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GLIA

Transporting cargo from A to B

Oligodendrocytes ensheath axons and provide trophic support, which is essential for long-term maintenance of the axon and oligodendrocyte as a functional unit. The mechanisms by which this is achieved are not known, but Frühbeis, Fröhlich *et al.* now demonstrate that oligodendrocyte-derived exosomes (cargo-containing microvesicles) are important for this process.

Oligodendrocytes are capable of releasing exosomes into the extracellular space, which can then be internalized by nearby cells. The authors showed that glutamate-induced increases in exosome release from oligodendrocytes was attenuated when glutamate was co-applied with antagonists of either NMDA or AMPA receptors (both of which are expressed on oligodendrocytes), with NMDA receptor antagonists having a greater effect. This suggests that neuronally released glutamate, acting mostly through NMDA receptors, stimulates exosome secretion from oligodendrocytes.

> “exosomes might confer neuroprotection”

To monitor the fate of oligodendrocyte exosomes after their release, the authors used fluorescent- or reporter enzyme-labelled exosomes and detected their uptake by neurons. They found that internalized exosomes accumulated in endosomal compartments in neurons and that preventing neuronal endocytosis (by inhibition of either clathrin or dynamin) reduced the uptake of exosomes. The reporter enzyme in the exosomes was working in the neurons, showing that the exosome cargo is functionally available to the target neurons.

What are the functional consequences of oligodendrocyte-to-neuron communication through exosome release and internalization? Comparing the viability of neurons cultured in the presence or absence of oligodendrocyte-derived exosomes, the authors found that under optimal conditions, the presence of exosomes did not change the metabolic activity of cultured neurons. Exposure to oxidative stress or nutrient deficiency, however, caused neurons with access to oligodendrocyte-derived exosomes to retain a level of metabolic activity that was closer to that under the unstressed condition, indicating that exosomes might confer neuroprotection.

Overall, these findings indicate that exosome-mediated glia–neuron communication is important for supporting metabolism and maintaining neuronal integrity under conditions of cellular stress.

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ORIGINAL RESEARCH PAPER Frühbeis, C. *et al.* Neurotransmitter-triggered transfer of exosomes mediates oligodendrocyte–neuron communication. *PLoS Biol.* **11**, e1001604 (2013)