High system segregation in resting fMRI predicts effects of top-down bias on pain perception.

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Introduction:

Pain – and how it is interpreted and mediated in the brain – is complex and involves many regions and cognitive phenomena like expectations from prior learning (1). Increase in perceived pain due to expectations has been widely linked with prior learning. Within the brain, learning has been associated with integration and segregation in networks formed by functional connections (2, 3), but the role of integration and segregation regarding pain experience is not understood. As pain is multi-modal, involves both learning and myriad regions, whole-brain segregation is a logical measure to consider.

Here, we hypothesize that higher segregation in baseline resting state networks predicts greater bias toward top-down cues in pain perception. We also questioned how segregation, nodal flexibility, and number of subnetworks traversed by nodes contribute and how these properties change between rest to task.

Methods:

Resting state fMRI scans were acquired at baseline (8 mins) and during three task scans (40 sec each, 10 total) in 38 healthy participants (18 females, mean age 31.7 +/- 10 years). The task protocol tested differences of perceptual bias in pain perception (4). 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.

fMRI time-series were extracted from 131 parcels (5) and adjacency matrices created with 0-lag Pearson correlations. Weighted and binarized networks were generated at a range of 0.05 to 0.5 densities using the Brain Connectivity Toolbox (6). Segregation (strength of within to between network connectivity) (2), flexibility (how many times nodes change network affiliation), and promiscuity (fraction of possible networks that each node affiliates with) (2,3) were evaluated using network communities identified with the Louvain method (7) and with 5 predefined resting state (5). Pain behavior was analysed for its link with baseline resting state scan. Windows of matched length were used for assessing changes in segregation between rest to task.

Results:

Pain ratings had high bias toward cues, with notable variance between participants. Both binarized and weighted resting state system segregation observed in baseline rest predicted individual differences in biased pain perception at a range of network densities ($p<0.05$), as did mean nodal promiscuity ($p<0.01$). Using matched window size, segregation values shifted to higher values from baseline to during task states, but this effect was significant only with fixed networks ($p<0.0001$) but not with the Louvain method.

Conclusions:

Previously, we reported that high clustering in resting state networks predicts effect of expectations on pain (8), and other work suggests network segregation and flexibility is a factor for learning performance (2, 3, 8). Here, learning induced bias in pain percept was associated with increased network segregation. This was observed before learning, suggesting an intrinsic characteristic of individuals' capacity for top-down bias where greater segregation at baseline is linked with stronger expectation effect. A higher nodal promiscuity also predicts greater learning induced bias, suggesting a balance of global integration vs changing nodal affiliation may contribute to how learning-based expectations inform perception.
Lastly, those with greater learning induced bias had greater difference between rest and task. This effect likely depends on intrinsic connectivity acting as a scaffold for facilitating task-effects and corroborates demonstrations of network reconfiguration correlating with task performance (2,3,9); here "task performance" is top-down processes informing perception.

Emotion and Motivation:

Emotional Learning

Higher Cognitive Functions:

Decision Making
Executive Function [2]

Learning and Memory:

Learning and Memory Other

Perception and Attention:

Perception: Pain and Visceral [1]

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[1|2]Indicates the priority used for review