Characterization of MS in a mouse model using the string-pulling behavioural task

Davis Juell, Luca Fascio, Behroo Mirzagha, Samsoon Inayat, Sophia Fraser, Jordan Dudley, Emily Hagens, Ian Whishaw, Majid Mohajerani

Motor defects produced from the disease in mouse models of multiple sclerosis are commonly assessed by researchers using manual observation of mouse movements. The assessment is subjective and prone to assessor dependent variability. This project focused towards creating an automatic and reliable characterization of MS in a mouse model using the string-pulling behaviour task in which an animal pulls a string using hand-over-hand movements in a sitting or a standing posture using online sensing with nose and whiskers. This task therefore allows observation of sensorimotor integration and both coarse and fine movements including motion of arms and hands, head, spine, and hind limbs. We hypothesized that using the string-pulling behavior and automatic analysis with machine learning and AI based software, we would detect abnormal movements early-on compared to manual observation and quantify the progression of motor deficits in MS mouse model. MS was induced in 14 mice by subcutaneous injections of 200 myelin oligodendrocyte glycoprotein 35-55 antigen (MOG35-55 or Ek-2110), a drug which triggers autoimmune encephalomyelitis (EAE) in mice producing key pathological features as in human MS. Starting Day 3 post-injection, mice were manually assessed for motor deficits and were also filmed while engaged in the string-pulling behavior. Offline analysis is being done using the Matlab-based toolbox developed in our lab. To date we have quantified the average velocity of whole-body movements, and patterns of hand movements of 4 mice with disease progression. These results show a significant decrease in average velocity (p=0.0060, ANOVA) and a significant increase in fractal dimensions (p=0.0001, ANOVA) which quantifies the irregularities of patterns of hand movements. Our results provide quantifiable characterization of MS through diminished movement kinematics, and increased degree of randomness of hand motion.