Altered Gastrointestinal Motility in a Mouse Model of Multiple Sclerosis

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Multiple sclerosis (MS) patients often experience constipation, but the etiology of this symptom is unknown. To study this in an animal model, we tested the hypothesis that mice with experimental autoimmune encephalomyelitis (EAE), would exhibit altered gastrointestinal (GI) transit and their blood serum would contain antibodies directed against targets in enteric ganglia. EAE was induced in C57BL/6J mice by injection of complete Freund's adjuvant (CFA) and myelin oligodendrocyte glycoprotein. After somatic motor symptoms developed, small intestinal transit was measured by calculating the leading edge (LE) and geometric center (GC) 20 minutes after oral gavage of rhodamine dextran. Whole GI transit time was determined by oral gavage of carmine red and calculating the latency for dye to appear in fecal pellets. Targets of antiserum were evaluated by immunohistochemical staining of guinea pig intestine whole mount preparations with EAE and control plasma. Small intestinal transit was significantly slower in EAE mice than in controls (LE, p<0.02; GC, p<0.01), and was not altered in CFA controls. The rate of whole GI transit was significantly longer in EAE mice versus CFA controls (p<0.05) and healthy controls (p<0.01). Plasma from EAE mice yielded more intense immunoreactivity in myenteric ganglia than plasma from control animals, with immunostained structures including neurons and nerve processes. In summary, EAE causes delayed small intestinal and whole GI transit time compared to healthy control mice, which could be representative of the bowel dysmotility exhibited by multiple sclerosis patients. The symptomology may be explained by the presence of GI-targeted antibodies in the blood of EAE mice.

Funding: National Multiple Sclerosis Society