GAIT COMPENSATIONS IN A RAT MEDIAL MENISCUS TRANSECTION MODEL OF KNEE OSTEOARTHRITIS

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INTRODUCTION

Osteoarthritis (OA) results in cartilage loss, bone remodeling, and up-regulation of inflammatory and catabolic mediators within a joint1. Despite a complex etiology, OA ultimately leads to pain and disability. Clinically, OA is diagnosed through physical exams and radiographs; however, OA assessments in the preclinical model focus on joint histology2. Behavioral analyses can be used to describe some symptomatic consequences of OA in the preclinical model3-5; however, these assays can have high variability and limited translation to the patient condition. Gait assessment provides a tool to evaluate the consequences of OA in both the preclinical model and the patient6. The objective of this study is to evaluate gait compensations, weight distribution imbalance, and limb sensitivity in a rat model post-traumatic OA.

METHODS

A medial collateral ligament transection (MCL sham, n=6) or a MCL and medial meniscus transection (MMT, n=6)4-5,7 was performed in male Lewis rats (200-250g); 4 additional rats received neither anesthesia nor surgery (naïve, n=4). Weight bearing, limb sensitivity, and gait were evaluated on post-operative day 9, 16, and 23. Weight bearing was assessed on an scale that records left-right weight distribution during rearing (incapacitance meter, IITC, Inc)3. Paw withdrawal thresholds were evaluated using von Frey filaments (Stoelting)8. Spatiotemporal gait data were collected by manual digitization of five high-speed videos of each rat at each time point (200 fps, Phantom V4.2)6. Similarly, 3-component ground reaction forces were obtained on a Hall-effect force transducer (AMTI) for each rat at each time point9. On day 28, serum and knees were collected. Cytokine activity in the serum was assessed with a 10-plex cytokine panel (Invitrogen). Knees were sectioned, stained, and graded with the OARSI histopathology scheme10. Two-way analysis of variance or two-way generalized linear models that included a linear dependence on trial velocity were used to detect differences between groups.

RESULTS AND DISCUSSION

Gait cycles became progressively asymmetric in the MMT group (Fig. 1, top), indicating syncopations in the foot-strike sequence. Moreover, left and right limb stance time (ST) tended to be imbalanced in MMT rats (Fig. 1, bottom), indicating that MMT rats spent less time on their operated limb while walking. Differences in stride length, step width, and stride frequency were not observed.

Ground reaction forces aligned with spatiotemporal changes. Peak vertical force and impulse were decreased in the operated limb of MMT rats (Fig. 2). Moreover, peak vertical force in the operated limb of MMT animals was lower than naïve controls (p=0.004) and vertical impulse in the operated limb of MMT animals was lower than MCL sham and naïve controls (p<0.02). Propulsive forces, but not braking forces, were altered in the hind limbs of MMT rats (p<0.05, not shown). Mediolateral forces did not vary amongst groups.
While gait data revealed limb compensations, imbalanced weight distribution was not observed on the incapacitance meter. This incongruity is likely due to differences between tests; incapacitance meters measure weight distribution during rearing, while ground reaction forces measure limb use during locomotion.

MMT and MCL animals had heightened sensitivity (lower thresholds) in their operated limb relative to their contralateral limb ($p<0.05$) and tended to be more sensitive than naïve controls ($p=0.056$), indicating limb sensitivity can occur with both MCL and meniscal injuries in rats.

Rats with the MMT surgery had severe lesions on the medial tibial plateau (Fig 3), ranking as either OARSI grade 4 or 5 (erosion or denudation). Severe lesions were not observed in MCL sham, naïve, or within the contralateral limb of MMT rats.

Serum cytokine concentrations were not different, though serum IL6 in MMT rats did tend to be higher than that of naïve controls ($p=0.072$, Fig 4).

**CONCLUSIONS**

To our knowledge, this is the first study to describe gait compensations in the rat MMT model of OA. The data reported herein indicate that gait analyses are sensitive to knee joint remodeling. In particular, gait parameters yielded more robust comparisons of the affected and contralateral limb than the incapacitance meter. Moreover, gait symmetry demonstrated a tendency to increase as OA progressed; no other parameter, including established assays of limb sensitivity and weight-bearing, demonstrated this potential. Future work will focus on correlating joint degeneration, sera biomarkers, and behavioral assessments in this rat model of knee OA.

**REFERENCES**


**ACKNOWLEDGEMENTS**

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<tr>
<td></td>
<td>Left</td>
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<td>23.3 ± 6.7</td>
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Table 1: Paw Withdrawal Thresholds in MMT Rats