Distinct neural mechanisms of pain modulation through distraction and placebo

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Introduction

- Distraction and placebo are two effective psychological mechanisms to alleviate pain.
- Our recent behavioral study1 showed that distraction and placebo had additive, not interactive, effects on pain, suggesting that two distinct neural mechanisms underlie the effects of distraction and placebo on pain.

Here, we examined whether there were separate neural mechanisms for distraction and placebo by answering the following questions:

- Do distraction and placebo influence pain by affecting brain regions that mediate nociceptive pain?
- What are the neural systems responsible for distraction and placebo?
- How do these systems interact with the primary nociceptive brain processes to reduce pain?

Methods

- N = 28, three experimental sessions on separate days
- In Session 2 and 3, we crossed a distraction task with an expectancy-based placebo treatment in the fMRI scanner while participants experienced thermal pain on their left volar forearm.

Trial structure

- Cognitive tasks for distraction

  1. Watch:
  2. Left-Right
  3. 3-Back

- Research questions

  - Pain modulation
  - Distraction
  - Placebo

Results

Analysis 1: Effects on the nociceptive brain system

- Neurologic pain signature (NPS)

  - Placebo Control

- Distraction

- Placebo vs. Control

- FDR p < .05

Take-home: 1. Both distraction and placebo produced significant, additive reductions in pain ratings, replicating previous work.
2. NPS mediated the distraction effects on pain, but not the placebo effects.

Analysis 2: Effects on the fronto-parietal control network

- FMRI multivariate signature for fronto-parietal control network (NPS: p < .05)

- Fronto-parietal attention neuromarker (FPAN) response

- Mediation effects Path: +0.40 (0.14)**

- Trial-by-trial Pain ratings

Take-home: 1. Increased fronto-parietal activity due to cognitive tasks was significantly correlated with the reductions in pain ratings, replicating previous work. This relationship was mediated by the NPS.
2. The relationship between the fronto-parietal network and the NPS was moderated by cognitive demand.

Analysis 3: Effects on the valuation system (ventro-medial PFC and nucleus accumbens)

- Three-path mediation for placebo effects (using a priori regions-of-interest)

- Whole-brain search for the second (top) or first (bottom) mediator

Take-home: Placebo effects, but not distraction effects, were mediated by the vmPFC-NAc pathway, which is previously shown to mediate the effects of cognitive self-regulation of pain.

Conclusion

- Distraction and placebo both reduce pain, but they rely on distinct neural mechanisms.
- Distraction reduces pain by competing for cognitive resources in fronto-parietal systems that nociceptive pain systems also need.
- Placebo reduces pain through a ventromedial prefrontal- striatal pathway associated with pain valuation.
- These findings provide empirical evidence that multiple systems are involved in pain relief, and demonstrate that these systems can work together to maximize pain relief without mutual interference.

References

1 Buhle et al., Psychological Science, 23, 246-253
2 Wager et al., The New England Journal of Medicine, 366, 1386-1397
3 Wex et al., PLoS Biology, 13, e1002036

Graphical summary