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ACUTE KINEMATIC AND KINETIC CHANGES IN RATS AFTER DIET INDUCED OBESITY AND ACL-X

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SUMMARY

Twelve preliminary kinematic and kinetic data sets from a longitudinal diet induced obesity osteoarthritis (OA) study (n=28) were analyzed from two time points. The baseline data was acquired at the end of the 12-week obesity induction and the post-surgical data was collected one week post-surgical intervention (ACL-X or sham). Hind limbs were analyzed for changes in kinetics and kinematics due to surgical intervention in both experimental and control contralateral hind limbs, and post-surgical asymmetries between limbs. Data was further stratified to determine effects of diet and obesity response on kinematic changes between responders and non-responders to dietary intervention. High fat diet responders demonstrated increased asymmetries irrespective of surgical intervention. ACL-X animals trended toward elevated kinetic asymmetries when compared to sham animals. We speculate that differences will become significant when the entire cohort of animals is included in the analysis. However, animals that received ACL-X had greater changes in 2-D sagittal plane peak knee angle during stance when compared with animals that received sham surgery, regardless of diet. These kinematic changes suggest that although kinetic differences were not observed in this data set, there are measurable changes due to surgical intervention despite small sample size.

INTRODUCTION

Both high fat feeding and resultant obesity are associated with inflammation, and this mechanism is thought to exacerbate OA.[1] Traditionally understood as a consequence of loading or trauma, OA is observed in non-loadbearing joints, such as the wrist.[2] Recent literature suggests that inflammation from high fat feeding is enough to cause OA, demonstrating a toxic effect of fat.[3] Sprague-Dawley rats respond best to diet-induced obesity (DIO) when compared with other rodents, and can be easily characterized as either obesity prone or obesity resistant when given ad libitum access to a high fat diet.[4] Recently, it has been speculated that OA progression with a high fat diet may occur independent of mass increase.[5] This animal model, with selective obesity response, provides the power to determine the contribution of impact loading to OA progression in the presence of low-level systemic inflammation.[6-8]

The **purpose** of this study is to evaluate the effect of high fat high sucrose diet on kinematic and kinetic changes post-surgery in diet induced obesity (DIO) rats. These data are from a longitudinal experiment that aims to validate a novel metabolic OA model against animals that have received anterior cruciate ligament transection (ACL-X), a validated OA progression model.

We **hypothesize** that (1) high fat diet animals that respond to the obesity induction will demonstrate exacerbated asymmetries and greater changes in peak knee joint angles during stance regardless of surgical intervention, (2) all animals will have kinetic asymmetries and changes in peak knee angles as a compensation mechanism post-surgery, and (3) ACL-X animals will demonstrate greater changes in kinematics and kinetics when compared with sham animals.

METHODS

Twelve male Sprague-Dawley rats (8-12 weeks old) were randomly separated into 2 groups as a preliminary representative analysis from a 6-month longitudinal study of 28 animals. Animals were individually housed. Prior to dietary intervention, all animals received tattoos on their hip, knee, and ankle joint centers to act as repeatable kinematic markers. The two groups, DIO (n=8) and control (n=4), were divided such that each animal received either high fat high sucrose food (40% fat, **Diet #102412, Dyets, Inc**) or lean chow (LFD, 13.5% fat, **LabDiet 5001**). After 12 weeks, the DIO group was split into responders (HFD-R, top 50% of weight gain, n=4) or non-responders (HFD-NR, bottom 50%, n=4), with average masses and percent change body mass in *table 1*.

Baseline sagittal plane 2-dimensional knee angle and 3-D kinetic measurements were collected post 12- week DIO on a 1-meter custom leveled runway with two embedded side by side 7.5 x 30 cm 3-dimensional force plates (Bertec, Columbus, OH). All animals were acclimatized to the force plate runway. Trials were deemed successful if the animal walked continuously over the dual force plates with one hind limb per plate and video data was acquired in concert. A minimum of two kinematics and kinetics trials from each hind limb were included in this analysis. After the baseline data collection, animals were further randomized to receive ACL-X (n=6) or surgical sham (n=6), and the experimental hind limb was assigned randomly. All surgical procedures were performed by the same individual and incisions were initiated on the lateral aspect of the experimental knee to prevent damage in the medial compartment. Sham surgery consisted of opening the capsule, spraying the knee joint with saline, and closing the incision. Kinematic and kinetic measurements were acquired one week post operation and

compared with baseline measures using a paired t-test, (α=0.05).

RESULTS AND DISCUSSION

After surgery, all animals demonstrated a significant decrease ($p<0.05$) in experimental limb pVGRF (-64.5 ± 98%), calculated as an average change ((post-surgery – baseline)/baseline). There were no significant differences in pVGRF change of the experimental limb between sham and ACL-X groups, but a trend toward larger changes in ACL-X animals was noted when changes were compared with sham animals. Also, significant decreases of the experimental compared to the contralateral control leg were observed in breaking and propulsive peak forces (breaking: -37.5 ± 64.5%, propulsive: -30.5 ± 50%, $p>0.01$) and medial-lateral peak forces (-29.3 ± 24.1%, $p>0.01$) across all animals. Decreased medial-lateral minimum and maximum forces were noted in experimental limbs, while increased medial-lateral forces were measured in control limbs. Significant increases in the control limb forces may suggest compensation (pVGRF 31 ± 20%, medial-lateral 91.6 ± 19%, breaking 15.1 ± 29.4%, propulsive: 21 ± 40.5%).

Additionally, there were no significant changes in peak knee angles during the swing phase in all animals post-surgery. Peak knee angle during stance was significantly decreased ($p<0.001$) in ACL-X animals regardless of diet group where full knee extension was defined as 180° (ACL-X: 128.2 ± 18° at baseline, 114.5 ± 12.2° post-surgery, Sham: 122.5± 4° at baseline, 115.5° ± 5.86° post-surgery). Although pVGRF changes were not significantly different between ACL-X and sham animals, the significant change in knee angle during stance demonstrates a surgery-specific change in movement patterns. Of note, HFD-R animals, regardless of surgery, had significantly decreased peak knee angle during stance ($p<0.001$).

CONCLUSIONS

There is evidence of compensation in all groups after surgical intervention. Some of the compensation mechanisms exhibited in this group of animals were decreases in experimental limb joint loading, evaluated by pVGRF, peak breaking force, peak propulsive force, and peak medial-lateral forces. However, we would have expected significantly larger compensation in the ACL-X animals due to instability when compared to sham animals. We attribute the lack of significance to the small sample size used in the preliminary analysis. Once the entire cohort of animals is included in the analysis, we speculate that this trend will become significant.

Acutely, after ACL-X or surgical sham, each HFD-R animal demonstrated increased kinematic changes when compared to HFD-NR or LFD groups, as expected. These kinematic changes suggest that although kinetic differences were not observed in this data set, there are measurable change in movement due to surgical intervention that are significant despite the small sample size of this preliminary data set.

Although the HFD-NR group is obesity resistant, we speculate that those animals will undergo a conversion of lean mass to fat mass from their limited activity and diet over time. This could lead to more pronounced kinematic changes, creating a muscle weakness model in the presence and absence of mass gain from all HFD animals longitudinally. As such, long term, we speculate that HFD-NR animals will demonstrate similar OA progression when compared to HFD-R animals because of a diet-associated low-level systemic inflammation, despite modest changes in movement patterns in the HFD-NR group presented here. Ultimately, this study will test the hypothesis that OA, when combined with obesity, may have a mechanism for OA onset independent of load.

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Table 1: Demographics of experimental animals grouped by surgical intervention and response to diet induced obesity. Final body mass after the 12-week feeding intervention and body mass increase ((week 12 mass –baseline mass) /baseline mass) are shown.

Group	Body Mass (g)	Body Mass % Increase	Group	Body Mass (g)	Body Mass % Increase
HFD-R ACL-X	653	55%	HFD-R SHAM	751	79%
	808	74%		636	48%
HFD-NR ACL-X	556	45%	HFD-NR SHAM	611	53%
	592	43%		579	59%
LFD ACL-X	477	21%	LFD SHAM	704	29%
	573	25%		553	24%