**Predicting MRI abnormalities with longitudinal data of the Whitehall II Substudy**

DPhil project – Supervisors: Dr Clare Mackay and Prof Klaus Ebmeier

The programme combines multi-modal imaging and cutting edge analysis of brain structure, brain perfusion, white matter integrity and brain function with a rich longitudinal data set, the Whitehall II cohort. Twenty-five year antecedent vascular and metabolic risk trajectories and morbidity, antecedent levels of physical and mental activity, baseline cognitive performance levels and 15-year slopes of memory decrement over time, history of depressed mood, genotype, and measured resilience will be used to model brain changes in 800 subjects. Hypotheses are predicated on the assumption that the brain responds adaptively to any age or illness-related lesion with compensating functional reorganization and repair that result in the restitution of cognitive and mental function and behaviour. Damage to this 'scaffolding structure', e.g. by widespread vascular damage to executive brain networks, will lead to decompensation of function, and result in clinical presentation with e.g. dementia or depression. We thus predict that highly functioning individuals may show structural or functional lesions in e.g. hippocampal networks, associated with an increase in activity in scaffolding (e.g. executive) networks. We further predict that such active protective mechanisms will be dependent on such antecedents as vascular risk related behaviour and (mental) activity, in addition to other factors less amenable to treatment and prevention. The presence of detailed and frequently sampled cohort data in the Whitehall II study allows for a unique prospective analysis of the effects of socio-demographic, physical and behavioural factors on brain integrity, and a powerful study design strategy that makes it possible to compare the two extreme expressions of a clinical feature (e.g. depression with first onset in the 60s versus no depressive symptoms over at least 25 years), by controlling and stratifying for potential confounders, such as the conventional variables age, gender and occupational level, but also crucial mechanistic factors, such as vascular risk. Short of a prospective interventional study this will be the most effective and efficient way of establishing time directed associations between socially important variables and brain structure and function in older age. Considering the crucial importance that the growing group of active over 60 year olds will have in society, and the effect that a small shift from disabled to able people will have in this part of society, this is important research.

We would be interested in hearing from strong candidates who would like to pursue one or more of these projects, or those who would like to develop their own ideas within our group. For more information about current projects please see our website: www.fmrib.ox.ac.uk/psychiatry

All of our projects would involve neuroimaging either in healthy or patient populations. Candidates should have a good degree in the field of neurobiology (Psychology, Neuroscience, Biology etc) and be technically competent. We would also be interested in hearing from candidates with technical backgrounds (Physics, Maths, Engineering etc) who have a strong interest in neuroscience.

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