Chronic intermittent hypoxia aggravates neurocognitive decline in an animal model of Alzheimer’s disease

Lida Du¹², Chun Kwan O¹², Linting Geng¹², Linhao Xu³, Ya Ke¹², Wing Ho Yung¹²

¹School of Biomedical Sciences, The Chinese University of Hong Kong, Hong Kong. ²Gerald Choa Neuroscience Centre, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong. ³Department of Anatomy, Hangzhou Medical College, China

Aims: Alzheimer’s disease (AD), characterized by progressive cognitive deficit, is a major neurodegenerative disease that affects tens of millions of patients worldwide. Obstructive sleep apnea (OSA) is another common pathological condition that has been implicated to be causally related to AD. This study aims to explore the impact of OSA-associated chronic intermittent hypoxia (CIH) on the pathogenic process in AD transgenic mice, and possible role played by endoplasmic reticulum (ER) stress. Methods: 3xTg-AD transgenic mice were treated by changing environmental oxygen levels between 10% to 21% for 8 hours per day for 4 weeks to mimic OSA-associated CIH. Control AD mice were exposed to normal oxygen level. Recognition memory and hippocampal long-term potentiation (LTP) were then assayed. The effect of an ER stress inhibitor GSK2606414 was also tested. Results: Recognition memory impairments were aggravated in AD mice receiving 4 weeks of CIH treatment, which was paralleled by increased impairment in LTP of the CA3-CA1 pathway. Interestingly, daily administration of GSK2606414 ameliorated LTP reduction in CIH-treated AD mice. Conclusions: Our results suggested that CIH could accelerate neurocognitive decline in AD transgenic mice. ER stress may participate in this process.