Expectancy-based enhancement of opioid analgesia:
An fMRI study of hidden vs. open remifentanil administration

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INTRODUCTION

It has long been believed that expectancies enhance the effects of active pharmacological treatments. Examples: Patient-controlled analgesia.

- Additive effects of treatment and expectancies (Pheno-drug synergy)
- Similar mechanisms are likely to underlie both placebo and opioid analgesia.
- Common effects on pain-evoked responses
- Decreases in pain processing regions (insula, thalamus, anterior cingulate)
- Increases in modulatory regions (ACC, orbitofrontal cortex)
- Placebo analgesia involves endogenous opioid release
- Reversibility by naloxone

- Opioid binding PET studies
- Expectancy-based enhancement of opioid analgesia: Remifentanil effects, high pain, early:
  - Opioids: Wise 02&04, Petrovic 02; Placebo: Wager 04, Price 07, Eippert 09

- Remifentanil effects, high pain, early:
  - Determined dose required to elicit analgesia without sedation
  - Remifentanil affects pain-processing brain regions differentially depending on expectancy

- Expectancies affect late components of the pain-evoked response

METHODS

Pharmacokinetic modeling:
- Fitted response in Right Anterior Insula.
- Main effects: Drug (p<0.01), context expectancy (O-H, p<0.05), intensity (p=0.01)
- Expectancy interactions in any context

![PhMRI RESULTS](image)

- Key findings:
  - Remifentanil and expectancy both contribute to analgesia with independent, additive effects that follow separate timescales across the session.
  - Remifentanil and expectancy modulate pain evoked responses both separately and interactively.
  - Remifentanil affects early components of the pain-evoked response.
  - Expectancies affect late components of the pain-evoked response, consistent with placebo analgesia.
  - Expectancies lead to stronger drug effects under Open administration.

- These findings have important translational implications: They suggest that psychological factors should be considered alongside traditional treatment considerations (e.g., drug dose) in clinical and research settings.

REFERENCES