Improving Diagnosis And Measurement Of Progression In Dementia: Longitudinal Clinical And MRI Studies

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Title of project or programme

Improving Diagnosis And Measurement Of Progression In Dementia: Longitudinal Clinical And MRI Studies

Principal Investigators of project/programme grant

Title	Forname	Surname	Institution	Country
Professor	Nick	Fox	University College London	UK

Address of institution of lead PI

Institution	Institute of Neurology, University College London
12 Queen Square Hills Road	
City	London
Postcode	WC1N 3BG

Country

United Kingdom

Source of funding information

Medical Research Council

Total sum awarded (Euro)

1365479.53

Start date of award

01-09-2007

Total duration of award in months

60

The project/programme is most relevant to

- Alzheimer's disease and other dementias
- Prion disease
- Huntington's disease

Keywords

Research abstract in English

Aims/objectives " Achieve earlier and more precise diagnosis in Alzheimer's disease (AD) and related disorders, including pre-clinical detection of disease; " Improve understanding of the pathophysiological evolution of neurodegenerative diseases and the relationships between imaging and clinical manifestations; " Measure disease progression, and assess its correlates and influences; " Evaluate symptomatic and potentially disease-modifying therapies. Design/methods Measures of cerebral change will be improved by optimising MRI acquisition reproducibility and post-acquisition artefact correction. Optimised protocols and artefact correction will be developed for 3T phased array acquisitions for 3D T2-weighted as well as T1-weighted volumetric studies. Linear and non-linear registration will be used to match imaging studies across modality and over time.

Registration-based measures of atrophy rates will be further developed – and different approaches critically compared and the topography of progression will be assessed. The precision of measures will be improved with multiple time point imaging. Registration and quantification techniques will be developed that fully incorporate multiple time point studies, fitting the time series rather than each pair of scans independently. I will determine the minimum scan-interval needed for serial MRI to a) detect and b) distinguish neurodegenerative disorders. I will pursue the potential for reduced sample sizes in trials by reducing within-subject variability in atrophy rate measures and investigating run-in designs.

I will further develop registration-based methods for quantifying progression of regional and global atrophy and parenchymal change and for measurement of cortical thickness changes: for these aims I will investigate combined serial 3D T2-weighted and T1-weighted imaging. I will combine and correlate atrophy measures with CSF markers and amyloid imaging (C11-PIB- PET) to determine the topography and association between amyloid deposition and neuronal loss. I will also correlate imaging changes with neuropsychometry to understand the temporal and topographical association between neuronal loss, amyloid deposition and cognition.

I will apply these techniques to well-characterised clinical cohorts with established disease and also to individuals at risk of familial AD, prion, Huntington's and fronto-temporal dementia. These cohorts offer a unique opportunity to study pre-symptomatic disease. Additionally I will study mild cognitive impairment (MCI) and subjects who have amnestic complaints but do have a sufficient memory deficit to fulfil criteria for MCI (which may represent a pre-MCI stage).

This programme of research offers clinical as well as scientific opportunities in the dementias but should also have relevance to other disorders where precise and yet easily applicable measurements of cerebral changes are important.

Lay Summary