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Transcranial Electric Field Treatments on Redox-Toxic Iron Deposits in Transgenic Alzheimer's Disease Mouse Models: The Electroceutical Targeting of Alzheimer's Disease

Authors : Choi Younshick, Lee Wonseok, Lee Jaemeun, Park Sun-Hyun, Kim Sunwoung, Park Sua, Kim Eun Ho, Kim Jong-Ki

Abstract : Iron accumulation in the brain accelerates Alzheimer's disease progression. To cure iron toxicity, we assessed the therapeutic effects of noncontact transcranial electric field stimulation to the brain on toxic iron deposits in either the Aβ-fibril structure or the Aβ plaque in a mouse model of Alzheimer's disease (AD). A capacitive electrode-based alternating electric field (AEF) was applied to a suspension of magnetite (Fe_3O_4) to measure the field-sensitized electro-Fenton effect and resultant reactive oxygen species (ROS) generation. The increase in ROS generation compared to the untreated control was both exposure-time and AEF-frequency dependent. The frequency-specific exposure of AEF to 0.7–1.4 V/cm on a magnetite-bound Aβ-fibril or a transgenic Alzheimer's disease (AD) mouse model revealed the removal of intraplaque ferrous magnetite iron deposit and Aβ-plaque burden together at the same time compared to the untreated control. The results of the behavioral tests show an improvement in impaired cognitive function following AEF treatment on the AD mouse model. Western blot assay found some disease-modifying biological responses, including down-regulating ferroptosis, neuroinflammation and reactive astrocytes that eventually made cognitive improvement feasible. Tissue clearing and 3D-imaging analysis revealed no induced damage to the neuronal structures of normal brain tissue following AEF treatment. In conclusion, our results suggest that the effective degradation of magnetite-bound amyloid fibrils or plaques in the AD brain by the electro-Fenton effect from electric field-sensitized magnetite offers a potential electroceutical treatment option for AD.

Keywords : electroceutical, intraplaque magnetite, alzheimer's disease, transcranial electric field, electro-fenton effect
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