Markers of cortical reorganisation in Complex Regional Pain Syndrome (CRPS): progress report.

Dr Christopher Brown, Department of Psychological Sciences, University of Liverpool.

Dr Michael Lee, Division of Anaesthesia, University of Cambridge.

Dr Nicholas Shenker, Department of Rheumatology, Addenbrooke's Hospital, Cambridge.

Progress and timeline to completion

The two major parts to the study are an EEG session and the MRI/fMRI session. PRF funding is largely contributing to the MRI scan costs (session 2). We have completed recruitment of 22 CRPS patients and 28 healthy controls. Of these, 19 CRPS patients and 13 healthy controls took part in fMRI scanning. This completes the planned data collection for the study.

Finances

All spending on the grant is completed and the grant is now closed with £1.87p left unspent.

Dissemination

Preliminary EEG results (from interim analyses) were presented as part of an oral presentation session at the EFIC (European Pain Federation) conference in Copenhagen in September 2017.

Three journal articles have been planned to disseminate the results:

1. The first paper (abstract below) is a combined analysis of EEG and behavioural data, expected to be submitted in May 2019.
2. The second paper (as yet untitled) is a further analysis of EEG data, likely to be submitted in 2020. This analysis is ongoing.
3. The third paper (as yet untitled) is an analysis of the fMRI data. Analysis for this paper will commence in 2019 with a likely submission date in early 2021.

Provisional title/abstract for first paper

Title: Computations of uncertainty underlie augmented somatosensory prediction errors in patients with Complex Regional Pain Syndrome

Abstract: Complex Regional Pain Syndrome (CPRS) is an often debilitating chronic pain condition with likely multifactorial origins, possibly including cerebral patho-mechanisms. We previously observed augmented late-latency somatosensory-evoked potentials in patients with CRPS that predicted behavioural response delays during tactile-spatial decision-making. Here, we test whether these observations can be explained by somatosensory prediction errors that update top-down processes (priors/predictions) influencing tactile-spatial perception. We employed a Bayesian model of hierarchical predictive coding to estimate individual differences in how the brain computes uncertainty in prediction and prediction errors during a tactile-spatial change-detection task. Initially, behavioural (response time) analyses (n=44) provided evidence of both bottom-up (sensory signal-to-noise) and top-down (learnt expectations about stimulus probabilities) influences on tactile-spatial change-detection. Strikingly, simulations of the predictive coding model reproduced these condition effects on behaviour, as well as individual differences in condition effects, providing predictive validity of the model. Model estimates indicated that CRPS patients (n=22), compared to healthy controls (n=22), were more uncertain in their top-down predictions of tactile-spatial changes; furthermore, this uncertainty was more stable (less volatile) over time. These factors explained larger model estimates of hierarchically mid-level precision-weighted prediction errors, which update the expected probability of tactile-spatial changes.

Model-based EEG analysis of somatosensory-evoked potentials (SEPs) revealed that these larger prediction errors partially explained augmented late-latency SEPs in patients. The results identify computational mechanisms underlying altered patterns of behavioural and neural responses in patients with CRPS, providing new insights towards the prevention or reversal of aberrant perceptual learning processes in the brain.