Multivariate Discrimination of Changes in Regional Cerebral Blood Flow Representing Ongoing Post-surgical Pain using Gaussian Process Classification.

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Introduction

Continuous arterial spin labelling (cASL), has been used to demonstrate regional cerebral blood flow-changes underpinning ongoing pain[1] in a reproducible network of brain regions. Such networks may be best detected by multivariate analysis techniques, which take account of spatial relatedness within the data. Here, we applied Gaussian Process Classification (GPC)[2], a supervised 'machine learning' image analysis technique, with the aim of providing probabilistic classification of individuals while pain-free, compared to the ongoing pain experienced following third molar extraction surgery (TME). A secondary aim was to ascertain the minimum amount of cASL data acquired to provide robust estimates of classification accuracy.

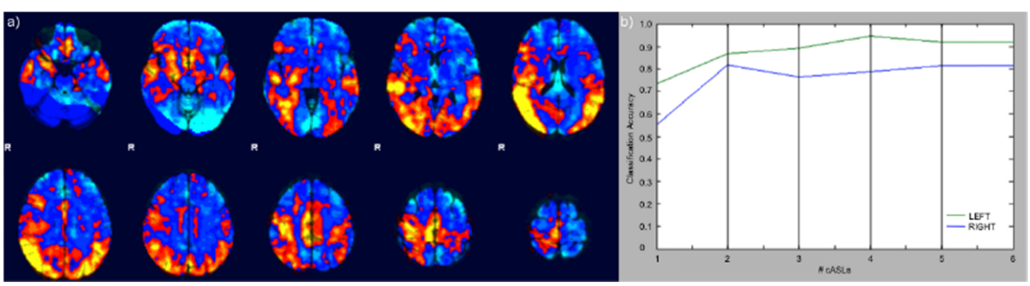
Methods

16 right-handed males requiring bilateral, lower-jaw TME were recruited. Four MRI examinations were performed, pre- and post-TME on both left and right-sided teeth. At each session, six individual resting-state cerebral blood flow maps were acquired using pulsed-continuous arterial spin labelling[3] (pCASL). A two-week recovery period separated surgeries.

Image analysis was performed using PROBID (www.brainmap.co.uk). Classification of pain-free, compared to post-surgical pain states, was computed individually for left and right-sided TME. Independent whole-brain linear GPCs were trained for each individual subject using leave-one-out cross validation. Permutation testing was performed across all subject predictions; the prediction model was calculated after randomly permuting classification labels (NoPain/Pain) 1000 times. p-values were derived by counting the number of permutations achieving higher sensitivity and specificity than non-permuted data. Classification accuracy was repeatedly recalculated as the number of pCASL volumes acquired per subject per session was exhaustively reduced from six to one.

Results

GPC correctly classified post-surgical pain, compared to pain-free pre-surgical states, with accuracies of 92% (Left tooth) and 82% (Right tooth). Multivariate discrimination maps underlying classification were physiologically plausible (Figure 1a). Classification accuracy remained above 80% using little as 2 pCASL exams per session (Figure 1b).



Conclusions

We demonstrate the potential of pCASL, in conjunction with GPC, as a robust, sensitive, time-efficient, and predictive assay of clinically relevant pain. The method has exciting potential for translation into the preclinical domain but also examination of persistent pain states, for example, osteoarthritis, cancer and HIV pain. Multivariate methodologies such as GPC may facilitate early decision-making in development of novel therapeutics for pain, including analgesics and other physical and behavioural therapies.

References

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2. Marquand et al. (2010) Neuroimage 49: 2178–2189.
3. Dai et al. (2008) Magnetic Resonance in Medicine 60: 1488–1497.