Investigating the hemodynamics of calf muscle during exercise using independent component analysis (ICA)

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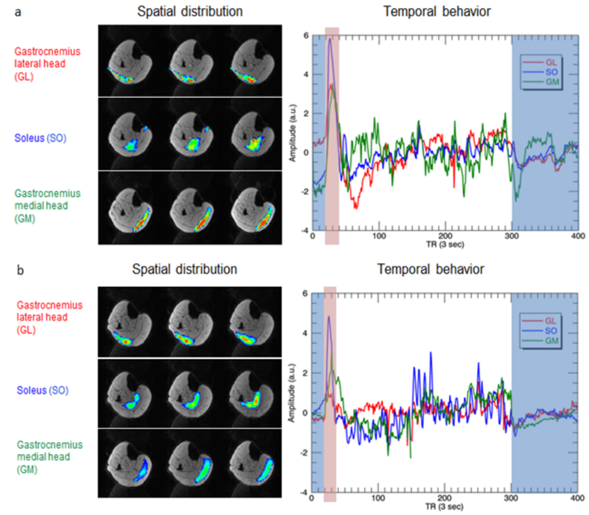

Fig. 1. The spatial and temporal behavior of 3 muscle groups during the exercise paradigm. Data from two healthy subjects are shown in a and b. Blue shaded area: baseline and recovery; orange shaded area: first minute after onset of the exercise paradigm.

Introduction: The hemodynamics of skeletal muscle and its alterations in diseases are important but not yet well studied. Studies have shown that postcontractile BOLD signal intensity (SI) changes in muscles are dependent on O_2 delivery and O_2 consumption [1]. However, performing group studies of the lower leg muscle signal during excise is challenging, because of the vast variations in individual morphology and muscle utilization strategy that entail a given task. As such, normalization to a common muscle template during exercise is difficult. We propose a novel approach of using single subject Independent Component Analysis (ICA) to simultaneously identify the lower leg muscle groups and their common hemodynamic behavior during a given exercise paradigm (rhythmic plantar-flexion) [2,3]. ICA results differentiate involvement of three muscle subgroups: gastrocnemius lateral head (GL), Soleus (SO) and gastrocnemius medial head (GM) and their dynamic BOLD signal behavior during an exercise paradigm.

Methods: The subject population included 4 healthy controls (HC) (mean age= 42.5 years, 1 female). Using a Siemens 3T scanner (Magnetom Trio), gradient echo EPI images of the calf muscles during exercise were acquired with the following parameters: voxel size = 2.5x2.5 mm, number of slices = 10, slice thickness = 5.0 mm, FOV= 160 mm^2, flip angle = 70^0, bandwidth = 2112 Hz/Px, TE = 25 ms and TR = 3 s. The exercise paradigm consisted of a one-minute baseline, a 14-minute rhythmic plantar-flexion exercise and a 5-minute recovery. Using a MRI compatible, custom made exercise machine, all subjects performed plantar-flexion with a 2 kg load at a pace of 20 times/min. To reduce the motion artifact, the exercise was performed only during the 2211-ms interval when no image acquisition was performed within each TR. This was achieved by providing sufficient instructions to subjects to follow the cue of gradient noise during image acquisition. MRI data were preprocessed using the SPM8 software (The Welcome Trust Centre for Neuroimaging, University College London, UK). The single subject ICA analysis was performed according to the methods outlined elsewhere [2, 3].

Results: Fig. 1a shows three individual IC maps corresponding to three muscle groups with unique temporal behavior during the exercise paradigm. Fig. 1b shows the results from a second healthy subject, demonstrating the reproducibility of our ICA approach. The BOLD signals from all three muscle groups, especially SO, exhibit a sharp increase and rapid decrease during the first minute after onset of the exercise paradigm and then remained slightly lower to the baseline. All components had a frequency power spectrum that was comparable to the low frequency of the exercise paradigm (~0.33 Hz).

Discussion: ICA requires no prior knowledge of the hemodynamic response function (HRF) of the muscle during a given exercise paradigm, which may vary across different muscle subtypes and subjects [2, 3, 4]. ICA was able to differentiate and identify GL, GM and SO muscles based on their unique hemodynamic characteristics during the exercising paradigm. A high inter-subject variability in muscle-condition, -size, -shape and -utilization with the corresponding BOLD signal behavior adds many levels of difficulty when conducting group studies in this field. The data driven methods utilized in this work can provide an avenue to address these issues by clearly identifying muscle subgroups: each having a unique temporal characteristic. Additionally, data point to a differential muscle physiologies during the first minute after the onset of the exercise paradigm. Our results support the notion of an intimate causal connection between the hemodynamic characteristic and muscle physiological conditions during exercising. As such, the current study demonstrate a novel and straight forward methodology to investigate muscle physiology during exercise and related diseases such as peripheral arterial disease (PAD).

Conclusion: Single subject ICA is shown to be a novel method for the study of muscle hemodynamics and associated physiology during exercise. This method automatically segments the muscle groups with respect to the matching hemodynamic characteristics. With further investigations on assessing its feasibility in differentiating the BOLD behavior in healthy and diseased subjects, this method can be a valuable tool for clinical applications in musculoskeletal diseases.

References:

[1] Towse et al. J Appl Physiol. 111 (2011) 27-39, [2] Calhoun, et al. Hum. Brain Mapp. 14(2001) 140-51, [3] Karunanayaka et al. HBM (2013), [4] Karunanayaka et al. NeuroImage (2010)

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