

Quantifying Metabolic and Neurologic Changes in Charcot Arthropathy Murine Models

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Disclosures: none

INTRODUCTION: Charcot arthropathy is a complication of diabetes mellitus that has significant impacts on patients' quality of life if there are delays in diagnosis of this condition. The pathophysiology is not fully understood, but existing research describes a proposed mechanism of joint degeneration due to a combination of neuropathy, inflammation and microtrauma. We aim to further elucidate the stages of neuropathic and physical changes in Charcot arthropathy by measuring metabolic parameters and sensation changes, with the future goal of correlating these findings with radiographic and histological findings.

METHODS: Characteristics of each group of C57BL/6J mice (from Jackson Laboratories, Bar Harbor, ME, USA) are described below in the table in panel A of Figure 1. Groups 2, 3, 4 and 5 were fed a 60% kcal from fat diet to facilitate diet-induced obesity (DIO). Initial body weights, DEXA scans, Von-Frey sensory testing, and hot plate sensory testing following the previously published murine model were performed prior to the start of the running protocol. The testing was repeated at weeks 4, 8, 12, and 16. Paired-t-Test and one-way ANOVA were utilized to determine significance of observed results. This study was approved by IACUC.

RESULTS SECTION: Trends in weight over the course of the study are represented in the graph in Figure 1B. Plantar temperature was measured before and after running on the treadmill; differences in plantar temperature for the running groups that had an endpoint of 16 weeks was not statistically significant (Figure 1C). Hot plate sensory testing initially demonstrated no significant difference in number of responses between groups during week 0. By week 16, group 1 was more sensitive than groups 3 and 5, demonstrating the development of decreased sensation in the hindfoot (Figure 1D). By week 12 and 16, mice eating the high-fat diet had a higher fasting blood glucose level than group 1 (normal diet). Additional results include statistically significant higher body fat percentage in groups eating a high fat diet, as well as a lower bone mineral density (BMD) at week 0 and 16. Von Frey sensory testing also showed more force was required to induce a positive response (paw withdrawal, licking), demonstrating a decreased hindfoot sensitivity in mice eating a high-fat diet.

DISCUSSION: Decreased number of responses with hot plate testing as well as increased force required to induce a response with Von Frey demonstrate development of decreased sensation in the hind-paw of mice being fed a high-fat diet. DIO-mice also have a statistically significant higher blood glucose than mice being fed regular diet. These changes represent diabetic neuropathy in this murine model and in the future will be correlated with radiographic and histological results collected from this study.

SIGNIFICANCE/CLINICAL RELEVANCE: The stages of sensory and neuropathic changes in Charcot arthropathy have been quantified by measuring metabolic changes as well as sensation changes over time in diet-induced obese mice completing a running protocol previously shown to induce joint degeneration representative of Charcot arthropathy.

Figure 1

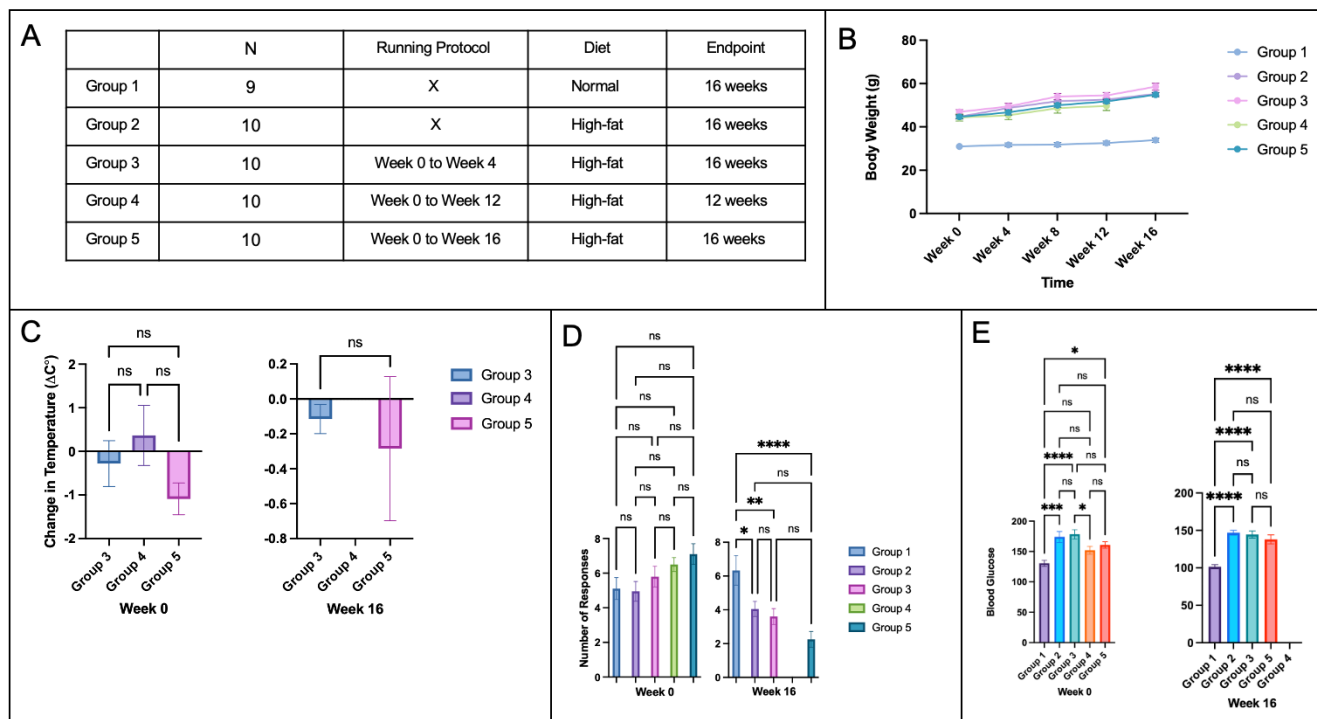


Figure 1A. Characteristics of each group of mice in the study. 1B. Change in body weight over time. 1C. Difference in plantar temperature before and after running. 1D. Number of positive responses during Von Frey sensory testing. 1E. Fasting blood glucose levels. Error bars represent standard error of the mean, * significant differences at $p \leq 0.05$.