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The Vulvosensation Matrix

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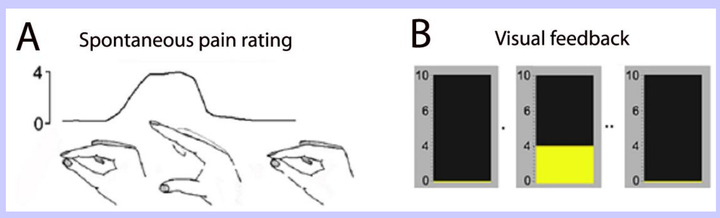
INTRODUCTION

- The existence of a pain "matrix" has been hypothesized for over 100 years and has received some support from neuroimaging
- More recently, the extracting pain related information from this network has become increasingly difficult as it is now more strongly associated to general attention and salience.
- We pitted the general linear model (GLM) solution to the analysis of touch versus pain perception against alternate models, including touch-pain differentiation based on temporal and network properties
- Whereas the GLM approach fails to distinguish between vulvar touch and pain perception, nuanced localized temporal differences, as well as global network properties,

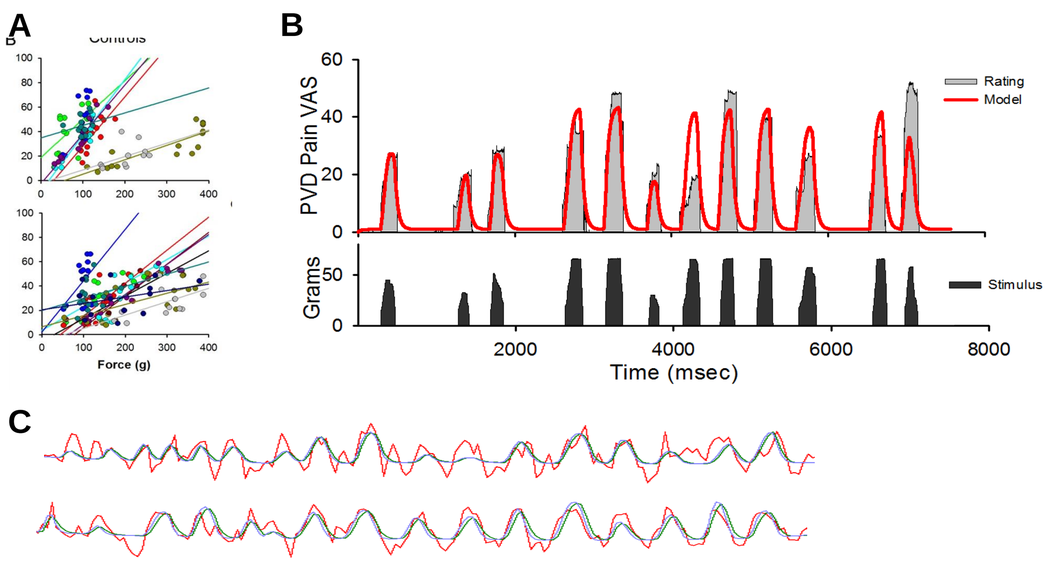
METHODS

- 16 healthy women (mean age = 25.6 years) were scanned during vulvar sensory testing
- An fMRI-compatible pressure deviceSubjects used a finger-span device to report their perception of vulvar touch and pain on a visual analog scale (0-100)
- The following stimulus parameters were equal between the touch and pain rating tasks: stimulus frequency, variability, duration, and interstimulus intervals; meanwhile, perception magnitude and variability were equated between touch and pain tasks.



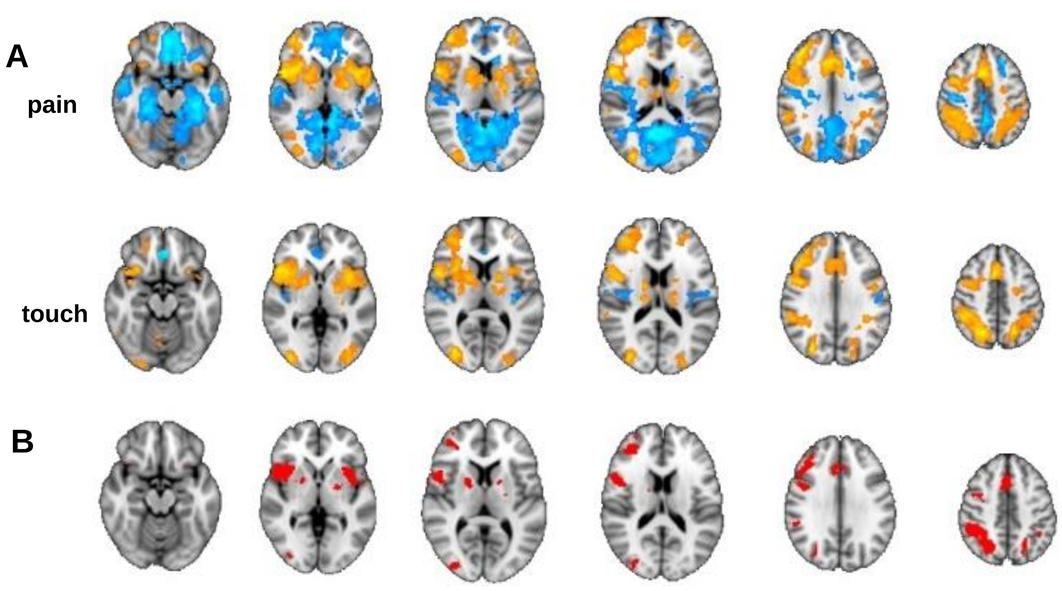
- Whole-brain functional MR data was acquired with a 3T Siemens Trio whole-body scanner. 42 slices were obtained in the axial plane covering the entire brain, flip angle = 90°, in-plane resolution = 64 × 64, TR/TE = 2500/30 msec and slice thickness of 3mm
- Group average time delay maps for were generated by averaging the time delay to the peak perception, across all subjects within each modality, after transformation of individual maps in standard space.
- Group comparisons were conducted with a paired t-test (fixed effect ordinary least squares analysis, z > 3.0 cluster-corrected for multiple comparisons at p<0.01).
- Network properties were extracted using the Sporns connectivity toolbox for Matlab, at different spatial resolutions and link densities, to determine differences in global connectivity between touch and pain.

1 Psychophysics and Temporal Modeling



A) Group average vulvar touch and pain activity maps similar and robust task-related activations in visual cortex, attentional networks, and regions classically associated with nociceptive processing.
B) The conjunction of (A) and (B) yields an activity map of mutually-recruited brain regions, referred to hereafter as the "task network."

2 GLM-based analysis fails to differentiate touch and pain



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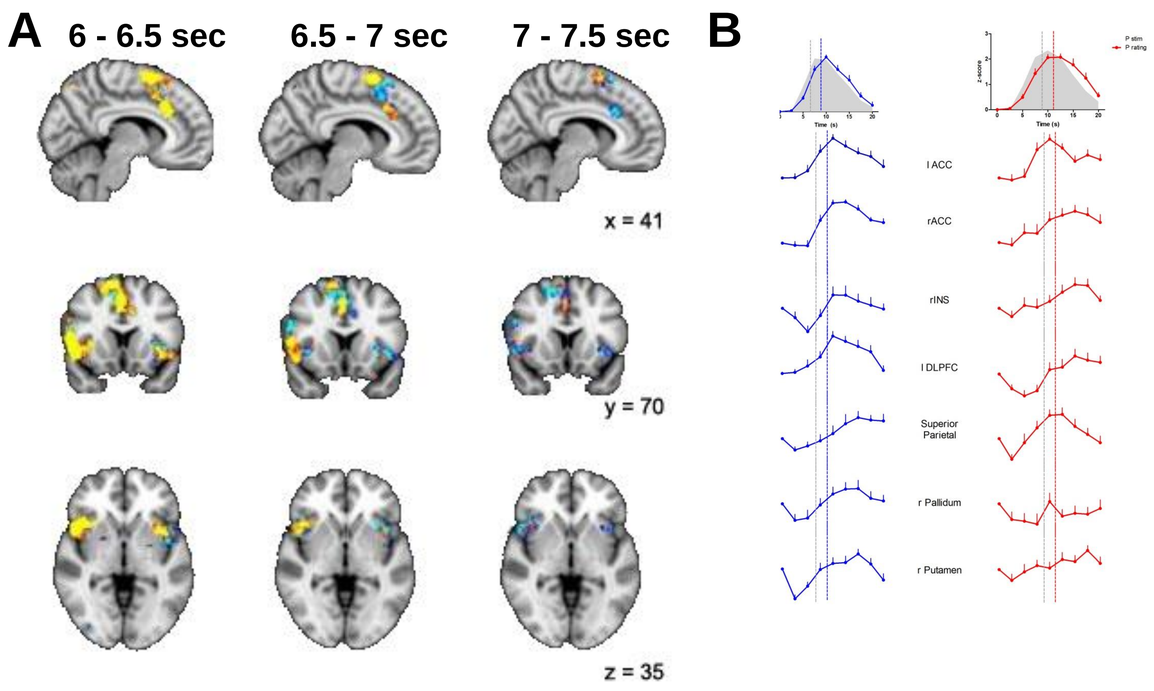
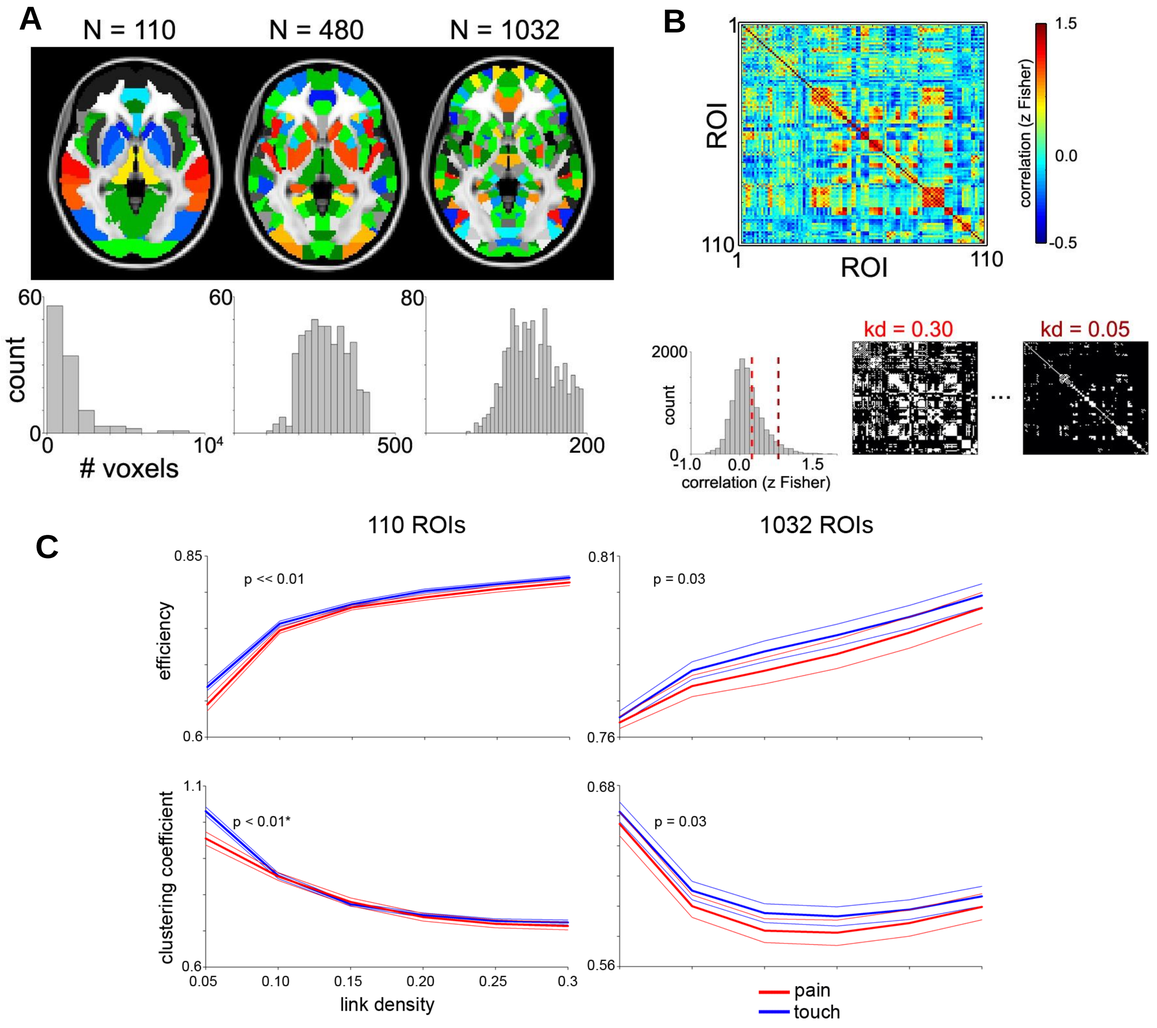
3 Temporal differences in vulvar touch vs pain perception



A) GLM-derived latency until peak perception of pain (red-yellow) and touch (green-blue) across 1.5 sec. Despite total spatial overlap of the peak latencies, pain perception peaks before touch perception In common regions, such as the bilateral insula, premotor cortex, paracingulate/midcingulate,
B) Triggered BOLD responses to touch (blue) or pain (red) stimuli for selected ROIs. Curves are averaged across runs and subjects, error bars are standard error. The top plot is the perception (line) and stimulus (shaded area).

4 Global network differences in touch and pain



A) ROIs were created covering the entire brain at different spatial resolutions by subdividing the Harvard-Oxford brain atlas. Histograms below demonstrate the distribution of ROI sizes. With the exception of the lowest resolution, ROI sizes were roughly equal.
B) Graph metrics were calculated from matrices representing the pairwise correlation of mean BOLD activity within each ROI. Matrices were thresholded for each individual subject according to link densities ranging from 0.05 to 0.30.
C) Global connectivity metrics were overall different between touch and pain across spatial resolutions and link densities. P-values indicate significance of main effect in a 2-way ANOVA testing for connectivity differences between pain and touch across all link densities. * indicates a significant interaction effect.

CONCLUSIONS

- Pain is distinguished by regions showing **enhanced network connectivity** properties that do not linearly map to stimulus perception.
- Pain reflects both **magnitude-related brain activity**, as well as widespread **shifts in synchrony** related to perception.
- In contrast to touch, **pain appears to be a flexible state** wherein diverse regions can more efficiently communicate, potentially to promote rapid planning and escape behavior to evade noxious stimulation and injury.

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