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Bone Characteristics and Fracture Risk in Adolescent Boys

➤ Rough play has its costs. Trauma-related fractures occur in approximately 162–257 adolescent boys per 10,000 person-years annually. During puberty, height growth rate peaks, but bone mineral density (BMD) does not accrue at an equal rate—an imbalance that might make bones temporarily more fragile.

However, this theory might not completely explain the increased fracture rate in puberty, because not all fractures result from equal trauma severity. This finding indicates that some bone is mechanically deficient. Moreover, although fracture incidence peaks between ages 11 and 12 years in girls and between 13 and 14 in boys, some bone deficiencies are detectable before puberty, between ages 7 and 8.

To investigate the association between congenital bone characteristics and fracture risk, Thierry Chevalley, M.D., at the Geneva University Hospitals and Faculty of Medicine in Switzerland, and his colleagues measured several bone variables in adolescent boys, including BMD (femoral neck), bone microstructure, and strength (distal tibia) using dual X-ray absorptiometry, high-resolution peripheral CT, and finite element analysis. They prospectively followed 176 healthy boys from ages about 7 to 15 years, half of whom had suffered fracture.

In their paper, to be published soon in ***The Journal of Clinical Endocrinology & Metabolism,**** the researchers report that lower femoral neck BMD, lower distal tibia trabecular volumetric BMD, and trabecular number, stiffness, and failure load contribute to bone weakness. They say these bone characteristics might have a genetic, rather than an environmental origin, because they can be detected at young ages and neither physical activity level nor protein and calcium consumption, measured at 7 and 15, contributed significantly to the fracture rate differences between the two groups. ■

* Chevalley T, Bonjour JP, van Rietbergen B, Ferrari S, Rizzoli, R. Fractures during childhood and adolescence in healthy boys: Relation with bone mass, microstructure, and strength. *J Clin Endocrinol Metab*, in press.

Vasopressin Aids Muscle Regeneration

➤ Skeletal muscle has a remarkable capacity to regenerate within 2 weeks of an injury. The peptide vasopressin, in vitro, is a potent myogenic promoting factor that is implicated in regeneration following experimental injury. The research team of Sergio Adamo, M.D., and Bianca Scicchitano, Ph.D., both at Sapienza University of Rome, Italy, further explored its effects in mouse muscle regeneration by manipulating the expression of its receptor, V1aR.

The team studied the consequences of overexpressing V1aR in specific muscles, thus sensitizing them to circulating vasopressin. Compared with controls, V1aR-overexpressing muscles showed significantly accelerated satellite cell activation, responded to injury to support regeneration, and exhibited increased expression of differentiation markers.

Investigating regeneration pathways, the researchers found that downstream from V1aR activation, calcineurin was strongly up-regulated in a way that led to increased expression of two of its downstream targets, the GATA2 and MEF2 transcription factors. V1aR also induced the calcineurin-dependent expression of interleukin (IL)-4, a potent mediator of myogenic cell fusion. These findings strongly suggest that vasopressin-induced IL-4 secretion sustains myogenesis in the later phases of regeneration.

Writing in ***Molecular Endocrinology,**** the researchers say their study demonstrates that skeletal muscle is a target of hormones of the vasopressin family and the research unveils several steps in a complex, vasopressin-dependent signaling pathway involving calcineurin, GATA2, MEF2, and IL-4. Knowing more about this pathway could lead to its manipulation in therapies for skeletal muscle regeneration, for instance, to minimize muscle wasting in aging, disuse, and neuromuscular disorders. ■

* Toschi A, Severi A, Coletti D, et al. Skeletal muscle regeneration in mice is stimulated by local overexpression of V1a-vasopressin receptor. *Mol Endocrinol*, in press.