Leucine-rich repeat kinase 2 expression in postmortem Parkinson’s disease brain

Dzamko1, N., Nichols2, J., Holten3, J., Van de Berg4 W., Takao5, M., Murayama5, S., and Halliday1, G.

1. Neuroscience Research Australia, University of NSW, Sydney, Australia
2. The Parkinson’s Institute, Sunnyvale, California, USA
3. Institute of Neurology, University College London, London, UK
4. Neuroscience Campus Amsterdam, VU University, Amsterdam, Netherlands.
5. Department of Neurology, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan.

Research question and background
Missense mutations in Leucine-Rich Repeat Kinase 2 (LRRK2) are a leading cause of inherited Parkinson’s disease. The most common Parkinson’s disease causing LRRK2 mutation increases the protein’s activity, and drugs that block LRRK2 have subsequently been developed as a potential Parkinson’s disease treatment. Whether LRRK2 is altered in more common sporadic Parkinson’s disease cases however, is unknown. Our project aims to measure LRRK2 protein in postmortem sporadic Parkinson’s disease brain tissue samples and determine if LRRK2 is altered and if/how such alterations may contribute to the disease process. This information will aid in determining if LRRK2 blocking drugs can be used to treat sporadic Parkinson’s disease.

Methods and tissues used
For this Michael J Fox Foundation funded project, Parkinson’s disease brain tissue has been sourced from The Sydney Brain Bank (Australia), Queen’s Square Brain Bank (UK), Tokyo Brain Bank for Ageing Research (Japan), The Parkinson’s Institute (USA) and the Netherlands Brain Bank. The following groups have been established - Long duration sporadic PD (n=24), short duration sporadic PD (n=12), preclinical PD (n=28) and neurologically normal matched controls (n=28). From these four groups four different brain regions have been selected for study. Substantia nigra (substantial cell loss and PD pathology), amygdala (limited cell loss and substantial PD pathology), frontal cortex (no cell loss but some PD pathology) and occipital cortex (no cell loss or PD pathology). Both Immunoblotting and immunohistochemistry are being performed to comprehensively determine the pattern of LRRK2 expression in PD brain and if/how LRRK2 changes in the brain with progressive PD pathology.

Results and conclusion
Initial studies have been performed and results are now being independently verified in a second location. The project is due for completion at the end of 2015.