

Neurodegenerative disease treatment

Focused ultrasound (FUS) is a **medical technology** that non-invasively stimulates the **brain** and has been applied in thermal **ablation**, **blood-brain barrier opening**, and **neuromodulation**. In recent years, numerous experiences and indications for the use of FUS in clinical and preclinical studies have rapidly expanded. Focused ultrasound-mediated BBB opening induces cognitive enhancement and **neurogenesis**; however, the underlying mechanisms have not been elucidated.

Kong et al. investigated the effects of FUS-mediated BBB opening on hippocampal long-term potentiation (LTP) and cognitive function in a 5xFAD mouse model of Alzheimer's disease (AD). We applied FUS with microbubble to the hippocampus and LTP was measured 6 weeks after BBB opening using FUS. Field recordings were made with a concentric bipolar electrode positioned in the CA1 region using an extracellular glass pipette filled with artificial cerebrospinal fluid. Morris water maze and Y-maze was performed to test cognitive function.

The results demonstrated that FUS-mediated BBB opening has a significant impact on increasing LTP at Schaffer collateral - CA1 synapses and rescues cognitive dysfunction and working memory. These effects persisted for up to 7 weeks post-treatment. Also, FUS-mediated BBB opening in the hippocampus increased PKA phosphorylation.

Therefore, it could be a promising treatment for neurodegenerative diseases as it remarkably increases LTP, thereby improving working memory ¹⁾

Although **microglial replacement therapy** is still in its infancy, it will likely be a trend in the development of treatments for **neurodegenerative diseases** due to its versatility and selectivity ²⁾.

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Kong C, Ahn JW, Kim S, Park JY, Na YC, Chang JW, Chung S, Chang WS. Long-lasting restoration of memory function and hippocampal synaptic plasticity by focused ultrasound in Alzheimer's disease. *Brain Stimul.* 2023 May 19:S1935-861X(23)01781-3. doi: 10.1016/j.brs.2023.05.014. Epub ahead of print. PMID: 37211337.

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Zhang L, Wang Y, Liu T, Mao Y, Peng B. Novel Microglia-based Therapeutic Approaches to Neurodegenerative Disorders. *Neurosci Bull.* 2023 Jan 3. doi: 10.1007/s12264-022-01013-6. Epub ahead of print. PMID: 36593381.

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