Postgraduate Research Scholarship on 'Uncovering the Brain Regions underlying REM Sleep Behaviour Disorder in Parkinson's disease'

Mission To evaluate the pathological basis of sleep-wake circuitry disruption from prodromal to advanced stages of Parkinson's disease to identify novel therapeutic targets for symptoms.

PROJECT SUMMARY

Sleep disturbances collectively represent one of the earliest and most prevalent non-motor symptoms reported by patients with Parkinson's disease. For instance, REM sleep behaviour disorder, in which patients will often lose the normal paralysis of REM sleep and enact their dreams, is now regarded the strongest clinical marker of developing Parkinson's disease or Lewy body dementia, often preceding the diagnosis by many years. Despite their importance, the neuropathological underpinnings of sleep disturbances such as RBD in Parkinson's disease are poorly understood in humans and targeted therapies are lacking. In the last decade, there has been a rapid expansion in our knowledge regarding the neurobiological mechanisms underpinning sleep biology that include brain regions that switch between REM and non-REM sleep and the critical roles of neurotransmitters like orexin, histamine noradrenaline, serotonin, and dopamine in sleep disturbances. However, the impact of Parkinson's disease on these brain regions has not been assessed at a cellular level. We hypothesise that pathological changes in these key subcortical nuclei and neurotransmitter systems underlie sleep-wake disturbances in Parkinson's disease. It is anticipated that new knowledge gained from this project may be used to guide targeted and novel therapeutic approaches for sleep and cognitive symptoms in Parkinson's disease.

Group/Team Join a multi-disciplinary lab with expertise in movement disorders and sleep biology with a collective aim of understanding the pathobiology of Parkinson's disease and related conditions. You will have access to world class research facilities in the Brain and Mind Centre (BMC).

Opportunities will be provided to support travel to national and international conferences and present your findings.

Project Details

This project will focus on analysing the pathology in brain regions associated with sleep-wake cycle disturbances (subcoeruleus nucleus, ventromedial medulla, ventrolateral periaqueductal gray and hypothalamus) in prodromal to advanced stages of Parkinson's disease. The project will assess tissue brain tissue donated for research, with the expected deliverables an improved understanding of the sequence and nature of the pathology within areas of the sleep-circuitry that will allow us to infer the relationship between sleep disturbance and progression of Lewy body pathology and local cellular vulnerabilities. The findings of this work may identify novel therapeutic targets such as the orexinergic system, and depending on the degree of co-pathology, may hint at the value of combination medications targeting multiple neuromodulator/neurotransmitter systems to help alleviate sleep disturbances and fluctuations in PD.

The student will learn to use many research tools including digital imaging, microscopy, protein profiling, histopathology, statistical inference, bioinformatics, and the application of artificial intelligence. The project not only gives comprehensive training on the use of traditional histological and microscopic techniques but also provides a unique opportunity to explore globally advancing techniques, like multiplex imaging, 3D imaging, and state-of-the-art high-resolution microscopy. Training will be provided in the writing and dissemination of scientific findings through presentations and academic publications.

For further information, please contact: Elie Matar (elie.matar@sydney.edu.au), Yuhong Fu (yuhong.fu@sydney.edu.au) or Glenda Halliday (glenda.halliday@sydney.edu.au)