Neuronal activity is closely associated with energy metabolism. In addition to glucose, astrocytederived lactate serves as an energy source for neurons. Chronic inflammation is a common pathological event that is associated with aging and neurodegenerative diseases. However, the mechanisms underlying inflammation-induced neuronal injury are not fully understood. Both microglia and astrocytes participate in the regulation of neuronal functions; therefore, Wang et al. used astrocyte-neuron co-cultures to investigate the effects of chronic microglial activation on neuronal lactate metabolism. Chronic low-grade inflammation was induced by repeated stimulation of primary rat microglia with low-dose lipopolysaccharide (LPS, 10 ng/mL). The medium from the LPS-activated microglia was collected and used to mimic the inflammatory environment in primary cultures. In monocultures exposed to an inflammatory environment, intracellular lactate decreased in neurons but increased in astrocytes. However, astrocyte-neuron co-cultures exhibited increased lactate levels in neurons and decreased lactate levels in astrocytes when exposed to an inflammatory environment. Inhibition of lactate transporters expressed on neurons or astrocytes reduced the intracellular lactate in co-cultured neurons exposed to inflammation, but not in those exposed to physiological conditions. Adenosine triphosphate (ATP) production was reduced in both mono-cultured and co-cultured neurons. These results indicate that a chronic inflammatory environment increases neuronal lactate supply by promoting the astrocyte-neuron lactate shuttle, but it impairs lactate oxidation in neurons. Additionally, chronic inflammation disrupts the neuronal cytoskeleton. This study highlights the importance of glial cells in regulating neuroenergetics and neuronal function and provides a comprehensive explanation for the neurotoxic effects of neuroinflammation¹⁾.

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Wang Y, Li J, Wang MY, Pan ZY, Li ZQ, Wang ZF. Chronic microglial inflammation promotes neuronal lactate supply but impairs its utilization in primary rat astrocyte-neuron co-cultures. Biochem Biophys Res Commun. 2022 Mar 26;607:28-35. doi: 10.1016/j.bbrc.2022.03.122. Epub ahead of print. PMID: 35366540.

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