

IL-6 as a Mediator of the Association between Psychological Risk Factors and Postoperative Pain in Patients Undergoing Joint Replacement

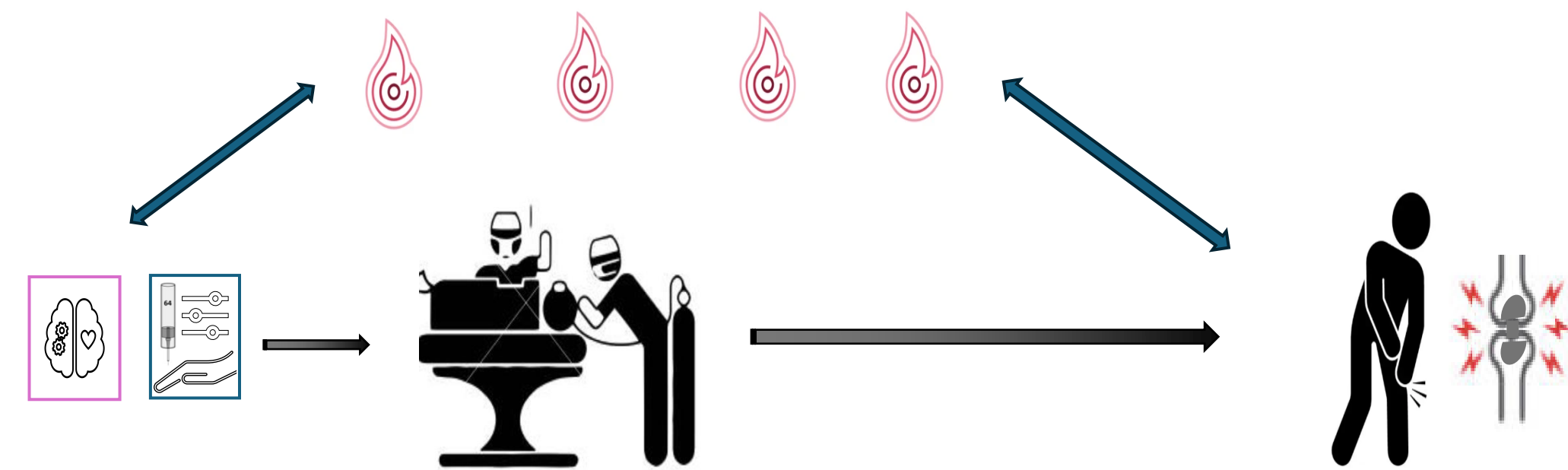
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BACKGROUND

- IL-6, a pro-inflammatory cytokine, plays a role in both surgical injury and the physiology of nociception.
- Pain Catastrophizing, an individual's tendency to think negatively about painful experiences, is related to greater pain and upregulation of IL-6, suggesting a potential link between psychosocial factors, pain, and inflammation.
- In prior work, we observed acute increases in IL-6 during experimental pain testing (IL-6 reactivity) both before and 3 months post-surgery.
- Notably, reductions in IL-6 reactivity from baseline to 3 months post-surgery were associated with improved clinical pain (Wilson et al., 2024)

STUDY AIMS

To understand the relationship of psychosocial risk and and proinflammatory propensity in increasing postoperative pain



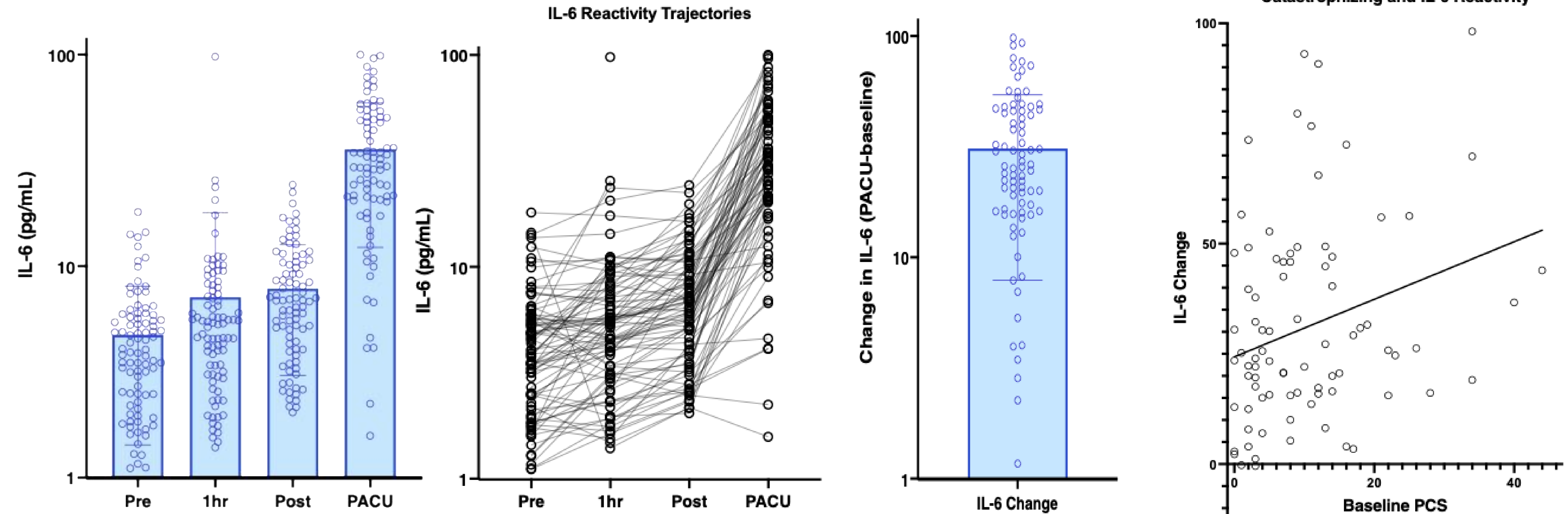
METHODS

- Population:** Patients undergoing total knee or hip arthroplasty.
- Design:** Prospective, observational study.
- Measures:**
 - Preoperative Pain Catastrophizing** assessed using the Pain Catastrophizing Scale (range: 0-52).
 - Postoperative Pain Severity** assessed using a numerical rating scale (0-10), approximately 2 hours after arriving in post anesthesia care unit (PACU) and on postoperative day 1 (POD1).
 - Postoperative Opioids** assessed in morphine mg equivalents (MMEs) in the PACU on POD1.
 - Perioperative IL-6** assessed via blood samples collected before surgical incision, 1 hour after incision, at the end of surgery, and 2 hours after surgery in PACU.

STATISTICAL ANALYSIS

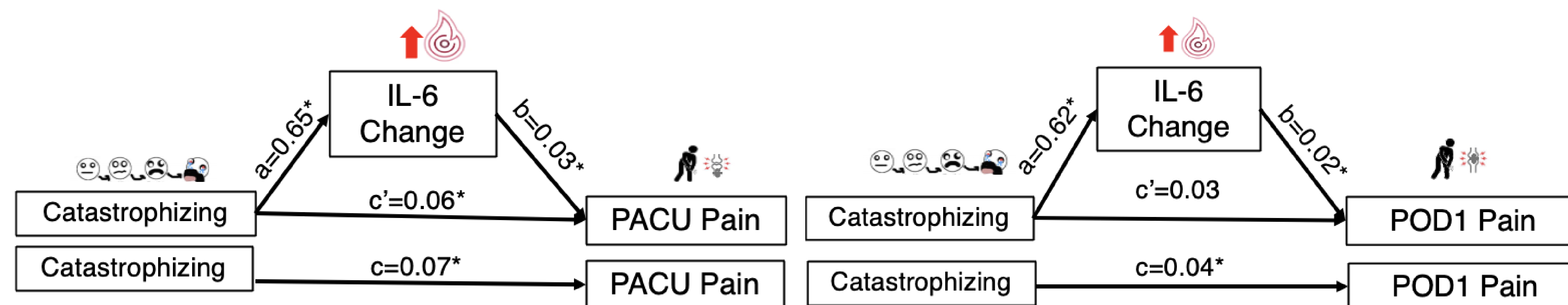
- A pre-to-PACU IL-6 change score was created to capture surgical IL-6 reactivity.
- Correlations examined associations between preoperative pain catastrophizing, IL-6 reactivity, and postoperative pain and opioids.
- Mediation analyses were conducted using the PROCESS macro to explore whether IL-6 reactivity mediated the association between preoperative catastrophizing and postoperative pain or opioids.

RESULTS



- Plasma IL-6 was variable among individuals
- Increase in IL-6 after surgery was variable among individuals

- Preoperative catastrophizing was associated with greater IL-6 increase.
- Preoperative catastrophizing was associated with greater postoperative pain and MME.



Mediation analysis showed that extent of increase in IL-6 partially mediates the relationship between preoperative catastrophizing and postoperative pain.

CONCLUSIONS

- The variability in IL-6 increase in response to total joint replacement was related to higher preoperative pain catastrophizing and greater postoperative pain.
- The surgically-induced IL-6 increase partially mediated the relationship between preoperative pain catastrophizing and greater postoperative pain.
- This raises a question for future investigations: could improving catastrophizing (negative pain-related thinking) before surgery positively impact the inflammatory response to surgery?

Reference: Wilson JM, Yoon J, Mun CJ, Meints SM, Campbell CM, Haythornthwaite JA, Smith MT, Edwards RR, Schreiber KL. The association between changes in clinical pain severity and IL-6 reactivity among patients undergoing total knee Arthroplasty: The moderating role of change in insomnia. Brain Behav Immun. 2024 Aug;120:199-207. PMID: 38838835.