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## Combined effects of aerobic exercise and 40-Hz light flicker exposure on early cognitive impairments in Alzheimer's disease of 3×Tg mice

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### Abstract

Alzheimer's disease (AD) is a progressive degenerative brain disease and the primary cause of dementia. At an early stage, AD is generally characterized by short-term memory impairment, owing to dysfunctions of the cortex and hippocampus. We previously reported that a combination of exercise and 40-Hz light flickering can protect against AD-related neuroinflammation, gamma oscillations, reduction in A $\beta$ , and cognitive decline. Therefore, we sought to extend our previous findings to the 5-mo-old 3×Tg-AD mouse model to examine whether the same favorable effects occur in earlier stages of cognitive dysfunction. We investigated the effects of 12 wk of exercise combined with 40-Hz light flickering on cognitive function by analyzing neuroinflammation, mitochondrial function, and neuroplasticity in the hippocampus in a 3×Tg-AD mouse model. Five-month-old 3×Tg-AD mice performed 12 wk of exercise with 40-Hz light flickering administered independently and in combination. Spatial learning and memory, long-term memory, hippocampal A $\beta$ , tau, neuroinflammation, proinflammatory cytokine expression, mitochondrial function, and neuroplasticity were analyzed. A $\beta$  and tau proteins levels were significantly reduced in the early stage of AD, resulting in protection against cognitive decline by reducing neuroinflammation and proinflammatory cytokines. Furthermore, mitochondrial function improved, apoptosis was reduced, and synapse-related protein expression increased. Overall, exercise with 40-Hz light flickering was significantly more effective than exercise or 40-Hz light flickering alone, and the improvement was comparable to the levels in the nontransgenic aged-match control group. Our results indicate a synergistic effect of exercise and 40-Hz light flickering on pathological improvements in the hippocampus during early AD-associated cognitive impairment. **NEW & NOTEWORTHY** Exercising in a 40-Hz light flicker environment was more effective than exercise or 40-Hz light flicker alone. This synergistic effect may prevent cognitive dysfunction by inhibiting A $\beta$ , tau pathway, and neuroinflammation and enhancing neuroplasticity and mitochondrial functions in the hippocampus during early Alzheimer's disease.

**Keywords:** 40-Hz light flicker; Alzheimer's disease; cognitive function; exercise; hippocampus.[PubMed Disclaimer](#)

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