INTRODUCTION

- Expectancies modulate both reported pain and responses in some brain regions, yet the key brain circuitry that mediates expectancy effects on pain experience has not been identified.
- Placebo expectancy manipulations decrease in “pain matrix” regions1,2, increases in control regions, particularly dACC.
- Placebo analgesic behavior correlations = between-subjects only.
- Event-related (cue-based) expectancy manipulations: modulation of pain matrix and control regions.
- Have not examined relationship between brain and pain reports.

Hypotheses

I. Expectancies modulate pain reports.
II. Expectancies modulate pain matrix activity (Path a).
III. Pain matrix activity affects perceived pain (Path b).
IV. Expectancy effects in pain matrix regions lead to changes in perceived pain (Mediation effect, A*B).
V. Higher order regions involved in cognitive control and value processing also mediate expectancy effects on perceived pain.
VI. Interactions among these mediators predict perceived pain.

METHODS

- Whole-brain multi-level mediation
- A test for mediation should satisfy the following criteria:
  1. M should be related to X (a effect).
  2. M should be related to Y after controlling for X (b effect).
  3. The indirect relationship (a*b) should be significant.

  - Linear equations within-subjects:
    - y = x + e_a
    - y = b + e_{a*b}
    - c = c' + a*b

- Whole-brain multi-level mediation

RESULTS

WHOLE BRAIN MULTI-LEVEL MEDIATION

1. Path c/c’
   - Path c: Expectancy modulates brain activity during pain.
   - Path c’: Brain regions mediate expectancy effects on pain perception.

2. Path a:
   - Expectancy (HM-LM) modulates brain activity during pain.
   - Perceived Pain (Path b):
     - Which brain regions mediate expectancy effects on pain perception?

3. Path b:
   - Controlling for expectancy and temperature, brain activity predicts perceived pain.

REFERENCES