

Neuroepidemiology of chronic pain: A meta-analysis of regional brain activation in chronic pain and healthy controls

Noah Waller, Semra Aytur, PhD, MPH and Donald A. Robin, PhD, University of New Hampshire, Durham, NH

Background/Purpose: Understanding the underlying brain regions and networks involved in chronic pain (CP) can help inform appropriate interventions. Meta-analyses allow for the distillation of myriad study data into statistical conclusions of greater power, thus facilitating evidence-based practice.

Objectives: To identify brain regions active while undergoing pain in patients with CP and in healthy controls (HC), including differences between groups and the underlying connectivity networks, using a comprehensive meta-analytic approach.

Methods: A systematic literature review was conducted for fMRI studies involving CP patients or HC undergoing pain induction via database searching and specific inclusion criteria. Studies were coded using brain mapping software and subsequently underwent an activation likelihood estimate (ALE) analysis. Peak activation coordinates from the ALE were used to create a meta-analytic connectivity model (MACM) with the CP data.

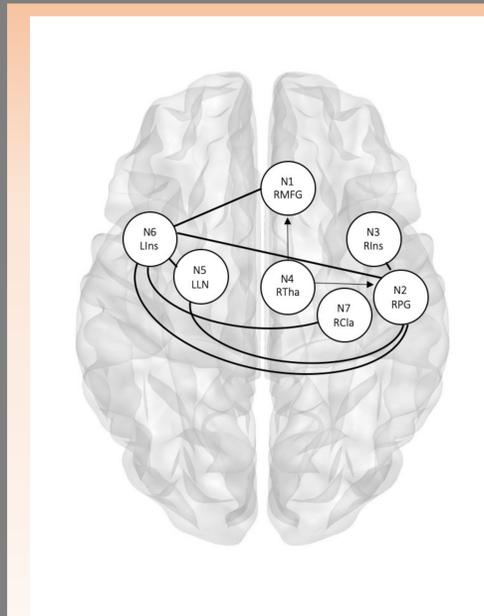
Results: The literature review yielded 92 studies involving HC undergoing pain induction and 21 studies involving CP patients undergoing pain induction.

- The ALE involving HC (1453 subjects, 2104 coordinate foci) revealed peak activation in 6 clusters including left thalamus, right cingulate gyrus, and right supramarginal gyrus.
- The ALE involving CP (419 subjects, 398 coordinate foci) revealed peak activation in 7 clusters including bilateral insula, right postcentral gyrus, and right thalamus.
- The MACM revealed two-way significant connections between the right medial frontal gyrus and the insula among other connections

Conclusion: Notable regional differences between the pain matrices of HC and CP were observed. Our connectivity model reveals significant associations between these regions that can further our understanding of CP mechanisms and interventions.

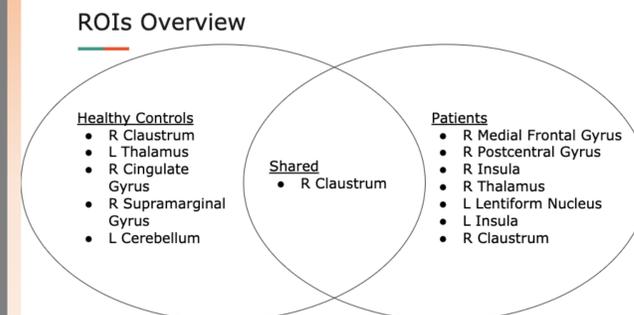
Brain activation during pain among patients suffering from chronic pain exhibits significant regional differences compared to the pain matrix in healthy controls.

Chronic Pain Meta-Analytic Connectivity Matrix (MACM)



MACM Parameters: CP
 ROIs = 12mm diameter
 Corrected P-Value = 0.007
 Significant 2-way connections = 6
 Significant 1-way connections = 4

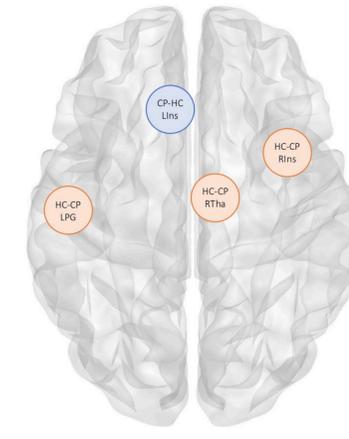
ALE Results/ROI Information



ALE Parameters: HC
 Cluster-level FWE = 0.05
 Threshold Permutations = 1000
 P-Value = 0.0001
 92 Papers
 1453 Subjects
 260 Conditions
 159 Experiments
 2104 Foci

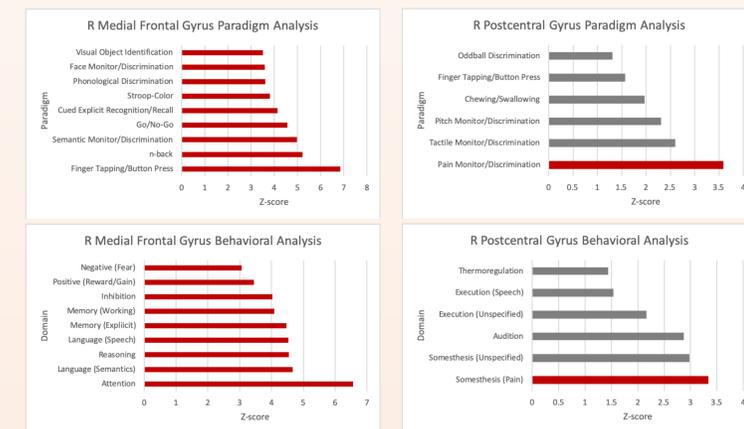
ALE Parameters: CP
 Cluster-level FWE = 0.01
 Threshold Permutations = 1000
 P-Value = 0.0001
 21 Papers
 419 Subjects
 54 Conditions
 40 Experiments
 398 Foci

Contrast Analyses

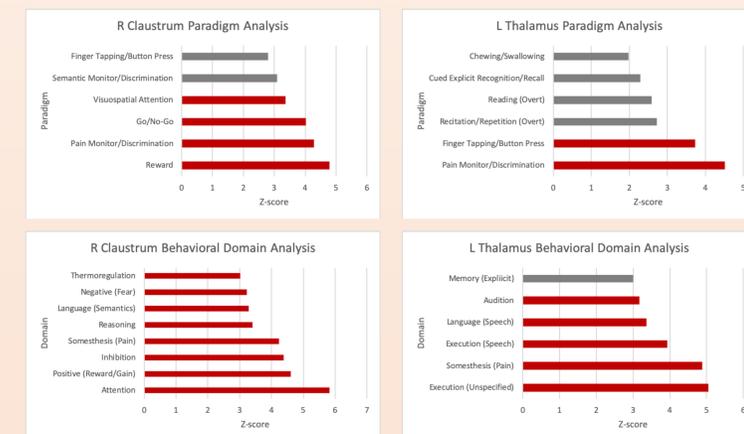


Regions highlighted in orange indicate peak activation regions resulting from a contrast analysis HC - CP (i.e. areas significantly more active in HCs than CPs). Region highlighted in blue indicate CP - HC contrast.

Chronic Pain Paradigm Class and Behavioral Domain Analyses (R MFG and RPCG only)



Healthy Control Paradigm Class and Behavioral Analyses (R Cla and L Tha only)



Red bars denote significant association within BrainMap database.

References

Eickhoff SB, Laird AR, Grefkes C, Wang LE, Zilles K, Fox PT. Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: A random-effects approach based on empirical estimates of spatial uncertainty. *Hum Brain Mapp* 30, 2907-2926, 2009.

Fiest, K., Pringsheim, T, Patten, S., et al. (2013). The Role of Systematic Reviews and Meta-Analyses of Incidence and Prevalence Studies in Neuroepidemiology. *Neuroepidemiology* 42(1):16-24

Fox PT, Lancaster JL. Mapping context and content: The BrainMap model. *Nature Rev Neurosci* 3, 319- 321, 2002.

Qureshia, AR., Ranaa, AQ., Malika, S., et al. (2018). Comprehensive Examination of Therapies for Pain in Parkinson's Disease. *Neuroepidemiology* 2018;51:190-206 205 DOI: 10.1159/000492221



University of New Hampshire
 College of Life Sciences and Agriculture