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In the rodent, the time to peak amplitude of nerve-stimulation induced signals were consistently faster than those obtained from human subjects. Their speed, however, is highly consistent with that of force-velocity measurements made in rat hind limb isolated muscle preparations, further corroborating the skeletal muscle hypothesis [14]. Moreover, by using a neuromuscular blocking agent or by surgically denervating lower limb muscles, the optical response was completely eliminated.

A proof of principle experiment (data not shown) in which both the kinetics of the optical signal and the muscle kinematics were concurrently measured demonstrated that muscle action as measured by direct movement of the muscle tendon were highly correlated. We currently speculate that the intermediate optical signal may provide a capacity to non-invasively monitor the electromechanical action of muscles on a millisecond time scale. This may have valuable clinical application if the features of this signal can be shown to be influenced by muscle fiber twitch kinematics that are altered at the structural molecular level in a variety of myopathic processes. It is also intriguing that metabolic derangements as well as mitochondrial disorders might alter the kinematics of muscle fibers at the millisecond time scale thus the optical signal may provide a clinical tool for the investigation of these important clinical diseases. Currently we are using both the animal and human models described in this paper in experiments that directly measure the muscle force and motion concurrently with the intermediate signal characteristics in an effort to elucidate of the dynamics and details of the intermediate optical signal as a biomarker for clinical muscular and neuromuscular physiology and pathbiology.

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