

What is new in Musculo-Skeletal Interactions

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Abstract

In this new column of the JMNI, we will give a six-monthly overview about new publications which, to our eyes, are interesting and relevant. Keeping in line with the 'spirit' of ISMNI, we take the freedom to discuss with a more holistic approach and most importantly, we encourage feed-back from the readers.

Muscle, Muscle & Bone, Motor Control, Exercise (J. Rittweger)

Muscle

A look at the latest editions of our textbooks of physiology teaches us that the world is simple. α -motoneurons release acetylcholine and thereby make the muscles contract. Diabetes is a disease in which insulin production or effectiveness is insufficient. A couple of recent publications makes perceivable a more holistic concept of the relationship between muscle contraction (i.e. mechanical power) and regulation of glucose uptake (i.e. chemical power delivery) by the organism's prevailing consumer of glucose, the muscle.

Ariel Zisman and co-authors show that it is mainly the glucose transporter 4 (GLUT4) of the muscles which plays an important role in glucose tolerance¹. It had been known before that the rate-limiting step in muscle glucose use is the transmembrane transporter GLUT4. Transport of glucose by GLUT4 can be stimulated both by plasma insulin and by contraction or exercise. Through the work of Zisman et al., we can appreciate the role of skeletal muscle in the homeostasis of plasma glucose.

The investigators developed a rat model in which GLUT4 was selectively non-functional in skeletal muscle after birth. As a consequence, the animals developed glucose intolerance, hyperglycemia, and hyperinsulinemia, that was resistant to insulin and muscle contraction/exercise. GLUT4, the 'bottle neck' in glucose uptake, seems

to be influenced independently by contraction and insulin, via different pathways. A possible mechanism that may explain the contraction coupled increase of glucose uptake is by the co-transmission of adenosin from the motor endplate. Interestingly, adenosin A_{2A} and A_{2B} receptors have now been found to be expressed on the muscle cell membrane².

The above results are interesting in several ways with respect to neuro-muscular interactions. Firstly, they increase our knowledge about the mechanisms that let the muscles adapt to their usage. Athletes, for example, have an increased capacity of glucose uptake. Secondly, they again indicate that the inhibited utilization of glucose by muscle is a crucial point in the development of diabetes mellitus (and not hypo-insulinemia alone). In support of this view, it has been known for some time now, that the expression of GLUT4 decreases with age³. And thirdly, they permit us to speculate about mechanisms that cause the muscles' power output to decline in the elderly: Is it possible that in some of our sedentary patients with unimpaired circulation, respiration and 'normal' mechanical power of their muscles have an impaired flow of glucose towards their muscle? Is there a 'hidden' group of patients, who suffer from unrecognised muscular dysfunction, but are currently treated as primarily diabetic? The lack of knowledge with respect to these questions is illustrated by a recent publication in which the correlation between fibre type composition and glucose sensitivity is significant, but remains poor ($r = 0.33$) even if adjusted by adequate, refined statistical tools⁴. New studies are required that compare energy flow, mechanical power production and GLUT4 activity to clarify these issues.

Muscle & Bone

Myostatin is a secreted growth and differentiation factor, which is expressed in skeletal muscle. It is believed to

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