Dysregulation in orexinergic system associated with Alzheimer disease

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In patients with Alzheimer disease (AD), increased cerebrospinal fluid levels of orexin, which helps regulate the sleep-wake cycle, may be associated with sleep deterioration, which appears to be associated with cognitive decline.

AD is a neurodegenerative disease marked by progressive memory loss and cognitive decline and often complicated by sleep disturbance. Orexin A is part of the orexinergic system and it helps regulate the sleep-wake cycle by increasing arousal levels and maintaining wakefulness. A relationship between the orexinergic system and the AD neurodegenerative process has been examined in a few studies with conflicting results.

The authors sought to evaluate the possible involvement of the orexinergic system by measuring CSF orexin levels in untreated AD patients and comparing them with healthy controls, as well as examining the role of the orexinergic system in sleep impairment in patients with AD. They measured CSF levels of orexin, the AD biomarkers tau proteins and ?-amyloid 1-42, as well as assessing sleep variables (including total sleep time, sleep efficiency, sleep onset, rapid eye movement [REM] and non-REM sleep stages). The study from August 2012 through May 2013 included 48 untreated patients: 21 patients were included in the mild AD group and 27 were classified as having moderate to severe AD. There also was a group of 29 healthy controls.

Patients with moderate to severe AD presented with higher average orexin levels compared with controls and they had more impaired sleep compared with controls and patients with mild AD. In the overall AD group, orexin levels were associated with total tau protein levels and sleep impairment. Cognitive impairment was associated with sleep deterioration.

"Our study has shown that, in AD, increased CSF orexin levels are linked to a parallel sleep deterioration, which appears to be related to cognitive decline. Hence, our results demonstrate that, in AD, orexinergic output and function seem to be overexpressed with disease progression and severity, possibly owing to an imbalance in the neurotransmitter networks regulating the wake-sleep cycle toward the orexinergic system promoting wakefulness."

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