# Animal study suggests inadequate sleep may exacerbate cellular aging in the elderly

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Researchers at the University of Pennsylvania School of Medicine have shown that the unfolded protein response, which is a reaction to stress induced by sleep deprivation, is impaired in the brains of old mice.

The findings suggest that inadequate sleep in the elderly, who normally experience sleep disturbances, could exacerbate an already-impaired protective response to protein misfolding that happens in aging cells. "Protein misfolding and aggregation is associated with many diseases like Alzheimer's and Parkinson's," notes first author Nirinjini Naidoo, PhD, Assistant Professor in the Division of Sleep Medicine. The study appears in the June issue of the *Journal of Neuroscience*.

The unfolded protein response (UPR) is one part of the quality control system for monitoring protein synthesis in the endoplasmic reticulum, the cellular compartment where some proteins are made. In this study, researchers found that the UPR was activated in 10-week old, sleep-deprived mice, so that misfolded proteins did not accumulate in the endoplasmic reticulum of brain cells in the cerebral cortex. However, in two-year-old, sleep-deprived mice, the UPR failed to do its job and misfolded proteins clogged the endoplasmic reticulum. Old mice that were not stressed by sleep deprivation were shown to already have an impaired UPR.

Sleep in mice is characterized by short periods of inactivity throughout the day and night. On average, mice sleep approximately one hour for every two they are awake. In order to deprive mice of sleep, researchers

constantly monitored and gently stroked the mice with a brush to disturb periods of inactivity.

At 3, 6, 9, or 12 hours of sleep deprivation, proteins were examined from the mouse brains. By six hours of sleep deprivation, young mice demonstrated that the UPR system was in place because protein synthesis was shut off by a chaperone protein called BiP/GRP78. In contrast, there was no BiP/GRP78 in old mice so protein synthesis continued.

Old mice also had less of the proteins that refold abnormal proteins than young mice, and old mice had more of the proteins that cause cell death than young mice. Thus, several processes are upset in old mouse brains by sleep deprivation, and the overall result is a further accumulation of misfolded proteins.

"We could speculate that sleep disturbance in older humans places an additional burden on an already-stressed protein folding and degradation system," says Naidoo.

Future studies will examine whether augmenting key protective proteins delays the effects of aging and reduces sleep disturbances.

Source: University of Pennsylvania School of Medicine