Title: Neuroplasticity of the visual cortex in multiple sclerosis

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**Background:** Multiple Sclerosis (MS) is the most common disabling neurological disease affecting young people. The cause of MS still remains unknown, but the mechanisms leading to disability have been identified. Demyelination and neuroaxonal loss are held responsible for the patients’ symptoms. Clinically it has long been recognized that some patients make an excellent recovery from disease attacks (relapses) whilst other progress inexorably. Development of disability in an individual patient likely depends on the balance between neurodegeneration and neuroplasticity. We and others found that the post-translational modifications of de- and regeneration in MS leave a molecular signature on proteins. For practical reasons we propose to investigate this signature within the visual system of MS patients who suffered during life from optic neuritis and donated their brain to the MS tissue bank.

**Methods:** Neuroimmunological (UCL) and functional (NIH/NINDS) experiments on proteins involved in neuroplasticity (e.g. neurofilaments). Patient material selection: during post-mortem optical coherence tomography (OCT) of the retina will be performed to identify areas with loss of retinal nerve fibre (RNFL). The corresponding retinotopic areas in the visual cortex will dissected from the post-mortem brain tissue. Matched brain tissue from patients with multiple sclerosis who did not suffer from impaired visual function and from patients who did not suffer from any neurological disease in whom OCT of the retina is normal will serve as control. We propose to study the post-translational modifications of neurofilament proteins (e.g. phosphorylation, citrullination) and other candidate protein biomarkers in micro-dissected brain slices using neuroimmunological, neurochemical and immunohistochemical techniques at UCL. The data generated by this part will be refined using quantitative phospho- mass spectrometry at the NIH/NINDS. This will allow narrowing of the spectrum of enzymes to be inhibited in order to minimize neurodegeneration or to activate in order to support neuroplasticity. Functional experiments of these enzymes on the candidate proteins will be performed using state of the art proteomic facilities at the NIH/NINDS or UCL according to the candidates' preference and future career objectives.

**References**

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