MRes in Translational Neurology
UCL Institute of Neurology
Abstracts of 2014-15 Research Projects
Inducing white matter microstructural change in Huntington’s disease using real-time fMRI neurofeedback training.

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Abstract:
Introduction: Huntington’s disease (HD) is characterised by progressive decline of motor, cognitive and behavioural function. Despite the early appearance of brain atrophy and connectivity loss being a major feature in disease pathology, HD gene mutation carriers remain symptom free for many years, suggesting the presence of compensatory mechanisms embedded in the brain. Real-time fMRI (rt-fMRI) neurofeedback training (nf-training), a novel non-invasive therapy being developed with the intent to harness these compensatory processes, was used in a pilot study in HD patients.

Objective: To measure plasticity-related microstructural changes in white matter (WM) that occur after one month of nf-training using Diffusion Tensor Imaging (DTI).

Methods: Analysis of diffusion weighted images involved using FSL for image pre-processing and tensor fitting, DTI-TK for spatial normalisation and TBSS for statistical analysis. Changes in structural connectivity were quantified using tractography.

Discussion: Our hypothesis is that WM density and structural connectivity in regions modulated by nf-training will increase. An increase in WM density will be indicated by an increase in fractional anisotropy and decrease in mean diffusivity. The results of this project will provide preliminary evidence on plasticity induced by rt-fMRI nf-training, as well as the underlying mechanism of nf-training.
Evaluating the use of the online Bradykinesia-Akinesia Incoordination (BRAIN) test in Parkinson’s disease in “On” and “Off” states

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Background
The BRAIN test is an online computer tapping task that has previously been validated and can differentiate individuals with Parkinson’s disease from healthy controls and also correlate with PD severity measured by disease-specific rating scales (Noyce ref). Motor fluctuations and wearing off symptoms develop in 40% of patients after 4-6 years and around 70% of patient after 9 years of dopaminergic therapy [1].

Aims
To evaluate the use of the BRAIN test as a test of upper limb motor function in individuals with Parkinson’s disease in the “On” and “Off” states

Methods
Validation of the online BRAIN test was undertaken in 62 patients with moderate stage Parkinson’s disease (Hohn and Yahr < 2.5) in the “On” state and the “Off” state. Kinesia scores (KS30), akinesia times (AT30), incoordination scores (IS30) and dysmetria scores (DS30) were compared between the two states. These parameters were also correlated against disease specific rating scale.

Results
Mean BRAIN test subscores were significantly different and correlated with disease rating scales between patients in their “On” and “Off” states.

Conclusions
This test may be used by patients in outpatient clinics or home settings to aid clinicians help identify motor fluctuations which may be used to guide future management, or by extrapolation, may help measure severity of bradykinesia for use in clinical trials.
Behavioural variant Frontotemporal Dementia (bvFTD) is a progressive neurodegenerative disease characterised by changes in personality, cognition and behaviour. Significant changes in eating behaviour, such as overeating and craving sweet foods, have also been found to affect over 80% of bvFTD sufferers. The hypothalamus is an important centre for feeding regulation, and previous studies have linked hypothalamic degeneration to feeding disturbance in FTD. This project aims to develop a targeted multiple reaction monitoring (MRM)-based mass spectrometric assay to measure 20 different hypothalamic and peripheral peptides and proteins that have been shown to regulate feeding behaviour, then use the assay to measure the levels of these peptides in cerebrospinal fluid (CSF) from bvFTD patients. We will also investigate the relationship between CSF peptide levels and behavioural measures in bvFTD patients. This work will provide important information about the neurobiology of FTD, especially the causes behind altered eating habits affecting the majority of bvFTD sufferers. The results may provide a route for therapies in FTD as well as identify new biomarkers that could help with the diagnosis and stratification of FTD.
James Parrott - Abstract

Introduction: The density of neurofibrillary tangles, made up of hyperphosphorylated tau, has been found to correlate strongly with disease burden. A PET tracer called T807 has been produced that allows imaging of this pathological tau, however the properties of this tracer has produced mix reports. Using the fluorescent analogue T726, the objective is to determine which inclusions in what disease binds to this tracer to understand which diseases the radioactive version can be used for.

Method: Fluorescence microscopy will be used in combination with thioflavin-s to identify the pathologies present and T726 to establish reactive inclusions in the tissue of Alzheimer's Disease (AD), Progressive Supranuclear Palsy (PSP), Corticobasal Degeneration (CBD), Pick's Disease (PiD) and Frontal Temporal Dementia with Parkinsonism 17 MAPT & TDPA (FTDP-17MAPT, FTDP-17TDPA). Quantification properties of T726 will then be investigated.

Results: Thioflavin-S staining has shown what pathologies are present in each disease and neurofibrillary tangles and neuropil threads can be visualised in the grey matter of AD. T726 binds to paired helical filaments, binds 3R tau and potentially 4R tau and can differentiate AD and PiD from healthy tissue in the grey matter of the frontal lobe. T726 does not react with TDP.

Discussion: The results suggest that the radioactive tracer T807 will be very useful clinically for AD and PiD, allowing staging and increase accuracy in diagnosis of these two diseases. Cross-reactivity is not an issue.