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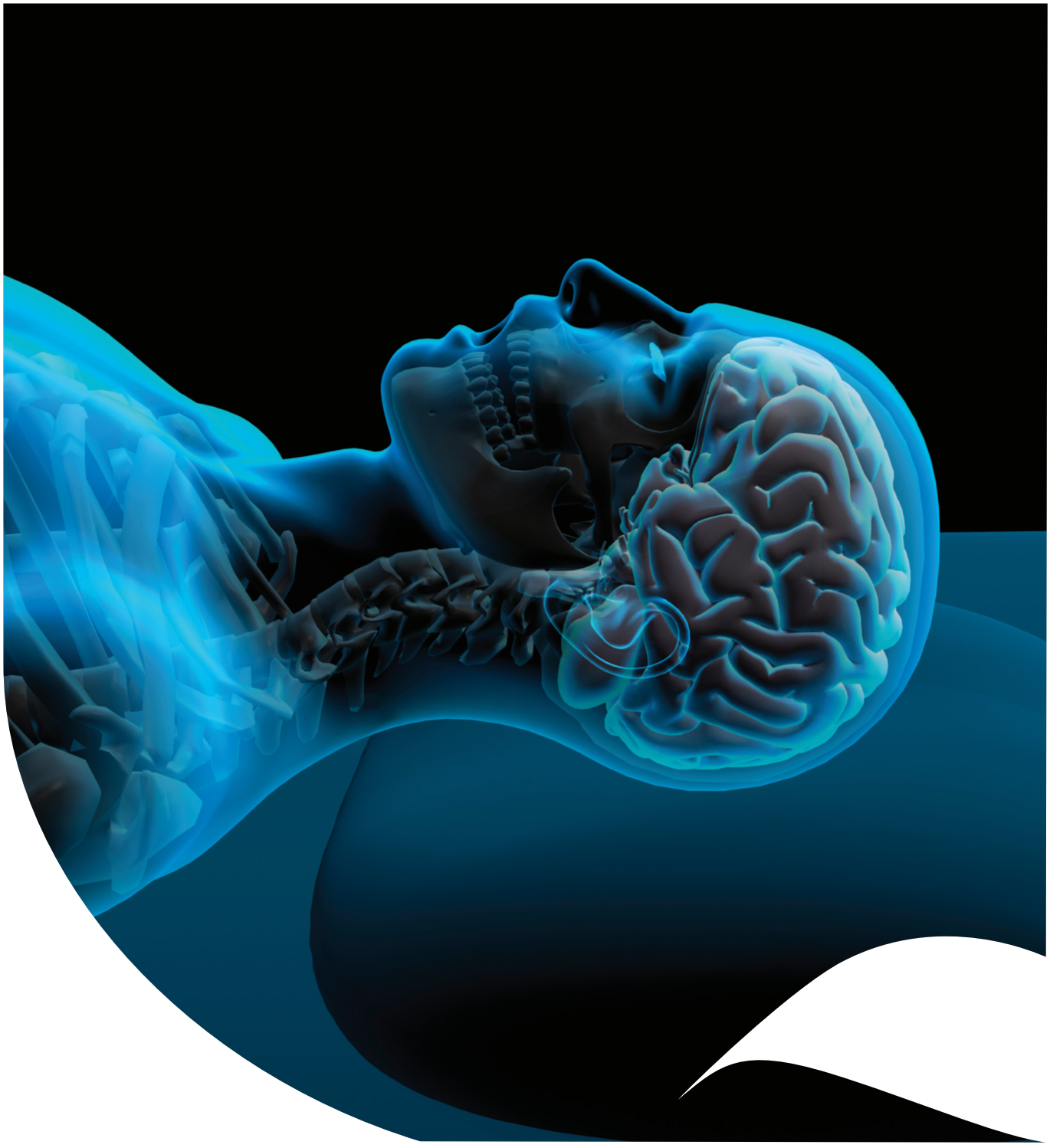
Biomedical Sciences

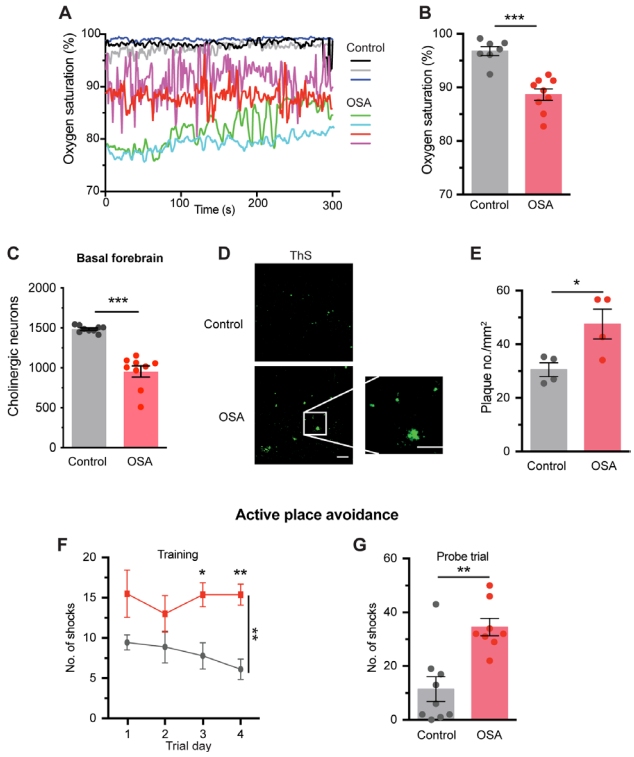
Obstructive Sleep Apnea (OSA) Model



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.



Obstructive sleep apnea (OSA) model

The Obstructive sleep apnea (OSA) mouse has altered breathing pattern and induces hypoxia.
The blood oxygen saturation is significantly reduced during the sleep period in OSA mice (A and B).

Obstructive sleep apnea exacerbates major AD hallmarks in the APP/PS1 mice.
The OSA APP/PS1 mice had lesions of cholinergic basal forebrain (C) and significantly increased levels of thioflavin S-positive Aβ plaques (D and E) in the cortex.

Obstructive sleep apnea exacerbates cognitive impairment in the APP/PS1 model.
The OSA APP/PS1 mice received significantly more shocks on the last two training days (F) and during the probe trial of the active place avoidance test (G).

UQ's School of Biomedical Sciences

The University of Queensland's School of Biomedical Sciences is making ground-breaking advances in modern medical science and providing students with the theoretical and practical skills for an exciting career in academia and industry. Our innovative research encompasses the research spectrum from basic discovery through translational pathways to medical solutions, including:

- Investigation of cellular processes such as protein trafficking, cell signalling and organelle function.
- 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.

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