

British Pain Society. Mildred Clulow Award Final Report

Principal Applicant: Professor Tara Renton

Address and Contact Details:

Amount Awarded:

Title: Mapping of central changes, using cASL, induced by post-surgical pain after third molar surgery before and after Perfalgan infusion.

Date of Award: October 2009

Use of Resource (equipment, recruitment costs etc):

Summary of achievements: (max 300 words)

The study aim was to demonstrate whether cASL imaging technique can quantify local changes in rCBF following attenuation of third molar surgery (TMS) acute pain using intravenous paracetamol. The grant was used to support scanning costs. Experimentation was completed in September 2011.

The study demonstrated the robust behaviour of the TMS model; mild to moderate reported pain following surgery and significant attenuation of pain following administration of intravenous paracetamol. Pain scores did not significantly differ between sides of tooth extraction, confirming the suitability of the 'cross-over' study design.

Whole brain voxel wise analysis demonstrated significant changes in regional cerebral blood flow (rCBF, 5-10%) between pre-surgical and post surgical states and pre and post IV paracetamol, however, the direction of rCBF changes was opposite to that predicted in the study hypothesis. Unilateral increases in rCBF were identified in the primary somatosensory cortex post-surgically whilst relative decreases in rCBF were identified bilaterally in the insula, hippocampus and posterior cingulate cortex (PCC). These latter regions are likely to be involved in the descending inhibition of pain. Investigation of the analgesic effect of paracetamol, independent of its central effects, demonstrated changes in rCBF bilaterally in the insula, thalamus, hippocampus and PCC. In the pre-surgical arm of the study, a decrease in activation of the right insula was demonstrated following IV paracetamol, demonstrating paracetamol's central effects, independent of its analgesic properties. Throughout the analysis no changes in rCBF were demonstrated, in the control region (the visual cortex).

This pilot study received 1st prize paper presentation at BPS conference, 2012 and has initiated two further, grant-funded studies, in order to clarify its findings. A repeat of this study, with an amended study design incorporating improvements identified during the running of the pilot study, is ongoing. This study design has also been applied to another study investigating the cerebral representation of oral ibuprofen.

Publications Arising Directly from the Award (max 5)

Howard, Krause, Khawaja, Massat, Zelaya, Schumann, Huggins, Vennart, Williams, Renton. 2011. Beyond patient reported pain: perfusion magnetic resonance imaging demonstrates reproducible cerebral representation of ongoing post-surgical pain. *PLoS One*, 6, e17096.

Hodkinson DJ, Krause K, Khawaja N, Renton TF, Huggins JP, Vennart W, Thacker MA, Mehta MA, Zelaya FO, Williams SC, Howard MA. Quantifying the test-retest reliability of cerebral blood flow measurements in a clinical model of on-going post-surgical pain: A study using pseudo-continuous arterial spin labelling. *Neuroimage Clin*. 2013;3:301-310.

Further Research Funding following the Award

Medical Research Council Grant - Cerebral Blood Flow Imaging - Towards an Efficient, Automated Assay of Ongoing Pain and its Treatment, August 2012, £500,000

Royal College of Surgeons Research Fellowship, April, 2011, £54,000

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