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

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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 injecting 100uL of myelin oligodendrocyte glycoprotein 35-55 antigen (MOG35-55 or Ek-2110) on the first day and then again 2 days later. This drug has been shown to trigger autoimmune encephalomyelitis (EAE) in mice producing the same key pathological features as in human MS. Starting Day 3, mice were manually assessed for motor deficits as well as were engaged in the string-pulling behavior and were filmed (were food deprived … ). Offline analysis (ongoing) is being done using the Matlab based toolbox developed in our lab. To date we have quantified the average velocity of whole-body movements, height of mice, and patterns of hand movements of 4 mice ….

Bimanual coordination can be calculated as the correlation between the distance each hand moves with the y-axis, the postural stability of the mouse can be determined from colour-based image segmentation, and movement kinematics can be discovered as an average velocity produced from optical flow estimation using the combined-local-global method. As MS is a human disease, experimental autoimmune encephalomyelitis (EAE) is induced within mice as it produces the same key pathological features as MS and is therefore useful as an experimental model. To induce EAE, we inject 100 uL of the myelin oligodendrocyte glycoprotein 35-55 antigen (MOG35-55 or Ek-2110) on the first day and then again 2 days later. A total of 14 mice were injected with the drug and recorded on the string-pulling task. As the drug was not effective in 100% of mice, we grouped them as either resistant or non-resistant. This data is still being processed, but the first 4 of the non-resistant mice have shown a significant decrease in their average velocity vs time (p = 0.0060; calculated through ANOVA) and a significant increase in fractal dimensions vs time (p=0.0001; calculated through ANOVA). That is, they slow down as MS neurodegeneration progresses and they show an increased degree of randomness in their hand motions.