



It's all in the technique! Meta-analytic evidence for distinct neural correlates of verbally induced only vs. verbally induced and conditioned placebo analgesia

* Shared first-authorship

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INTRODUCTION

Placebo effects in pain can be induced in several ways.¹

RESEARCH AIM

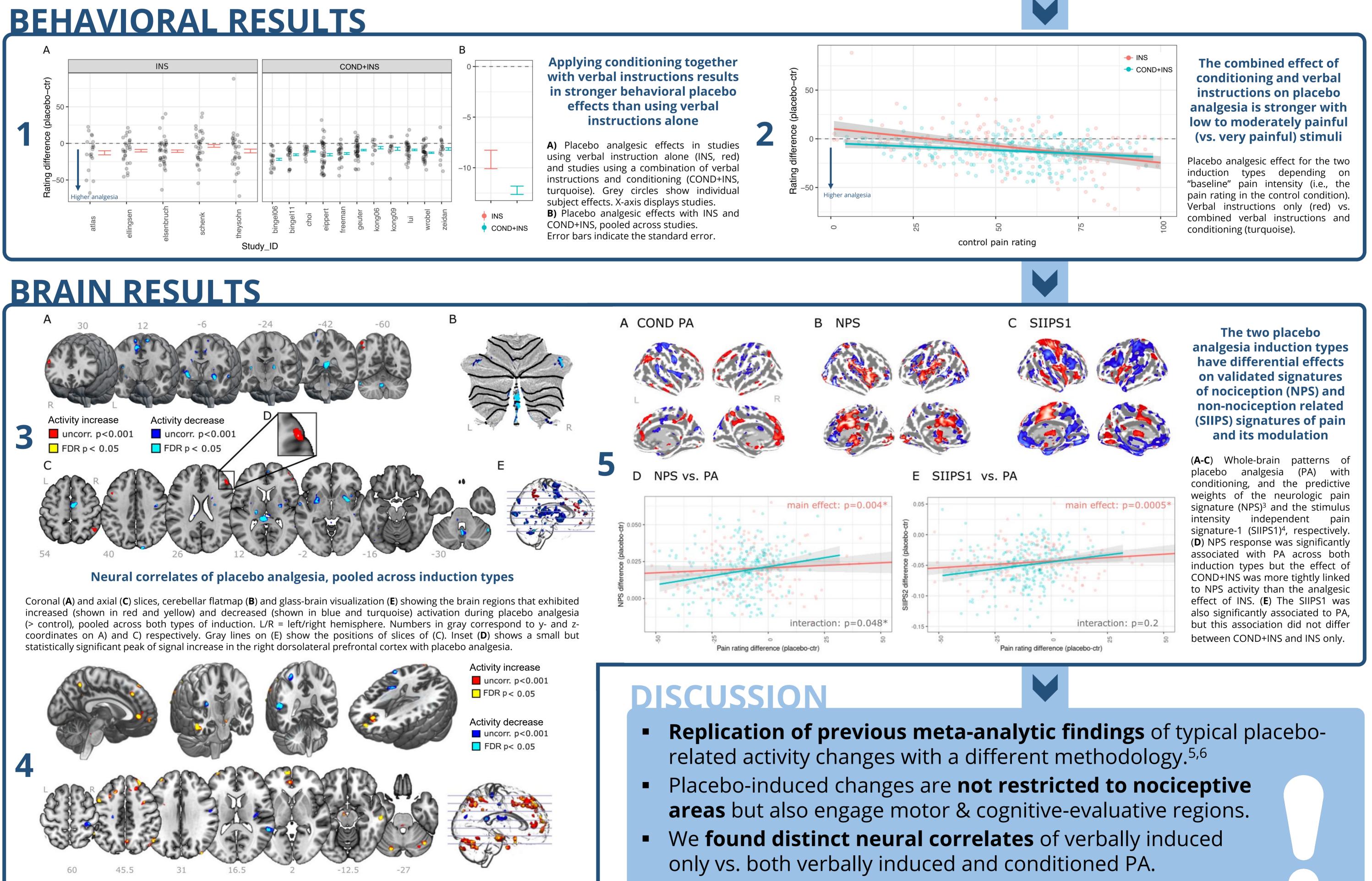
- Verbal instruction and conditioning procedures, alone or in combination, are the most commonly used approaches in experimental settings.
- Conditioning procedures consistently enhancing the efficacy of **placebo** treatments and analgesic effects.²
- However, the **underlying neural mechanisms and differences** between these two placebo analgesia (PA) techniques are not yet well understood.

Are there **behavioral and** neurophysiological differences (in PA-associated brain activity) depending on whether **conditioning was used** to induce placebo analgesia or not?



METHODS

- Systematic meta-analysis of individual participant data from 16 within-subject placebo neuroimaging studies (total n = 409)
 - Instructions alone: 5 studies, n = 147
 - Instruction combined with conditioning: 11 studies, n = 268
- **Placebo manipulations**: Topical cream (*k* = 7), intravenous infusion (k = 5), sham acupuncture (k = 2), sham TENS (k = 1), or nasal spray (k = 1)
- **Noxious stimulation applied**: Thermal (*k* = 11), laser (k = 2), distension (k = 2), or electrical (k = 1) stimulation
- Analysis: Rank-harmonized individual-level data in a permutation testing framework
- **Linear model**: analgesia rating ~ induction type * pain rating + gender + age



Distinct neural correlates of the two placebo analgesia induction techniques

Brain regions exhibiting stronger activation during placebo analgesia induced by combined verbal instructions and conditioning are shown in red and yellow. The opposite contrast identifying regions with stronger activation decrease during placebo analgesia is shown in blue and turquoise. L/R = left/right hemisphere. Gray numbers = z-coordinates. Slice positions are indicated by gray lines in the glass brain visualization.

- Results may reflect differences in the underlying neural **mechanisms** over and above the differences in the magnitude of behavioral analgesia induced by the two different induction types.

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REFERENCES

1) Enck et al. (2013) 4) Woo et al. (2017) 2) Vase et al. (2002) 5) Zunhammer et al. (2018) 3) Wager et al. (2013) 6) Zunhammer et al. (2021)



