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. Arterial spin labelling (ASL) has recently been applied in studies of acute, tonic, post-surgical and osteoarthritis pain, 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) was performed using the following scanning parameters: TR/TE = 2200 ms/19 ms; TI1/TI2 = 700 ms/1350 ms; 24 cm 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 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/para hippocampus, 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, FMRI, http://fsl.fmrib.ox.ac.uk/fsl/).

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.

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 and in post-surgical pain, 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 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.