disadvantages are – clinical examples

- Selected fcMRI literature on: mild cognitive impairment and Alzheimer's disease, movements disorders, neuropsychiatric disorders

- Combining information of fcMRI with structural connectivity or structural covariance – clinical examples

- Dangers of over-interpreting the fcMRI results (e.g., higher is not necessarily better)

- Is "disease of connectivity" the same thing as "disconnection"?

References/preparatory reading - Reviews:

- Fox, M. D. & Greicius, M. Clinical applications of resting state functional connectivity. *Frontiers in systems neuroscience* **4**, 19 (2010).

- Buckner, R. L., Krienen, F. M. & Yeo, B. T. Opportunities and limitations of intrinsic functional connectivity MRI. *Nature neuroscience* **16** (2013).

- Sheline, Y. I. & Raichle, M. E. Resting state functional connectivity in preclinical Alzheimer's disease. *Biological psychiatry* **74** (2013).

- Kleinschmidt, A. & Vuilleumier, P. Disconnecting cognition. *Current opinion in neurology* **26** (2013).

Further reading:

- Seed-based fcMRI study on Parkinson's disease: Helmich, R. C. *et al.* Spatial remapping of cortico-striatal connectivity in Parkinson's disease. *Cerebral cortex* **20** (2010).

- ICA-based fcMRI study on Alzheimer's disease (using grey matter as covariate): Zamboni, G. *et al.* Resting functional connectivity reveals residual functional activity in Alzheimer's disease. *Biological psychiatry* **74** (2013).

- Graph theory fcMRI study on schizophrenia: van den Heuvel, M. P. *et al.* Abnormal rich club organization and functional brain dynamics in schizophrenia. *JAMA Psychiatry* **70** (2013).

- Study combining fcMRI and structural covariance in five neurodegenerative disorders: Seeley, W. W., Crawford, R. K., Zhou, J., Miller, B. L. & Greicius, M. D. Neurodegenerative diseases target large-scale human brain networks. *Neuron* **62** (2009).

- Study combining fcMRI and structural connectivity in amyotrophic lateral sclerosis: Douaud, G., Filippini, N., Knight, S., Talbot, K. & Turner, M. R. Integration of structural and functional magnetic resonance imaging in amyotrophic lateral sclerosis. *Brain* **134** (2011).