Pervasive axonal transport deficits in multiple sclerosis models.

Impaired axonal transport can contribute to axon degeneration and has been described in many neurodegenerative diseases. Multiple sclerosis (MS) is a common neuroinflammatory disease, which is characterized by progressive axon degeneration—whether, when, and how axonal transport is affected in this condition is unknown. Here we used in vivo two-photon imaging to directly assay transport of organelles and the stability of microtubule tracks in individual spinal axons in mouse models of MS. We found widespread transport deficits, which preceded structural alterations of axons, cargos, or microtubules and could be reversed by acute anti-inflammatory interventions or redox scavenging. Our study shows that acute neuroinflammation induces a pervasive state of reversible axonal dysfunction, which coincides with acute disease symptoms. Moreover, perpetuated transport dysfunction, as we found in a model of progressive MS, led to reduced distal organelle supply and could thus contribute to axonal dystrophy in advanced stages of the disease.