Neurology

https://neurodegenerationresearch.eu/survey/neurology-2/

Principal Investigators

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Institution

Imperial College London

Contact information of lead PI
Country

United Kingdom

Title of project or programme

Neurology

Source of funding information

MRC

Total sum awarded (Euro)

€ 2,013,973

Start date of award

05/05/2011

Total duration of award in years

5.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias|Parkinson's disease & PD-related disorders|Huntington's disease

Keywords
Research Abstract

This programme, based at Imperial College London, targets the use of positron emission tomography (PET) to image the functional changes associated with Alzheimer‘s, Parkinson‘s, and Huntington‘s diseases. In subjects who have amnestic mild cognitive impairment and so are at risk of progressing to dementia the time course of amyloid deposition and microglial activation (inflammation) and relationship between these pathologies is being examined. Brain imaging findings with PET are being correlated with amyloid and cytokine levels in spinal fluid and

plasma proteomic profiles. The time course and pattern of amyloid deposition in carriers of gene mutations predisposing to Alzheimer‘s disease (presenelin and APP) is also being tracked. The efficacy of anti-amyloid strategies such as passive immunotherapies is being trialled using PET amyloid imaging as a proof of mechanism. Parkinson‘s disease (PD) patients with memory or gait difficulties are also at risk of developing dementia. Again, the prevalence of cortical microglial activation and amyloid deposition in these high risk cases and the relationship between these pathologies is being examined. Asymptomatic LRRK2 and glucocerebrosidase A gene mutation carriers at risk for PD are also being ascertained to determine the time course of inflammatory changes in the brainstem. PD is also associated with other non-motor problems such as sleep disorders, fatigue, depression, and impusle control disorders. PET is being used to study the relative contributions of brainstem and limbic dopaminergic and serotonergic dysfunction to these syndromes in PD in the belief that it may throw light on the mechanisms underlying these problems in the general population. The implantation of fetal midbrain cells into the putamen of advanced PD patients has previously been associated with variable efficacy and disabling graft-associated involuntary movements (dyskinesias). We are studying the mechanisms underlying development of thesias. Additionally, a trial using PET to measure graft function in transplanted patients with early rather than advanced PD is underway. Huntington‘s disease (HD) gene carriers inevitably develop symptoms but it is now possible to detect functional changes with PET some years ahead of clinical disease manifestation. The programme is examining the time course of striatal microglial activation in asymptomatic HD gene carrtiers and how this correlates with spinal fluid and plasma levels of cytokines and other inflammatory markers. The role of cannabinoid CB1 radioligands as markers of striatal degeneration in HD is also being explored. In summary, this MRC programme is designed to determine the efficacy of functional imaging as a prognostic biomarker of dementia, to determine the role of microglial activation in driving neurodegeneration, and to provide proof of mechanism when putative neuroprotective and restorative therapies are being trialled.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
United Kingdom

Diseases:
Alzheimer's disease & other dementias, Huntington's disease, Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

Database Tags:
N/A