Remote, Tunable Modulation of Astrocytic Calcium Signaling via an Engineered Paramagnetic Matrix: A Non-Invasive Platform for Neuroprotection in CNS Disease

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Dysregulated astrocytic Ca2+ signaling is a key driver of high-burden CNS disorders, including Alzheimer’s and stroke, yet existing neuromodulation strategies remain invasive and neuron-centric, failing to target glial dysfunction. Here, we present a non-invasive platform using magnetism to achieve precise modulation of astrocytic Ca2+ dynamics through an engineered paramagnetic extracellular matrix, magnesium-iron hydrotalcite (MgFe-HTlc). Building on prior evidence of MgFe-HTlc biocompatibility and Ca2+ activation via the mechanosensitive TRPV4 channel, we investigated whether magneto-mechanical coupling enables tunable control of astrocytic Ca2+ states and restoration of Ca2+ and osmotic homeostasis following pathological disruption. Ca2+ imaging in primary astrocytes first demonstrated that MgFe-HTlc induces mild, oscillatory Ca2+ activity via TRPV4-mediated influx. Static magnetic fields enabled tunable modulation: acute stimulation elicited sustained Ca2+ elevations and chronic stimulation induced robust, wave-like responses. Under oxidative stress, a neural injury model, MgFe-HTlc significantly suppressed aberrant Ca2+ hyperactivity and reduced astrocyte swelling, quantified via fluorescent cell area analysis as a proxy for cytotoxic edema. Unexpectedly, TRPV4 inhibition enhanced magnetically induced Ca2+ responses under stress, revealing a previously uncharacterized negative feedback mechanism where TRPV4-mediated Ca2+ influx activates downstream suppressive pathways, potentially involving Ca2+-activated chloride channels. This work establishes an innovative engineered platform harnessing magnetism for remote, tunable glial modulation, offering a transformative approach for non-invasive therapeutic restoration of astrocytic homeostasis in CNS diseases.

Awards Won:
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