

Altered Gait in Charcot Neuropathic Mice: A Kinematic Analysis

Zachary Koroneos¹, Shelby Alwine¹, Indigo Milne¹, Nicole Fye¹, Chris Stauch¹, Dr. Michael Aynardi¹
¹Penn State College of Medicine, Hershey, PA

Disclosures: none

INTRODUCTION: Charcot arthropathy is known to cause neurodegenerative as well as physical skeletal changes that can affect gait. A verified model of inducing Charcot arthropathy in mouse hindlegs exists, but clinical data has yet to be gathered from this model. This is a pilot study with the purpose of gathering clinical data on mouse gait and joint reactive forces that occur over time as a result of Charcot arthropathy utilizing MatLab software.

METHODS: Eleven wild-type 25-week-old C57BL/6J mice were obtained. Group A included 6 mice that were fed a high fat, 60% kcal diet starting at the age of 6-weeks. Group B included 5 mice, which were fed a normal murine diet. Group A became obese and developed neuropathy as the result of their hyperglycemic state. Group A also completed a verified running protocol to induce microtrauma leading to Charcot-type changes in mice hindfeet.

Data was collected at the time points of 0 and 16 weeks between a control group and mice with induced Charcot-type joint changes. To obtain gait analysis videos to process using our program in Matlab, brightly colored dots were placed on the mice's hindlimbs. Mice first had their left hind leg shaved while under brief anesthesia using isoflurane. Skin safe non-toxic markers of various colors were used to mark the hip, knee, ankle, and tarsal joints.

The mice were then placed on the treadmill at a constant speed and were recorded in slow motion for 1 minute. The videos were then edited to include 2-3 full gait cycles and uploaded into MatLab for analysis. A novel code was then utilized to measure gait angles and coordinates in space by following the corresponding-colored dot for each joint on the mouse. This entire process is shown in Figure 1.

RESULTS SECTION: The control mice did not have significant changes in range of motion of the knee, ankle, or midfoot while walking between weeks 0 and 16. In contrast, the mice fed a high-fat diet had statistically significant differences in ankle range of motion ($p=0.0275$), nearly significant differences in knee range of motion ($p=0.0991$), and insignificant differences in midfoot range of motion between weeks 0 and 16. In addition, the differences between range of motion of the knee of the control vs. C57BL/6J mice were significantly different between groups at both weeks 0 ($p=0.0016$) and 16 ($p=0.0201$). In the ankle, the difference was statistically significant at week 0 ($p=0.0275$) but not week 16 ($p=0.7066$), presumably due to a large standard deviation in ankle range of motion.

DISCUSSION: Results of this gait analysis indicate that mice with Charcot-like arthropathic changes demonstrated gait differences that affected the range of motion of the knees and ankles of the mice, but not the midfoot. These changes could be due to the neuropathic abnormalities induced in mouse feet that would cause gait changes. Future studies will include a larger sample size of mice with gait analysis done at intermediate time points to further quantify how gait changes over time with Charcot arthropathy.

SIGNIFICANCE/CLINICAL RELEVANCE: This novel method for analyzing gait in rodent models of human disease is inexpensive and easy to perform. It has the potential to replace more expensive methods of gait analysis in rodents and allow researchers to study the changes of gait as disease progresses in rodent models of human disease.



Figure 1. Illustration of process utilized to induce Charcot and analyze mouse gait.