## Using Arterial Spin Labeling to Image the Changes in Cerebral Blood Flow Caused by Sustained Muscular Pain

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*Introduction*: Most imaging studies of pain have involved superficial stimuli, such as contact heat, of brief duration (less than 30 seconds), whereas, clinical pain is generally prolonged and arises from deep tissues [1,2]. Having demonstrated that arterial spin labeling (ASL) is sensitive enough to detect pain-related activation in a conventional paradigm [3], the purpose of the current study was to use perfusion MRI to identify neuronal activation caused by experimental tonic (sustained) muscular pain. An ASL technique was chosen expressly for this purpose since it is well suited to stimulation paradigms with low task frequency [4].

*Materials and Methods*: A multi-slice, spiral ASL sequence was used to collect CBF images on a 3T magnet equipped with an 8channel, receive only, phased array coil (GE medical systems) [5]. Ten axial perfusion-weighted images were acquired every 7.5 s with an in-plane resolution of 3.75 mm and a slice thickness of 6 mm. Eleven healthy male volunteers (aged 23-41, mean:  $29\pm5$ ) were imaged during 10 minutes of baseline (no pain) followed by 15 minutes of pain from the intramuscular infusion of hypertonic saline (HS) (5% NaCl) into the left forearm. After an initial 0.5ml bolus, the infusion rate was adjusted to maintain a subjective pain intensity rating of 7/10 on a visual analog scale. Eight healthy male controls (aged 25-42, mean:  $31\pm6$ ) were imaged during infusion of normal saline (0.9% NaCl).

*Results*: The largest CBF increases occurred within the 1<sup>st</sup> 5 min of pain and these were observed bilaterally in the insula, thalamus, putamen, anterior and middle cingulate, as well as contralateral S2 and ipsilateral middle frontal gyrus. Initial significant decreases in CBF were seen mainly in the parietal cortex and S1. Levels of CBF increase and decrease both dissipated over time, except for a region in the left, superior temporal lobe, in which CBF continued to decrease. Group analysis of controls revealed no statistically significant activations.

*Discussion*: This study demonstrated that ASL is able to track changes in regional CBF that occur during sustained muscular pain. The initial bolus of HS caused the greatest CBF increases. Interestingly, these increases diminished over the following 10 min even though the subjective pain intensity ratings remained greater than 5/10. This may be due to a decrease in the unpleasantness of the pain. Future studies will involve modifying the stimulus in order to maintain the duration of the pain, and in particular its unpleasantness, in order to more closely emulate the clinical pain experience.



**Fig. 1 Group Activation Map**: Areas of significant CBF increases (red) and decreases (blue) during the tonic pain stimulus. A:  $1^{st}$  2.5min; B:  $1^{st}$  5min; C  $2^{nd}$  5min; D:  $3^{rd}$  5min. Corrected for multiple comparisons (FDR, p < 0.05). Images displayed in neurological convention.

## References

- (1) Shipton et al., Eur J Anaesthesiol 2005;22(6):405-12.
- (3) Owen et al., *Pain* 2007 Aug 21; [Epub ahead of print].
- (5) St. Lawrence et al., *MRM* 2005;53(3):735-738



**Fig. 2 ROI Time Courses:** CBF changes (relative to baseline) as a function of time in the anterior cingulate (blue), and left temporal lobe (red).

- (2) Schreckenberger et al., *Neurology* 2005;64:1175-1183.
- (4) Wang et al., MRM 2003;49:796-802.