

# Sleep apnea leading to Parkinson's disease – an important association

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## Dear editor

We read with great interest the recently published article “Sleep apnea and the subsequent risk of Parkinson disease: a 3-year nationwide population-based study” by Chou et al.<sup>1</sup> The study is a step forward in understanding the underlying pathophysiology of Parkinson's disease, the authors have deduced sleep apnea as one of the possible risk factors.

Parkinson's disease is a disorder of the central nervous system (CNS) causing depletion of cells (dopaminergic neurons) in the part of the brain that controls movement (specifically substantia nigra). People with Parkinson's disease experience a wide range of symptoms, which include: tremor (shaking), rigidity/slowness of movement, and postural instability due to problems with balance and coordination. The potential risk factors for Parkinson's disease, in addition to increasing age and sex are: family history positive for Parkinson, depression, constipation, and sleep disorders.<sup>2</sup>

According to the review article “Sleep disturbances associated with Parkinson's disease” published in 2011 by Suzuki et al, sleep disturbances are a documented risk amongst people with non-motor symptoms with a prevalence ranging from ~40%–90%.<sup>2</sup> Evidence from previous studies suggest that the chronic intermittent hypoxia, and possibly sleep loss and fragmentation associated with sleep apnea, increase the levels of various markers of inflammation and cause oxidative stress.<sup>3,4</sup> Studies have demonstrated that oxidation promotes  $\alpha$ -synuclein oligomerization in cells.<sup>3,4</sup> Aggregation and neurotoxicity of misfolded  $\alpha$ Syn are crucial mechanisms for progressive dopaminergic neuro-degeneration associated with Parkinson's disease.<sup>5</sup> From these studies one can deduce that sleep apnea-induced hypoxia causes oxidative stress which leads to aggregation of  $\alpha$ Syn – one of the possible mechanisms of neuron cell loss.

In this retrospective cohort study Chou et al intended to demonstrate a possible temporal association between sleep apnea and Parkinson's disease. The study revealed that after adjustment of possible confounders, the risk of developing Parkinson's disease in the sleep apnea cohort was 1.85 folds higher than in the non-sleep apnea cohort. It was further analyzed that women and young males did not exhibit a significantly increased risk of Parkinson's disease in sleep apnea cohort compared to those in the non-sleep apnea cohort during the 3-year follow-up period. According to the results of this cohort study, sleep apnea is an age- and sex-dependent longitudinal risk factor for Parkinson's disease in elderly men.

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We suggest that further well-designed longitudinal and interventional studies of longer duration are needed to demonstrate a causal link between Parkinson's disease and sleep apnea and should take into account other common confounding variables to assess specific mechanisms that could explain this association. Furthermore, prospective studies should be conducted in the future in order to establish the underlying definitive pathophysiological mechanism of developing Parkinson's disease.

## Disclosure

The authors report no conflicts of interest in this communication.

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