Differential Diffusion Behaviour in Human Calf Muscles following Voluntary vs Electrically-Stimulated Contractions

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Target audience: Researchers and clinicians interested in the short-term physiological effects of electrical stimulation versus voluntary movement in skeletal muscle as assessed using diffusion tensor imaging (DTI).

Purpose: To demonstrate the temporal differences in DTI response immediately following skeletal muscle contraction when contractions are induced voluntarily versus electrical stimulation.

Methods: *Subjects:* Three healthy male volunteers (mean age 33.6 yrs) were scanned prior to and immediately following a 5-minute "contraction period", during which muscle contractions were induced either by electrical stimulation or voluntarily. *Contraction*: In the "stimulation" condition (STIM), two surface electrodes were fastened to the skin above the common peroneal nerve superior and lateral to the fibular head of the dominant leg. Stimulation of the common peroneal nerve was expected to affect (via deep and superficial branches)muscles such as tibialis anterior (ATib), extensors digitorum longus and hallucis (Ext), peroneus longus (Peron)[1]Stimulation consisted of a 0.1msec pulse at 2Hz and 35mA using a commercial EMG/stimulator unit modified for MRI-compatibility. Briefly, a commercial EMG/stimulator unit (XLTEK, NeuroMax 1004) was used for generating stimulation pulses. Standard MR-compatible electrodes (Cleartrace REF2700-003) connected to clip electrodes (Invivo Adult Quadtrode MRI ECG Cable) were attach to the subject's skin. These were connected via 9m of coaxial cable to the EMG/stimulation unit (through the waveguide) in the MR control room. Voluntary muscle contraction (VOL) consisted of repeated dorsiflected foot eversions at 1 Hz with instructions to mimic the muscle contraction and foot movement induced by electrical stimulation. These movements typically involved ATib, Ext, and Peron.[1] *MRI:* Scanning was done using a GE 3T (GE Healthcare, Milwaukee WI) and an 8-channel lower extremity coil. DTI data was acquired using a dual echo spin echo EPI sequence (b=400s/mm^2, TR/TE=4000/70ms, 6 directions, 16 slices 4mm thick, 16cm FOV, 64x64) prior to (4 volumes) and immediately following the exercise (13 volumes). The DTI volumes were collected every 35s from the thickest cross-section of the calf of the volunteer's dominant leg. *Analysis:* Regions-of-interest (ROIs) were drawn on ATib, Ext, Peron, soleus (SOL), and gastrocnemius lateralis (LG), and subsequently spatially and temporally registered using FSL[2] to create a time course of diffusion behaviour. ROIs were drawn separately for pre- and post-contraction volumes to prevent misregistration due to bulk movement during exercise. ROIs consisted of two 2x2 squares across 5 slices placed to avoid fascia, blood vessels, or artifacts from chemical shift. Mean diffusivity (MD) was then calculated for each volume using FSL[2]. Percentage MD change from baseline was calculated for each post-contraction time point in order to normalize diffusion changes between individuals.

Results: Following *VOL*, all active muscles (ATib, Ext, Peron) showed ~10% increase in diffusion at the first post-contraction time point **[Fig1]**, subsequently decreasing or increasing depending on the predominant fiber type (slow- vs fast-twitch, respectively). For the remainder of the post-VOL time period (~7.5 minutes), mean diffusivity in active muscles ranged from 5-23% above baseline, while inactive muscles ranged from ~-3-+2 % of baseline. Following *STIM*, the percentage MD increase of Peron was ~4% initially, while remaining muscles showed no significant change from baseline**[Fig2].** For the rest of the post-STIM time period, mean diffusivity in Peron ranged ~2-5.5% above baseline while remaining muscles fluctuated between approximately -2 to +2% change from baseline. In comparing *VOL* vs *STIM*, Peron showed consistently greater increases in MD above baseline, although both post-contraction conditions display a similar trajectory of diffusion across time **[Fig3]**.

Discussion: Mean diffusivity displays greater magnitude and variance in diffusion change when muscle contractions are elicited voluntarily rather than by electrical stimulation. Given that diffusion in tissue has been associated with blood flow, this could indicate that nervous processes governing bloodflow regulation of bloodflow are somehow circumvented following electrically-induced muscle contractions. While these results do not negate the effectiveness of electrical stimulation as a muscle activation tool, its use in muscle contraction appears to have very different MRI results compared to similar voluntary movements. Electrical stimulation of skeletal muscle should not be considered a substitute for voluntary exercise, but instead an alternate form of muscle activation by contraction. Further investigations into voluntary vs. stimulated contractions should include examination of BOLD and ^{31}P-MRS data as well as measures of blood flow. Furthermore alternate forms of electrical stimulation should be considered.

Conclusions: DTI is only marginally sensitive to muscle changes induced by electrical stimulation, while greatly influenced by mild voluntary exercise. Due to differences in post-contraction behaviour, electrical stimulation should not be considered a substitute for voluntary exercise, but rather an alternate regimen of muscle activation and contraction.

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References: [1] Snell RS. Clinical Anatomy for Medical Students, 3rd ed. Toronto: Little, Brown & Co, 1986.; [2] http://fsl.fmrib.ox.ac.uk/fsl/;

Fig1

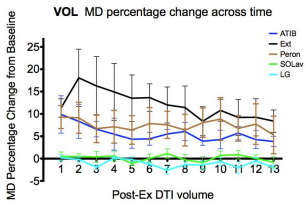

Fig 2

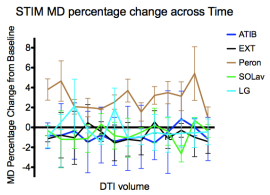

Fig 3