Sleep deprivation and the Alzheimer’s disease phenotype

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Recent studies have highlighted the frequency of sleep disturbances in Alzheimer’s disease (AD). However, whether they are secondary to the disease or per se increase the risk of dementia and AD remains to be investigated. The aim of the current investigation was to study the effect of sleep deprivation (SD) on the development of AD phenotype in a transgenic mouse model with plaques and tangles, the 3xTg mice. Compared with controls, behavioral assessment showed that SD-treated mice had a significant decline in their learning and memory abilities. While no differences were detected in the levels of soluble Aβ peptides, the same animals displayed a decrease in tau phosphorylation, which associated with a significant increase in its insoluble fraction. In addition, we observed that SD resulted in lower levels of post-synaptic density protein 95 and increased glial fibrillary acidic protein levels. Finally, while total levels of the transcription factor CREB was unchanged its phosphorylated form was significantly diminished in brains of sleep-deprived mice when compared with controls. Our findings underline the importance of SD as a chronic stressor which by exacerbating biochemical processes influences the development of memory impairments and AD neuropathologies. Correction of SD could be a viable therapeutic strategy to prevent the onset or slow the progression of AD in individuals bearing this risk factor.

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