

# Regional Brain Activation in Chronic Pain: A Meta-analysis for Therapeutic Protocol

Noah C. Waller  
Dr. Donald A. Robin, Faculty Advisor  
Interdisciplinary Program in  
Neuroscience and Behavior  
University of New Hampshire, Durham NH

## Impact & Objectives

- Impact**
- Over 100 million Americans suffer from chronic pain, causing more disability than any other medical condition in the U.S. at a cost of \$560-\$635 billion per year.
  - Brain stimulation techniques (such as transcranial magnetic stimulation [TMS]) can target brain areas to induce neuro-plastic changes to achieve therapy.
- Objectives**
- To identify regions in the brain active when undergoing pain - in patients with chronic pain and in healthy controls.
  - To accomplish this by examining the broad scientific literature base related to regional brain activations in pain induction – performing a *meta-analysis*.

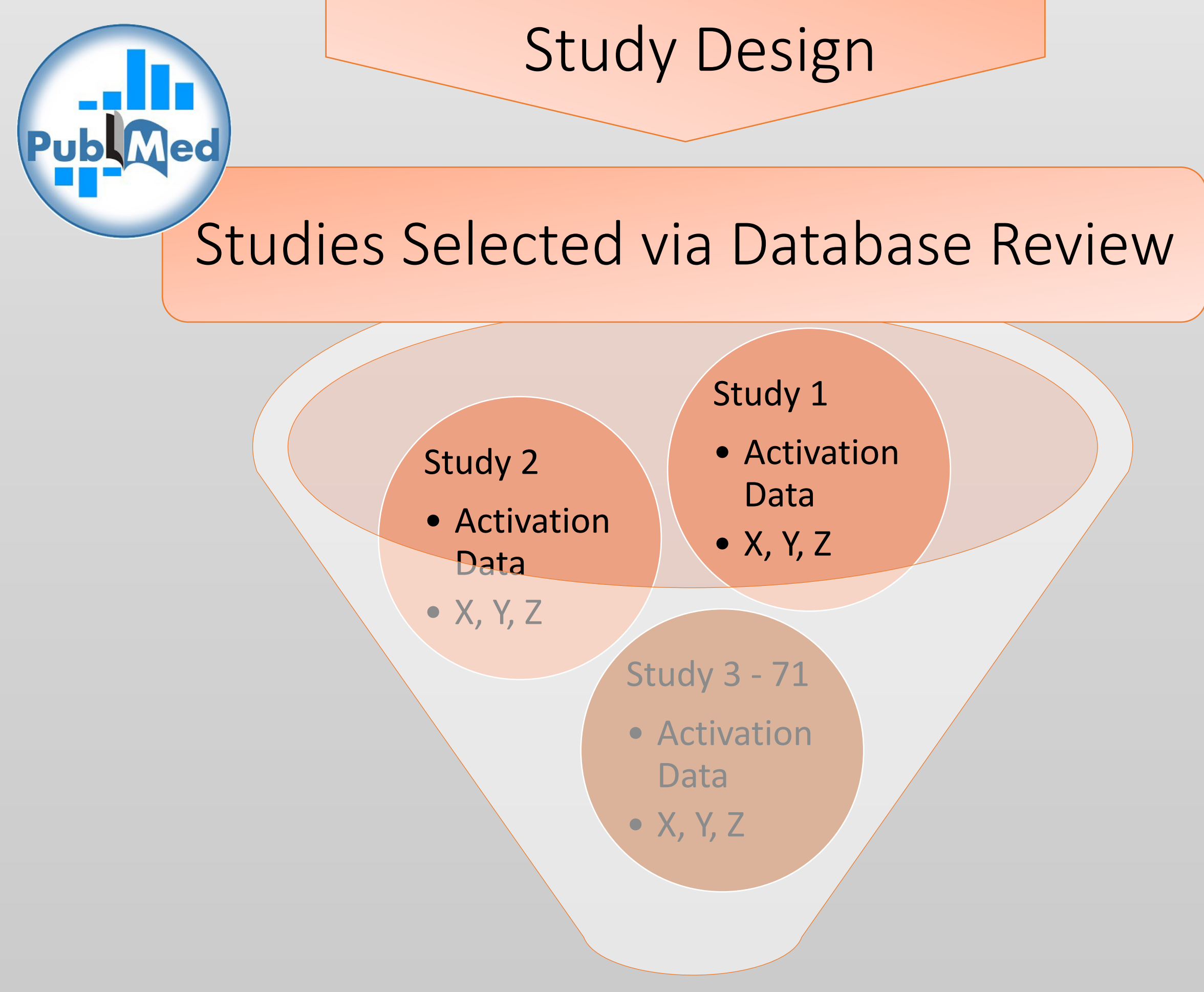
## Data Collection

- Extensive database searching of PubMed yielded nearly 4,000 papers meeting the general *inclusion criteria* for the study.
- Upon review and criteria refinement, 71 papers met the specific requirements for inclusion. Notably, the eligible studies were restricted by *timespan, coordinate-based data, functional magnetic resonance imaging (fMRI) usage, and subject diagnoses*.
- Inclusion Criteria Specifics:  
What studies were selected?
- 2008-2018
  - Pain Induction
  - Humans
  - Whole-brain data
  - Coordinate data
  - fMRI
  - No ROI data

## Data Analysis

- Each study's coordinate-based data (X, Y, Z) were entered into Scribe, a BrainMap software used as a database for fMRI brain activity.
  - Software within the same BrainMap suite – known as GingerALE – was used to run an Activation Likelihood Estimate (ALE) statistical analysis.
  - Resulting convergent coordinates were viewed and analyzed on a template brain with Mango software.
- ALE Test: What and Why?**
- ALE is a method for identifying convergent coordinates in brain activation meta-analyses.
  - ALE allows for a distillation of large numbers of brain activation coordinates into discrete statistic conclusions of greater power.

### Study Design



### Coordinate Data Input into Scribe

Hemisphere	X mm	Y mm	Z mm	SPI Value
Right	28	-12	66	3.14
Right	40	-14	62	2.65
Right	28	-20	66	3.01
Right	22	-32	70	2.08
Left	-2	-40	64	5.35
Left	-40	-42	-24	3.24
Left	-12	-46	2	3.62
Left	-40	-50	10	3.24
Left	-6	-40	42	2.53
Left	-24	4	-32	4.07
Left	-10	20	4	3.05
Right	10	18	0	5.03
Left	-6	16	6	2.89
Right	10	14	0	5.26
Left	-6	14	-6	4.34
Right	6	6	-8	4.45
Left	-26	-36	-26	3.08
Right	24	-62	-56	3.13

### ALE Performed on Aggregated Data

### Results Viewed on Template Brain



## Results

Chronic Pain Patients	Healthy Controls	Patients vs. HCs
<ul style="list-style-type: none"> <li>202 foci in 7 studies</li> <li>ALE at P Value of 0.01</li> </ul>	<ul style="list-style-type: none"> <li>1556 foci in 41 studies</li> <li>ALE at P Value of 0.001</li> </ul>	<ul style="list-style-type: none"> <li>1758 foci in 48 studies</li> <li>ALE at P Value of 0.01</li> <li>Contrast image</li> </ul>

Low → High Activation

## Conclusions & Next Steps

- Conclusions**
- Activation in patients revealed activity in 10 clusters, including the left medial frontal gyrus, bilateral insula, and bilateral thalamus.
  - Activation in healthy controls revealed activity in 7 clusters, including the right cingulate gyrus, bilateral insula, and right thalamus.
  - Notable differences in the patients include the bilateral activation of the thalamus, activity in the medial frontal gyrus, and activity in the transverse temporal gyrus.
- Next Steps**
- Performing a meta-analytic connectivity modelling (MACM) of these regions to determine functional connectivity.
  - Preparing a study involving TMS brain stimulation to alleviate chronic pain in patients.

## Acknowledgements & References

Thank you to Dr. Robin of the Communication Sciences and Disorders Department for working with me to organize this project, to Kimberly Ray for her experience in meta-analyses and the BrainMap software, to Zoe Weston for her experience in paper collections and review, and to the BrainMap team.

Thank you to the Hamel Center for Undergraduate Research and the SURF Grant that allowed this research to be possible.

**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.

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