

## Placebo Analgesia Accompanies Large Reductions in Pain-Related Brain Activity in Irritable Bowel Syndrome Patients

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### Introduction

Using a clinically relevant model of placebo analgesia (PA) in irritable bowel syndrome patients and fMRI data, we investigated whether placebo analgesia (PA) is accompanied by reductions in BOLD signals in pain-related areas of the brain *during the time of stimulation*. Our hypothesis was that PA effects accompany reduced neural activity in brain regions implicated in afferent processing of evoked pain in IBS [1] including thalamus, somatosensory cortices, insular cortex, and anterior cingulate cortex. Our choice of this experimental model was based on our previous work, including one that failed to show naloxone antagonism [2]. As previous PA neuroimaging studies implicate opioid mechanisms [3-6], the lack of naloxone effects suggests multiple PA mechanisms possibly unrelated to afferent inhibition.

### Experimental

The study was performed at the University of Florida McKnight Brain Institute in Gainesville. The rectal placebo agent consisted of 200 mg saline jelly. The agent was kept in medical container and applied to the rectal balloon (500 ml polyethylene bag) used for visceral pain stimulation. Patients were placed in the left lateral decubitus position and the rectal balloon was lubricated and placed into the rectum (this lubricant was used in all conditions). A visceral stimulator rapidly distended the rectum (14.5ml/s) to a precise pressure (10 or 55mm Hg), and recorded pressure, volume, and compliance.

### Results and Discussion

Repeated measures ANOVA for pain ratings revealed a significant main effect for condition. A whole-brain GLM analysis of fMRI data revealed large reductions in brain activation within pain-related regions occurred during the placebo condition. Although many factors influence placebo analgesia, it is accompanied by reduction in pain processing within the brain in clinically relevant conditions.

### Conclusions

The results of this study provide evidence that PA decreases pain-related signals during the period of stimulation; and, when combined with our previous results [1, 2, 7], underscores the biological and psychological significance of the placebo effect. As these effects can be quite large [1, 2, 7, 8] and embedded within active treatments, the potential exists to enhance chronic pain treatments.

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