

# Placebo effects: From sociodemographic aspects to sleep

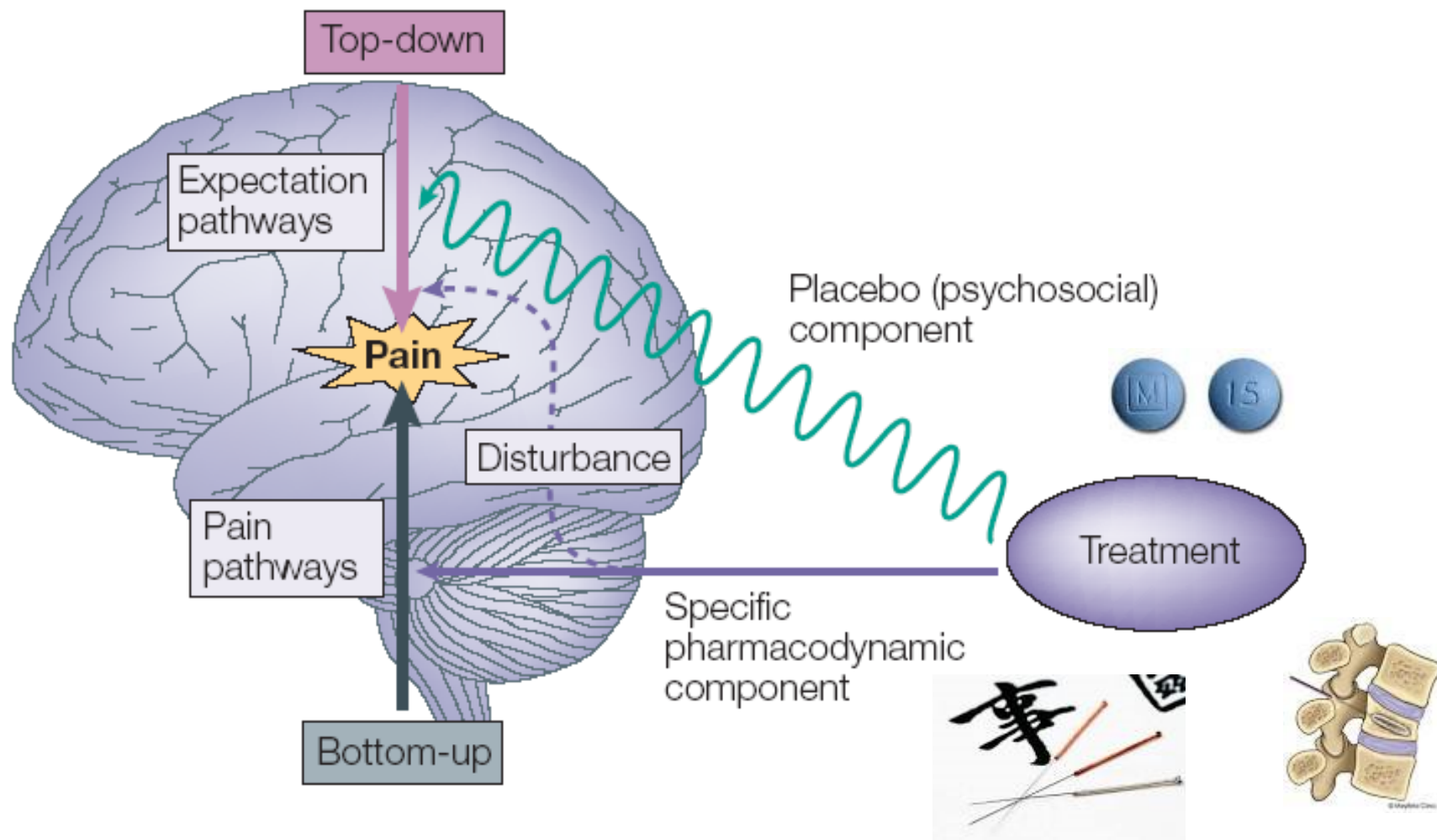
Luana Colloca, MD, PhD, MS  
[colloca@umaryland.edu](mailto:colloca@umaryland.edu)

# Learning objectives

- Predictive factors of placebo effects in chronic pain:
  - Sociodemographics / disparities (e.g., sex, race/ethnicity)
  - Psychological and clinical factors (e.g., fear of pain, insomnia)
  - Biological signatures (e.g., omics)
- Sleep phenotypes and placebo effects in chronic pain



# Placebo and drug effects



Colloca and Benedetti. Nature Rev Neurosci 2005

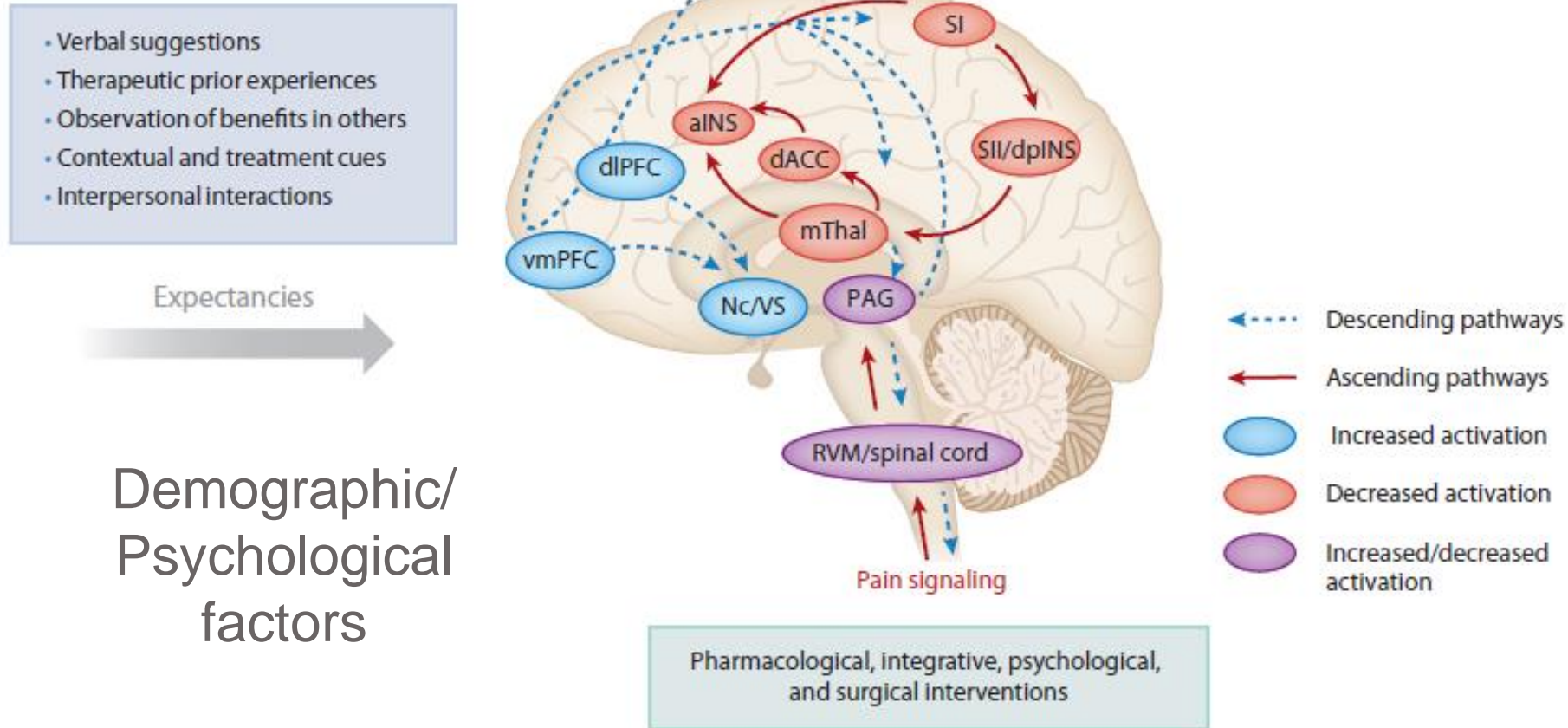


# Placebo effects without placebos



# Placebo effects: Psychoneurobiological mechanisms

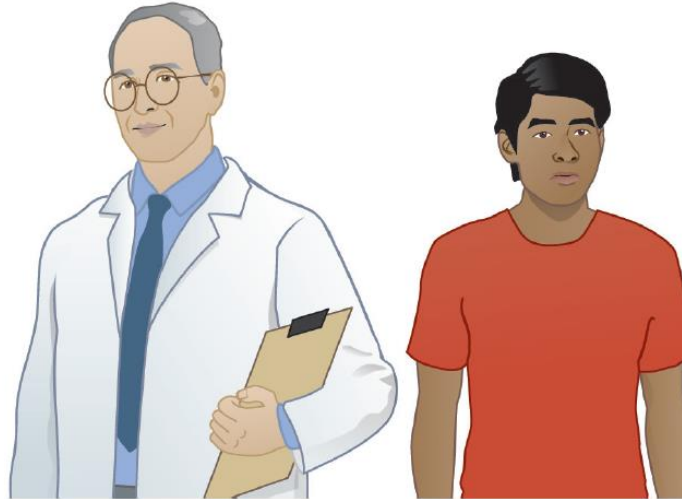
Genetic factors



# Nocebo effects

## EXTERNAL FACTORS

- Negative verbal suggestions
- Prior therapeutic experiences
- Social observation
- Mass psychogenic modeling
- Treatment leaflets
- Patient-clinician communications
- Informed consent process
- Contextual cues
- Clinical encounters



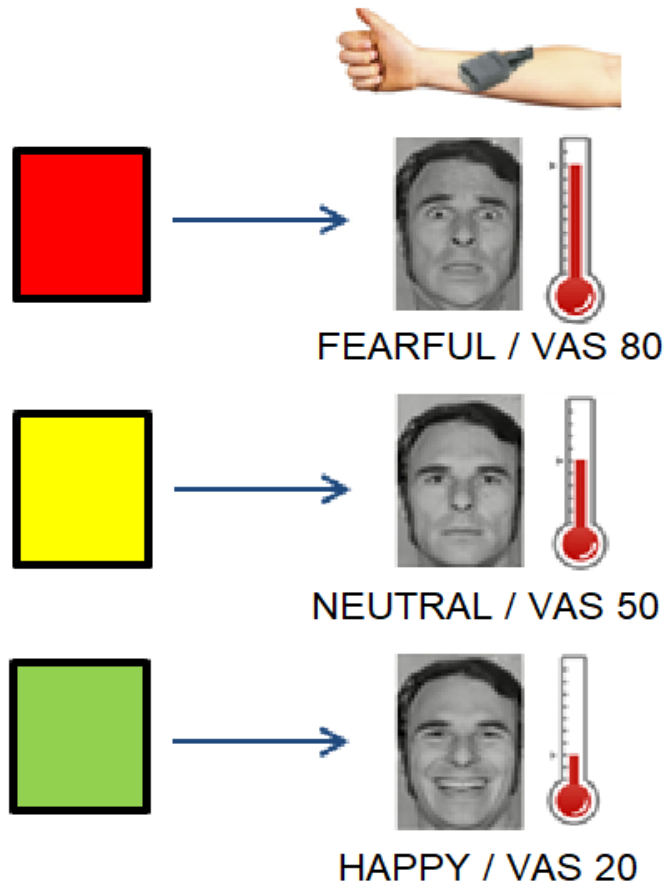
## INTERNAL FACTORS

- Emotion and mood
- Maladaptive cognitive appraisal
- Negative valence factors
- Personality traits
- Somatosensory features
- Omics

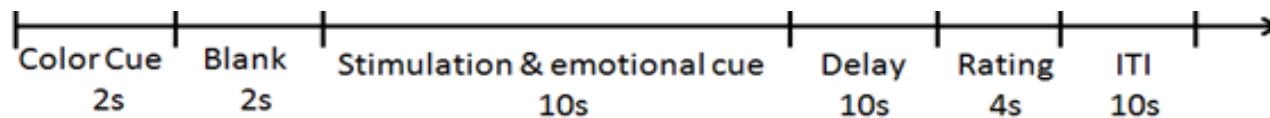
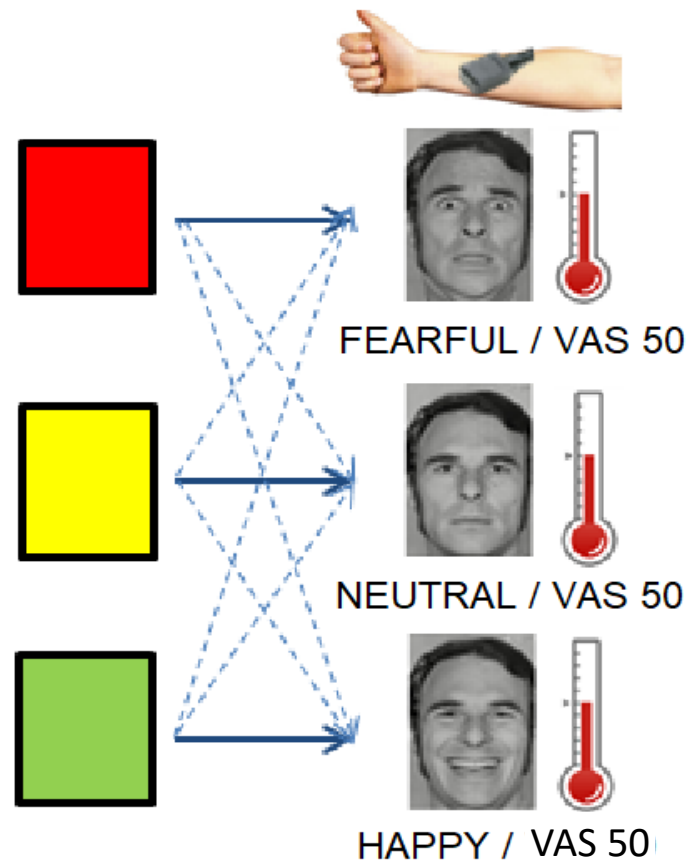


# Prior experiences and expectancies

Day 1: Conditioning

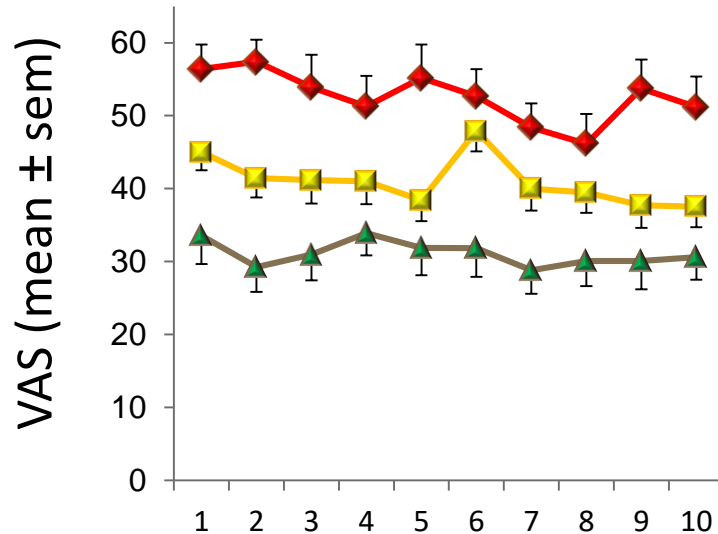


Day 2: Testing

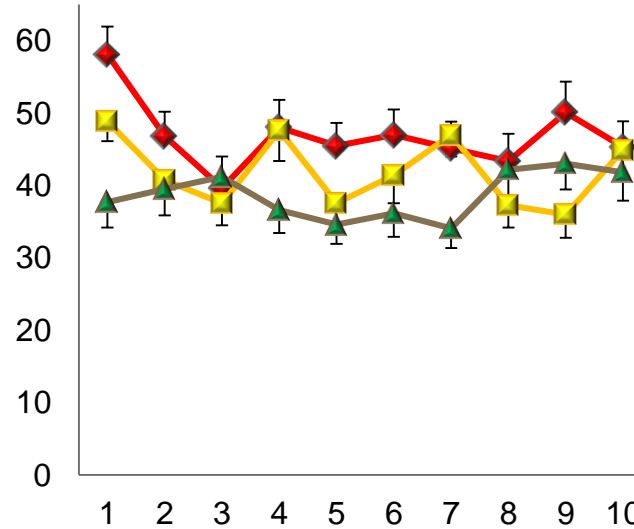


# When expectancies are violated

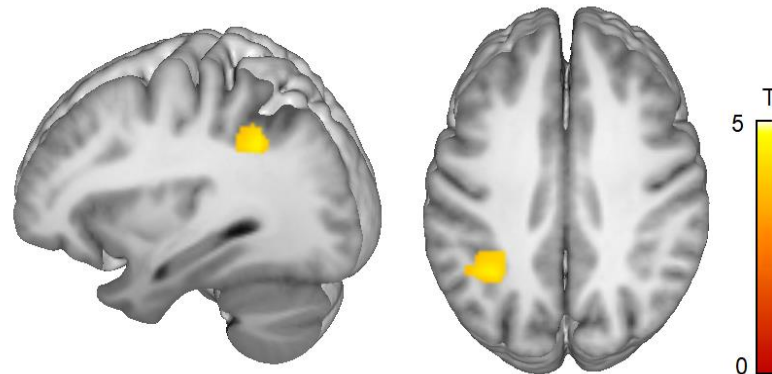
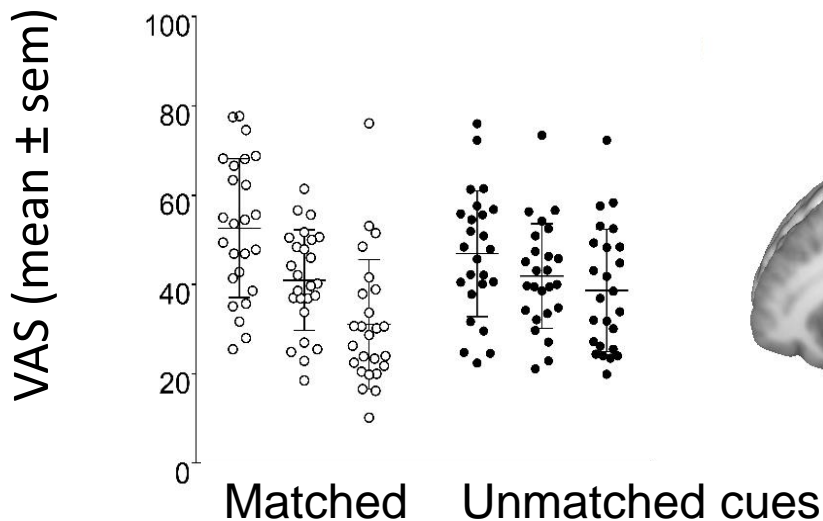
Matched cues (50%)



Unmatched cues (50%)

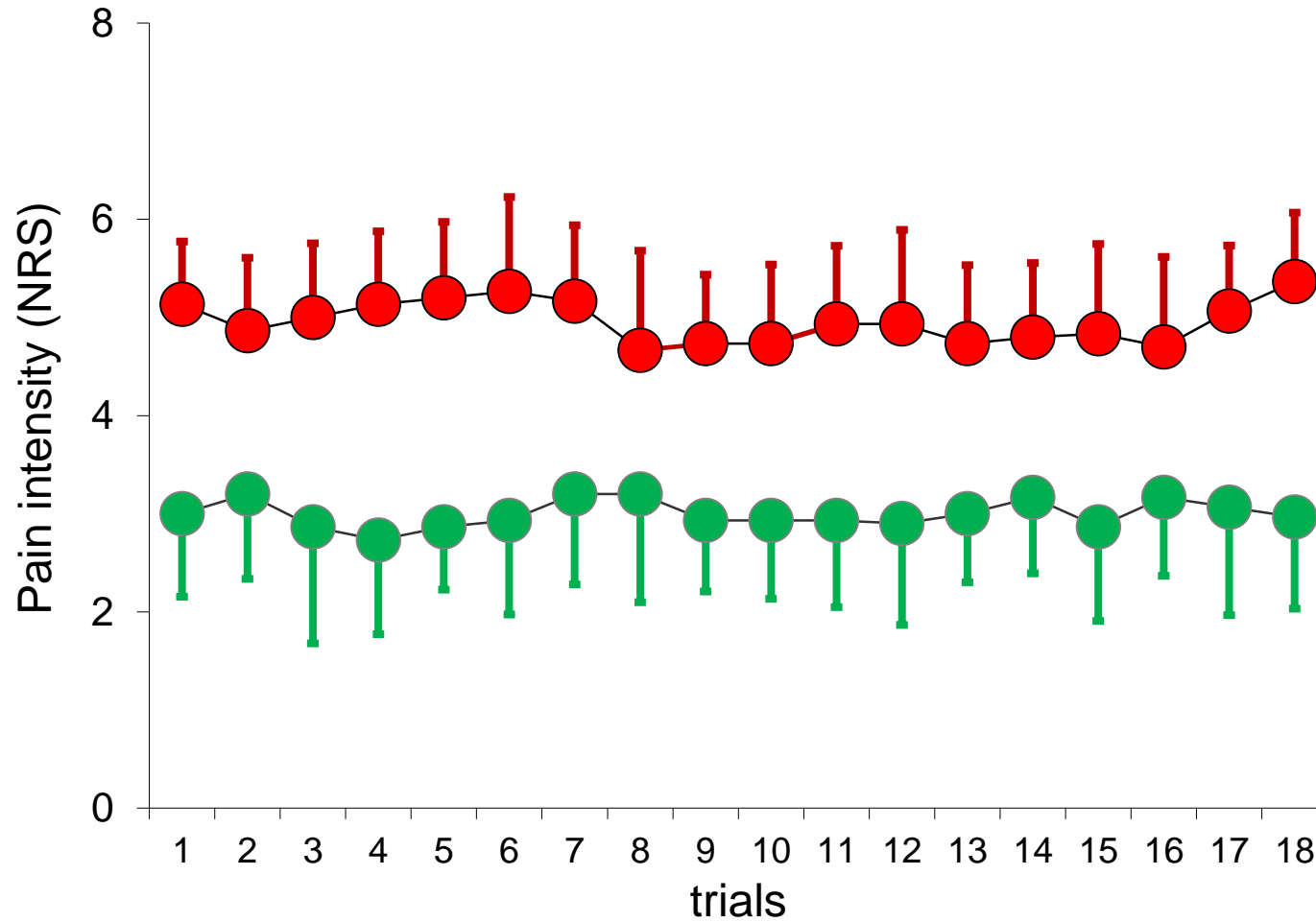


left inferior parietal cortex, including the  
supramarginal gyrus and angular gyrus



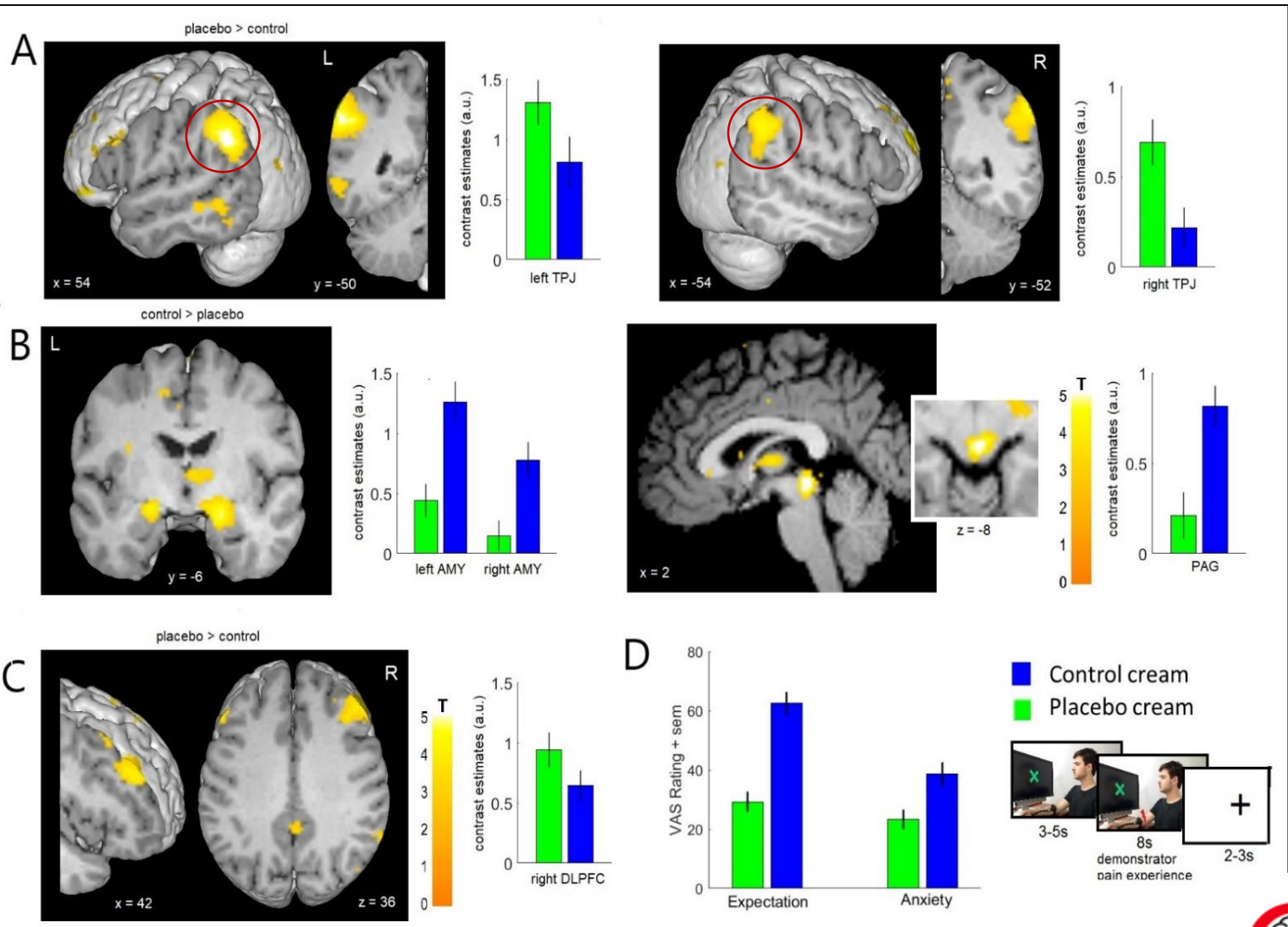


# Observe to get pain relief



# Transfer of placebo analgesia

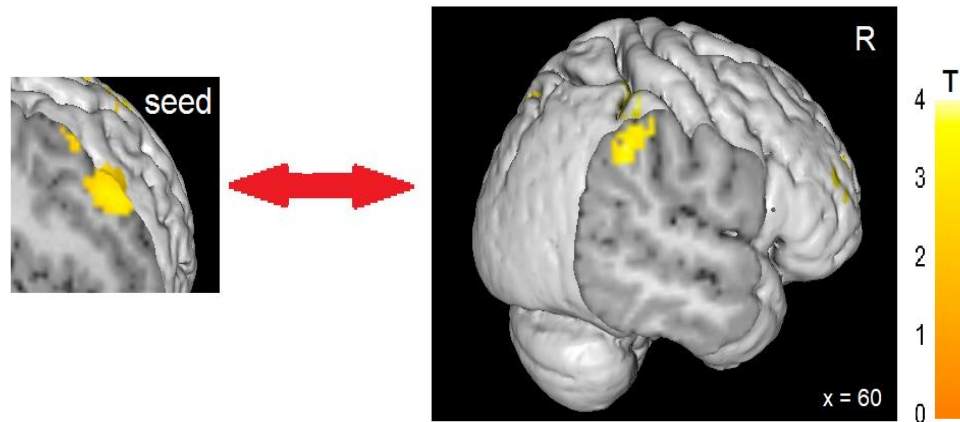
Observation phase



Test phase

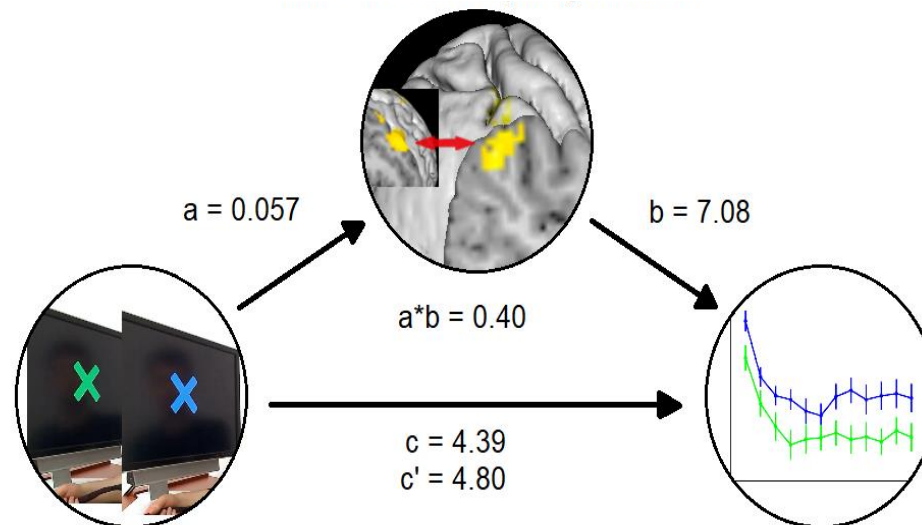


# DLPFC-TPJ connectivity and placebo effects

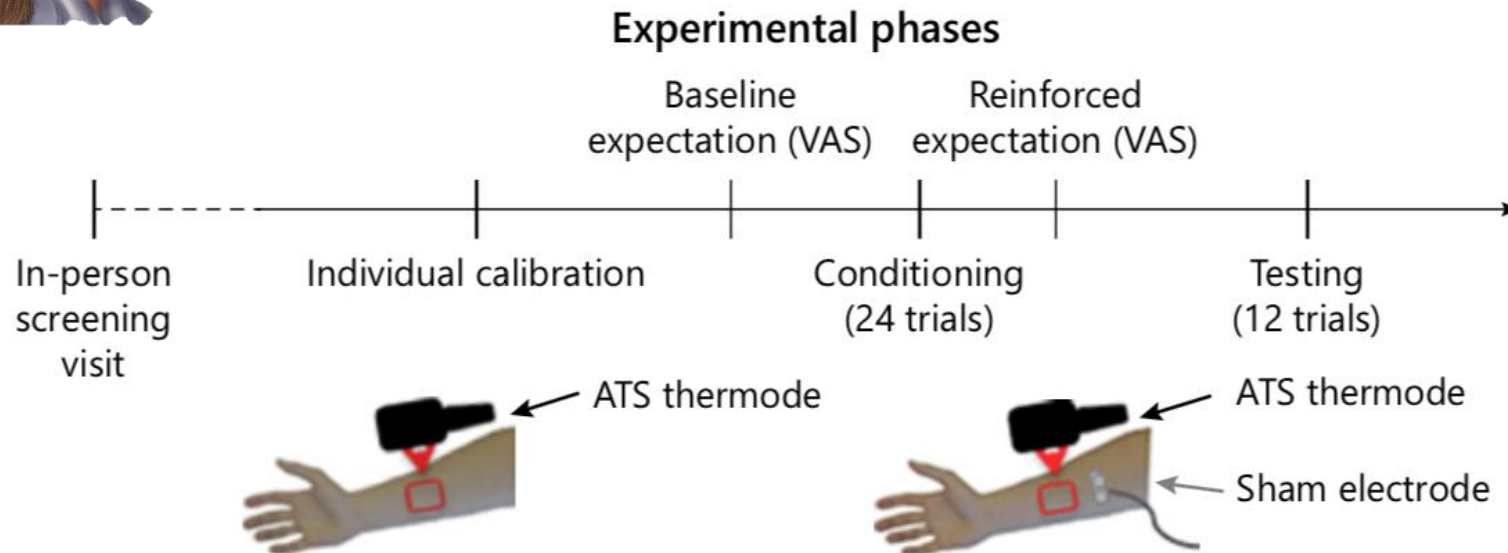


DLPFC = Dorsolateral prefrontal cortex

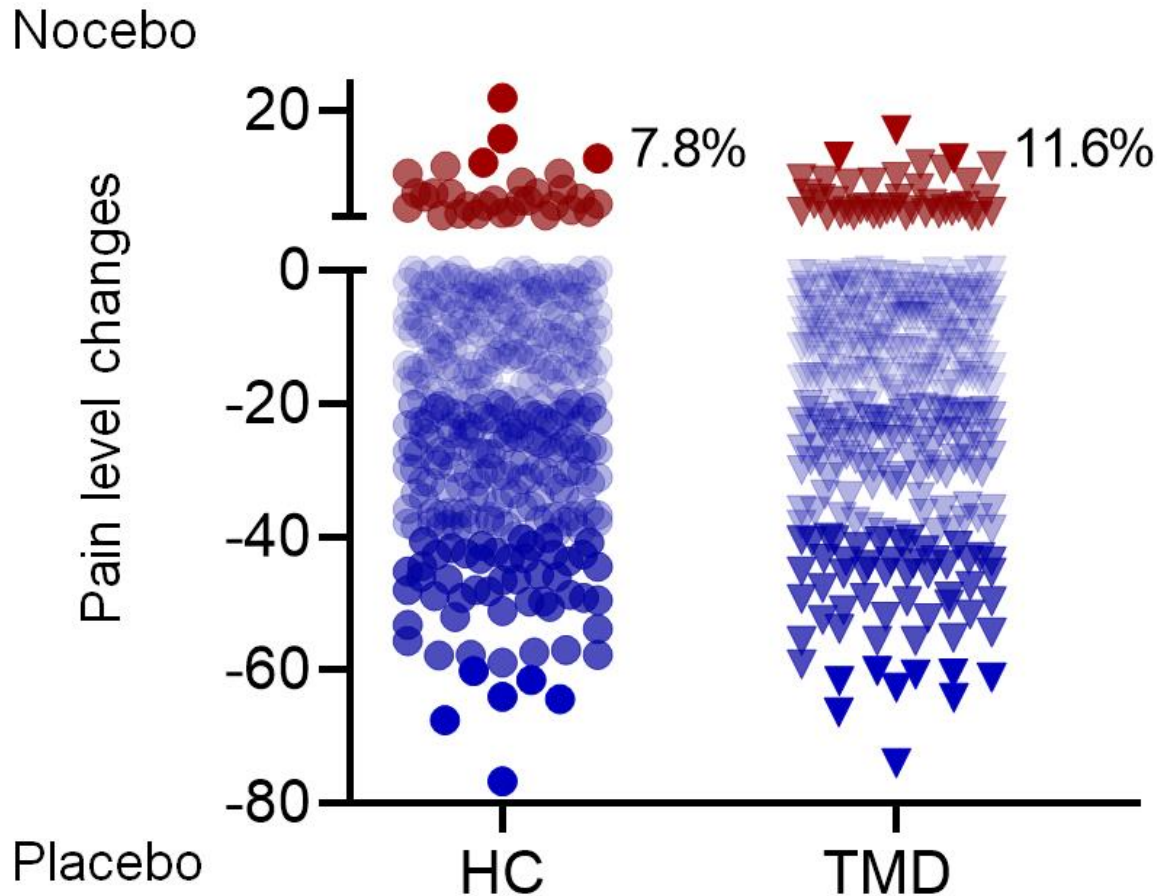
TPJ = Temporoparietal junction



# Placebo effects and translational research



# Distribution of individual placebo effects



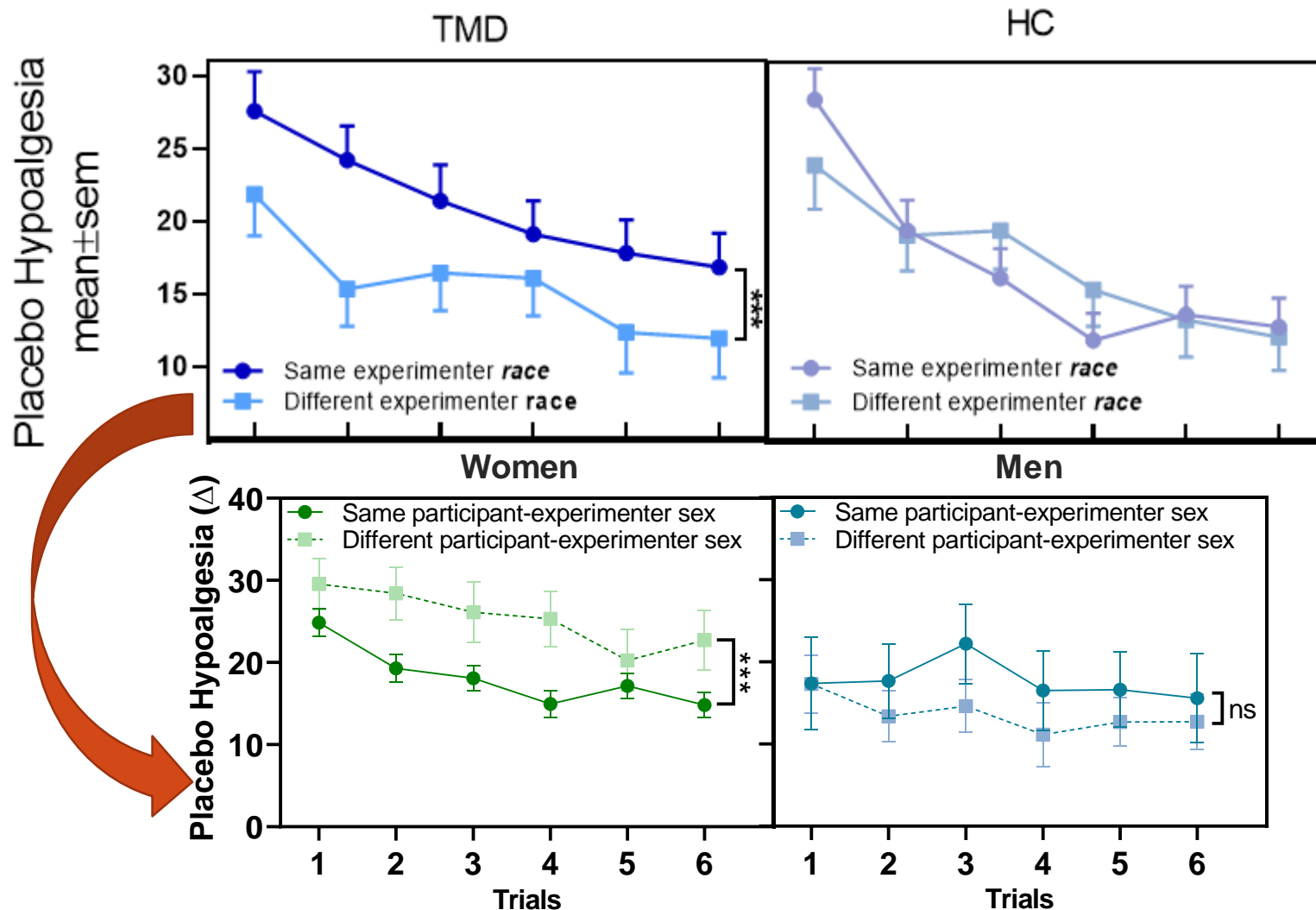
TMD = temporomandibular disorder, HC = Healthy controls

Colloca et al. Psychother Psychosom. 2020

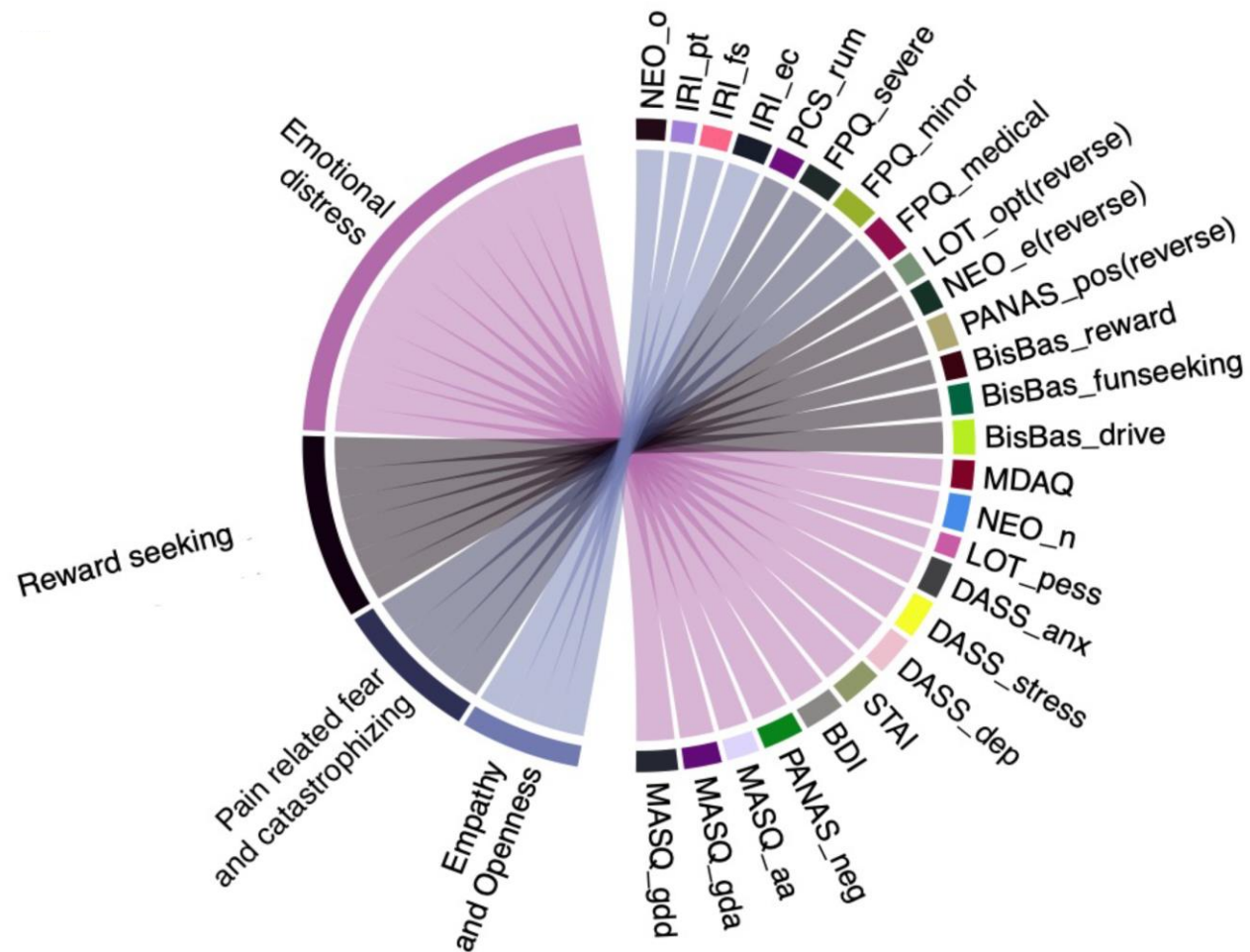
Colloca Ann Review Toxicol and Pharmacology 2024



# Participant-experimenter race/ethnicity and sex concordance

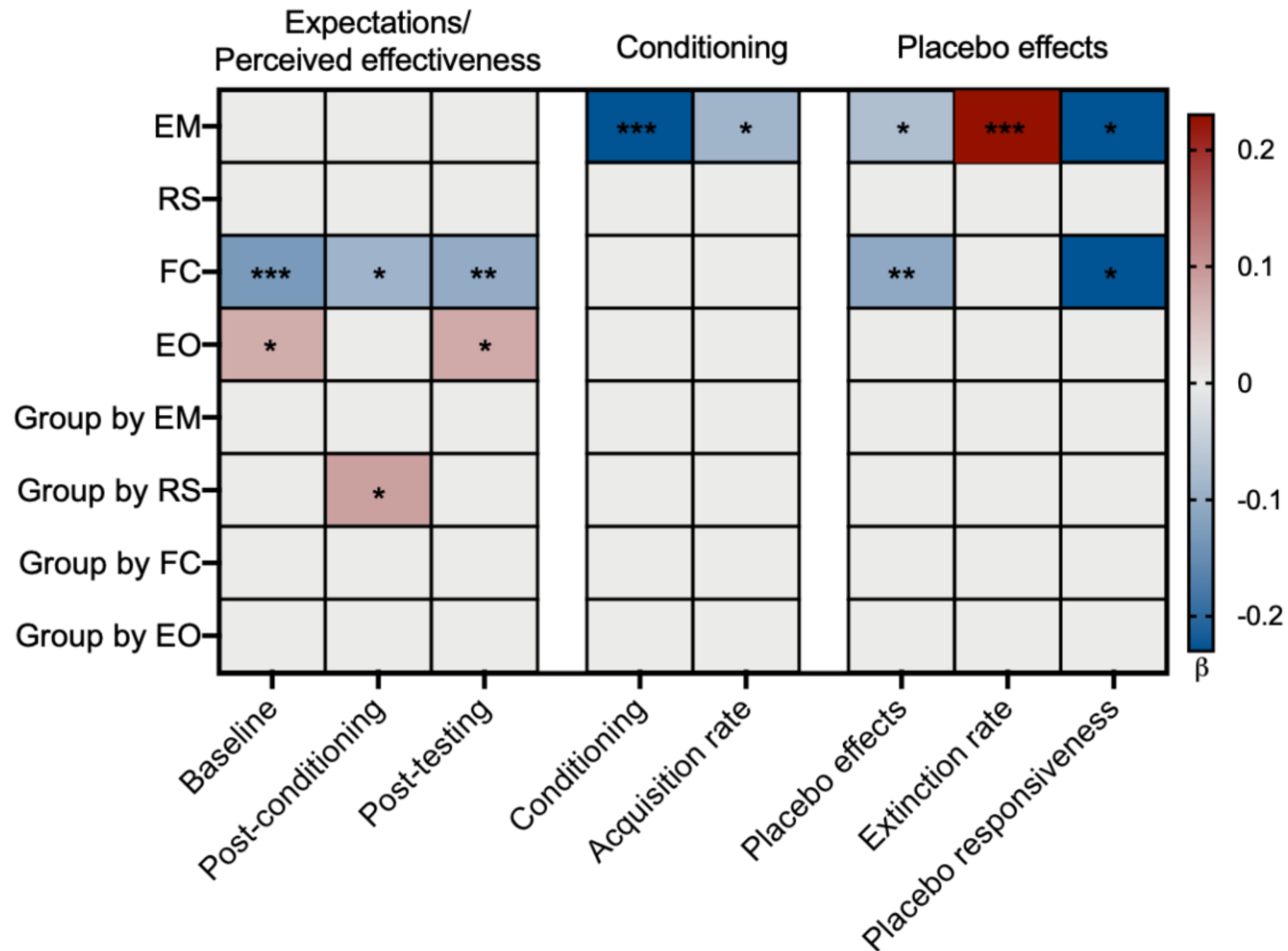


# Placebo responders vs non-responders: Contribution of psychological factors





# Expectations, conditioning, and placebo effects



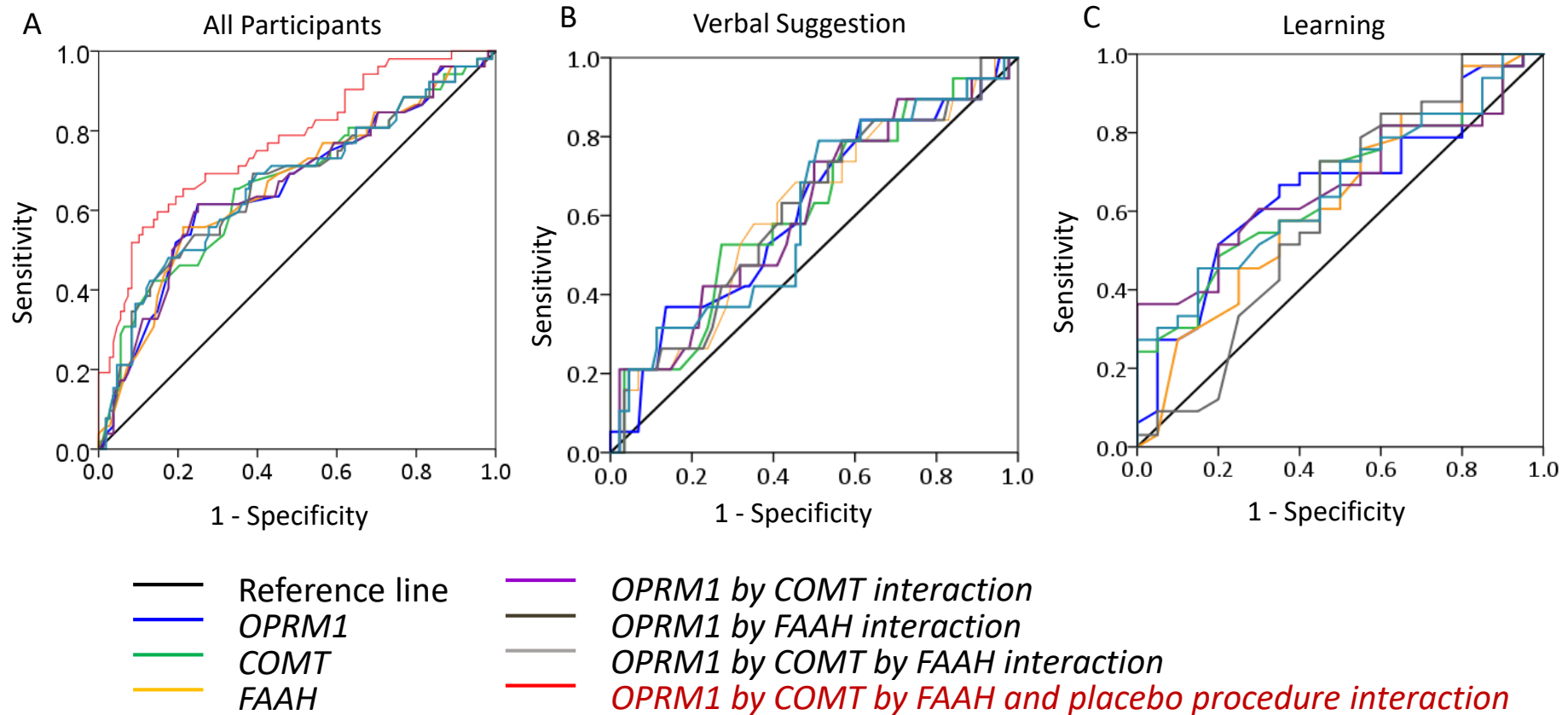
**EM** = Emotional distress    **RS** = Reward seeking

**FC** = Pain related fear and catastrophizing    **EO** = Empathy and openness





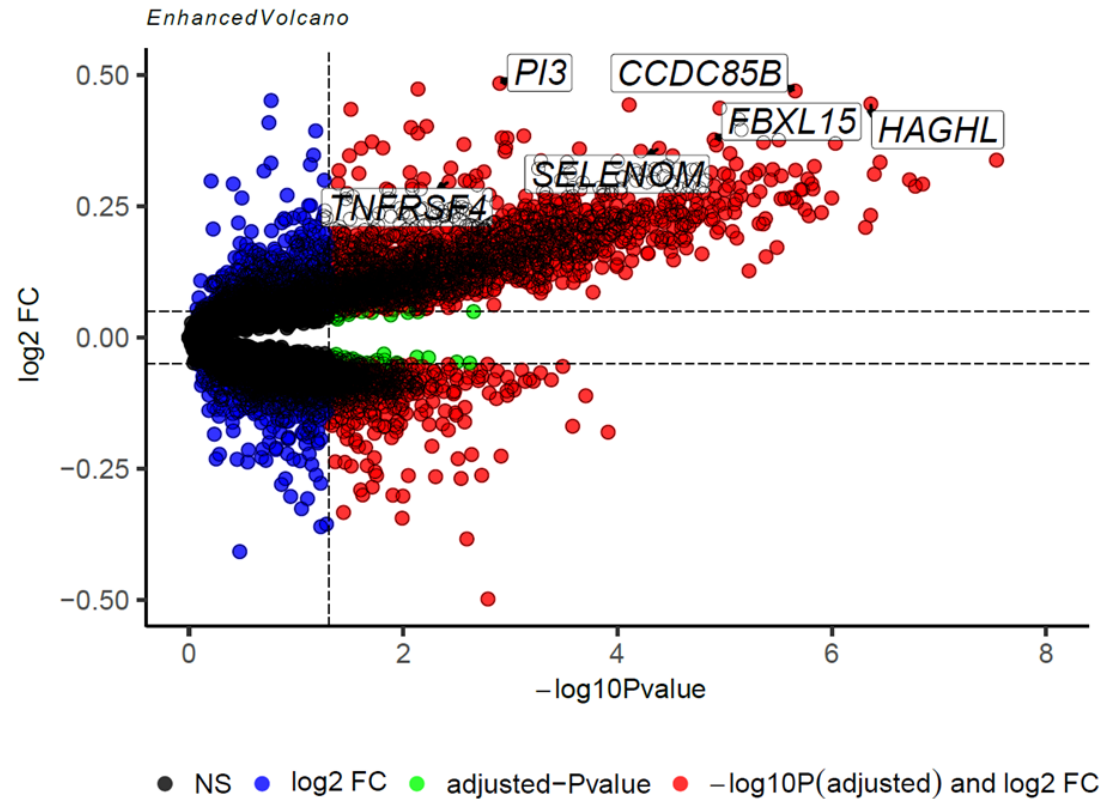
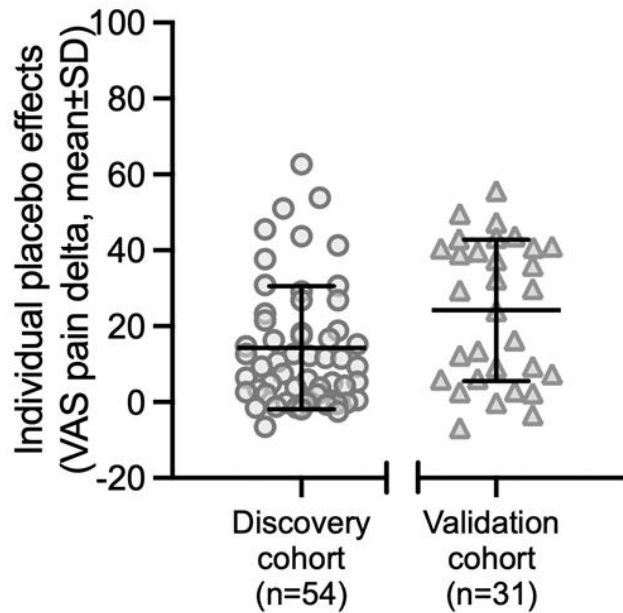
# *OPRM1*, *COMT*, and *FAAH* genetic variants for estimating placebo effects



3 SNPs in the opioid receptor mu subunit (*OPRM1* rs1799971), catechol-O-methyltransferase (*COMT* rs4680), and fatty acid amide hydrolase (*FAAH* rs324420) genes have been associated with placebo hypoalgesia



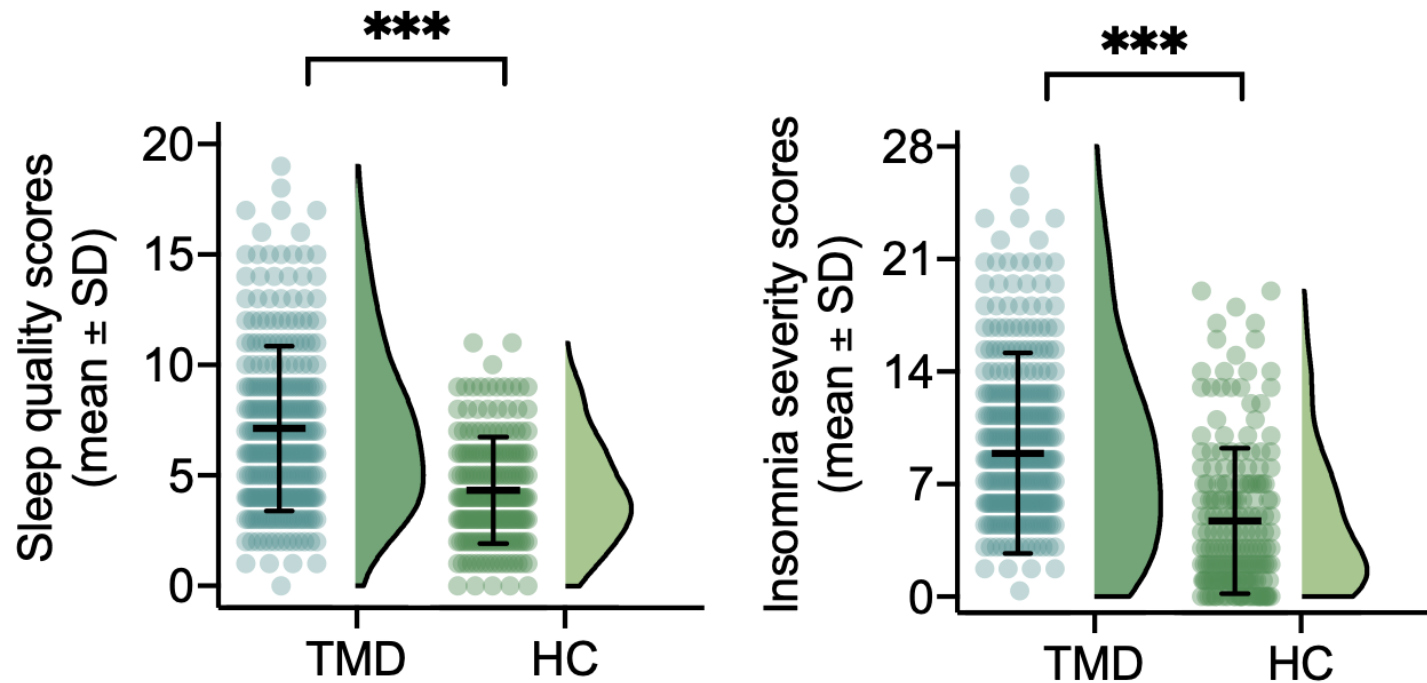
# Transcriptomic profiles and placebo effects



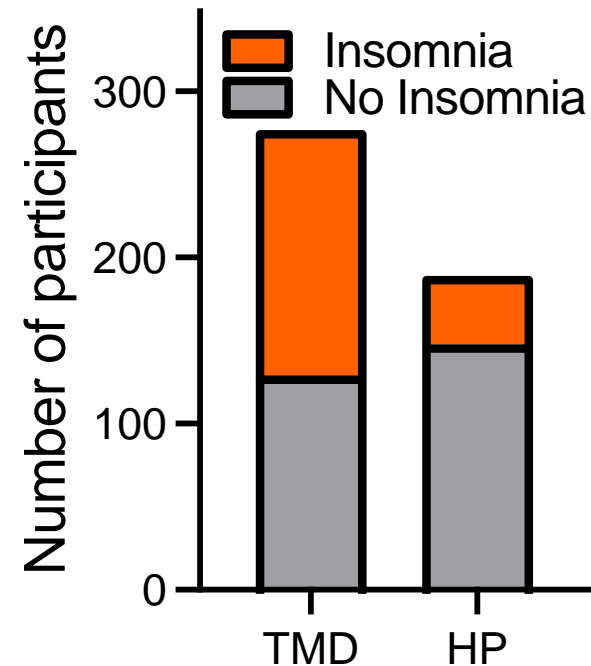
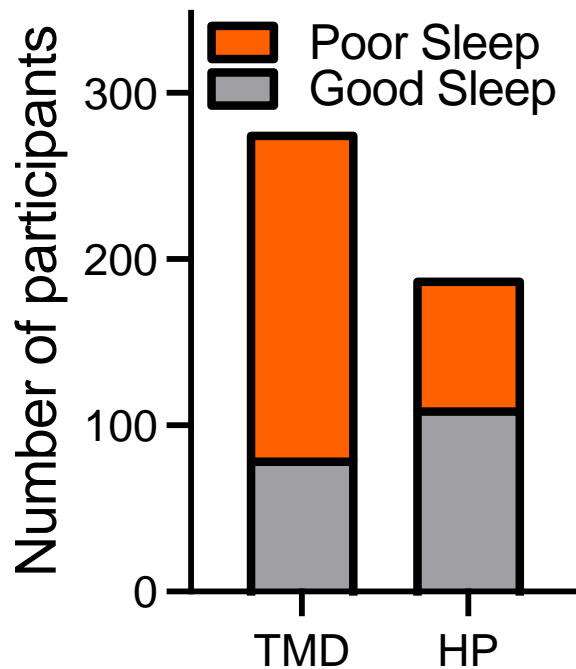
total = 10873 variables



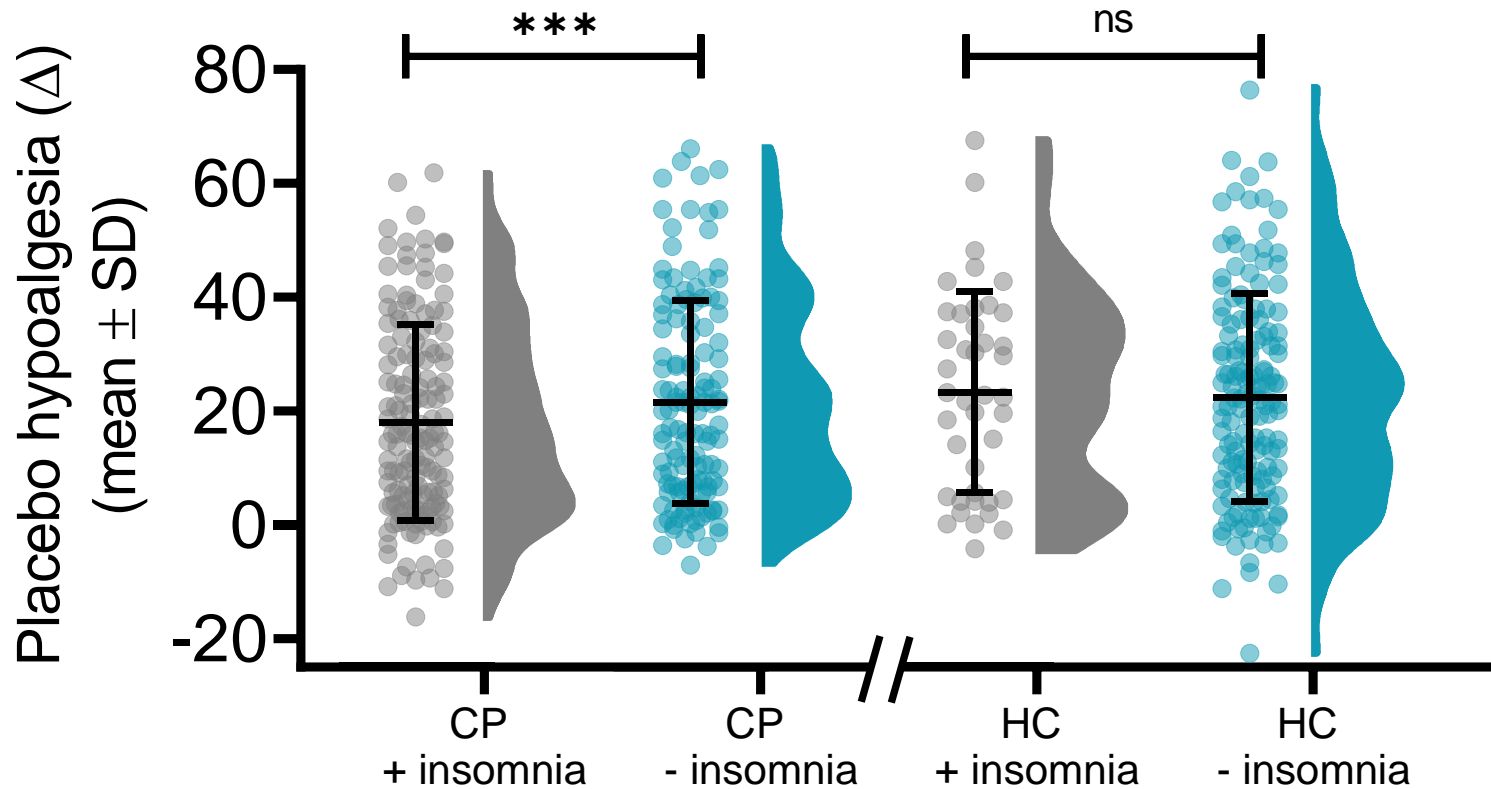
# Distribution of poor and good sleepers



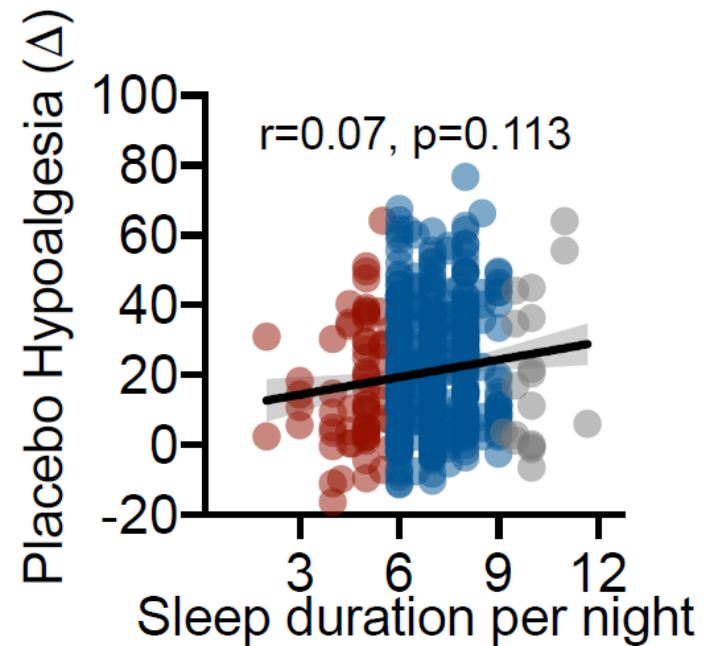
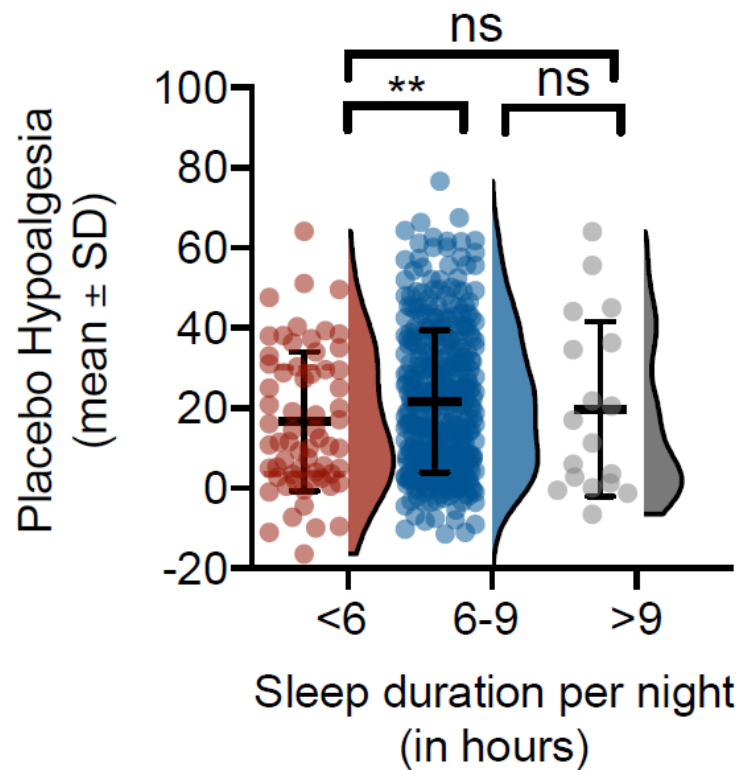
# Distribution of poor and good sleepers



# Insomnia reduces placebo effects



# Number of hours of sleep and placebo effects



# Overall take-home messages

- Placebo effects are neurobiological responses
- Sociodemographic factors influence placebo effects with AfroAmerican Blacks having smaller placebo effects and women having larger placebo effects
- Sleep patterns influence placebo effects: long-term insomnia reduces placebo effects in the presence of chronic pain.





<http://colloca.wixsite.com/colloca-lab/staff>



@Colloca\_Luana

Email: [colloca@umaryland.edu](mailto:colloca@umaryland.edu)





# Funding agencies



NIDCR (R01DE025946 - PI)

NIDCR (R21DE032532-01 - multiPIs)

NCCIH (R01AT010333- PI)

NCCIH (R015R01AT011347-PI)

NIAAA (R13 – multiPI)

MPOWERING THE STATE (PI)

ATIP/ICTR - UMB (multi-PI)

CARES - UMB (multi-PI)

Samueli Foundation

TRR/Germany

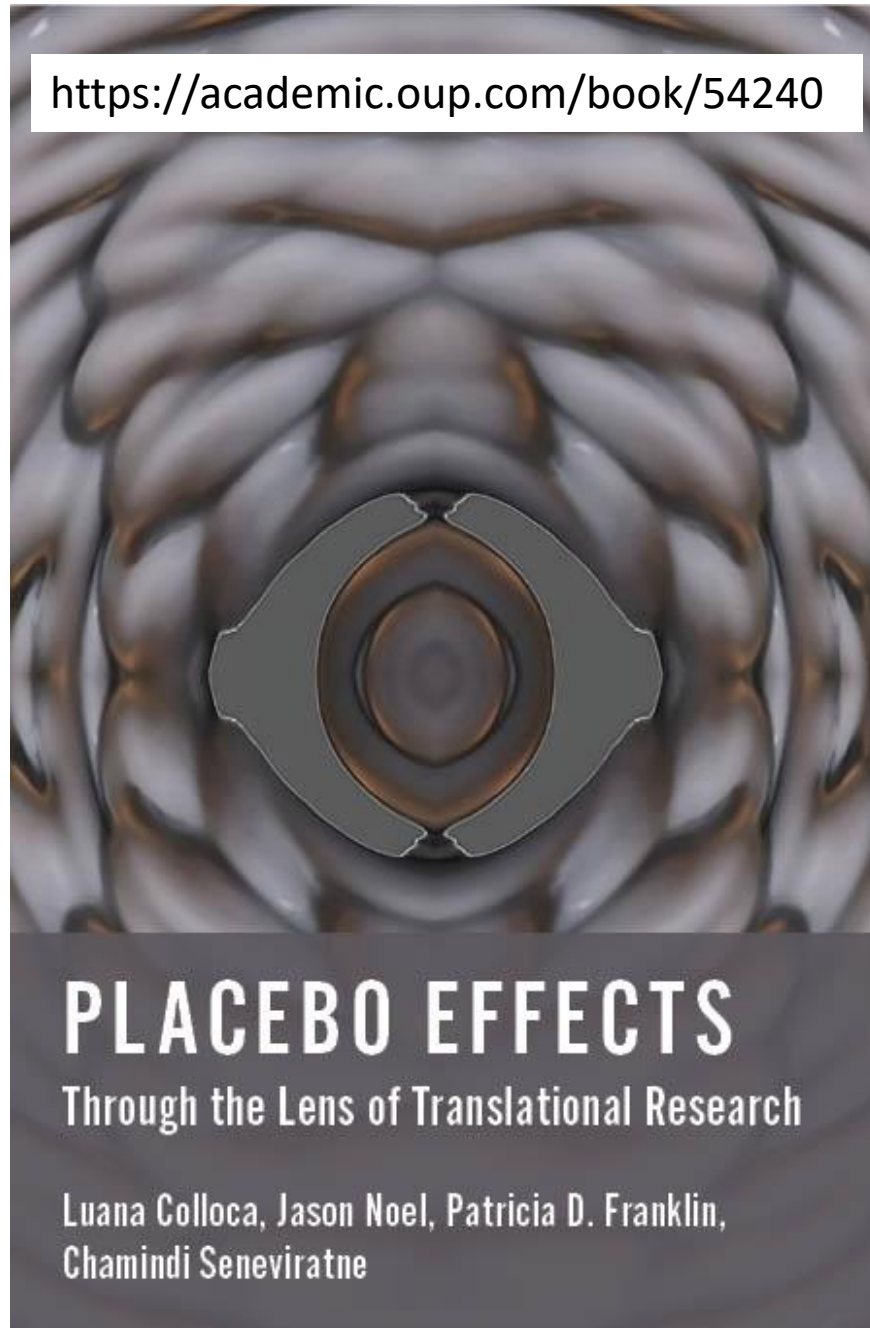
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The name "Placebo Beyond Opinions" (PBO) reflects the Center's **commitment to moving beyond mere opinions or assumptions** about the placebo effect and delving into rigorous scientific investigation. It emphasizes the Center's focus on advancing beyond subjective beliefs or unsubstantiated claims about placebos, **instead aiming for a deeper understanding through empirical research** and interdisciplinary collaboration. The term "Beyond Opinions" refers to a departure from speculation and a **dedication to evidence-based inquiry**.

## Mission:

The Placebo Beyond Opinions (PBO) Center is committed to advancing interdisciplinary research and education on placebo, nocebo, and expectation effects, with a particular focus on addressing disparities and integrating digital therapeutics. Collaborating with global leaders, we investigate these mechanisms and their impact on symptom variability, treatment responses, and clinical encounters, especially among underserved populations. Through rigorous research, we seek **to improve clinical trials, educate future clinicians, and integrate placebo knowledge into precision medicine practices**, leveraging digital therapeutics (e.g., virtual and augmented reality) to ensure equitable access and optimal patient care.

## Goals:

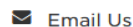
- 1. Addressing Socio-Economic Factors and Disparities:** The PBO Center aims to focus on socio-economic factors and disparities that influence clinical outcomes in underrepresented populations. Through comprehensive research on placebo, nocebo and expectations, we hope to contribute to mitigate these disparities and ensure equitable access to effective healthcare (e.g., digital therapeutics).
- 2. Educating Medical Providers on Placebo Effects:** A primary objective of the PBO Center is to educate clinicians about the significance of placebo, nocebo and expectancies effects in healthcare delivery. By incorporating knowledge of placebo mechanisms into medical education, we empower clinicians to deliver targeted and more effective patient care, ultimately improving treatment outcomes.

## Initiatives Supported by the PBO Center:

- Creating an Interdisciplinary Entity for Global Collaboration:** The PBO Center serves as an interdisciplinary hub that fosters collaboration among centers and scholars dedicated to advancing placebo science. By facilitating the exchange of ideas and resources, progress in understanding and harnessing placebo, nocebo and expectancy effects for improved patient care.
- Developing an Elective Lecture on Placebo Effects:** The PBO Center offers ad-hoc elective lectures on Placebo Effects designed to highlight the importance of patient-provider communication in enhancing treatment outcomes. Through interactive learning, clinicians and students can gain insights into the role of placebo mechanisms in healthcare delivery.



## Contact



[Email Us](#)



655 West Lombard  
Street, Room 729A  
Baltimore, MD 21201



410-706-5975

