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INFLAMM-AGING AND OSTEOPENIA IN A RODENT MODEL OF SPINAL CORD INJURY

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INTRODUCTION

After spinal cord injury (SCI), approximately 80% of individuals are diagnosed with osteopenia or osteoporosis. Bone loss begins immediately after injury, continuing for at least the next 2 years. It is estimated that there is a 30-40% decrease in bone mineral density in the legs following SCI. Consequently, people with SCI are up to 104 times more likely, than the general population, to have a fracture by the age of 50, and post fracture complications will occur in 54% of cases. These complications include, but are not limited to, respiratory and urinary tract infections, venous thromboembolic events, fracture non-union, and depression. Bone loss significantly affects physical health and quality of life for people with SCI.

This SCI-induced bone loss is likely to be further exacerbated in older individuals. There is a relatively slow rate of decline in bone mineral density beginning at age 40 and continuing throughout adult life. We know that the age of individuals sustaining an SCI is increasing. To date, however, there has been no study of the effects of aging on bone loss after SCI.

We hypothesized that an SCI-induced reduction in weight bearing on the hind limbs would further exacerbate age-induced bone loss.

METHODS

Both young (2-3 mos) and old (20-30 mos) male and female mice served as subjects. The mice were given a moderate spinal contusion injury (T9-T10, SCI), or no injury (Sham), and recovery was assessed for 28 days post injury.

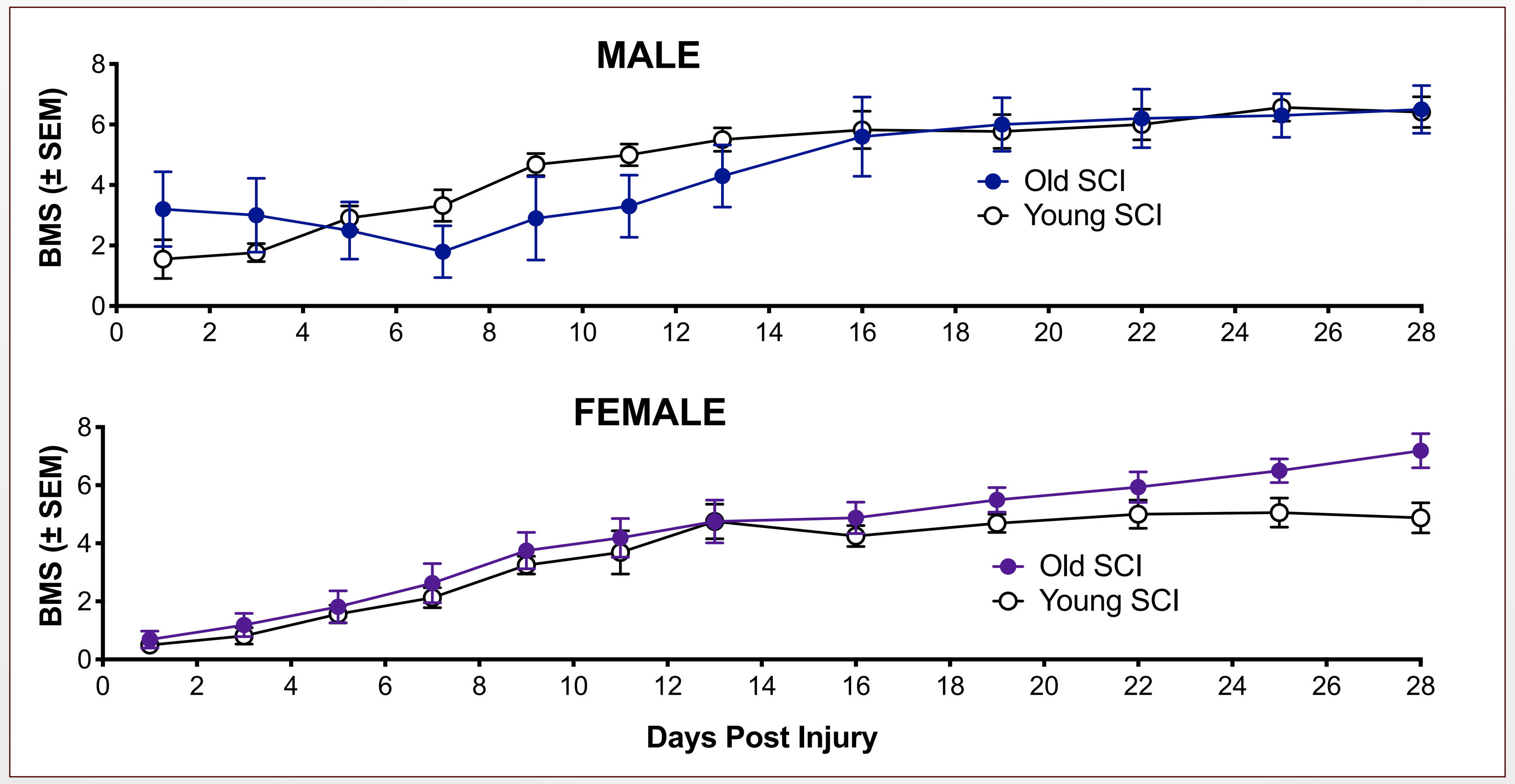
Post-surgery motor recovery was measured 3 ways:

1. **The Basso Mouse Scale (BMS):** BMS was used to determine locomotor recovery for 28 days post-injury. The test measures hind limb motor movement ranging from movement of the hip, knee, and ankle joints to coordinated walking.
2. **Rearing Activity:** Mice were placed in a high-ceiling chamber for 5 minutes to assess total number of rears prior to surgery and every 7 days until day 28. Higher rear count indicated greater motor recovery.
3. **Total activity:** Subjects were placed in automated activity chambers prior to surgery and every 7 days until day 28. Total activity was recorded in an automated activity chamber during a 5 minute interval and expressed as Total Distance traveled.

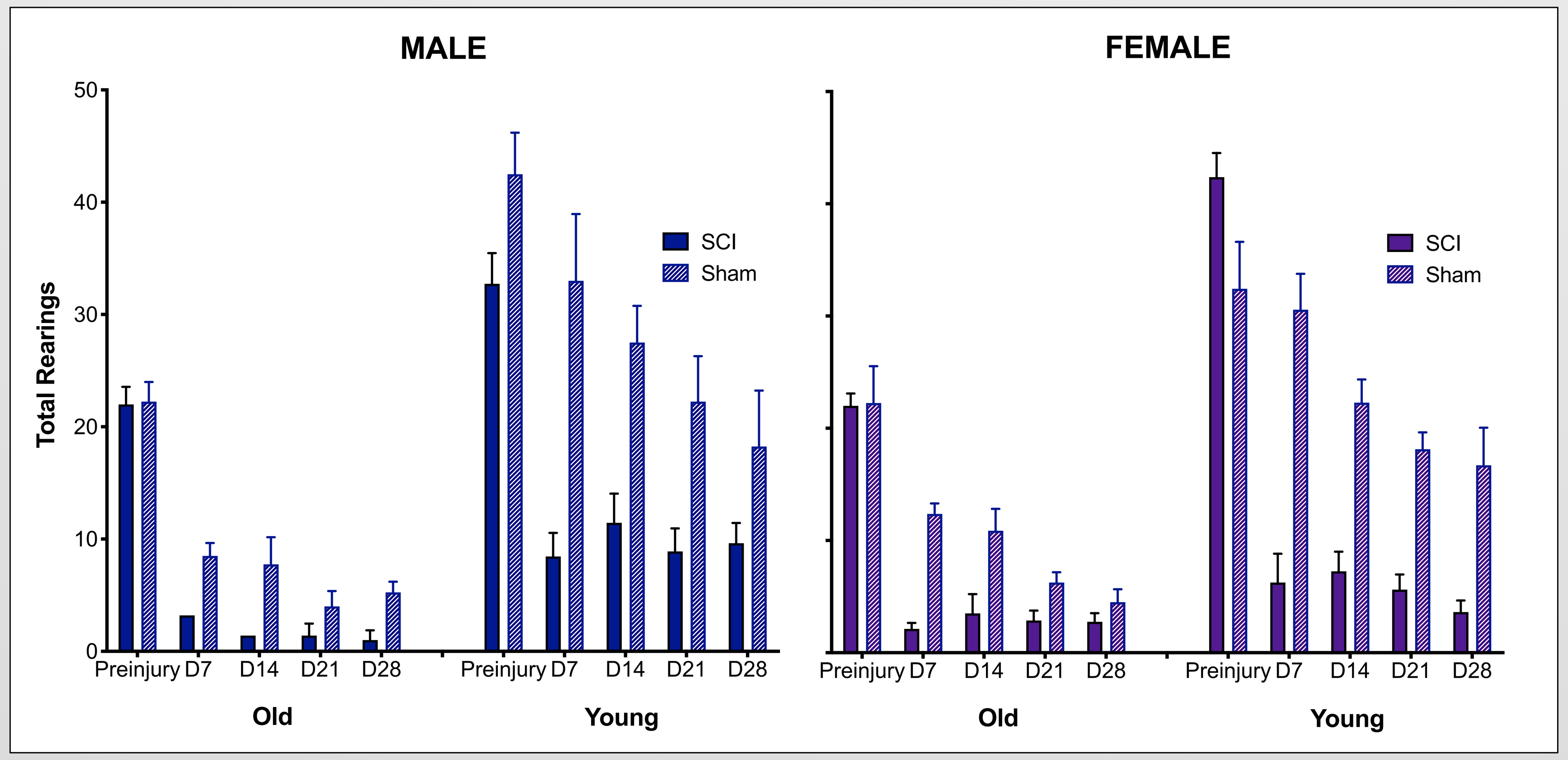
The effects of SCI on bone volume was assessed by ex vivo microCT: Tibial bones were harvested at sacrifice at 28 days post-surgery and fractional bone volume to total tissue volume (BV/TV) was analyzed in the proximal tibia metaphysis.

Correlation of Post-SCI Activity and Bone Volume: To determine if decreased activity following SCI correlated with decreased bone volume, rearing time and total distance traveled of all SCI mice (male and female, young and old) were correlated to their individual fractional BV/TV.

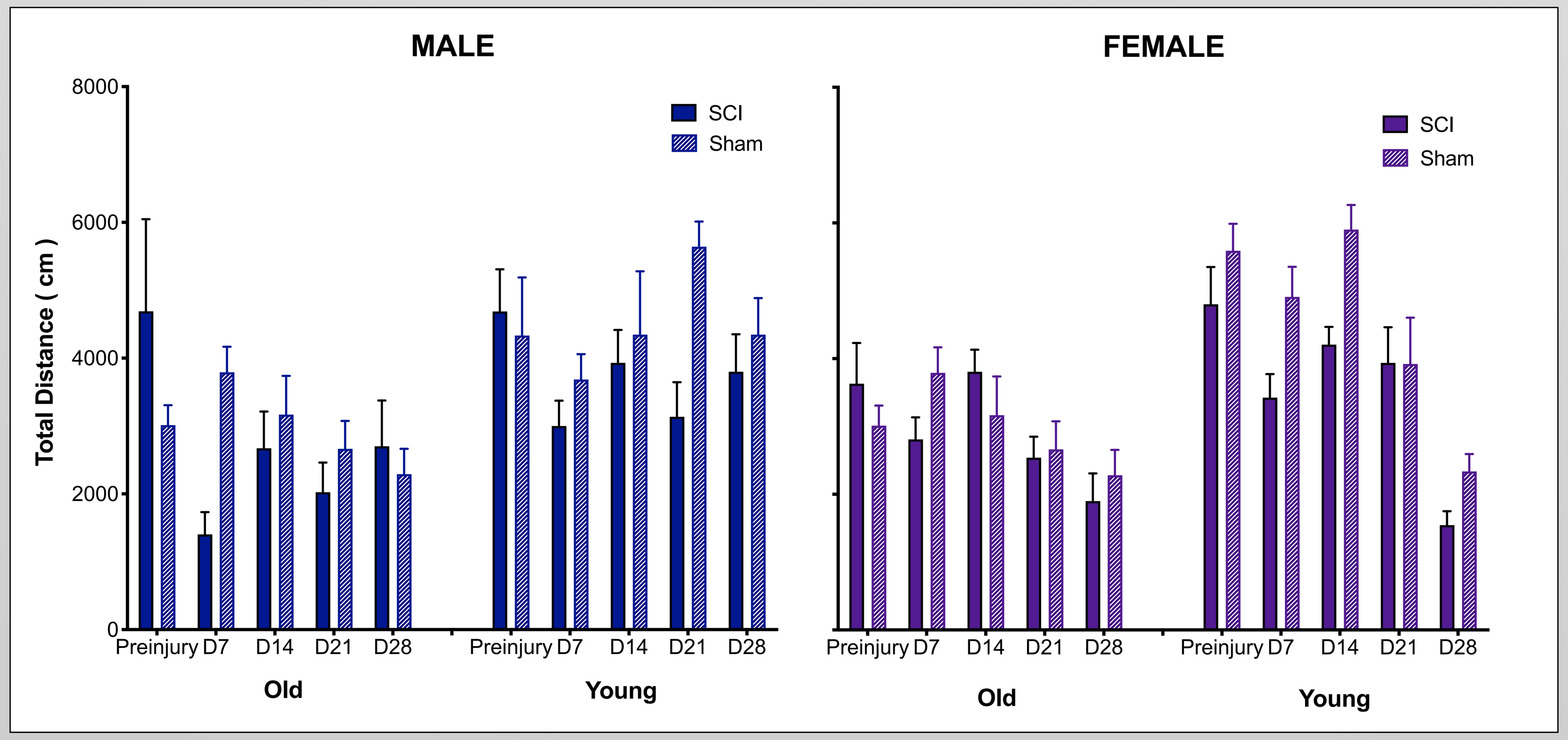
AGE AND SEX DID NOT AFFECT LOCOMOTOR RECOVERY AFTER SCI



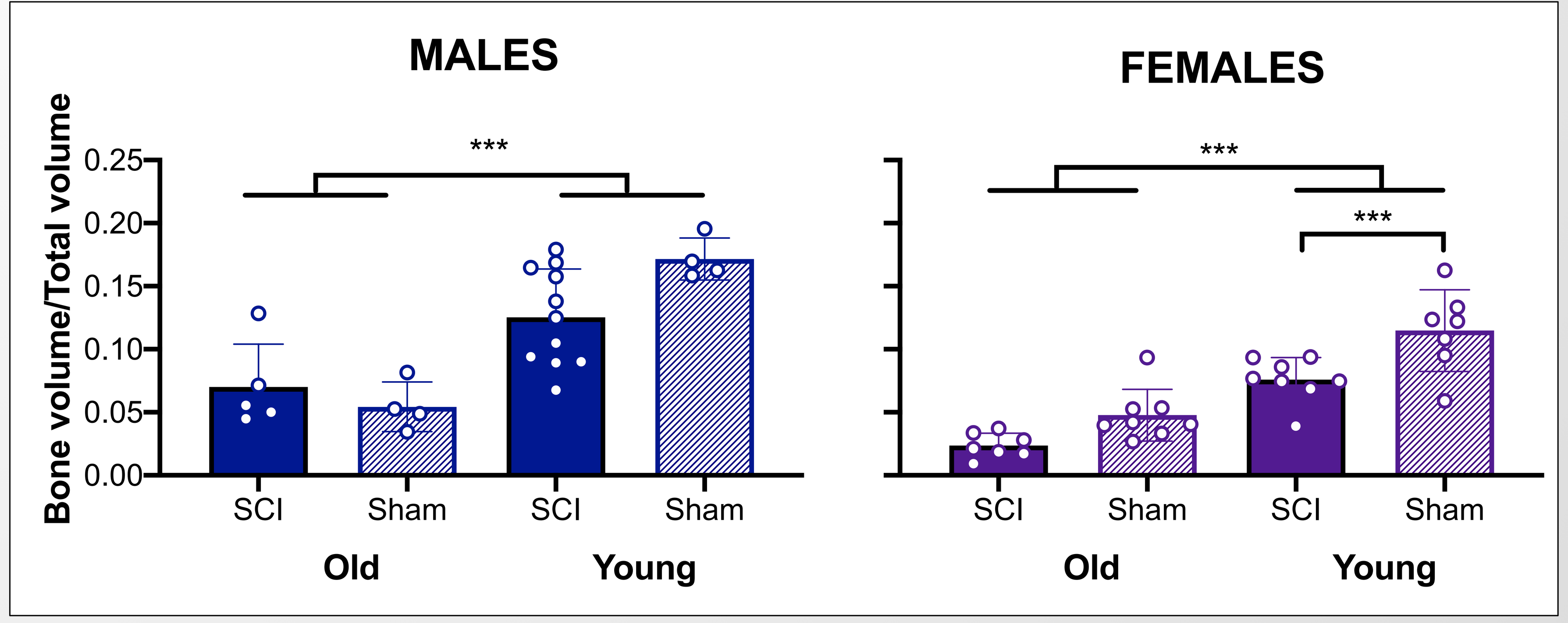
BOTH AGE AND SCI SIGNIFICANTLY DECREASED REARING ACTIVITY



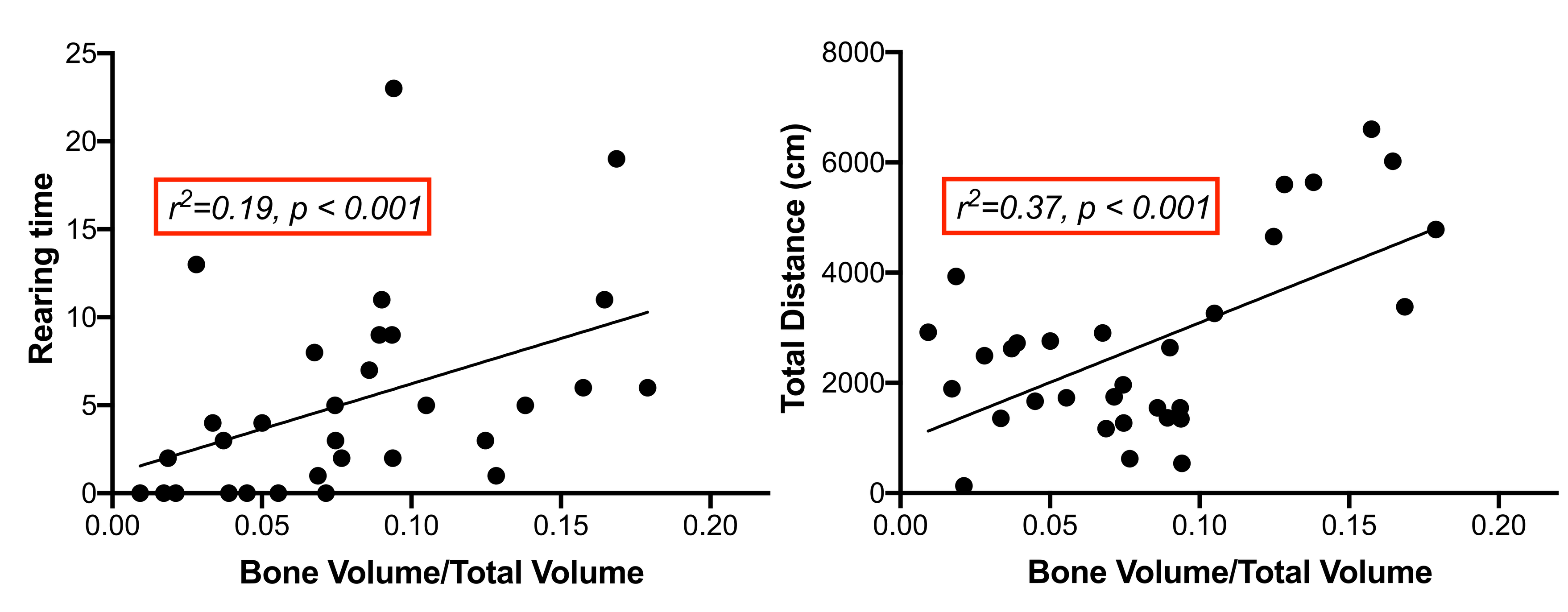
AGE DECREASED ACTIVITY, SCI AND SEX DID NOT



BOTH AGE AND SCI SIGNIFICANTLY DECREASED BONE VOLUME



SCI-INDUCED DECREASED ACTIVITY CORRELATES WITH DECREASED BV/TV



SUMMARY AND CONCLUSIONS

Post-SCI activity recovered within 28 days, regardless of age or sex. Most mice were stepping by day 13 post injury, and all were stepping by 28 days.

SCI and age significantly suppressed the recovery of rearing and total activity. These effects only appeared 'additive' in the rearing test. Old mice also reared substantially less than the young mice. Age more consistently affected the distance traveled in the activity chambers, compared to the effects of SCI.

Both SCI and age decreased bone volume. Significant effects of SCI in female subjects and a trend in males (that was not significant) were observed.

SCI-induced diminished activity levels (both rearing time and distance traveled) were significantly correlated with decreases in tibial trabecular bone volume.

These data underscore the importance of *load and use* on the maintenance of bone mass. Rather than simply being whether subjects are loading on the hindlimbs or not, active loading may be critical. Indeed, partial weight-bearing in humans during physical therapy does not stabilize or reverse bone loss. Our data support this finding but indicate that therapies that could completely load the bones may be effective. A comparison of the efficacy of different types of physical activity on bone loss is warranted, as well as testing whether intervention after bone loss has occurred could reverse effects of SCI on bone health.

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