

THE IMPACT OF NEUROIMAGING ON NEUROSCIENCE

Richard Frackowiak

Neuroimaging of the human brain with MRI has a number of essential advantages. From the physics viewpoint, there are no known deleterious effects which permits repeat scanning and measurement of indices in time. There are opportunities for adjusting scanning sequences to obtain tissue contrasts and properties, often with quantitative measurements and combining them in single experimental periods. Whole brain scanning, advantageous because it gives the possibility of unambiguous anatomical interpretation and of accurate normalisation can be supplemented by higher sensitivity local scanning with special antennae. These factors combine to give what is essentially *in vivo* pathology - the capacity to follow the evolution of a pathological process to tissue characterisation post-mortem. Because clinical neuroscience is classically based on making correlations between post-mortem characteristics and *in life* clinical syndromes (which evolve), the scanning technologies add precious longitudinal data to clinical neuroscience.

What lies ahead now? Has the time come to radically overhaul our epistemological approach to understanding human brain disease. We now know a great deal about brain structure and function. Additionally, advances in information technologies in the last three decades, from supercomputers to distributed and interactive databases, make integration of very large and diverse datasets and advanced data-led analysis possible. We can envisage data-mining analyses of large image datasets, to look for biologically homogeneous “constructs”, defined by common characteristics, that indicate a shared pathological mechanism, which would lead to a neuroimaging oriented redefinition of disease. Reverse engineering by clinicians will refine the new phenomenology and hence nosology of such disease constructs. This trend is already visible with the dementias, which over the last four decades have been redefined as a number of dementia-producing diseases each defined in biological terms.

That momentum for such imaging directed change is building. The ADNI initiative, generating a large database of scans from 4000 Alzheimer patients and normal subjects is typical of the proof-of-concept efforts now underway. Clinicians and scientists use the ADNI data extensively to test hypotheses, which has already generated many publications. Large databases are common in hospitals where PACS systems in radiological departments represent extended databases that could potentially be interrogated with technology such as that used by web search engines. We have tested machine-learning techniques to analyse complex data such as structural MRI images to show that they can be classified using scalable mathematical techniques to provide a way of identifying uniform diagnostic categories. Methods of combining data using multivariate analytical techniques are also becoming increasingly common in genetics-imaging experiments.

I believe that, thanks to these developments, we are now on a trajectory towards a more objective, epistemologically valid nosology that will be of benefit to doctors, patients and anyone else interested in how the brain is organised in health and disease.

References

1. <http://www.adni-info.org/>
2. <http://www.adni-info.org/Scientists/ADNIScientistsHome/ADNIPublications.aspx>
3. <http://bluebrain.epfl.ch/>
4. http://en.wikipedia.org/wiki/Blue_Brain_Project
5. <http://www.humanbrainproject.eu/index.html>
6. Tan GCY, Doke TF, Ashburner J, Wood NW, Frackowiak RSJ. (2010) Normal variation in fronto-occipital circuitry and cerebellar structure with an autism-associated polymorphism of CNTNAP2. *NeuroImage* 53, 1030–1042.
7. Knyazeva MG, Carmeli C, Fornari E, Meuli R, Small M, Frackowiak RSJ, Maeder P. (2011). Binding under conflict conditions: State-space analysis of multivariate EEG synchronization. *Journal of Cognitive Neuroscience*, 23: 2363-2375.
8. Stonnington CM, Chu C, Klöppel S, Jack Jr CR, Ashburner J, Frackowiak RSJ. (2010) Predicting clinical scores from magnetic resonance scans in Alzheimer's disease. *NeuroImage* 51: 1405-1413.
9. Draganski B, Schneider SA, Fiorio M, Klöppel S, Gambarin M, Tinazzi M, Ashburner J, Bhatia KP, Frackowiak RSJ (2009) Genotype-phenotype interactions in primary dystonias revealed by differential changes in brain structure. *Neuroimage*. 47, 1141-47.
10. Klöppel S, Stonnington CM, Chu C, Draganski B, Scahill RI, Rohrer JD, Fox NC, Jack CR, Ashburner J, Frackowiak RSJ. (2008) Automatic classification of MR scans in Alzheimer's disease. *Brain* 131, 681-689.
11. Gurling HM, Critchley H, Datta SR, McQuillin A, Blaveri E, Thirumalai S, Pimm J, Krasucki R, Kalsi G, Quedsted D, Lawrence J, Bass N, Choudhury K, Puri V, O'Daly O, Curtis D, Blackwood D, Muir W, Malhotra AK, Buchanan RW, Good CD, Frackowiak RSJ, Dolan RJ. (2006) Genetic association and brain morphology studies and the chromosome 8p22 pericentriolar material 1 (PCM1) gene in susceptibility to schizophrenia. *Arch. Gen. Psychiatry* 63, 844-54.