Chronic low back pain patients exhibit distinct patterns of increased resting cerebral blood flow

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Purpose

BOLD FMRI has been used to reveal brain networks responding to acute administration or modulation of painful stimulation. Regions forming these networks include the primary and secondary sensory-motor cortices, thalamus, cingulate, and insula as well as regions involved in attentional and cognitive processes such as the amygdala and hippocampus/parahippocampus[1]. Arterial spin labelling (ASL) has recently been applied in studies of acute[2], tonic[3,4], post-surgical[1] and osteoarthritic pain[5], revealing regions with increased cerebral blood flow (CBF). Here, we examine resting CBF in patients with chronic low back pain compared to controls.

Methods

Thirteen patients with a physician diagnosis of chronic (>1 year) low back pain and fourteen controls were included in this study. At 3 T (HDx, General Electric Healthcare), pulsed ASL (PICORE-QUIPSSII)[6] was performed using the following scanning parameters: TR/TE = 2200 ms/19 ms; TI1/TI2 = 700 ms/1350 ms; 24 cm^2 field of view: 64 x 64 matrix; 16 slices, 7.0 mm with a 1.0 mm gap. Quantified CBF maps were calculated using the single compartment model[6] and then registered to standard space (MNI) using the T1-weighted image (1x1x1mm voxels). Regions generally accepted to be a part of the pain network (the thalamus, postcentral gyrus, anterior and posterior cingulate, hippocampus/parahippocampus, amygdala and insula) were examined in a region of interest analysis and CBF was compared between groups. CBF was also compared in a voxel-wise analysis between the patient and control groups using a GLM. The *Z*-statistic map ($Z > 2.3$) was cluster corrected for multiple comparisons ($p<0.05$) (FSL, FMRIB, http://fsl.fmrib.ox.ac.uk/fsl/).

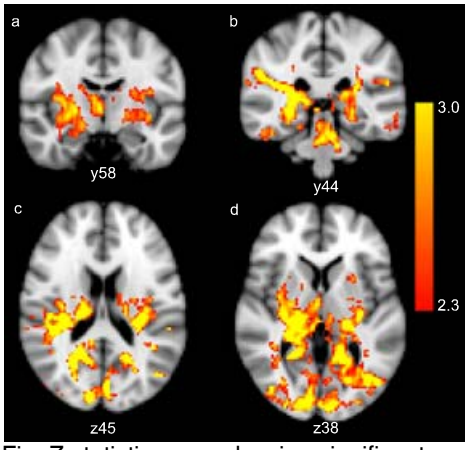

Fig. Z-statistic maps showing significant CBF increases in the whole brain analysis.

Results

The regional analysis showed increased CBF in the right and left thalamus, the right hippocampus/parahippocampus and right insula. From the whole-brain analysis (Fig), the regions and corresponding peak *Z*-statistic with significantly increased CBF in the patient group are summarized in the Table. We detected no areas of reduced CBF in the patient group compared to controls.

Table. Regions showing increased CBF in the whole-brain analysis

Region	Z-stat
Temporal Occipital Fusiform Gyrus	5.08
Occipital Fusiform Gyrus	5.00
Lateral Occipital Cortex, inferior region	4.91
Precuneus	4.85
Inferior Temporal Gyrus, temporooccipital part	4.83
Posterior Cingulate Gyrus	4.75
Lingual Gyrus	4.75
Cuneal Cortex	4.59
Occipital Pole	4.59
Insula	4.53
Parietal Operculum	4.49
Right Thalamus	4.49
Posterior Supramarginal Gyrus	4.21
Right Putamen	4.18
Intracalcarine Cortex	4.15
Right Caudate	4.13
Left Putamen	4.10
Inferior Temporal Gyrus, posterior division	4.03
Posterior Parahippocampal Gyrus	3.97
Left Thalamus	3.94
Precentral Gyrus	3.94
Anterior Supramarginal Gyrus	3.89
Brainstem	3.63
Left Pallidum	3.57
Central Operculum	3.55
Right Pallidum	3.42
Left Caudate	3.37

Discussion

We have identified brain regions with increased CBF in chronic low back pain using pulsed ASL. No differences in grey matter density were detected. Some of the observed areas of increased CBF are consistent with regions that show increased CBF in osteoarthritis of the thumb[5] and in post-surgical pain[4], suggesting that some regional CBF changes are associated with long-term pain. Regions that consistently showed increased CBF in chronic low back pain and thumb osteoarthritis[5] such as the insula, posterior cingulate, parietal operculum, hippocampus, thalamus, cuneus, precuneus, precentral gyrus and inferior temporal gyrus are suggested to be involved in chronic pain processing regardless of body location. Regions such as the central operculum and pallidum that are unique to this study, may be related to the co-morbidities associated with chronic pain, such as catastrophizing, fear/anxiety and depression. The post-central gyrus, posterior cingulate and amygdala, often implicated in pain imaging studies, did not show a significant difference between groups in both the regional and the whole-brain analysis.

Conclusion

ASL measurements have the capacity to detect regional differences in CBF associated with chronic low back pain. The application of ASL is likely to assist in understanding chronic pain and treatment efficacy as, unlike BOLD FMRI, it is sensitive to long term alterations in CBF and is not restricted to acute events. Pain is a multifactorial condition and understanding the underlying mechanisms in pain conditions using robust imaging markers of chronic pain may accelerate the development of new treatments.

References: [1]Howard et al. *PLoS One* 2011; 6: e17096. [2]Owen et al. *Pain* 2008; 136: 85. [3]Owen et al. *J Magn Reson Imaging* 2012; 35: 669. [4] Owen, et al. *Pain* 2010; 148: 375. [5] Howard, et al. *Arthritis Rheum* 2012;EPub ahead of print. [6]Wong, et al. *Magn Reson Med* 1998; 39: 702.