Toward Remote Control of Neural Function: Extracellular Matrix Paramagnetic Hydrotalcite Renders Brain Astrocytes Responsive to Static Magnetic Field via TRPV4 Ion Channel-Mediated Calcium Influx

Liedtke, Illaria (School: Rye Country Day School)

Central nervous system (CNS) diseases such as Alzheimer's, epilepsy, and stroke affect over 1 billion people globally, and dysregulated astrocytic calcium signaling can drive these pathologies. In healthy brains, astrocytes, a key component of the blood-brain-barrier, maintain CNS homeostasis through calcium signaling. Specifically, they rely on TRPV4 calcium-permeable ion channels to sustain neurovascular homeostasis. When dysregulated, adverse consequences ensue such as defective neural signaling and neuronal cell death. Developing methods to control astrocytic calcium signaling is thus key to generating new therapies for CNS disorders. Current methods are limited, such as invasive approaches using brain implantation. Remote magnetic control approaches offer promise, but are still under-explored and limited in effectiveness. Therefore, this study combines the extracellular matrix, paramagnetic magnesium-iron hydrotalcite (MgFe-HTlc), with static magnetic stimulation (SMS) to affect calcium dynamics in rat primary astrocytes. Fluorescein diacetate vitality assays demonstrated that MgFe-HTlc is biocompatible for primary astrocytes, enhancing their differentiation. Calcium imaging revealed that MgFe-HTlc induces an oscillatory response— baseline waves necessary for neural plasticity and signaling. When applying SMS to primary astrocytes grown on MgFe-HTlc, a sustained calcium response was observed, which can stimulate repair mechanisms defective in aging and disease. Both calcium responses were eliminated with selective TRPV4 inhibitors. These findings suggest the ability of a novel engineered magnetic extracellular matrix, paired with SMS, to evoke and sculpt astroglial calcium responses via TRPV4, setting a path to remote therapeutic management of CNS diseases.

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