Graduate Studies

Department of Physiology
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Skeletal Muscle Energetics and Magnetic Resonance Imaging

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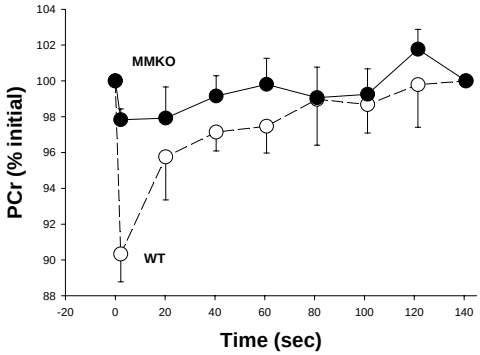
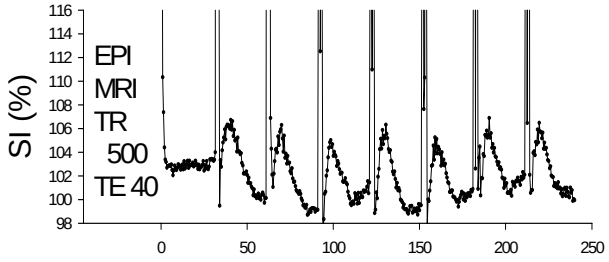
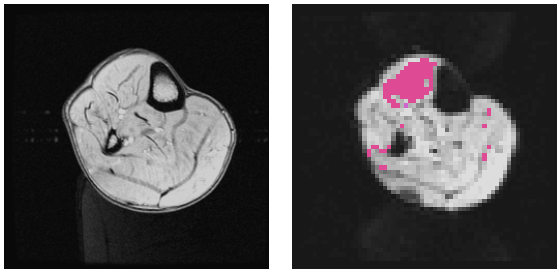
Healthy skeletal muscle is important not only for locomotion, but also for cardiovascular fitness and whole body metabolic balance. Thus, lack of regular muscular activity is a major contributing factor in the development of many chronic diseases, including heart failure, diabetes, and obesity. Furthermore, loss of muscle mass, strength, and coordination with age is a major cause of falls and other catastrophic injuries in the elderly population. In aggregate, skeletal muscle inactivity or weakness directly or indirectly cost the US health care system over $75 billion per year. Research in our laboratory ranges from basic studies aimed at understanding the regulation of muscle metabolism and energetics, to applied studies aimed at developing new diagnostic tools for the study of diseased muscle. Many of these studies involve NMR spectroscopic and imaging (MRI) measurements, for which we use both the NMR equipment available in physiology, and the human MRI equipment in the Department of Radiology. Some recent examples:

The role of muscle phosphocreatine. Creatine kinase catalyzes the rapid rephosphorylation of ADP to ATP from the hydrolysis of the phosphocreatine (PCr) stored in muscle. Phosphocreatine may also play roles in intracellular ATP transport and in regulation of mitochondrial oxygen consumption. We examined the function of phosphocreatine by comparing rates of PCr breakdown at the onset of contractions in leg muscle of wild-type vs. MM-creatine kinase knockout mice. (Roman et al, AJP:Cell 283:C1776, 2002). The results demonstrated that PCr breakdown is dramatically slower at the onset of contractions (2 s @ 5Hz) in the knockout mice. Because muscle force and ATP utilization were not seriously compromised, we concluded that oxygen consumption must be very rapidly activated in the knockout muscle, contrary to current dogma. Further studies are examining the energetic and functional consequences of other genetic manipulations of muscle metabolic enzymes, e.g., adenylate kinase knockout.



MRI studies of muscle oxygenation and blood flow. We recently showed that a single, brief contraction of human muscle results in a delayed, transient increase in blood flow and oxygenation which can be non-invasively measured by MR imaging or by near-infrared spectroscopy (Meyer et al, NMR in Biomed. 17:392, 2004). The magnitude of the transient change after brief contractions was 4-fold greater in physically active subjects compared to inactive subjects, although peak muscle blood flows in these two groups of subjects were the same after a more strenuous repetitive exercise. This suggests that measurement of flow or oxygenation transients after single contractions might provide a much more sensitive measure of peripheral vascular health than more conventional measures of limb vascular anatomy or post-exercise flow. Ongoing studies are exploring the use of these measurements for the early detection of diabetic peripheral vascular disease.





MRI of motor recruitment and fatigue. For many years our lab has been interested in using MRI to study patterns of motor unit recruitment in human subjects (see Meyer and Prior, Exerc. Sport Sci. Rev. 28:39, 2000 for review). We recently extended these studies to include brain functional MRI imaging (Fig. 3). We demonstrated that muscle fatigue in healthy young subjects is associated with increased activity of the motor areas, consistent with the recruitment of additional motor units to overcome peripheral fatigue. Future studies may examine brain activity in subjects with fibromyalgia and other poorly understood chronic fatigue syndromes.