# Nicotine Induced Changes in Muscle BOLD Signal at 3T

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## Introduction

Substances which affect brain blood flow are known to cause perturbations in brain BOLD signal. However, vasomodulators also affect the BOLD signal in skeletal muscle [1,2]. Previously we have demonstrated that oscillating subject breathing of 100% $O_2$ with normoxia can produce a 'boxcar-like' pattern in muscle BOLD signal similar to that seen in fMRI brain activation studies [1,2]; the amplitude of which is likely related to voxel blood perfusion and volume. Hyperoxia results in an increase in $T_2$ and reduced blood volumes [3,4]. Using oxygen-enhanced BOLD imaging of human calf muscles, we proposed that muscle fibre differences (fast twitch vs. slow twitch) would be observable and that nicotine a powerful vasomodulator, could result in differences between pre and post exercise states, providing blood flow and perfusion information. Nicotine is known to be a vasoconstrictor in some vascular beds, and is suggested to be a vasodilator in others. There is some debate as to whether it acts as a constrictor or a dilator in skeletal muscle, and as to its effect on type I and type II muscle [5,6].

Hyperoxia can produce a constriction of small vessels in skeletal muscle [7]. However, the change in oxygen content in the blood, and blood volume changes dominate the BOLD signal. Breathing 100% $O_2$ results in an increase in $pO_2$ in the plasma which is preferentially extracted above the oxygen bound to haemoglobin. As the hyperoxia paradigm has no direct functional aspect, the $O_2$ demand remains constant throughout the imaging sequence. Thus, the periods of hyperoxia produce an increase in dissolved $O_2$ which is paramagnetic and a relative decrease in deoxyHb, also a paramagnetic species. An increase in the BOLD signal intensity with hyperoxia would suggest that the decrease of deoxyHb dominates the effect; a decrease in signal would imply that the increased $pO_2$ dominates.

## Methods

The right calf in 5 subjects (3♂, 2♀) was immobilised and imaged using a GE Excite 3T MRI and a transmit-receive extremity coil. An EPI sequence was employed to collect 180 temporal points, during which the subjects periodically inhaled 100% $O_2$ (4 cycles of 90s normoxia each followed by 45s of 100% $O_2$). Subjects then exercised (200 rapid calf-raises, with straight knees) and the imaging protocol was repeated. For studies to evaluate nicotine subjects fasted for 8 hours and then were similarly evaluated, however the imaging/exercise paradigm was performed 1/2 hour following administration of 4mg of nicotine. Nicotine was administered via a nicotine polacrilex gum (Nicorette, Pharmacia AB, Sweden). Muscle BOLD dynamic range, (%BOLD signal difference, post vs. pre-exercise) was calculated and compared between slow and fast twitch muscles.

## Results and Discussion

Regions of interest (ROI) were analysed using AFNI [8] for the fast-twitch gastrocnemius and the slow-twitch soleus muscles. The number of activated voxels increased in both muscles following exercise, as did the mean intensity of activated voxels. The soleus muscle showed dramatic activation with hyperoxia (Figures 1 & 2) reflecting the high vascular density compared with the gastrocnemius. The soleus also displayed a marked increase in BOLD response with nicotine, whereas the gastrocnemius, showed much less activation, and less response to exercise and nicotine. These results confirm the vasodilation effect in type I skeletal muscle, but indicate that type II muscle perfusion is not affected by nicotine. They also show that the increased $pO_2$ and blood volume effects dominate the hyperoxic BOLD effect in muscle.

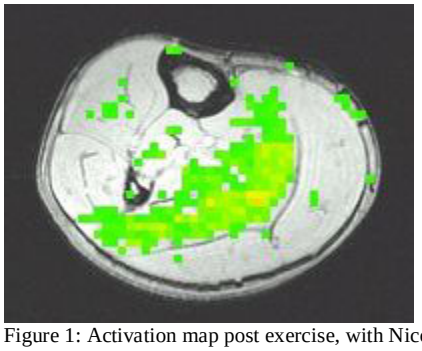

Figure 1: Activation map post exercise, with Nicotine, clearly depicting the soleus.

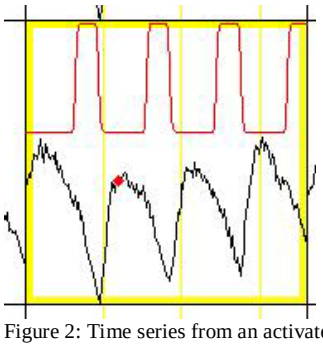

Figure 2: Time series from an activated voxel in Fig. 1.

## Conclusion

Muscle BOLD imaging using hyperoxia dramatically differentiates between muscle fibre types at 3T. Nicotine was shown to increase the muscle BOLD signal in type I, slow-twitch skeletal muscle, yet have little effect in type II, fast-twitch muscle.

References

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