The pathological mechanisms of gender and menopause factors influencing cognitive impairments in Alzheimer's mice: role of autonomic nervous system and sleep.

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Background: Previous studies indicated that the risk of dementia differs by gender. Prevalence of dementia is higher and the symptoms are more severe in women after menopause, which may suggest the beneficial effect of estrogen. The underlying pathogenic mechanism, however, have not been investigated clearly. The preliminary results from our laboratory showed that male Alzheimer's disease transgenic (APP/PS1) mice have had sleep problems and autonomic dysfunction before cognitive decline.

Aims & Objectives: We aimed to investigate the pathophysiological mechanism of gender and menopause factors influencing cognitive impairment, as well as investigate the protective role of estrogen in Alzheimer's disease transgenic (APP/PS1) mice.

Methods: Male and female APP/PS1 mice underwent ovariectomy or sham surgery and received estrogen or vehicle at 16 weeks old and were recorded 24-hour physiological signals per week for 2 weeks continuously. Moreover, the cognitive function and β-amyloid levels were measured.

Results: Compared with female sham-operated wild-type mice, the high-frequency power (HF) of heart rate variability in female ovariectomized wild-type mice decreased. Moreover, while APP/PS1 mice have had sleep fragmentation problem, female ovariectomized APP/PS1 mice got further worse. By the treatment of estrogen, the HF power increased and the number of sleep-wake transition decreased. Besides, APP/PS1 mice had lower delta power during sleep compared with wild-type mice, and after ovariectomized, it got further decreased but not statistically significant. In addition, trend of memory deficits were observed in female ovariectomized mice in the Morris water maze test.

Discussion & Conclusion: After menopause, women have autonomic dysfunction and sleep fragmentation, as well as poorer sleep quality. The early treatment of estrogen, however, may improve the parasympathetic function and the sleep quality of postmenopausal women, and delay Alzheimer's dementia.