Hyperemic Flow Heterogeneity in Human Leg Muscle: An MRI Study Using Arterial Spin Labeling

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Introduction

Previous studies in non-diseased skeletal muscle have shown that flow and oxygen consumption are not uniform between muscle groups during exercise (1,2). Flow measurement based on whole limbs as the case with plethysmography can therefore be confounded if the spatial heterogeneity is not taken into account. Arterial spin labeling (ASL) (3) is a noninvasive MR technique for perfusion measurement that has been widely used in the brain. So far, only few ASL studies have investigated the spatial flow distribution in extremity muscles (4,5). In the present work, we report the results of the application of continuous ASL (CASL) to systematically study perfusion differences between all major muscle groups in the calf.

Materials and Methods

1. Experiment paradigm In skeletal muscle, flow during exercise or following a period of ischemia is several-fold higher than at rest, and is measurable as an indicator for both normal and pathophysiology (6). Considering that exercise may preferentially stimulate certain muscle groups and complicate flow comparisons between them, we elected to employ a brief ischemic-hyperemic paradigm to more uniformly challenge all muscle groups. A nonmagnetic tourniquet was used with the cuff placed on the thigh to create a 5-min period of ischemia followed by a period of hyperemic flow. The occlusion pressure was 250 mmHg. ASL imaging commenced 2 min before cuff inflation and ended 3 min after cuff deflation.

2. Human subjects and MR scans Nineteen healthy subjects (ages 28-45 years, F=8, M=11) were scanned after IRB approval and appropriate consent were obtained. None of the subjects had evidence of vascular disease as assessed by medical history and noninvasive vascular systolic pressure indices. MR imaging was conducted on a 3.0 T Siemens Trio system (Erlangen, Germany) with a transmit/receive knee coil. Subjects were placed supine. Perfusion-weighted images were obtained using a single-slice version of the CASL sequence (7) with single-shot gradient-echo echoplanar readout. Our previous study suggested a prolonged tagging bolus in skeletal muscle and existence of venous outflow during hyperemia. Such confounds can be minimized by using a post-labeling delay of 1900 msec in combination with a 4-sec TR. Other imaging parameters were: FOV = 22 cm (mid-calf), in-plane matrix size = 64 x 64, slice thickness = 1 cm, TE = 17 msec, tagging duration = 2 sec. The labeling plane was 6 cm proximal to the imaging slice for the tag scan and 6 cm distal for the control scan. A 2D high-resolution anatomic image was acquired at the same slice at which ASL imaging was performed.

3. Data analysis Subject motion was corrected by obtaining navigator echoes along three orthogonal directions prior to data acquisition. ASL signals were generated by pair-wise subtraction of tag and control images and converted to quantitative flow. Two adjacent data points in time were averaged, resulting in an effective temporal resolution of 16 sec. The anatomic image was used to define regions of interest (ROI) for six muscle groups in the calf (Fig.1). Any vessels visually discernible on the anatomical image were excluded from further analysis. For each muscle group, peak and average flow were computed for the hyperemic duration.

Results and Conclusions

Statistical flow differences were observed between muscle groups (one-way ANOVA, p = 0.002). Tukey's HSD post hoc test then showed a mild statistical difference (p = 0.08) between deep muscles (deep flexor and soleus) and superficial muscles (anterior/lateral extensors, medial/lateral gastrocnemius) whereas no significant differences were found within deep muscles and within superficial muscles (Table 1, Fig 2). The higher hyperemic flow response in the soleus muscle can be attributed to the higher fraction of slow-twitch type I fibers (70-80%) with a greater capillarity and oxidative capacity (8). Hence, after the depletion of oxygen during the occlusion, the soleus muscle recruits more flow to replenish the blood/oxygen reserve. By contrast, gastrocnemius and anterior/lateral extensors are more evenly mixed with type I fibers (50–60%) and type II fibers (8). One notices that the deep flexor in the mid-calf exhibits a peak hyperemic flow comparable to that in the soleus muscle. Particularly noteworthy is the high resting flow of the deep flexor compared to other muscle groups.

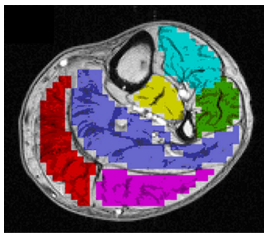

Fig 1. Mid-calf muscles: medial/lateral gastrocnemius (red/pink), soleus (purple), deep flexor (yellow) and anterior/lateral extensors (blue/green).

Table 1. Hyperemic flow (mean±std)

Muscle Groups	Peak	Mean
Lateral Gastrocnemius	87±32	49±20
Medial Gastrocnemius	85±43	49±25
Soleus	116±57	67±39
Deep Flexor	127±49	69±20
Anterior Extensor	86±33	72±33
Lateral Extensor	75±47	64±49

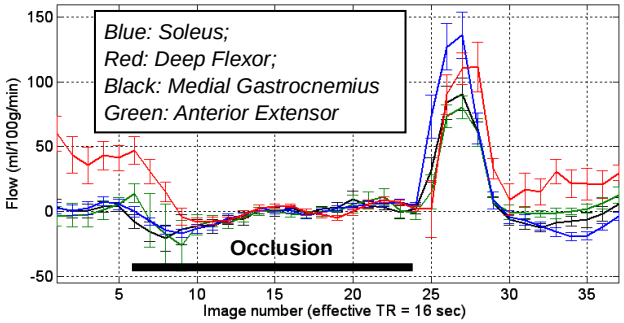

Fig 2. Error bars indicate the standard error across subjects.

Finally, computer simulations were conducted to estimate possible dependence of the results on T_1/T_2*. However, variations in these parameters were found to account for less than 10% of the observed differences among muscle groups. As a result, the discrepant hyperemic flow between deep and superficial muscles as shown in Fig. 2 can be considered physiological. In summary, CASL proves to be able to detect the flow heterogeneity between muscle groups in human extremities. The ability to reliably measure heterogeneity may help understanding the vascular/metabolic mechanisms in skeletal muscle and possibly provide diagnostic information for the assessment of peripheral vascular disease.

References

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