Effect of altered 5HT homeostasis on femur bone parameters

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Aims

The aim of this research was to assess the effect 5HT has on bone in a Wistar-Zagreb 5HT (WZ-5HT) rat model at the site of distal femur.

Method

Wistar-Zagreb 5HT (WZ-5HT) rat model is a physiological animal model of altered serotonin (5HT) homeostasis. By crossing male and female Wistar rats selected for high or low platelet 5HT levels and the velocity of platelet 5HT uptake two distinct sublines, high-5HT and low-5HT, were created (1). Bone analysis was performed on 8 months old female WZ-5HT rats.

For analysis distal part of the femur was scanned using 1076 µCT scanner. Images were obtained using 48 kV and 200 µA, corresponding to 18 µm isotropic resolution, with a 0.6° rotation step, 0.5 mm aluminum filter and to reduce image noise frame averaging was set to a value of 2. Images were reconstructed using NRecon software, employing range of 0-0.07 on a histogram scale. DataViewer software was used to align scanned bones with the concurrent saving of transaxial data set for further analysis.

In order to determine the effect of altered serotonin homeostasis on fracture repair a femur osteotomy was introduced using an oscillatory saw. Bone fragments were repositioned and fixed using Kirchner’s intramedullary pin (2). Animals were monitored for 8 weeks after which bones were analyzed.

Beside micro CT analysis functional testing of femur biomechanical properties was done using a Texture Analyzer HD.Plus (Texture technologies, USA). Cortical bone was assessed using the three-point-bending test while trabecular bone was analyzed using the indentation test (3).

Results

No change in cortical bone volume (BV/TV) and thickness (Co.Th) was observed between the sublines of WZ-5HT rat model. Conversely increase in endosteal volume (EV) was observed in high-5HT subline (Fig.1A). Biomechanical testing confirmed the results obtained by micro CT with no change in bone tissue properties (Fig. 1B).
Trabecular bone at the site of distal femur was markedly different between the sublines. Bone volume (BV) and trabecular number (Tb.N.) were decreased (Fig.2A), while the trabecular separation (Tb.Sp) was increased in high-5HT subline with no change in trabecular thickness (Tb.Th.) (Fig.2B). Biomechanical properties confirmed the results obtained by micro CT with lower trabecular bone strength in high-5HT rats (Fig.2C).

Fracture repair was impaired in high-5HT rats with lower callus bone volume (Fig.3A) and lowered biomechanical properties of the healed bone (Fig.3B).
Conclusion

We showed that an elevated level of 5HT has a diminutive effect on the trabecular bone and compromises the long bone fracture repair in rats with increased plasma and platelet 5HT levels.

References: