Chronic sleep disturbance could trigger onset of Alzheimer's

18 March 2014

People who experience chronic sleep disturbance—either through their work, insomnia or other reasons—could face an earlier onset of dementia and Alzheimer's, according to a new pre-clinical study by researchers at Temple University.

"The big biological question that we tried to address in this study is whether sleep disturbance is a risk factor to develop Alzheimer's or is it something that manifests with the disease," said Domenico Praticò, professor of pharmacology and microbiology/immunology in Temple's School of Medicine, who led the study.

Initially, the researchers looked at longitudinal studies which indicated that people who reported chronic sleep disturbances often developed Alzheimer's disease.

For the study, they used a transgenic Alzheimer's mouse model that begins developing memory and learning impairment at about one year—the equivalent of a human that is mid-50-60 years in age—and at 14-15 months have the typical human brain pathology of Alzheimer's, including amyloid plaques and tau protein tangles, the two major brain pathological/lesion signatures for the disease.

The eight week study began when the mice were approximately six months old, or the equivalent of an adult human in their 40s. One group of mice was kept on a schedule of 12 hours of light and 12 hours of darkness, while a second group was subjected to 20 hours of light and only four hours of darkness, greatly reducing their amount of sleep.

"At the end of the eight weeks, we didn't initially observe anything that was obviously different between the two groups," said Pratic?, who is also a member of Temple's Center for Translational Medicine. "However, when we tested the mice for memory, the group which had the reduced sleep demonstrated significant impairment in their working and retention memory, as well as their learning ability."

The researchers then examined the mice's brains to look at the different aspects of the Alzheimer's pathology—mainly the amyloid plaques and tau protein tangles.

"Surprisingly, we didn't see any difference between the two groups in the amyloid plaques," noted Pratic?. "However, we did observe that the sleep disturbance group had a significant increase in the amount of tau protein that became phosphorylated and formed the tangles inside the brain's neuronal cells."

Tau protein acts as an important component for neuronal cell health, but elevated levels of phosphorylated tau can disrupt the cells' synaptic connection or ability to transport a nutrient/chemical or transmit an electrical signal from one cell to another, said Praticò.

"Because of the tau's abnormal phosphorylation, the sleep deprived mice had a huge disruption of this synaptic connection," he said. "This disruption will eventually impair the brain's ability for learning, forming new memory and other cognitive functions, and contributes to Alzheimer's disease."

Pratic? said that since the sleep deprived mice developed the Alzheimer's brain pathology earlier than the mice who were not deprived, sleep disturbance acts as a trigger that accelerates the pathological process of tau becoming phosphorylated and irreversibly damaging the synaptic connection.

"We can conclude from this study that chronic sleep disturbance is an environmental risk factor for Alzheimer's disease," he said. "But the good news is that sleep disturbances can be easily treated, which would hopefully reduce the Alzheimer's risk."

More information: The researchers published their findings, "Sleep deprivation impairs memory, tau metabolism and synaptic integrity of a mouse model of Alzheimer's disease with plaques and tangles," in the journal *Neurobiology of Aging*.

Provided by Temple University