Biomedical Sciences
Obstructive Sleep Apnea (OSA) Model
Obstructive sleep apnea (OSA) is the most common type of sleep disruption. It affects more than 50% of the elderly adult population and occurs due to the collapse of the upper airways, particularly during rapid eye movement (REM) sleep and it is usually associated with a reduction in blood oxygen saturation. OSA is a strong epidemiological risk factor for the development of dementia, but also cardiovascular disease and diabetes.

We have developed a naturalistic mouse model of OSA through selectively ablating cholinergic neurons in the brainstem with injection of a ribosomal inactivating saporin-conjugated urotensin-2 peptide (UII-SAP) in the brain. The mice replicate key features of human OSA: altered breathing during sleep, sleep disruption, moderate intermittent hypoxemia and cognitive impairment. When we induced OSA in a familial AD model, the mice displayed exacerbation of cognitive impairment and pathological features of AD, including increased levels of amyloid-beta (Aβ) and inflammatory markers, as well as selective degeneration of cholinergic basal forebrain neurons. We also revealed that the above neurodegenerative symptoms could be prevented by inhibition of neural cell death receptor p75 neurotrophin receptor (p75NTR) and/or hypoxia inducible factor 1 alpha activity (HIF1α).

It is the first naturalistic OSA mouse model in the field which otherwise uses fluxing oxygen concentrations in piped air requiring expensive hypoxia chambers and gas mixtures. Our OSA mouse display the above symptoms from two weeks after surgery, and mice can be group housed in standard cages with assessments performed at any time without disrupting OSA conditions. The model can be used to investigate the effects of sleep apnea including in vivo testing of drugs in development for a variety of chronic conditions.

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- Study of how the dysregulation of bodily processes can cause serious human disorders such as infertility, Alzheimer’s disease and autism.
- Musculoskeletal and neuromotor analyses to improve whole-body movement performance.
- Novel approaches to heal conditions such as spinal injury, motor neuron disease and cancer.