J Musculoskelet Neuronal Interact 2008; 8(1):12

Black Forest Forum / Presentation
May 10-13, 2007
Castle Bad Liebenzell, Germany

Hylonome

Mechanostat function during skeletal development

T. Skerry

Academic Unit of Bone Biology, School of Medicine & Biomedical Sciences, University of Sheffield, Sheffield, UK

Keywords: Bone, Disuse, Exercise, *In Utero*

It is well known that the effects of mechanical loading on bone are greater in growing children and animals than in adults. Typically, children who begin playing racket sports at less than 5-years-old may have double the difference between serving and non-serving arms after 5 years, compared with those playing for the same duration who begin later in life. This poses the question, "how early in life does the skeleton begin to show adaptive responses?". Studies of babies born with so-called fetal akinesias, in which muscle development or function are abnormal, resulting in decreased or absent fetal movement, show that the skeletons of affected individuals are poorly developed and less well mineralized than normal. To study the role of mechanical loading in development of the skeleton we have analyzed the skeletons of mice engineered to lack the genes for two muscle transcription factors Myo-D and Myf-5. The absence of these genes prevents development of skeletal muscle and mouse pups are born with a skeleton that lacks many of the features seen normally. Bones are straight instead of curved, and lack either the narrowing of the mid-shaft of the cortex or the flaring of the metaphyses seen in WT controls. Even more striking is the absence of the traction epiphyses, proving Julius Wolff's assertion over 100 years ago that these develop because of muscular activity. MicroCT analysis of neonatal skeletons revealed reduced lengths of mineralized cortex, and low mineral density. These findings show that bone's adaptive response to exercise begins *in utero* and that movement during skeletogenesis is a powerful influence on skeletal form at birth. If the fetal origins of adult disease hypothesis are applicable to bone, then the movements of the fetus may affect susceptibility to bone disease in later life some 50-60 years later.

The author has no conflict of interest.

Corresponding author: Professor Tim Skerry, Professor of Orthopaedic Biology, Academic Unit of Bone Biology, Section of Musculoskeletal Science, School of Medicine & Biomedical Sciences, Beech Hill Road, Sheffield, S10 2RX, UK
E-mail: t.skerry@sheffield.ac.uk

Accepted 1 June 2007