Uncovering the Benefits of Ultrasound: Effects on Colocalization of Microglia and Amyloid-Beta Plaque in Alzheimer Mouse Models

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Alzheimer's Disease (AD) is a debilitating neurodegenerative condition, characterized by amyloid-beta plaque deposition in the brain. Focused ultrasound (FU) may have a therapeutic modulating effect on the brain of AD. Close approximation of microglia with amyloid-beta plaque, colocalization, is an essential step for microglia to clear amyloid-beta plaque. Therefore, quantification of colocalization is important to assess the effect of an intervention. However, until now, colocalization has been manually counted by visual observation, which is labor intense and prone to errors. Solidity (the degree of fulness of microglia) is a morphological feature of activated microglia and can be used to assess the effect of an intervention but has been rarely studied. To overcome this, I programmed a Python™ code that enables quantification of colocalization by counting the number of microglia within a 15-μm distance of an amyloid-beta plaque and the solidity degree of the colocalized microglia. We tested the performance of the code-based counting method against the manual counting method in 10 AD mice. Bland-Altman analysis showed a nearly perfect agreement of counts (Bias of the ratio: 1.002 [95% CI: 1.001~1.004]). Based on the code-based method, FU treated mice had significantly higher amounts of colocalization compared to untreated mice (The FU brain slices were approximately 90% colocalized, whereas untreated brain slices were 67% colocalized). FU also increased the solidity of colocalized microglia (from approximately 83% to 88%), indicating an effective response to amyloid-beta plaque. Computational tools offers a novel method for characterizing the therapeutic effect of FU on microglia.

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