# How does the Alzheimer's disease brain respond to optomechanical stimuli? A narrative review

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## Abstract

Alzheimer's disease (AD) is a neurodegenerative condition with enormous social and economic impact at a global scale. Given the inefficacy of the pharmacological treatments developed so far in decelerating/blocking AD pathology, the study and development of so-called alternative (i.e., non-pharmacological) and non-invasive therapies has become one of the major focuses of biomedical research on AD in recent years. Indeed, several researchers have demonstrated the therapeutic potential of optical and mechanical (i.e., optomechanical) stimuli in brain lesions. Among them, photobiomodulation (PBM, the application of modulated red/NIR light for therapeutic purposes) and tailored ultrasonic waves applied to the brain through transcranial ultrasound stimulation (TUSS) are at the forefront of clinical interventions with the potential to improve associated neuropathology and symptomatology of AD (e.g., reduction of protein aggregates deposition in the brain, increased functional connectivity and synchronization of neuronal activity, cognitive improvements), both at the preclinical and clinical levels. However, the biologic mechanisms differentially activated/stimulated during optomechanical stimulation are far from being understood. There are no proven data about the bioavailability of the stimulus energy and their bioeffects on signaling pathways, inflammation and clearance mechanisms, as well as on how these alterations relate with the behavioral improvement observed. Thus, this review compiles and describes possible biological mechanisms and alterations through which optomechanical stimuli can be effective in mitigating AD neuropathology and clinical symptoms. The topics reviewed here will be crucial for further development in the field of alternative, noninvasive brain stimulation approaches against AD, also contributing to all therapeutic interventions by transcranial stimulation in the future, enabling the development of customized therapies.

**keywords:** Alzheimer's disease, immunoregulation, photobiomodulation, neuroprotective effect, optomechanical stimuli, ultrasound.