Integrity of structural pathways of the brain predicts effects of top-down bias on pain perception.

Submission No:

4690

Submission Type:

Abstract Submission

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Introduction:

Expectations play a key role in biasing pain perception (1,2,3). This represents a cognitive function that can alter the perception of pain depending on context and prior information. This effect was measured in an experiment designed to evaluate a participant's pain ratings to incoming heat stimuli preceded by a visual cue. The visual cue served to rate the incoming heat stimulus intensity, thus introducing an expectation component. Eventually the visual cue would incorrectly predict the incoming heat stimulus.
Previous studies using dMRI have shown promising results in predicting placebo analgesia in clinical trials by inspecting integrity of white matter tracts (4,5). However, the study of top-down mechanisms that influence pain perception and play a key role in positive placebo outcomes has not received equal attention using the same technique.
Applying Mrtrix3's fixel-based analysis, diffusion Magnetic Resonance Imaging (dMRI) is used here, to investigate whether microstructural differences in white matter pathways (8,9,10) within a population sample can serve as a predictor of a subject's adherence to expectations for pain perception. White matter microstructural differences can manifest as differences in Fibre Density (FD), Fibre Cross-Section (FC) and a combination of the two, Fibre Density and Cross-Section (FDC), all of which underlie intra-axonal volume of fibre bundles and overall structural connectivity. Hence this method offers certain advantages over previously used diffusion methods (9,10).

Methods:

Using a heat stimulus system, healthy participants (n=38) were subjected to multiple trials involving pain stimulus preceded by a visual cue that induced expectations. Followed by each trial, participants were prompted to rate their pain on a 0-100 pain rating scale. The task protocol tested differences of perceptual bias in pain perception (2). Numerical visual cues were paired with matched heat stimuli to encode linear association with pain intensities. Extent of bias toward cues was tested by presenting stimuli that deviated from expectations engendered by cue values at a range of prediction errors. The extent of perceptual pain bias was quantified as the difference in pain rating at zero versus maximum prediction error.
Diffusion MRI data was collected on a 3.0T GE scanner before assessing task performance. Diffusion images were

obtained using 60 directions, 2mm isotropic resolution at 7 b=0 interleaved acquisitions. An additional scan with 7 reversed phase-encoding b=0 images were acquired to facilitate distortion correction. General preprocessing was performed followed by whole-brain fixel-based analysis. GLM regression analyses correcting for age using connectivity-based fixel enhancement, 5000 permutations and FWE error correction were performed on all white matter fixels identified across subjects and evaluated whether fixel parameters underlying intra-axonal volume significantly mapped to perceptual pain bias.

Results:

Individuals that demonstrated a higher learning bias in pain perception showed reduced combination of fibre density and bundle cross-sectional area (FDC) in the splenium (posterior corpus callosum). On seeding this region using tractography to observe its connectivity with the brain, we found that this was an important pathway connecting the two cerebral hemispheres particularly along the temporal and visual pathways, as indicated in previous tracing and tractography studies.

Conclusions:

Taken together, this study demonstrates that inter-individual differences in white matter structure may play an important role in countering effects of top-down bias from prior learning. The predictive relation mapped to posterior corpus collosum. This region is an important pathway for interhemispheric communication between three lobes (parietal, temporal, visual (6,7)). Taken together, structural pathways as observed with fixel-based analysis (8,9,10) can predict an individual's capacity to overcome effects of learning induced bias.

Emotion and Motivation:

Emotional Learning

Higher Cognitive Functions:

Decision Making
Executive Function [2]

Imaging Methods:

Diffusion MRI

Perception and Attention:

Perception: Pain and Visceral [1]

Keywords:

Cognition
Perception
Tractography
White Matter
Other - predictive processing

[1|2]Indicates the priority used for review