GLIAL MICROVESICLES IN MOTION AT THE NEURON SURFACE: IMPLICATION IN ALZHEIMER’S DISEASE

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Extracellular vesicles (EVs) released from astrocytes and microglia are key players in glia-neuron communication in the healthy and diseased brain (Antonucci et al., 2012; Gabrielli et al., 2015; Prada et al., 2018). However, how EVs move across the extracellular space to reach target neurons and whether EVs interact with neurons at preferential sites remain elusive. Here, we show that gial EVs efficiently bind to both the cell body and neurites of primary hippocampal neurons. Surprisingly, after the neuron contact, a large fraction of EVs move along the surface of axons and dendrites in both retrograde and anterograde directions. Extracellular EV motion may be driven by binding to neuronal receptors, that ay drift on the plasma membrane following cytochalasin-sensitive and nocodazole-resistant cytoskeleton rearrangements. However, a fraction of MVs contain actin filaments and have an independent capacity to move along the gradient of neuronal receptors in an actin-dependent manner. Our results demonstrate, for the first time, that gial EVs exploit surface neuronal receptors to passively/actively reach their target sites. The implication of extracellular EV movement in the rise and propagation of synaptic dysfunction in the early stages of Alzheimer’s disease will be discussed.

Riferimenti:

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