

# Placebo effects in the era of the epidemic of opioids

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Dean's Lecture Series - Virginia Lee Franklin Lecture, Oct 25, 2018

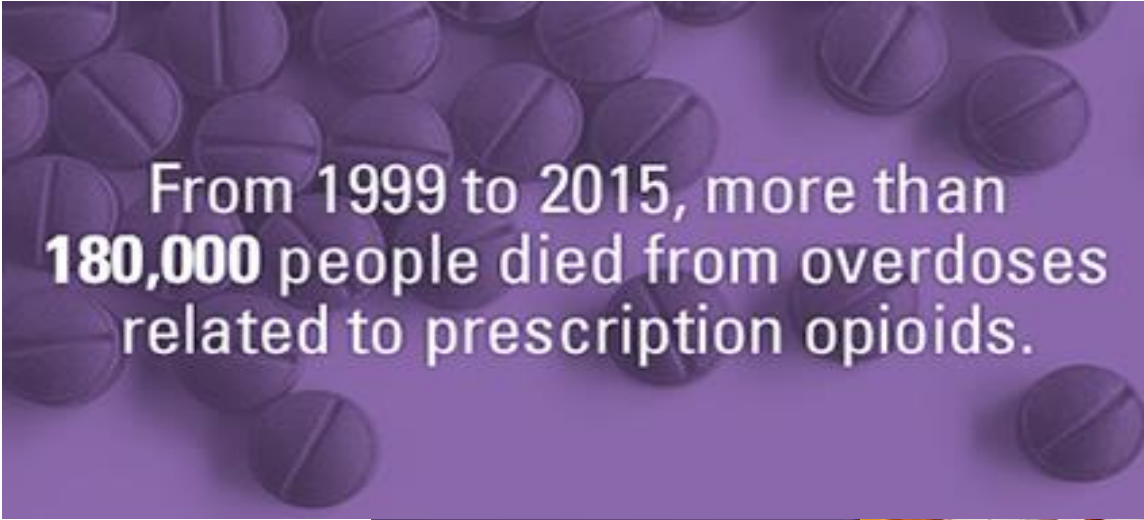
# Prevalence of chronic pain



In 2012, approximately 55% of all US adults experienced some form of pain




# The epidemic of opioids

A close-up photograph of numerous purple, round, scored tablets scattered on a dark purple background.

From 1999 to 2015, more than **180,000** people died from overdoses related to prescription opioids.

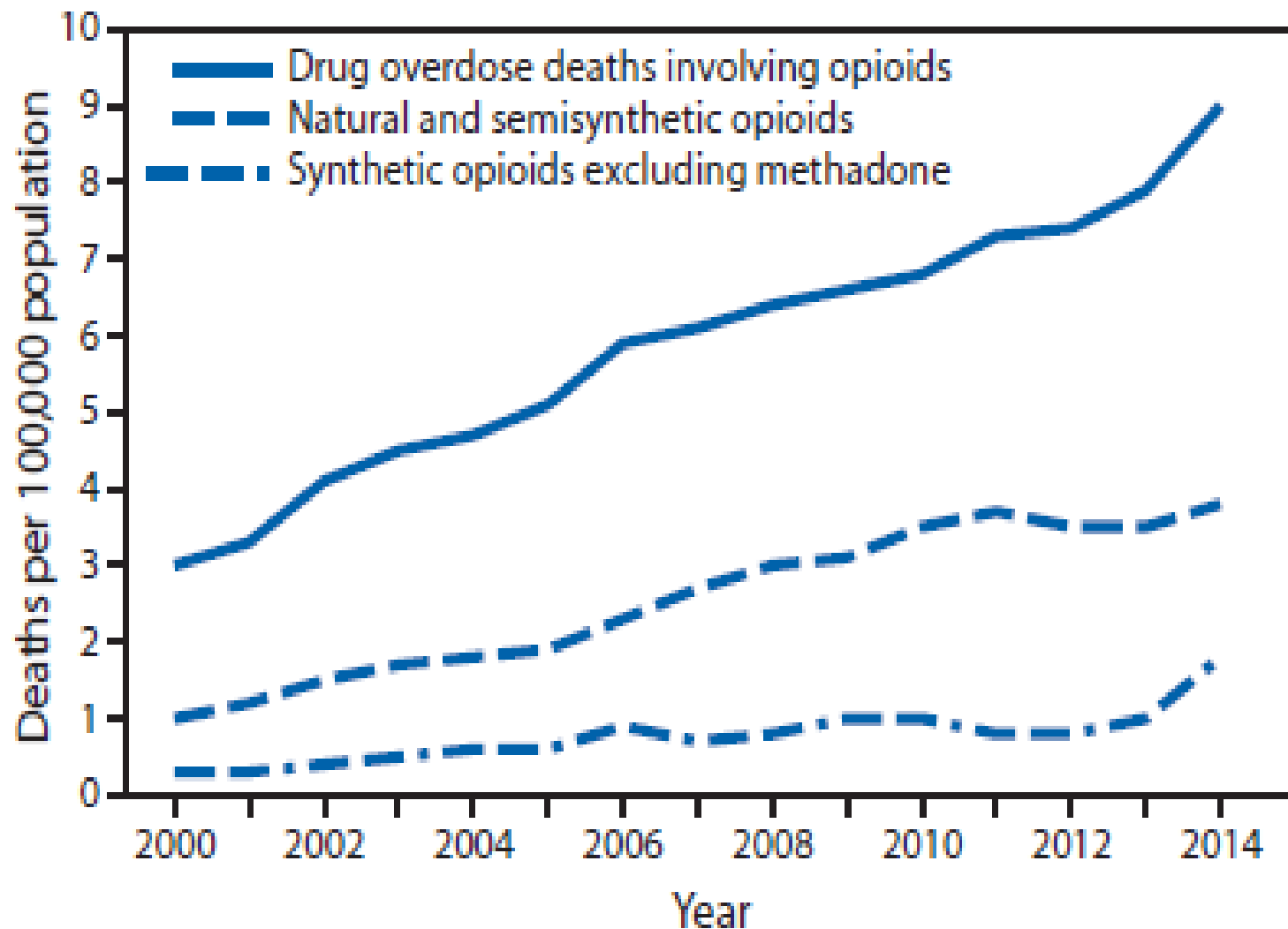
A photograph showing a pile of orange plastic prescription bottles with white labels and caps, some with their caps removed.

Nearly **2 million** Americans abused or were dependent on prescription opioids in 2014.

A photograph of a person's head and shoulders, seen from the side, with their hand pressed against their forehead, suggesting pain or distress. The background is a dark purple gradient.

An estimated **1 out of 5** patients with non-cancer pain or pain-related diagnoses are prescribed opioids.

# The opioid overdose death epidemic in the US



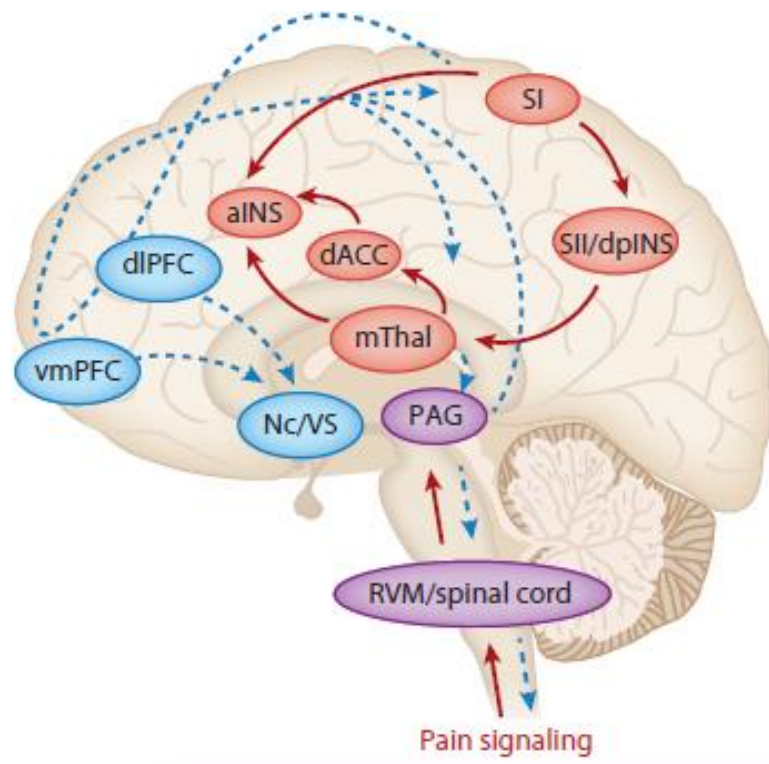
Adapted from:

Rudd et al. 2016;64(50-51):1378-1382

# PAIN EXPERIENCE IS MODULATED BY...

- Verbal suggestions
- Therapeutic prior experiences
- Observation of benefits in others
- Contextual and treatment cues
- Interpersonal interactions

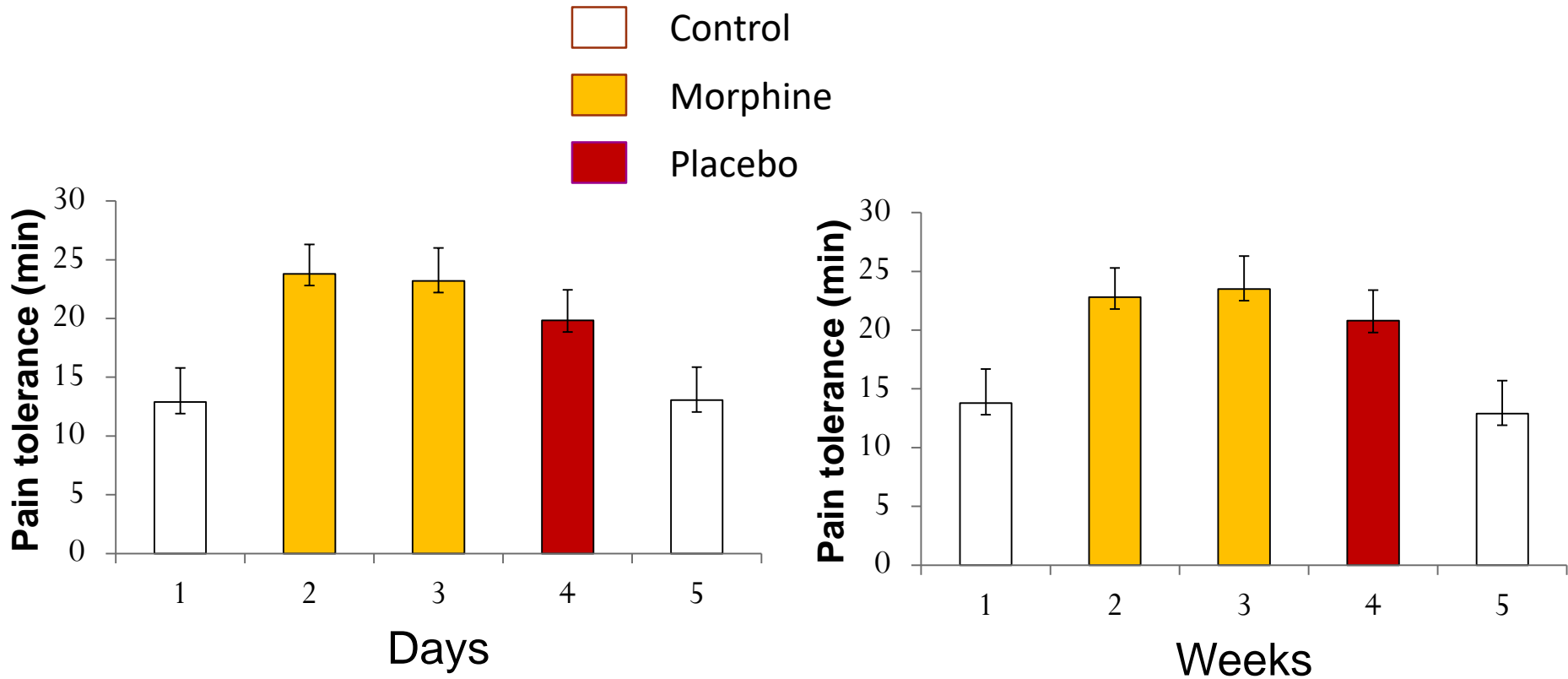
Expectancies



- ← - - - Descending pathways
- ← Ascending pathways
- Increased activation
- Decreased activation
- Increased/decreased activation

Pharmacological, integrative, psychological, and surgical interventions

# Conditioned responses and pain tolerance



Amazio and Benedetti, J Neurosci. 1999 Jan 1;19(1):484-94

Benedetti, Pollo, Colloca. J Neurosci. 2007 Oct 31;27(44):11934-9.



# Dose-extending placebos

Week 1



Week 2



Week 3



Week 4





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## RAP study – SON&STC&SOM



Sarah Murthi – Division of Trauma and Critical Care R Adams Cowley STC

L. Yvette Fouche – Department of Anesthesiology

Luana Colloca – Pain Translation Symptom Science School of Nursing

Patricia Casper – Acute Pain Management Service, University of Maryland

# RELIEVING ACUTE PAIN (RAP) STUDY

HP#: 00078742

NTC: NCT03426137

**SCOPE:** Explore dose-extending placebos as a novel strategy to reduce overall opioid intake  
**159** trauma patients

## Inclusion Criteria

- Aged 18 to 65 years old
- Admission to the Shock Trauma Center
- **Trauma**
- Predicted length of stay  $\geq$  3 days
- Plan by primary service to follow the Shock Trauma Guidelines for Acute Pain in Orthopedic Injury

## Exclusion Criteria

- Non english speaking
- Spine or spinal cord injury
- Severe Traumatic brain injury
- Patient-controlled analgesia
- Admission Creatinine  $>$  1.4
- History of chronic kidney disease
- Methadone or heroin use in the 3 months prior to admission (patient self report)
- Methadone or heroin positive toxicology screen for opioid drugs not prescribed during current hospitalization
- Severe psychiatric condition (e.g. schizophrenia, bipolar disorders, mania, autism) and /or psychiatric condition leading to treatment and/or hospitalization within the last 1 year.
- Pregnancy or breast feeding
- Contraindication to NSAIDS, including high risk of bleeding or known severe coronary artery disease

# VIRTUAL REALITY, Music and PAIN



CellPress

Neuron  
NeuroView

## NIH/Kennedy Center Workshop on Music and the Brain: Finding Harmony

Thomas Cheever,<sup>1,11</sup> Anna Taylor,<sup>1,11</sup> Robert Finkelstein,<sup>1,\*</sup> Emmeline Edwards,<sup>1,\*</sup> Laura Thomas,<sup>1</sup> Joke Bradt,<sup>2</sup> Steven J. Holochwost,<sup>3</sup> Julene K. Johnson,<sup>4</sup> Charles Limb,<sup>5</sup> Aniruddh D. Patel,<sup>6,7</sup> Nim Tottenham,<sup>8</sup> Sunil Iyengar,<sup>9</sup> Deborah Rutter,<sup>10</sup> Renée Fleming,<sup>10</sup> and Francis S. Collins<sup>1</sup>

# VIRTUAL REALITY and UM COLLABORATION



Amitabh Varshney - University of Maryland, College Park

Sarah Murthi – Maryland Blended Reality Center STC

Craig Kier - Maryland Opera Studio, College Park

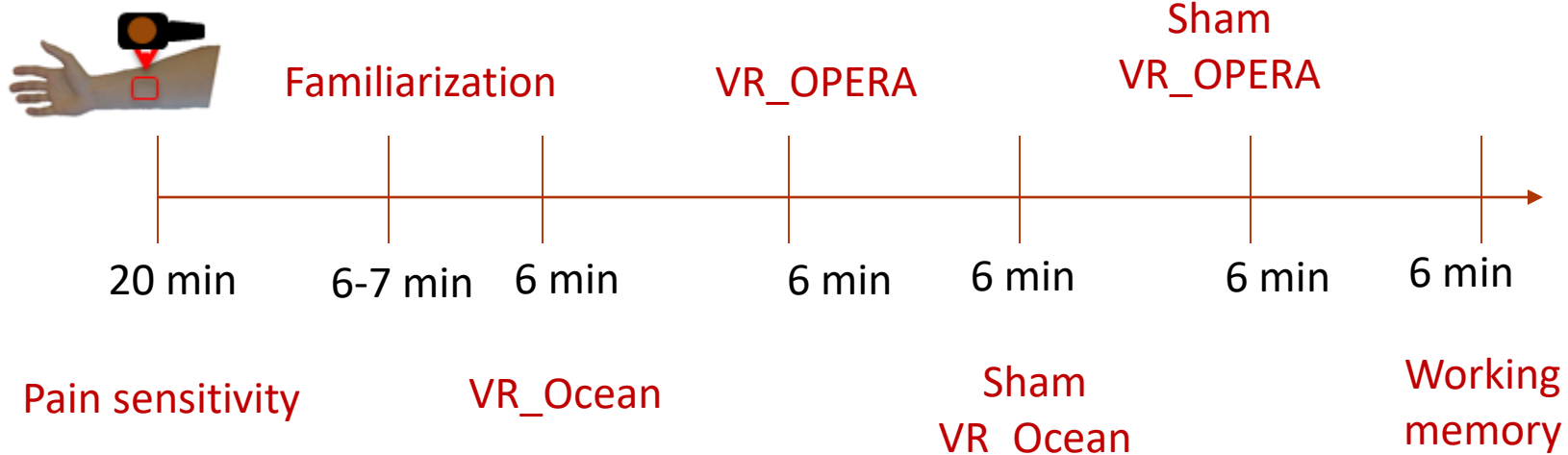
Luana Colloca – School of Nursing



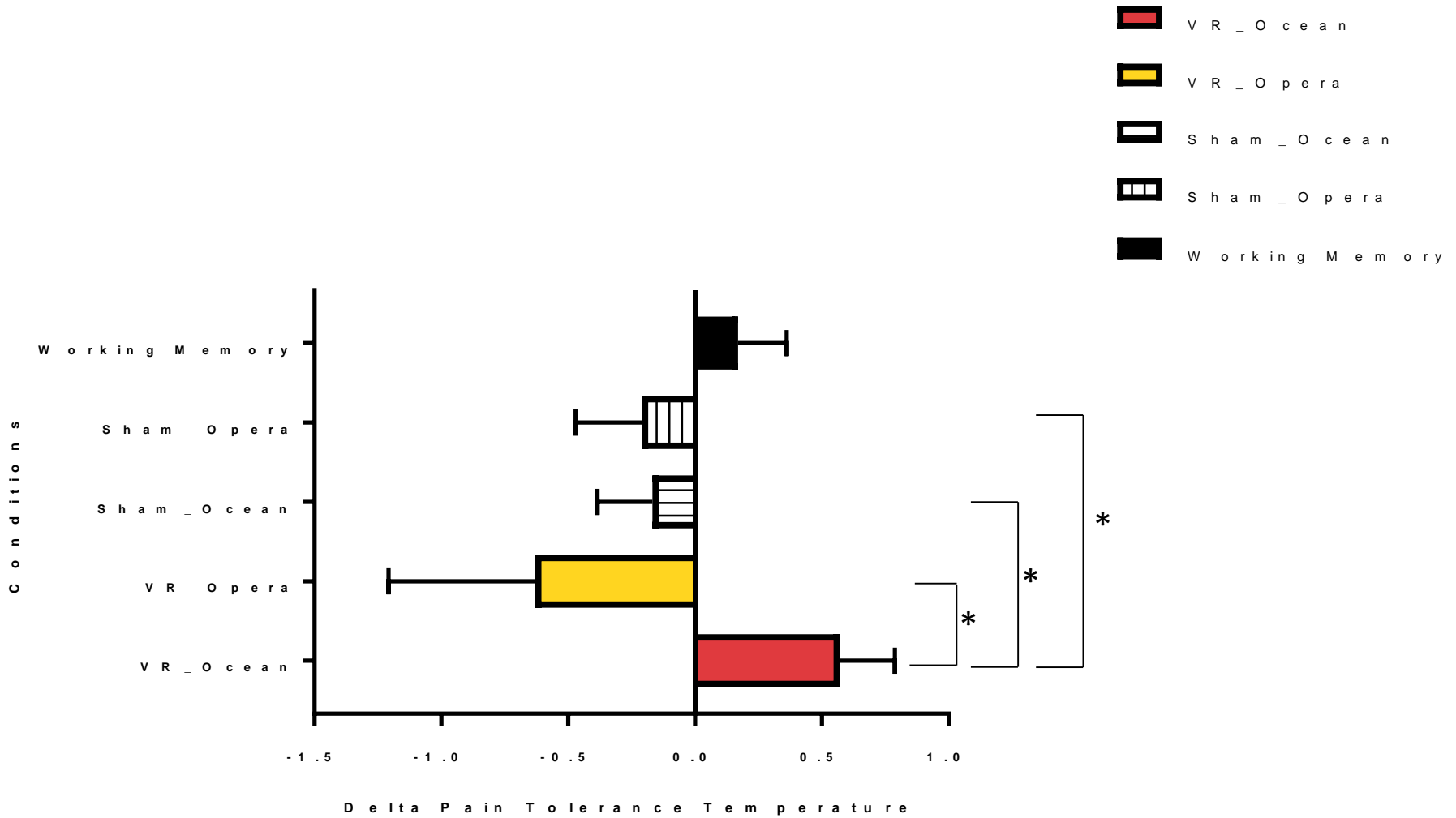
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# VIRTUAL REALITY and PAIN MODULATION

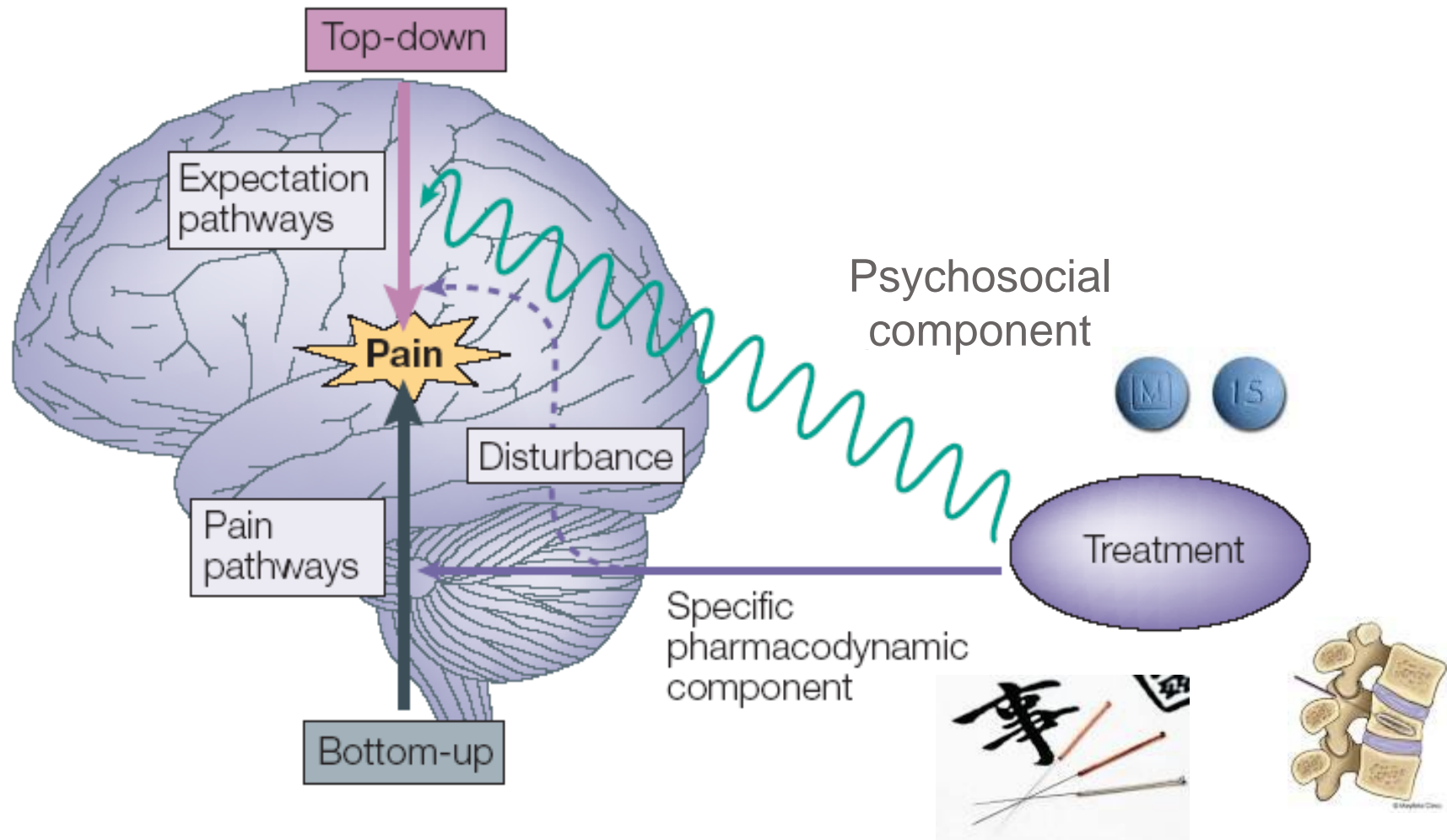
-  VR\_Ocean
-  VR\_Opera
-  Sham\_Ocean
-  Sham\_Opera
-  Working Memory



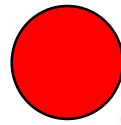
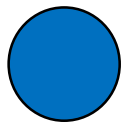
# Virtual reality and pain tolerance changes



# Placebo and drug effects



Colloca and Benedetti, Nature Rev Neurosci 2005; 6:545-52



### BUPRENORPHINE

### TRAMADOL

### KETOROLAC

### METAMIZOL

open

hidden

open

hidden

open

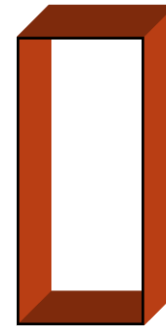
hidden

open

hidden

Pain reduction

0  
-1  
-2  
-3



## Conclusive remarks

- Placebo effects depend upon the activation of the descending pain modulatory systems and the release of endogenous opioid substances
- This research hints to a need for harnessing endogenous modulatory mechanisms to optimize clinical outcomes in daily clinical practice
- The developed approaches can be powerful therapeutic tools to reduce overall opioid use for treating acute and chronic pain in clinical settings

# Funding agencies



NIDCR (R01DE025946-03 - PI)

MPOWERING (PI)

PCORI (co-I)

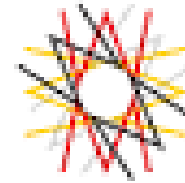


AHRQ (R24HS022135 - PI)

CACPR (co-PI)

ICTR (co-PI)

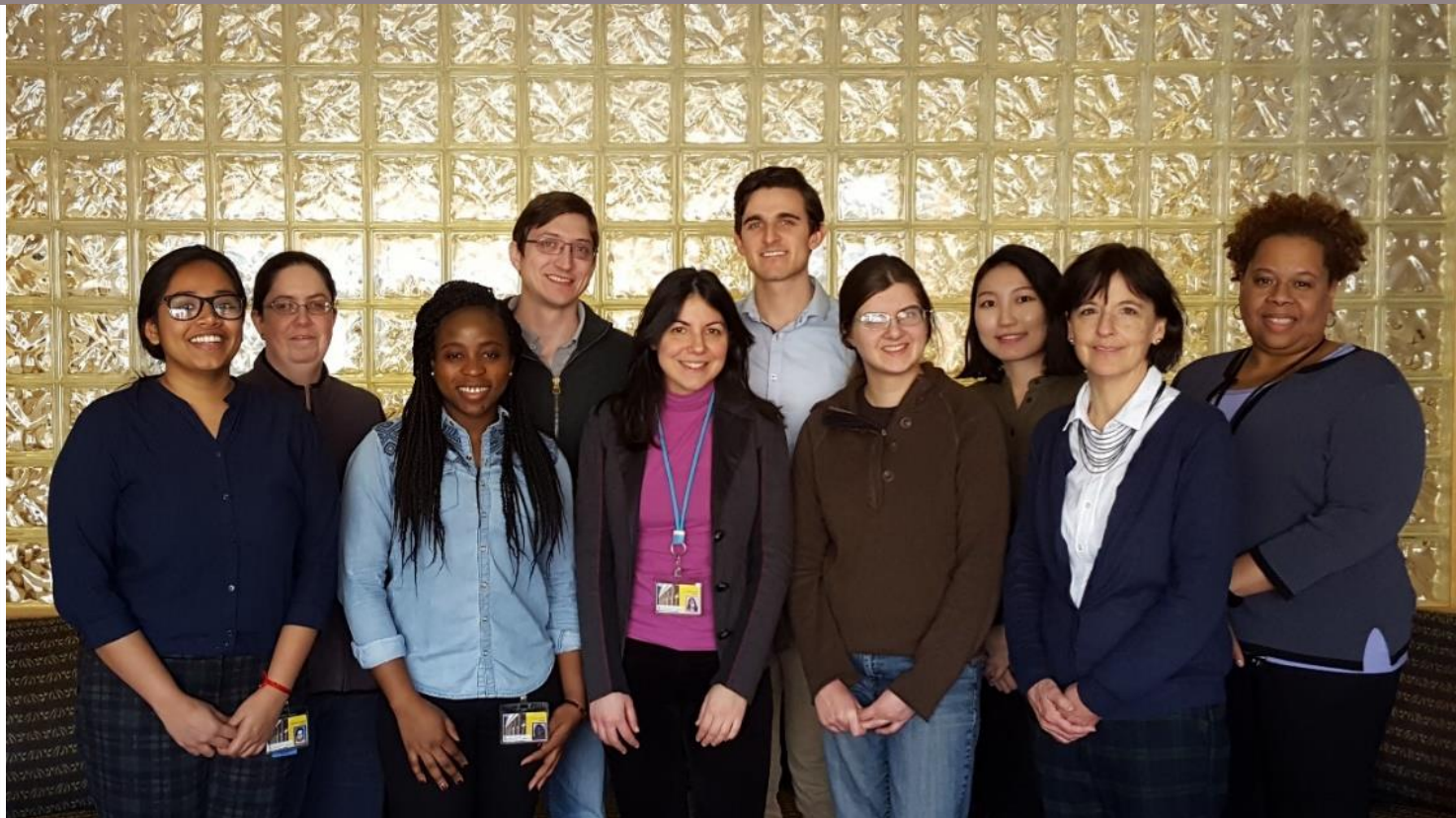
CARES (co-PI)



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# The Colloca lab:

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



# Educational tools

