

Preliminary results pre-registration overview

Neural correlates of expectations
of pain, perceived pain, and cognitive effort

Aug 24th, 2021. Heejung Jung

Goal of presentation

- Behavioral Pilot data (updated N: 21 → 48)
- Submitted version of Pre-registration
- Univariate gym results (updated N: 17)
- Future plan: Multilevel mediation analysis

Design

expectations can shape experiences

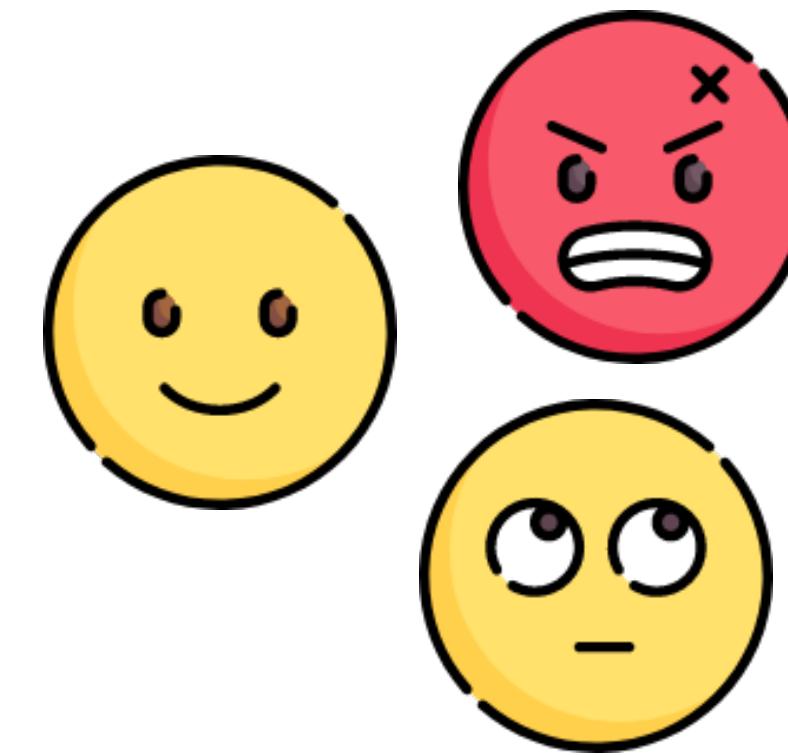
Social influence



Expectations



Subjective experiences



Design

Independent variables

- 3 tasks (pain vs. vicarious vs. cognitive)
- 2 Social Cue (high vs. low)
- 3 Stimulus intensity (high vs. med vs. low)

Dependent variables

- “expect” ratings
- “actual” ratings

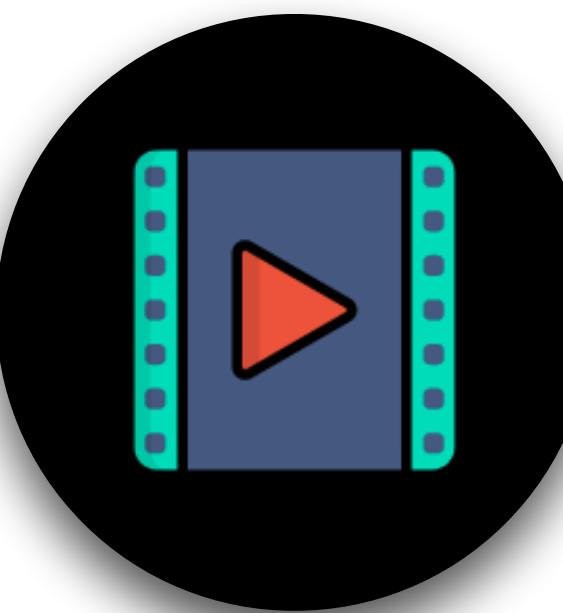
- **3 tasks**
- 2 Social cue
- 3 Stimulus intensity

Pain



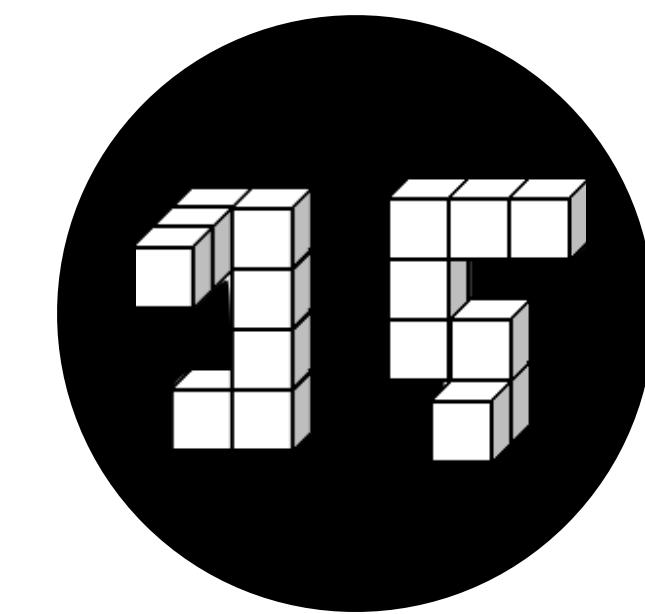
Thermal pain

Vicarious



Vicarious pain videos

Cognitive

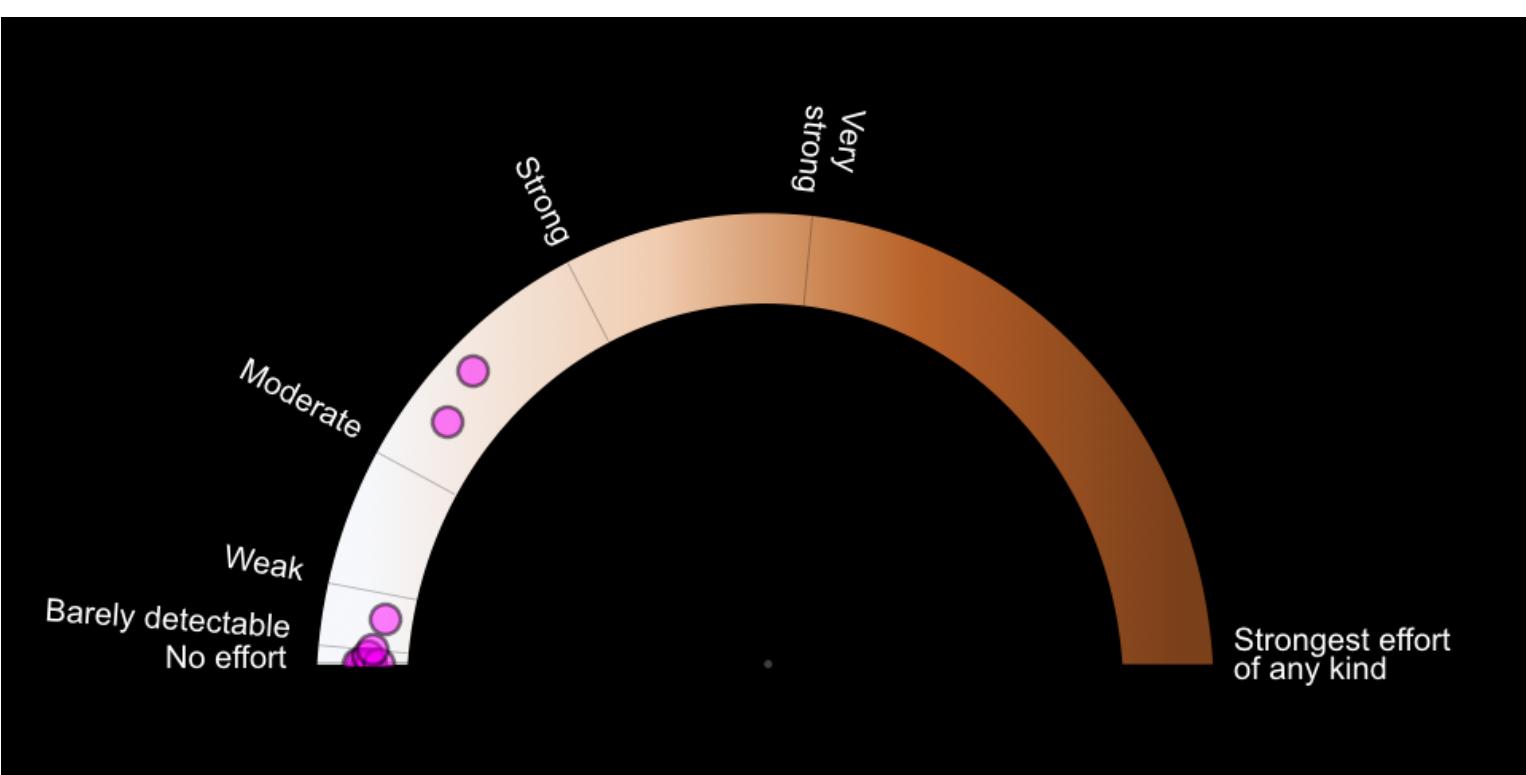


Mental rotation

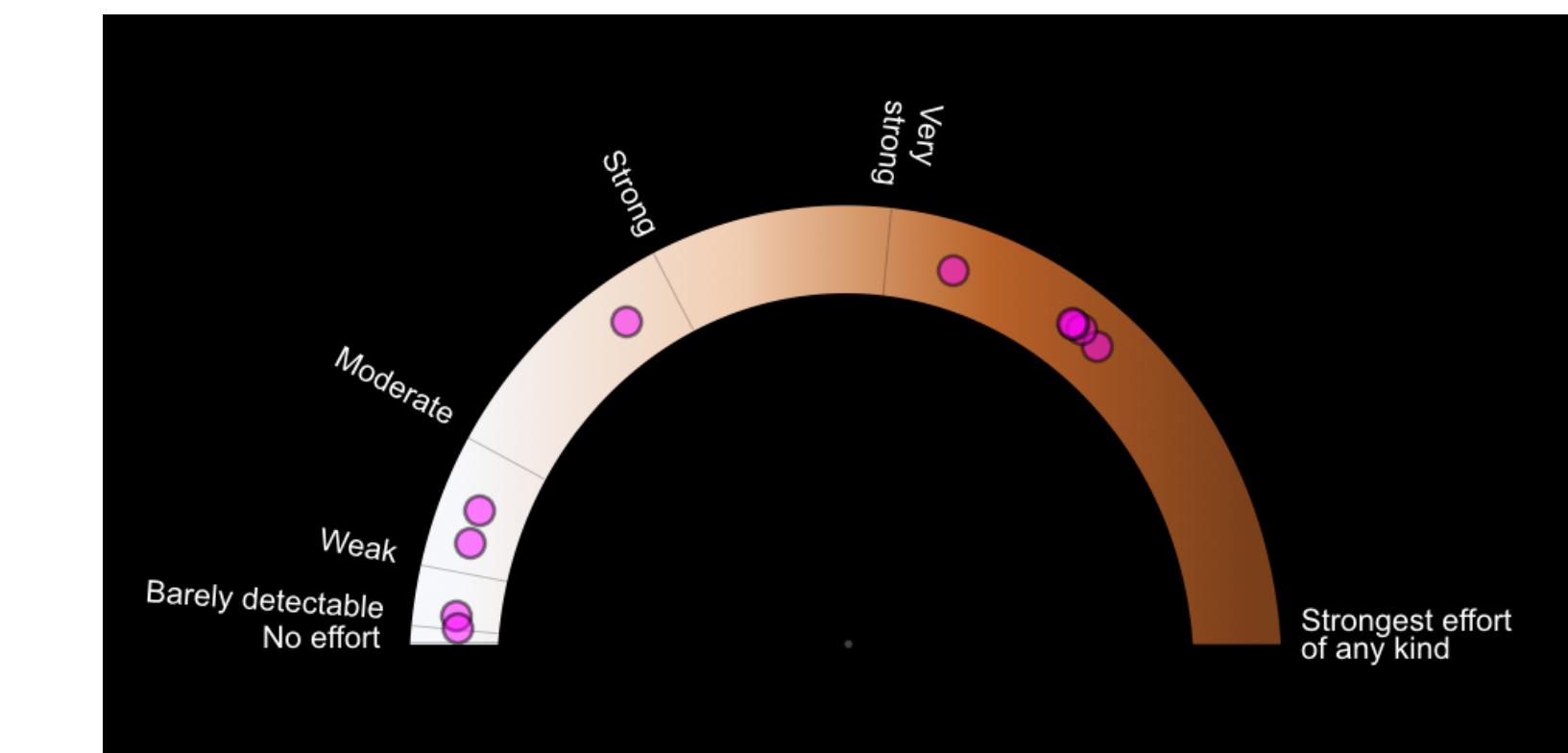
- 3 tasks
- **2 Social cue**
- 3 Stimulus intensity

- Based on pilot data N=5
- Generated cues from beta distribution

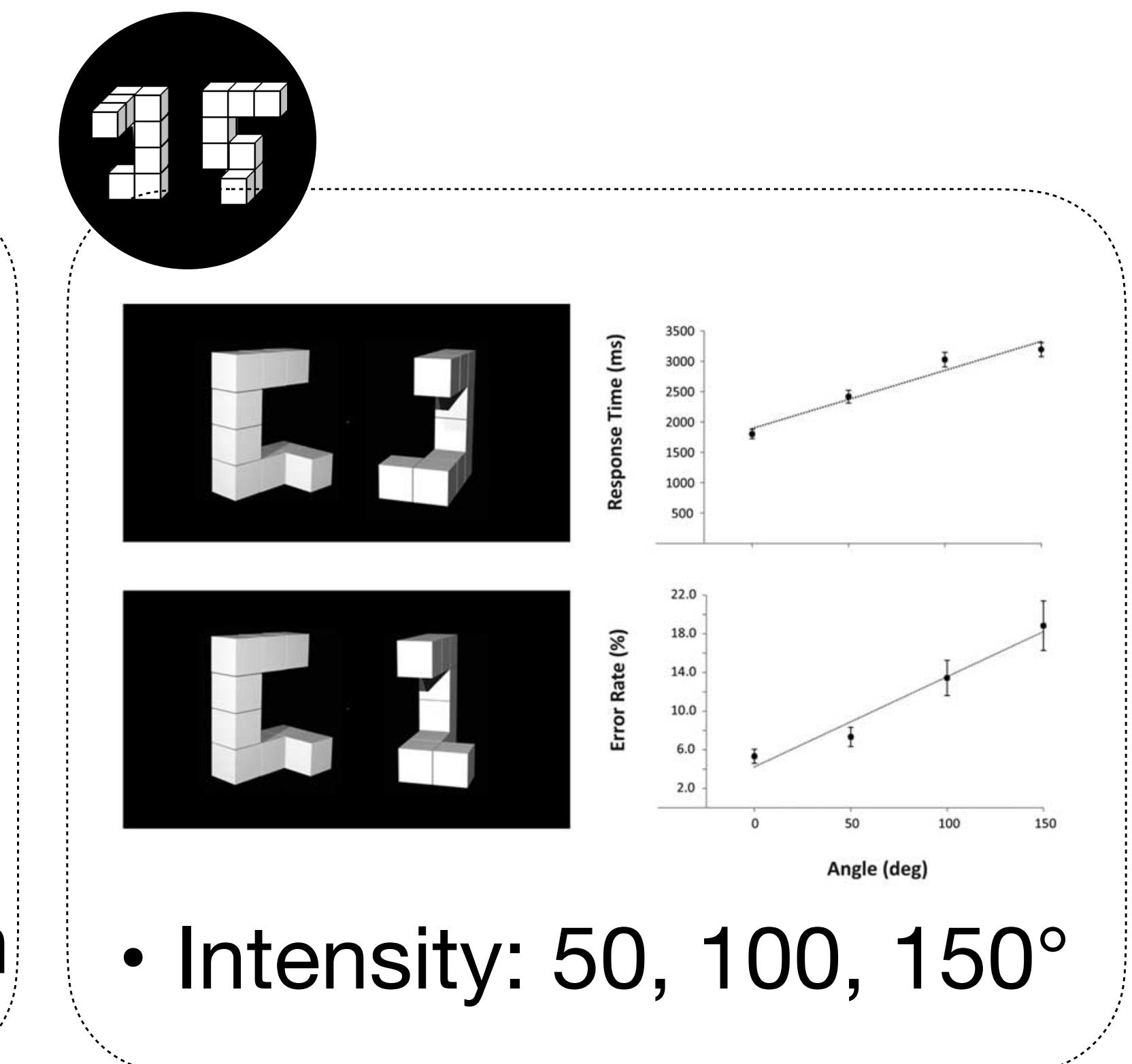
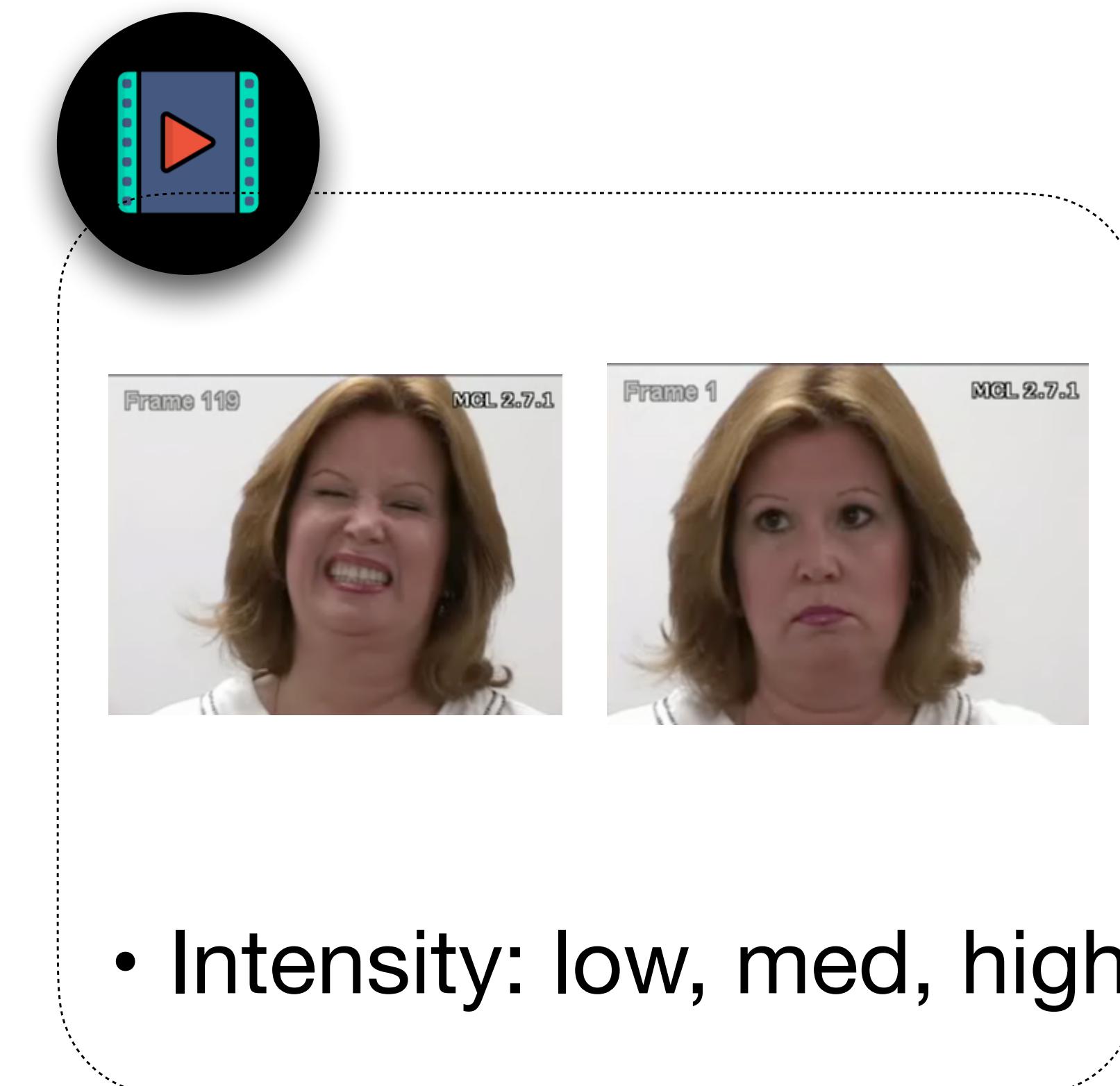
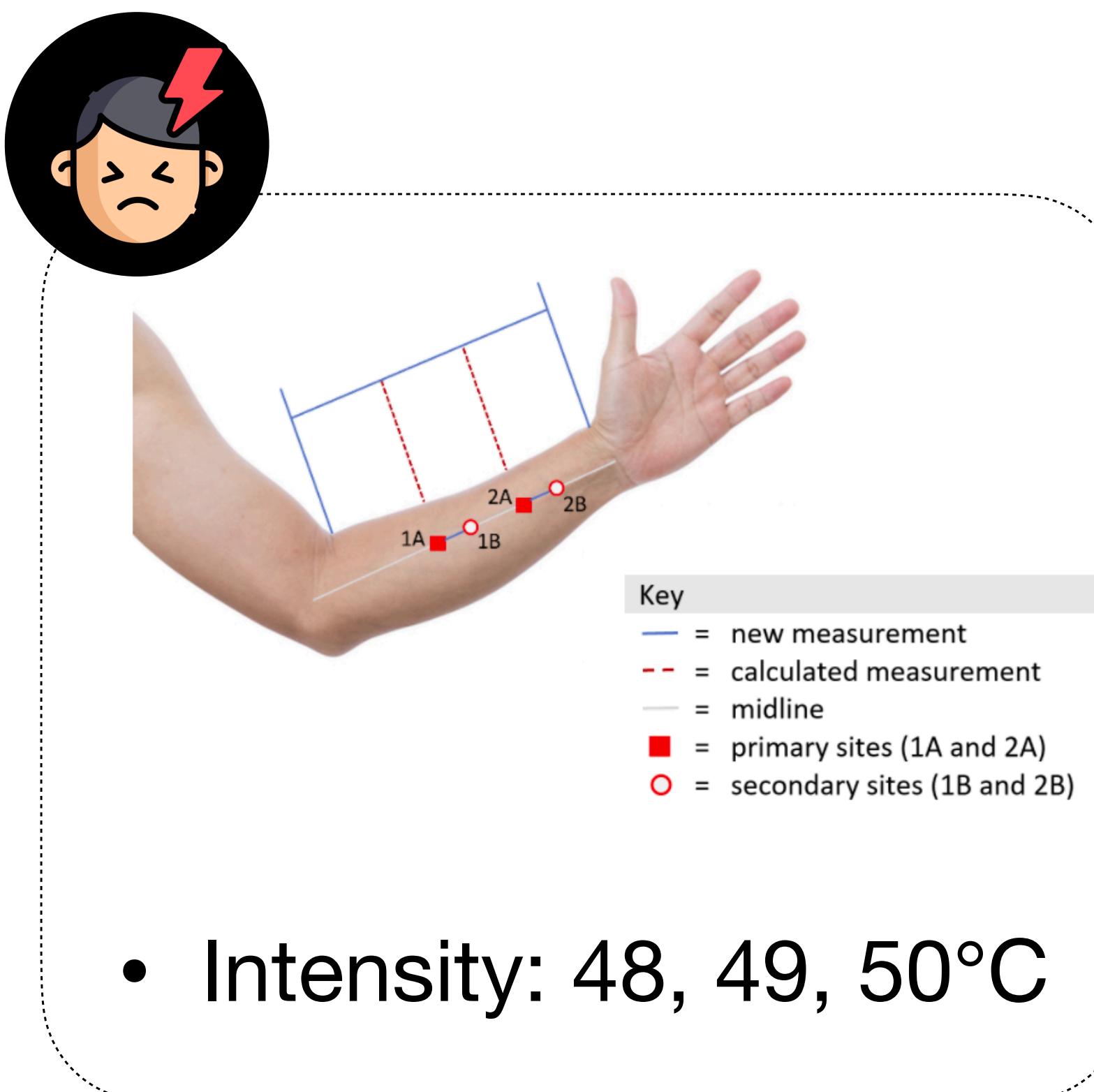
Low cue



High cue

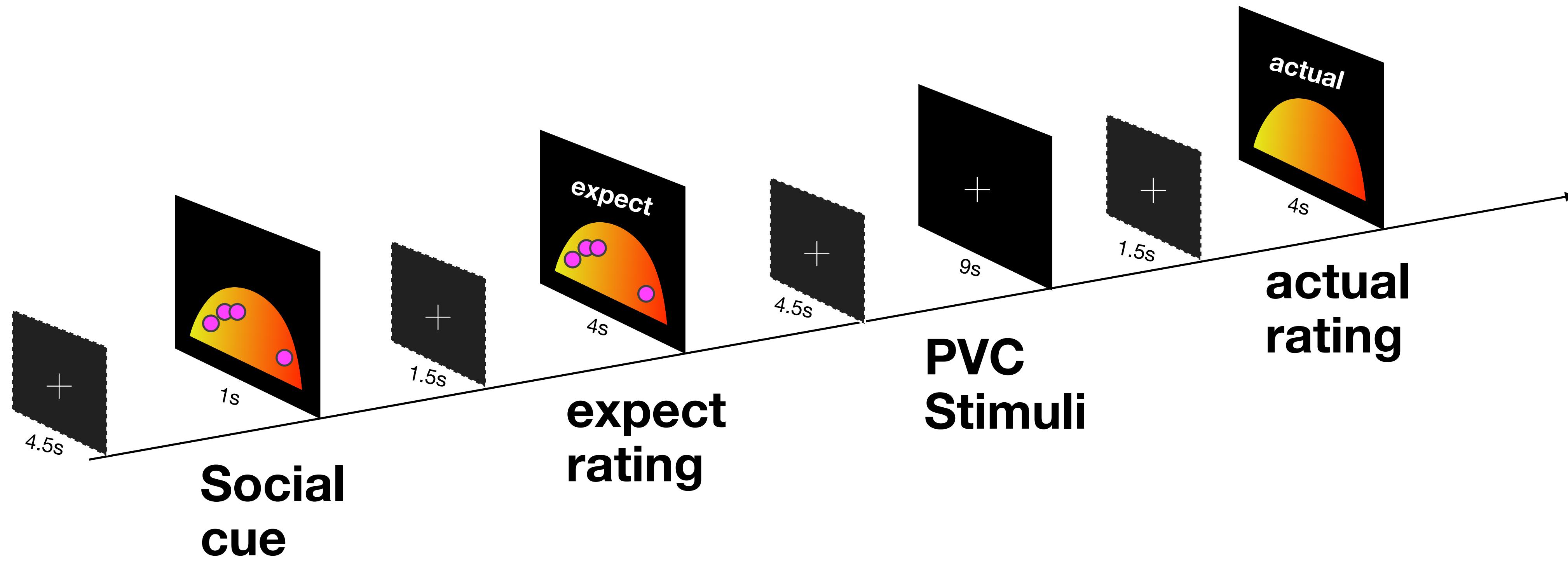


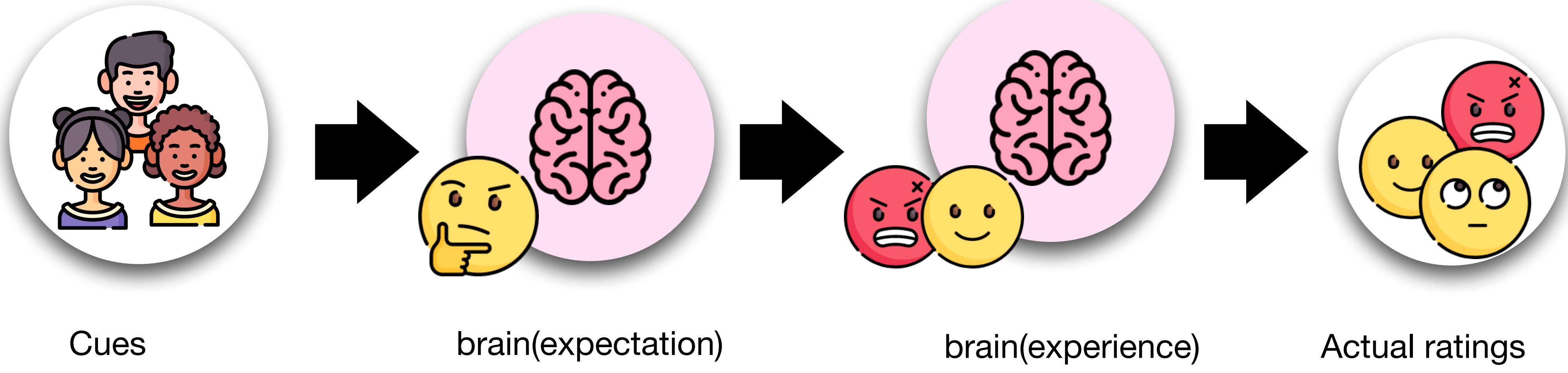
- 3 tasks
- 2 Social cue
- **3 Stimulus intensity**



Lucey et al. (2011)

Ganis & Kievit (2015)
Shepard & Metzler (1971)

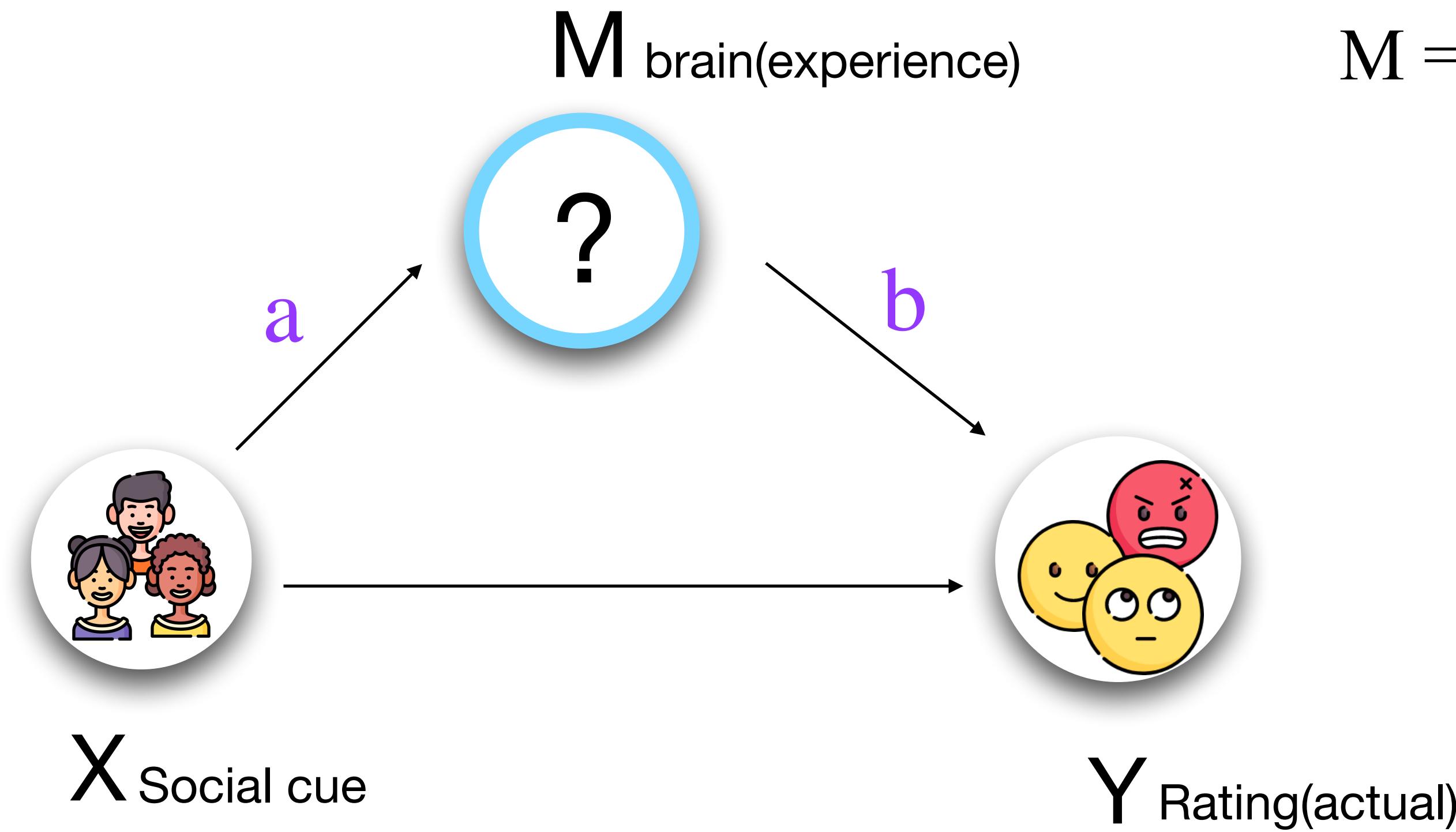




how do expectations shape actual experiences?

Mediation

Two-path mediation

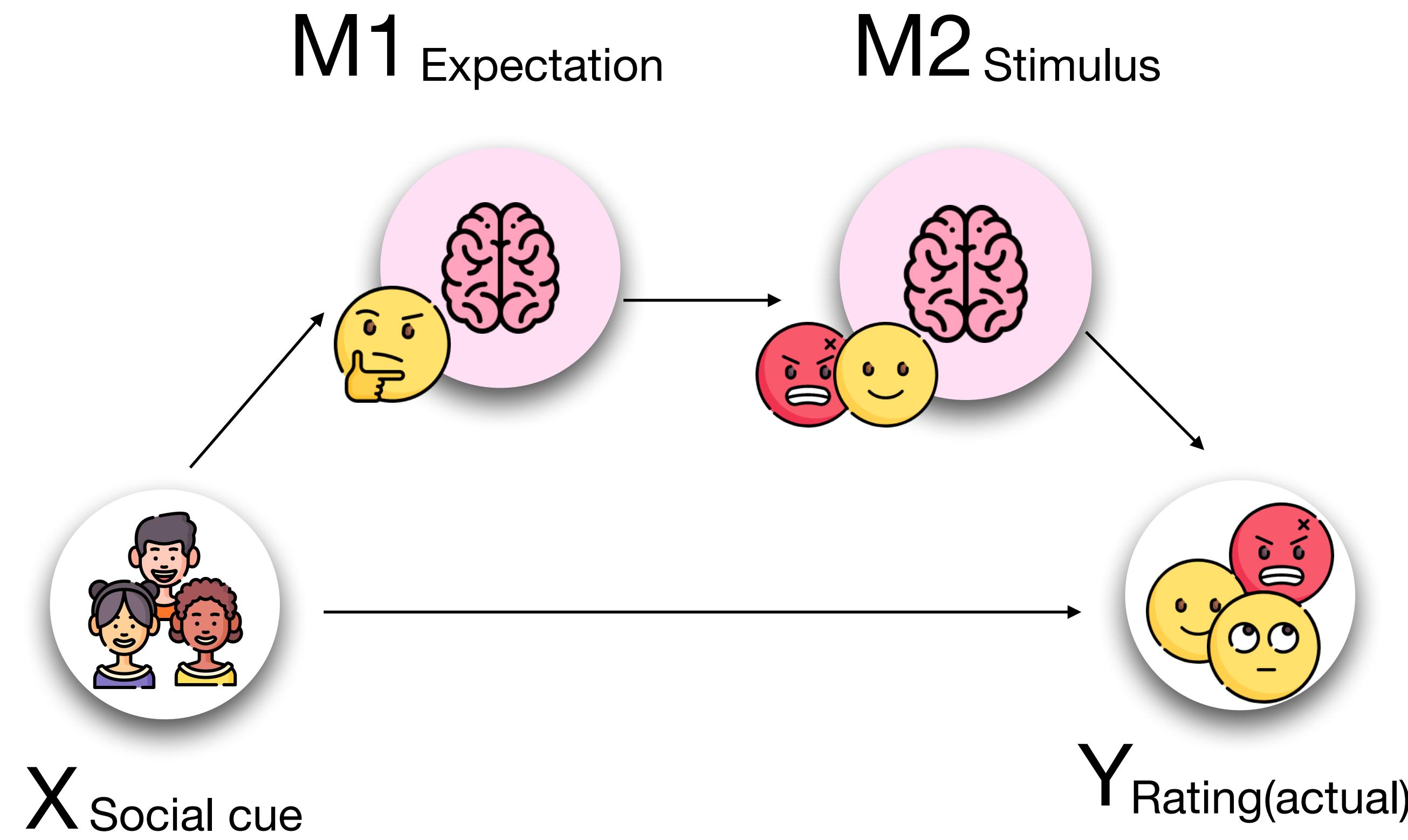


$$Y = \beta_0 + cX$$

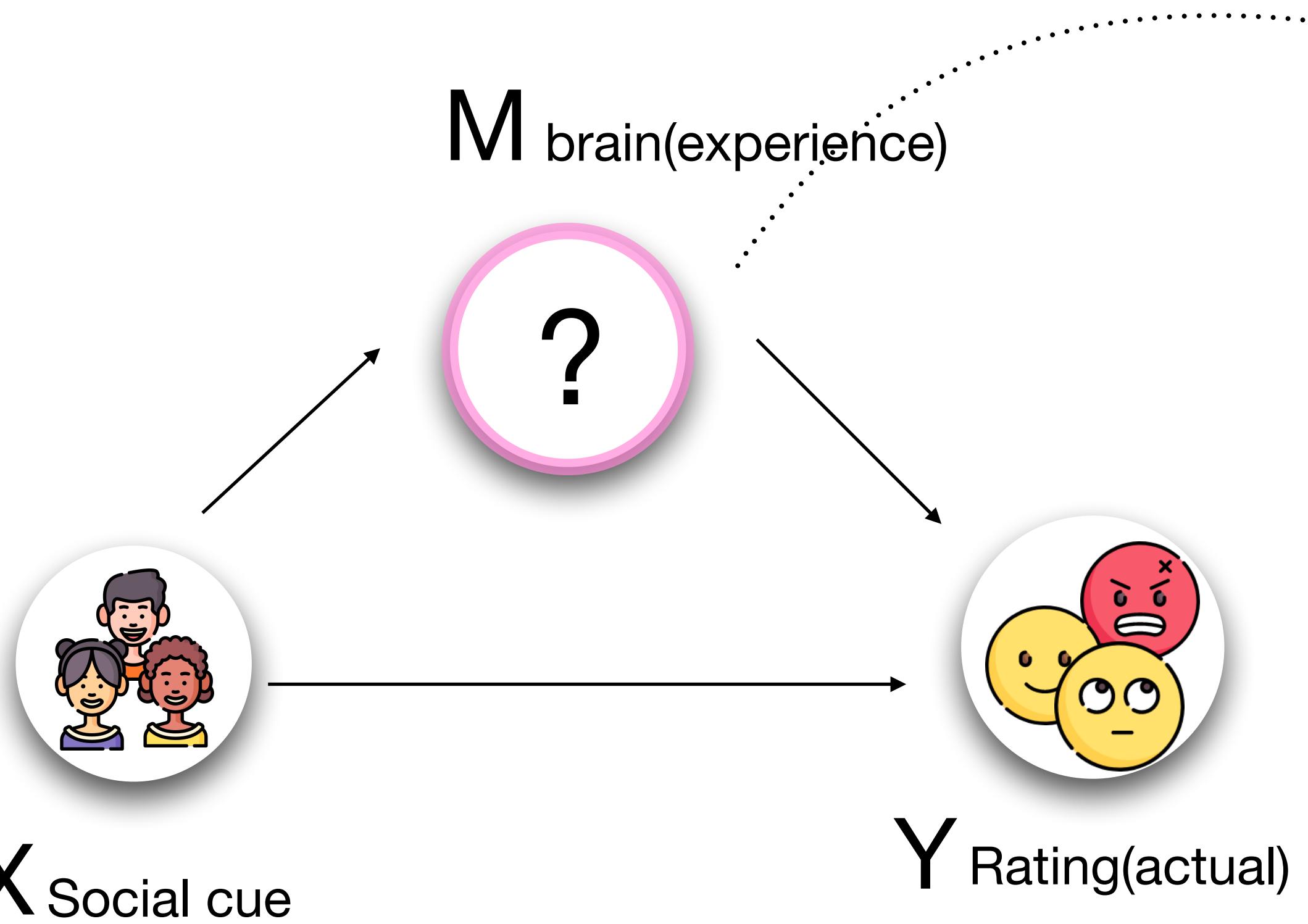
$$Y = \beta_0 + c'X + bM$$

$$M = \beta_0 + aX$$

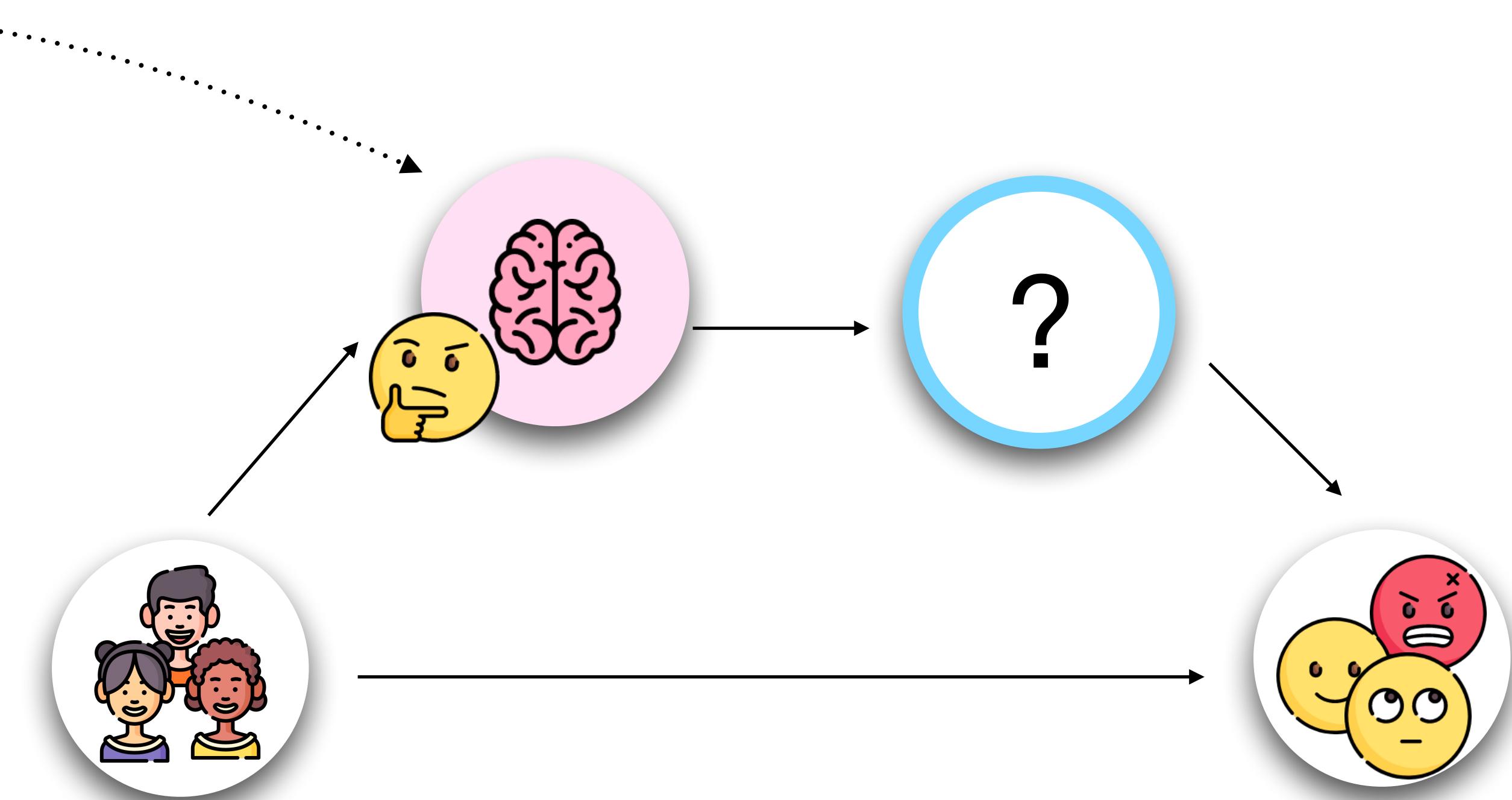
$\therefore ab = \text{indirect effect (mediation)}$



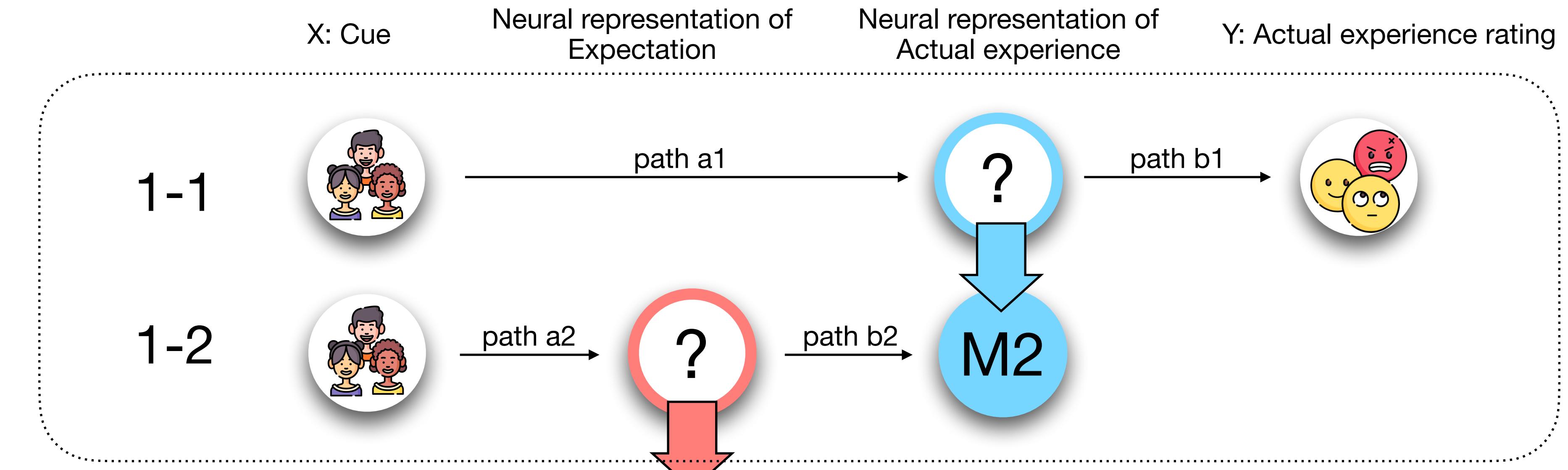
Two-path mediation



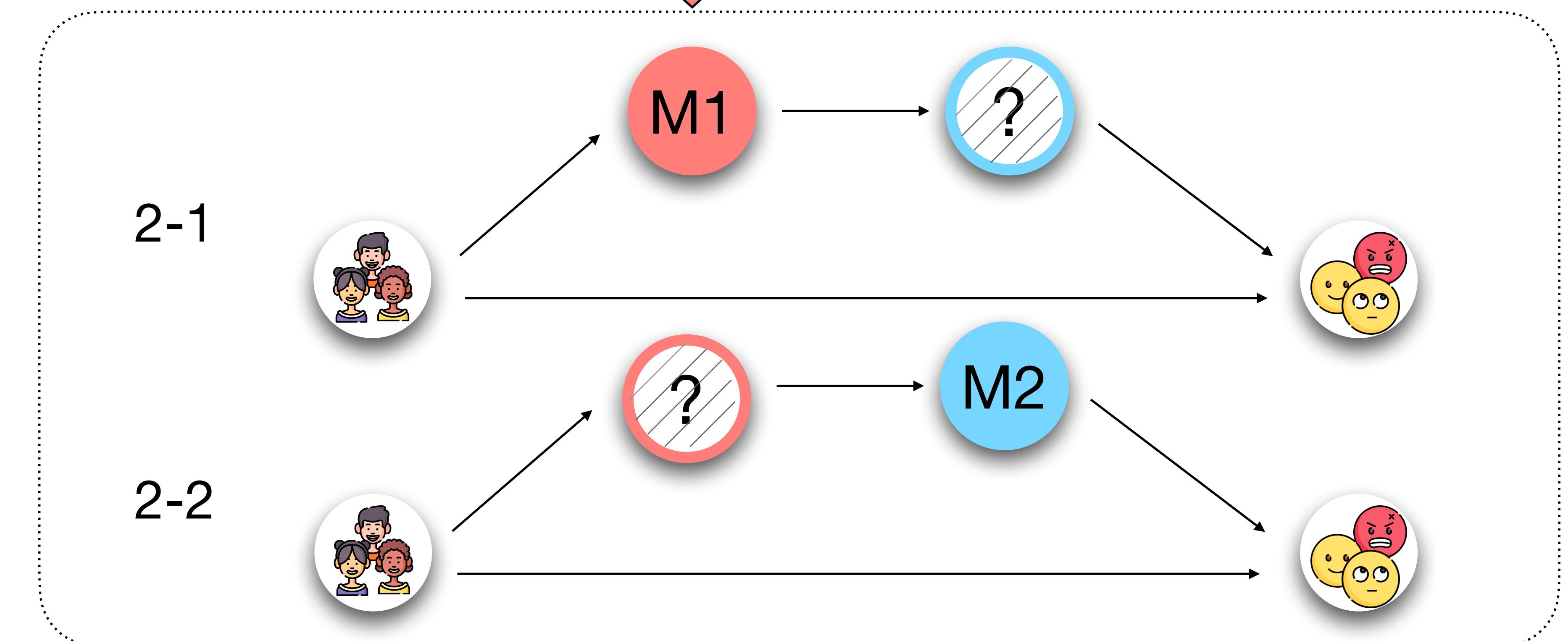
Multi-path mediation



Analysis 1 Two-path

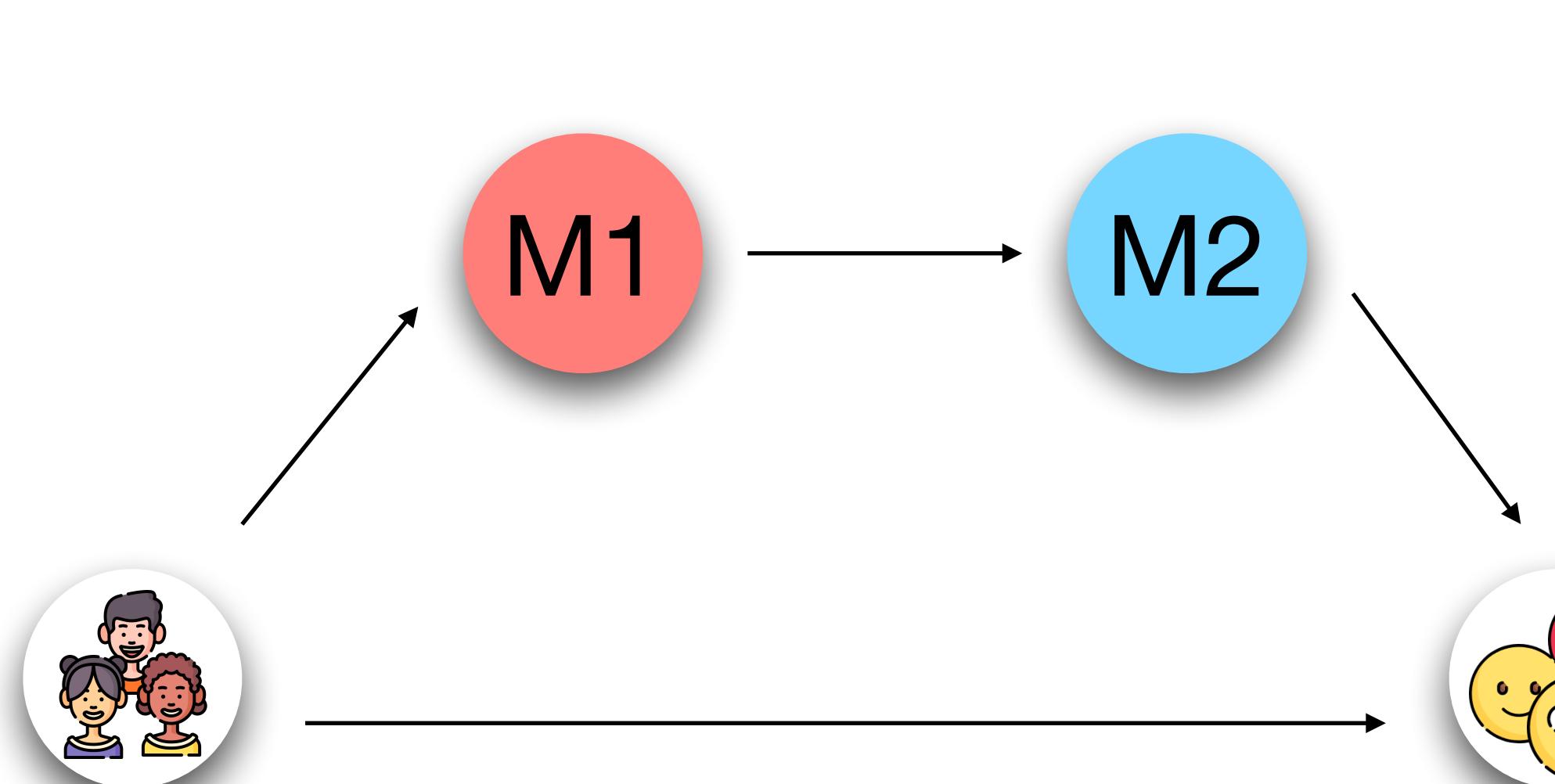


Analysis 2 Multi-path



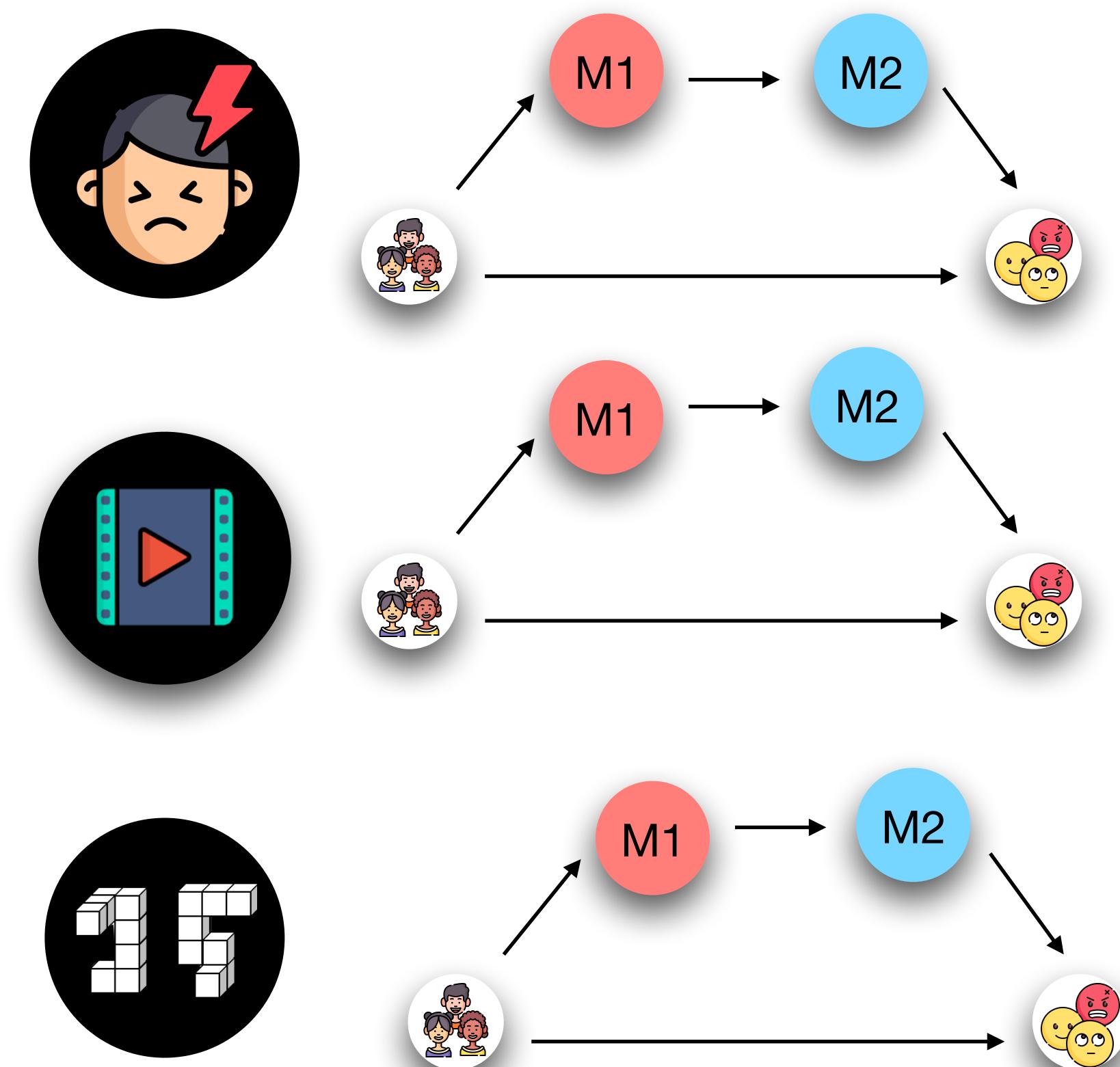
Domain-general

Include all PVC trials



Domain-specific

Include P, V, C trials respectively



Pre-registration

OSF | Spacetop - Social Influenc x +

osf.io/639fg/

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Spacetop - Social Influence

Contributors: Heejung Jung

Affiliated Institutions: None

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| OSF_analysisplan_diagram.png | 2021-07-06 08:48 PM |

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Tags

Add a tag to enhance discoverability

Analysis Plan

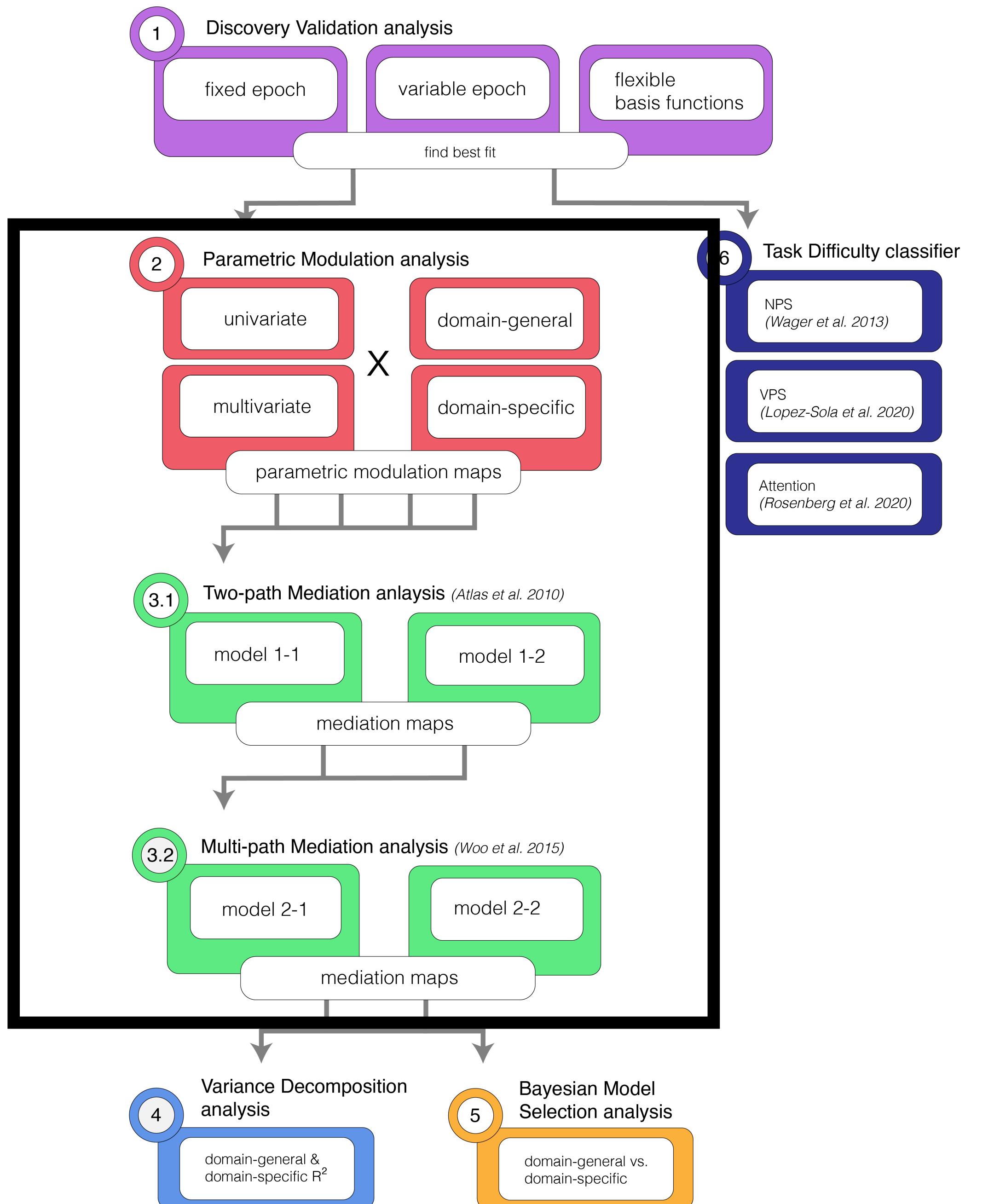
I. Neuroimaging analysis

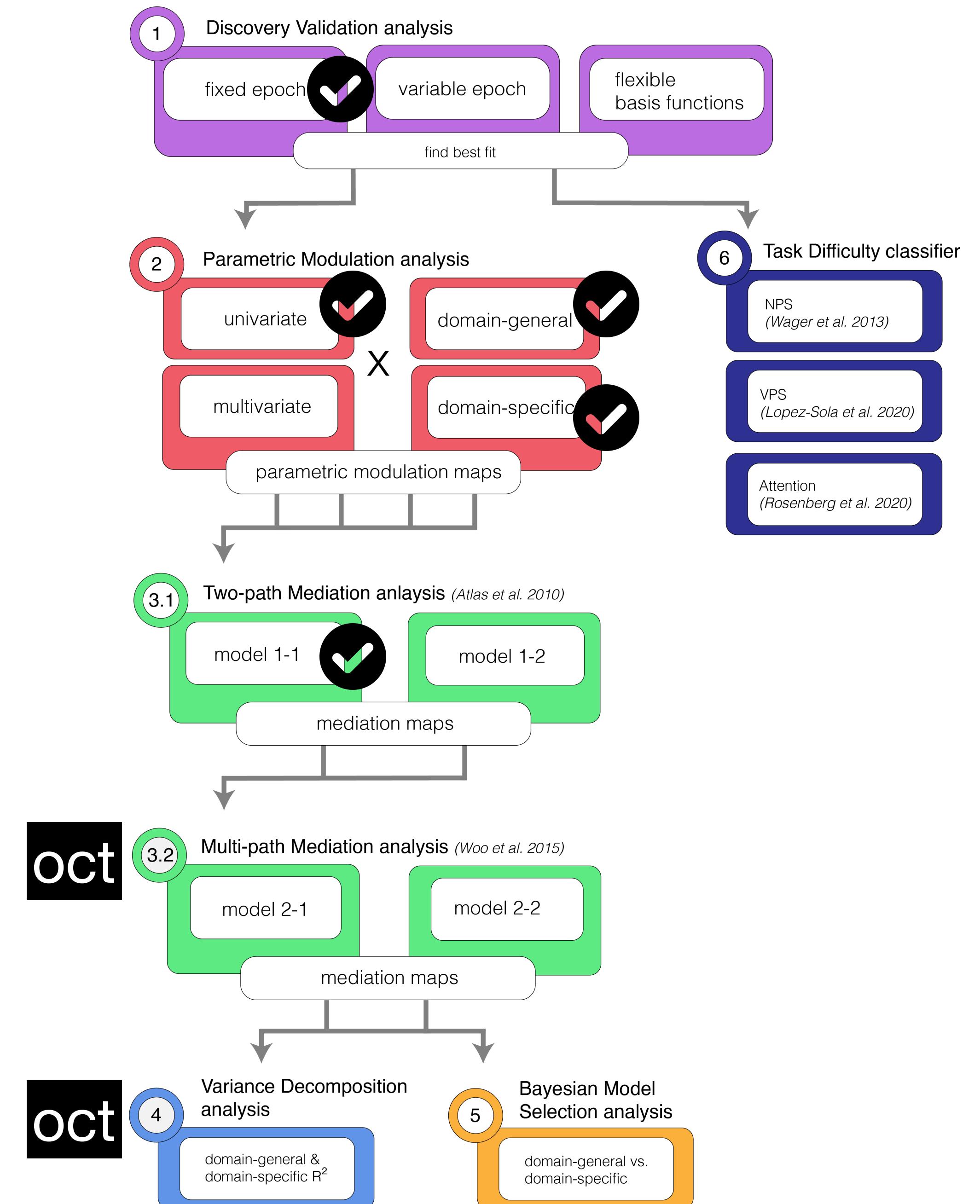
- 1. Neuroimaging Discovery validation analysis
- 2. Neuroimaging Parametric modulation analysis
- 3. Neuroimaging Mediation analysis (two-path, then multi-path)
 - 3.1. Two-path mediation analysis
 - 3.2. Multipath mediation analysis
- 4. Neuroimaging Variance decomposition analysis
- 5. Neuroimaging bayesian model selection
- 6. Neuroimaging task difficulty classification

II. Behavioral analysis

Analysis Plan

A screenshot of a web browser displaying a PDF document titled "OSF_analysisplan.pdf" on the Open Science Framework (OSF). The browser's address bar shows "osf.io/yg6b3/". The OSF navigation bar includes links for "My Quick Files", "My Projects", "Search", "Support", "Donate", and a user profile for "Heejung Jung". Below the navigation bar, there are tabs for "Files", "Wiki", "Analytics", "Registrations", "Contributors", "Add-ons", and "Settings". The main content area shows the PDF document. On the left, a sidebar displays the file structure: "Spacetop - Social Influence" contains "OSF Storage (United States)" which holds "OSF_analysisplan.pdf", "OSF_analysisplan_diagram.png", and "OSF_studydesign.png". A "Tags" section allows adding tags to enhance discoverability. The PDF document itself has a header "Analysis Plan" and is divided into two sections: "I. Neuroimaging analysis" and "II. Behavioral analysis". "I. Neuroimaging analysis" contains six numbered items, each with a blue link. "II. Behavioral analysis" is currently collapsed. The PDF viewer includes standard controls like zoom, page number (1 of 9), and print.

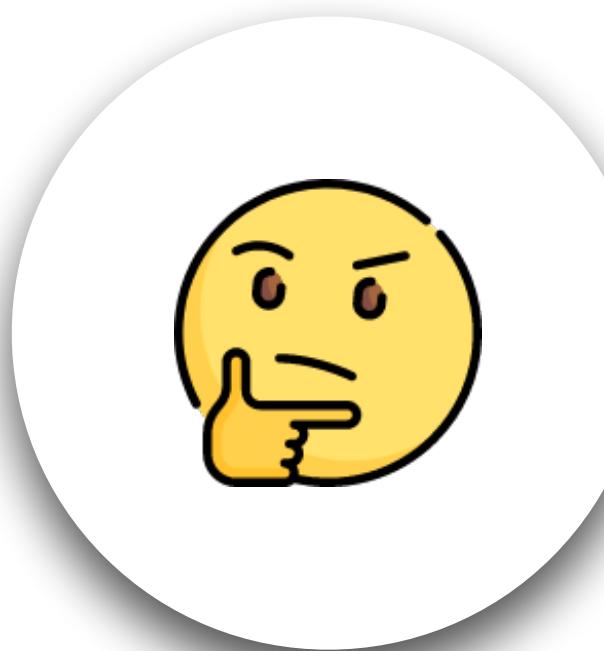




Behavioral analysis



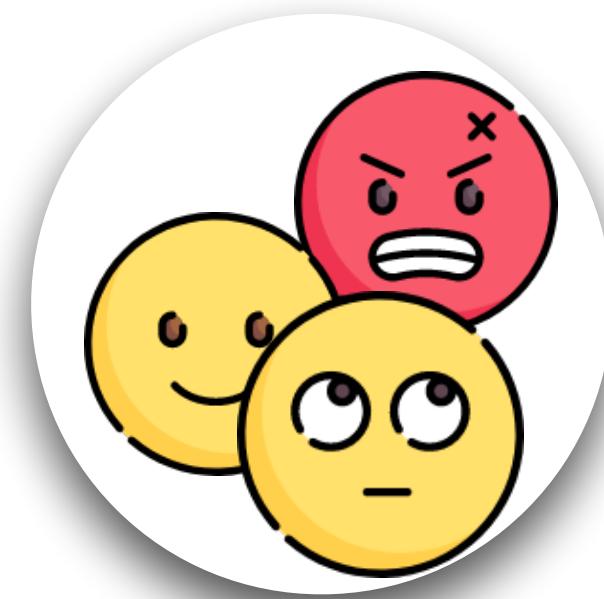
2 Social
cues



expectations



3 stimulus
intensity



Actual
experience



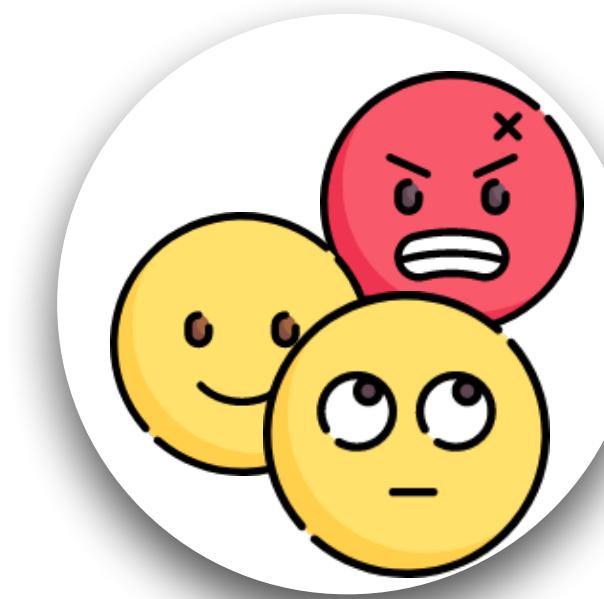
2 Social
cues



expect
rating



3 stimulus
intensity



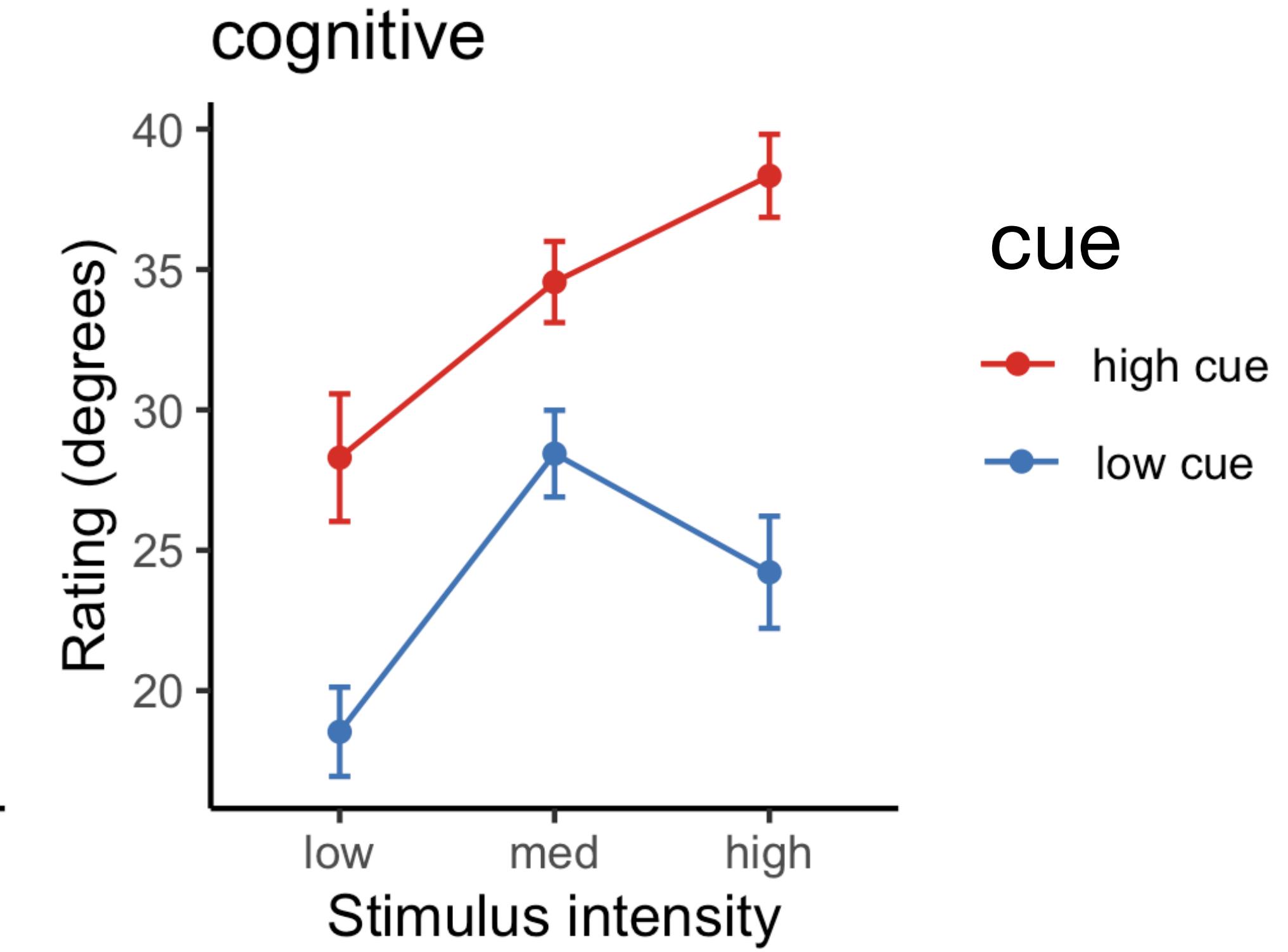
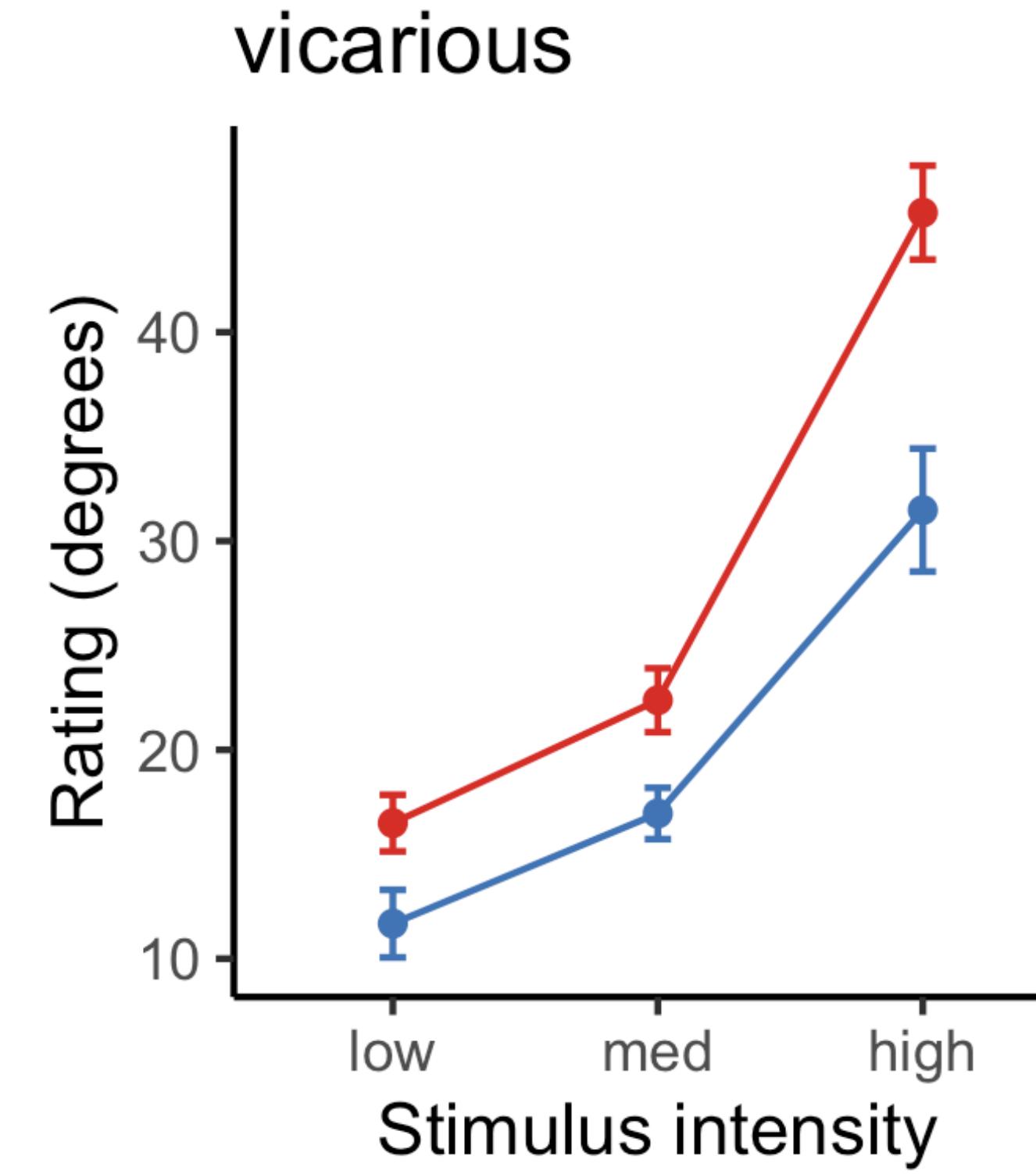
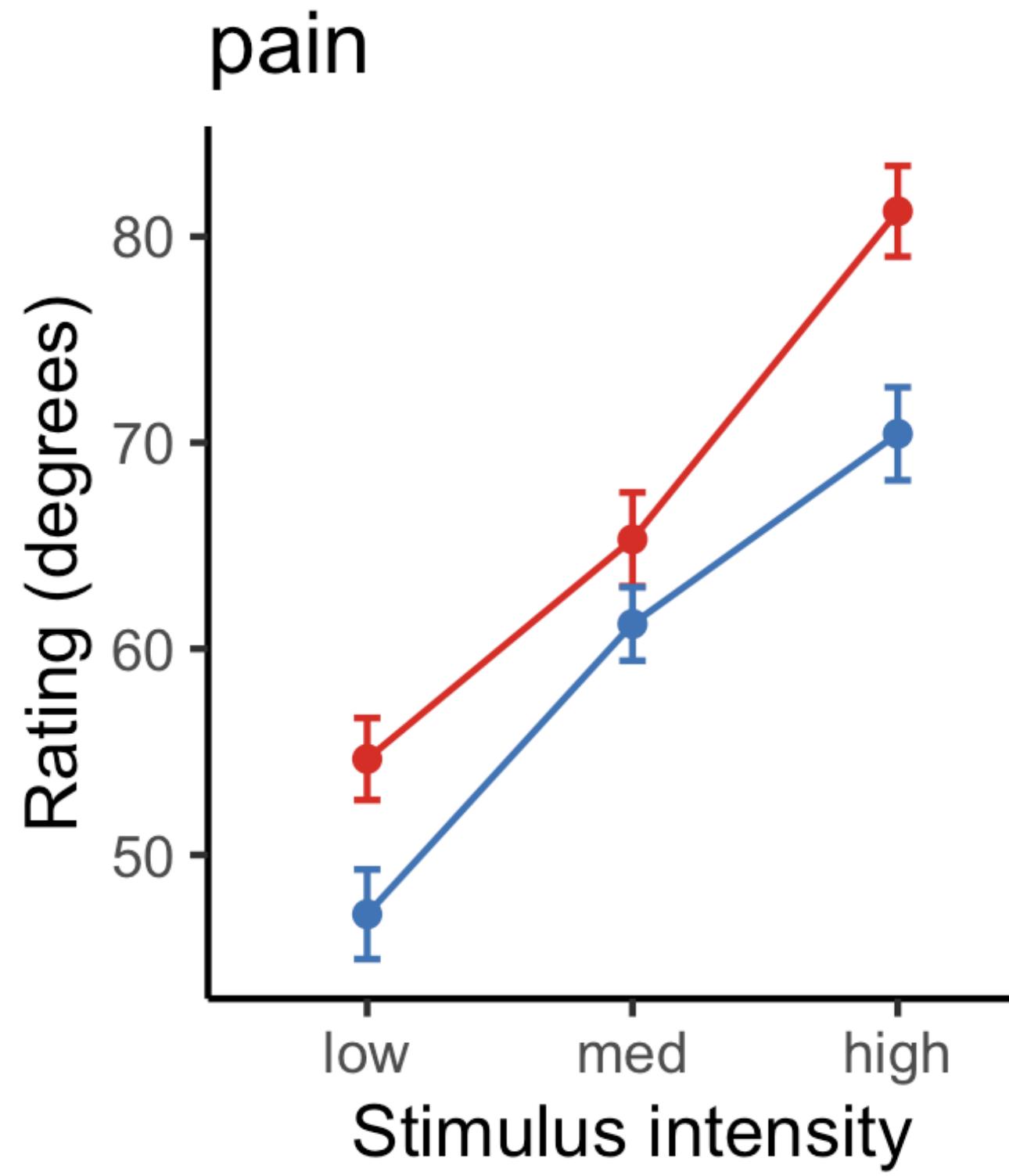
Actual
experience

Can social cues modulate actual experiences?

Subjective ratings on stimulus intensity experie

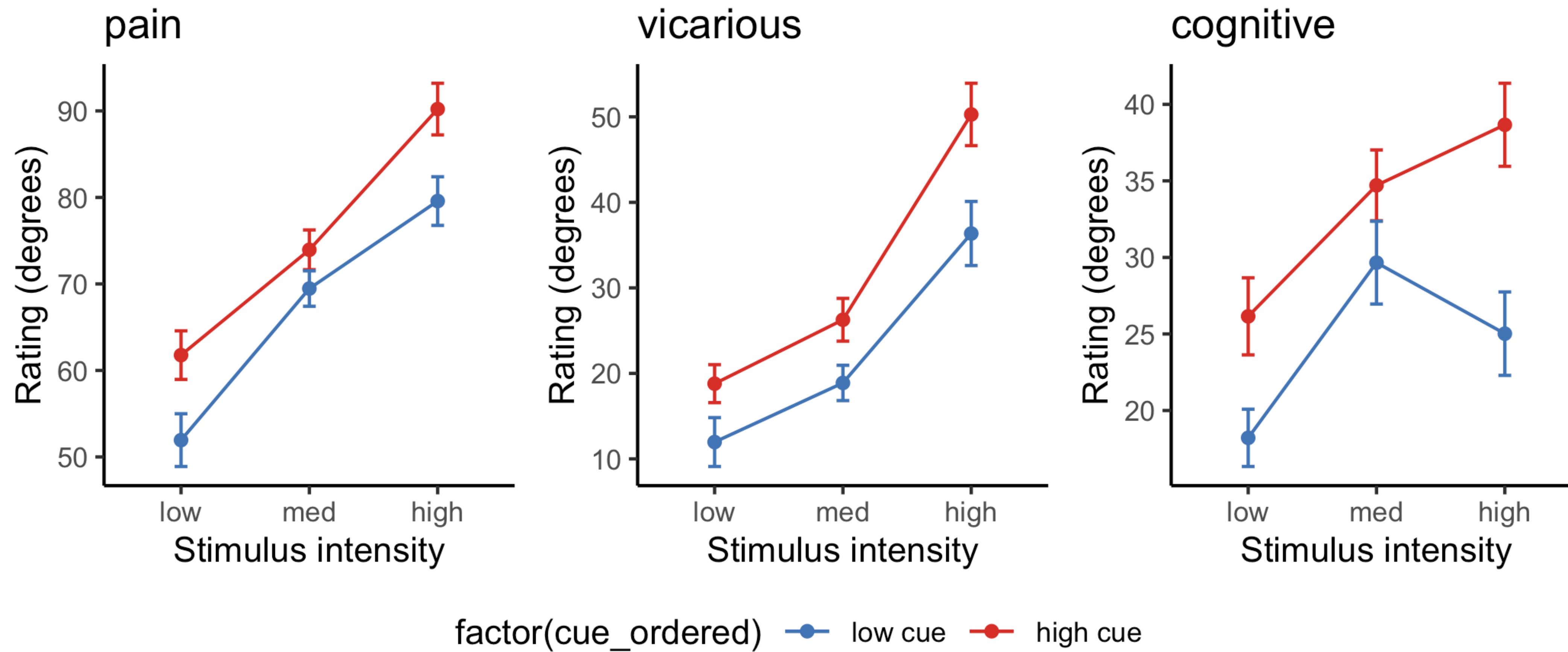
Can social cues modulate actual experiences?

N = 21



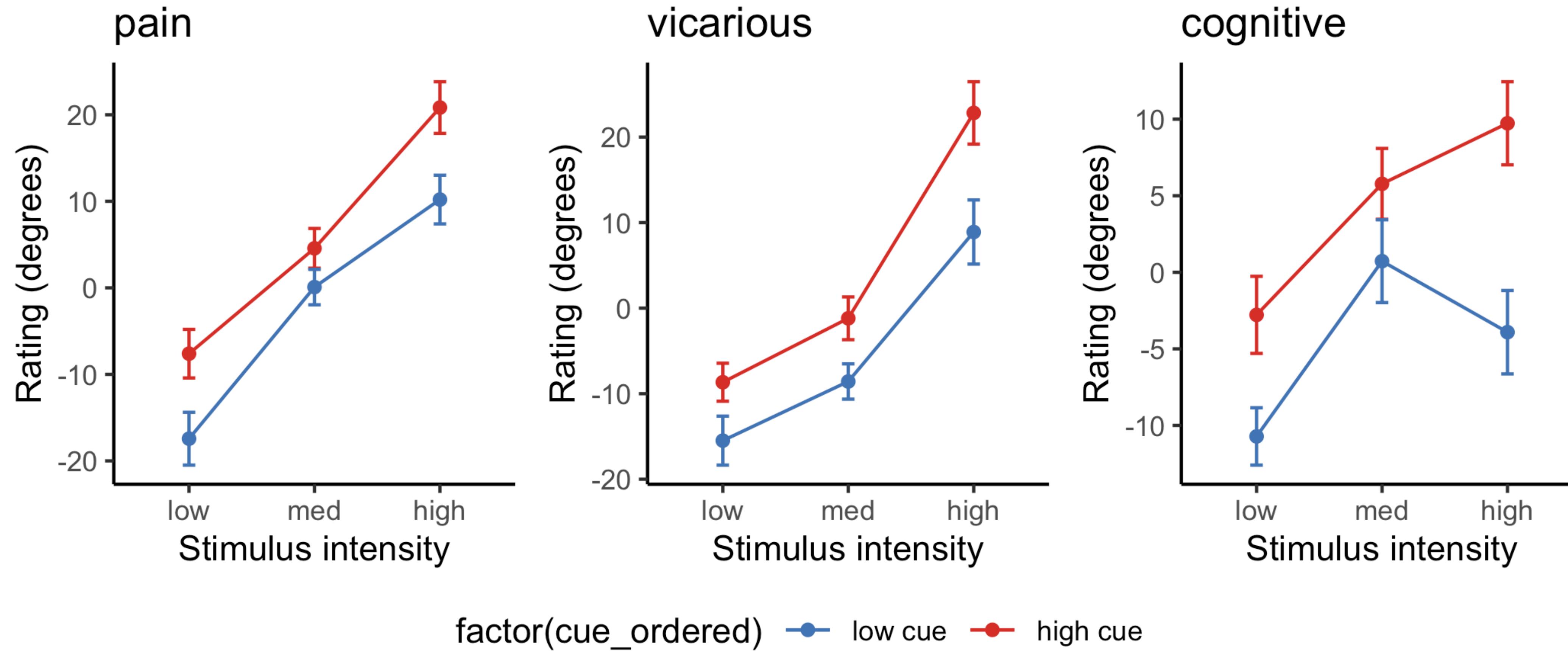
Can social cues modulate actual experiences?

N = 48



Can social cues modulate actual experiences?

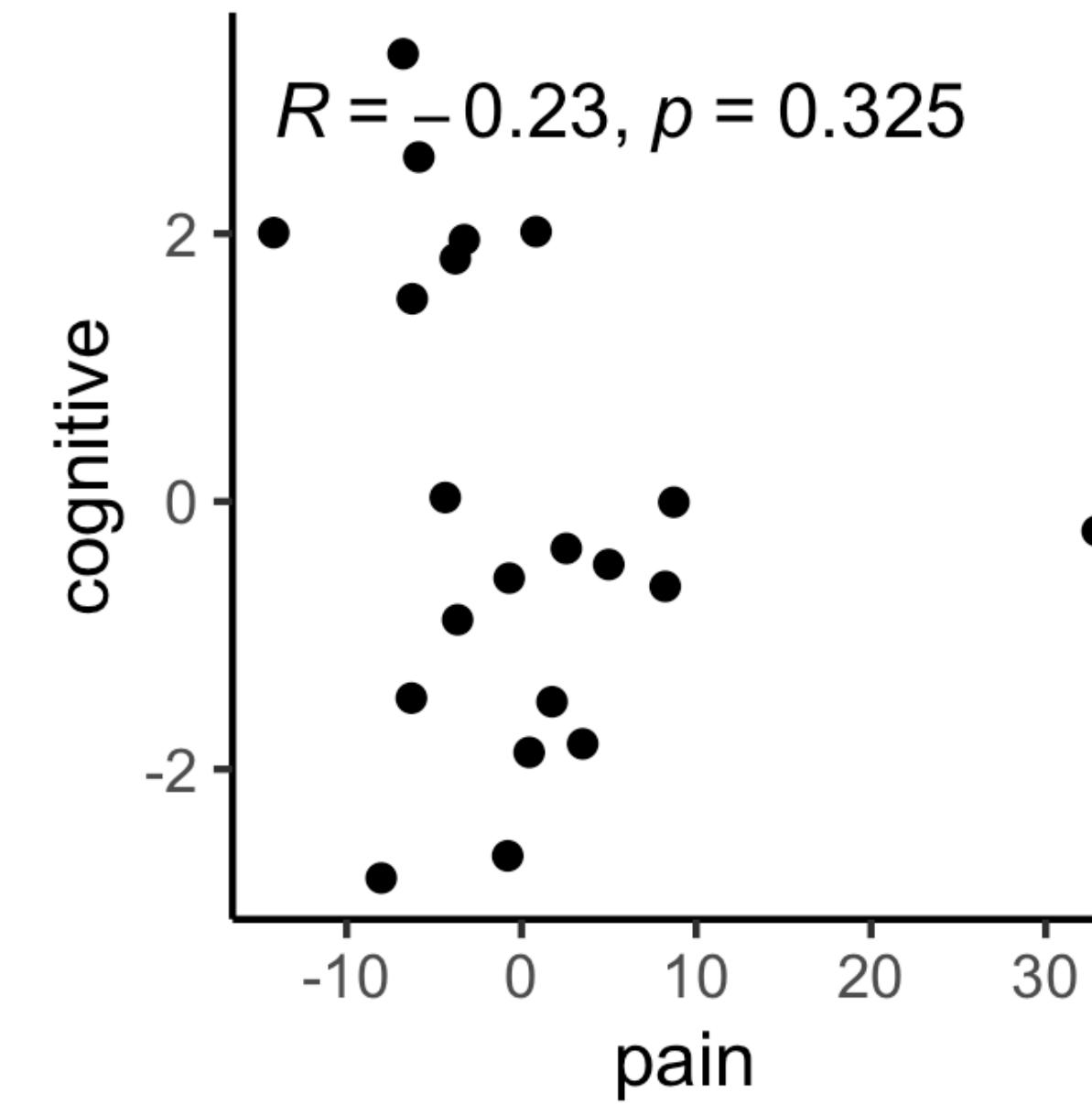
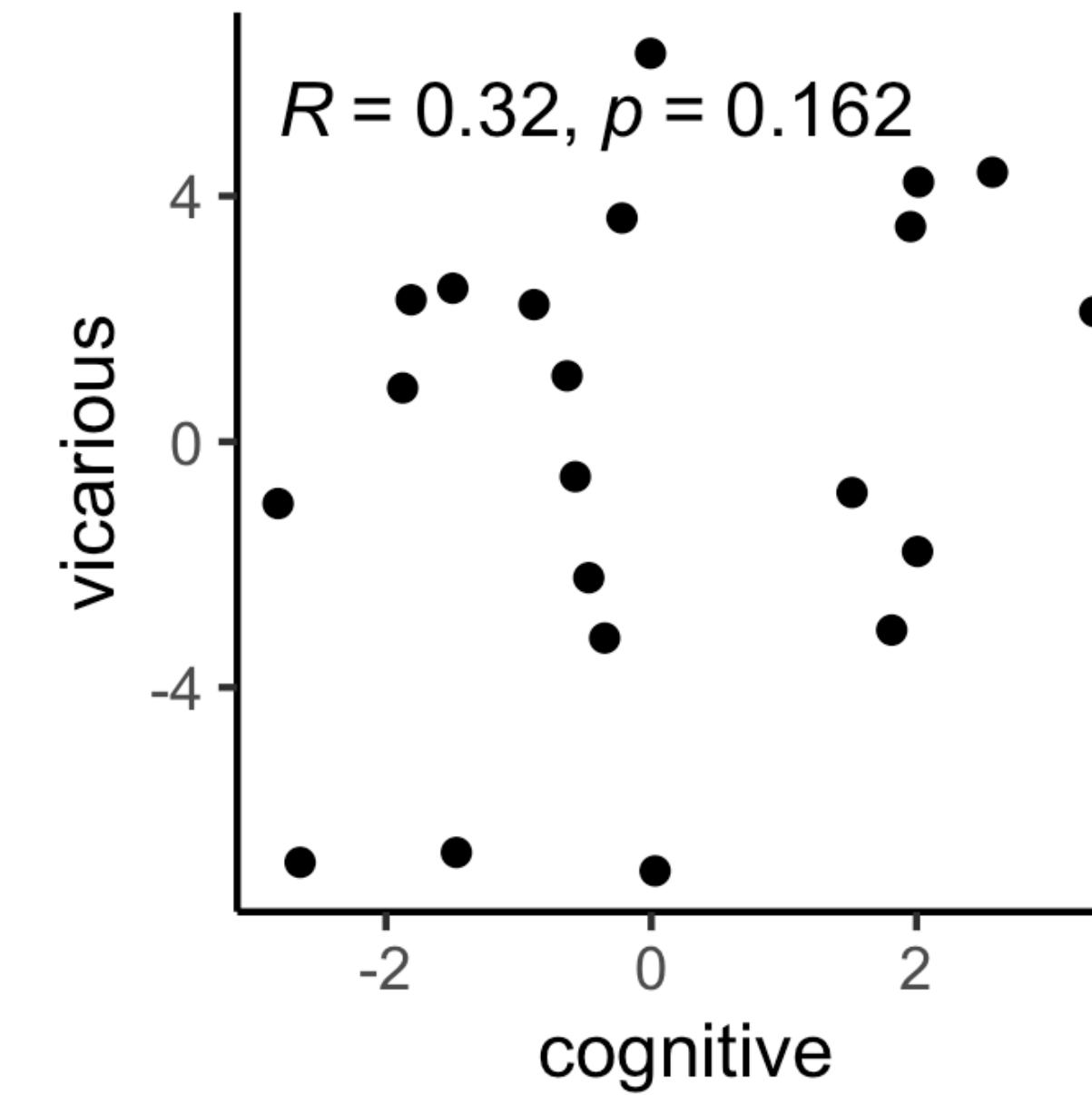
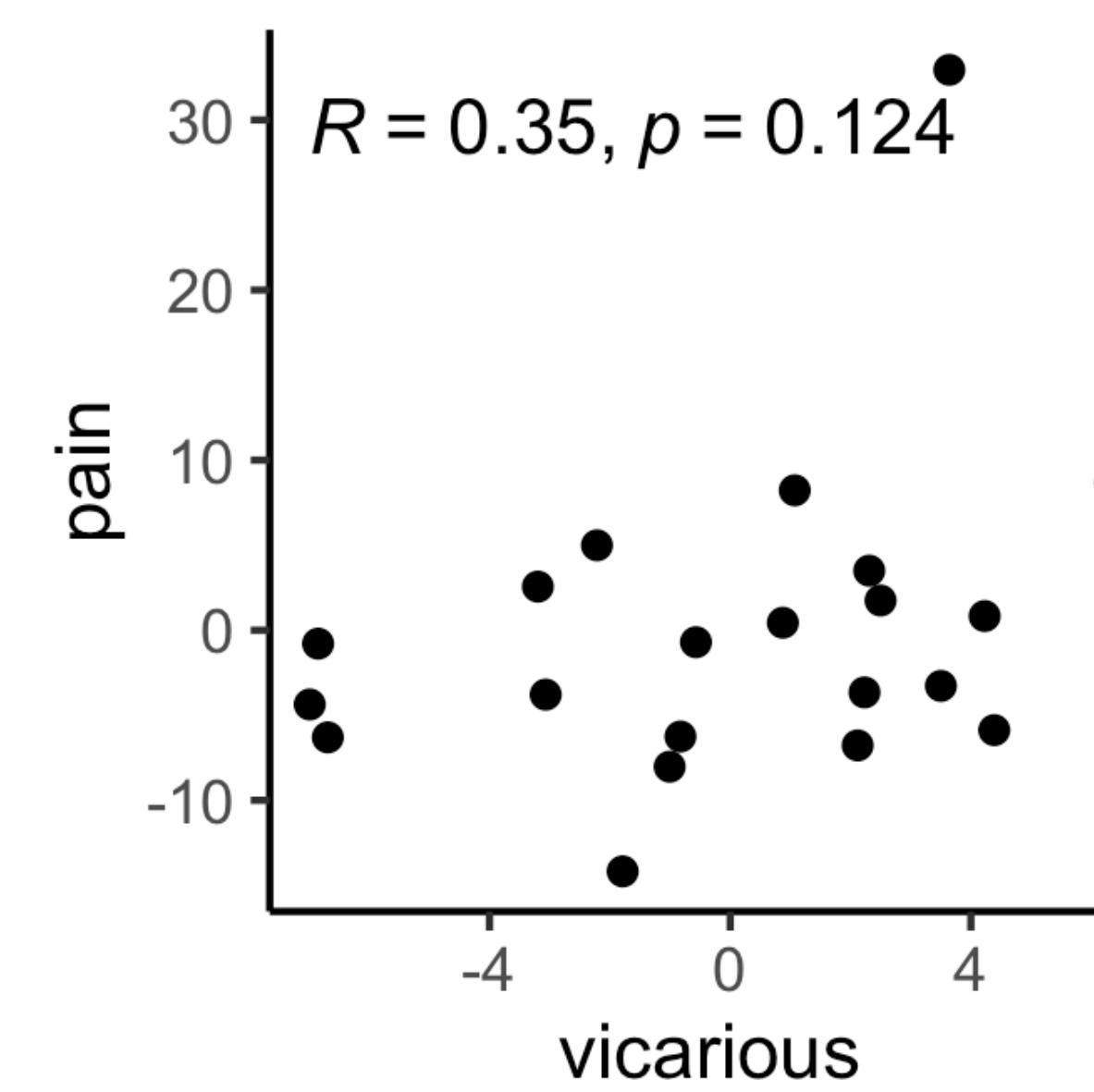
N = 48 demean



Are individual differences in cue effects domain-general?

N = 21 Plot random slopes of “cue effect on actual ratings”

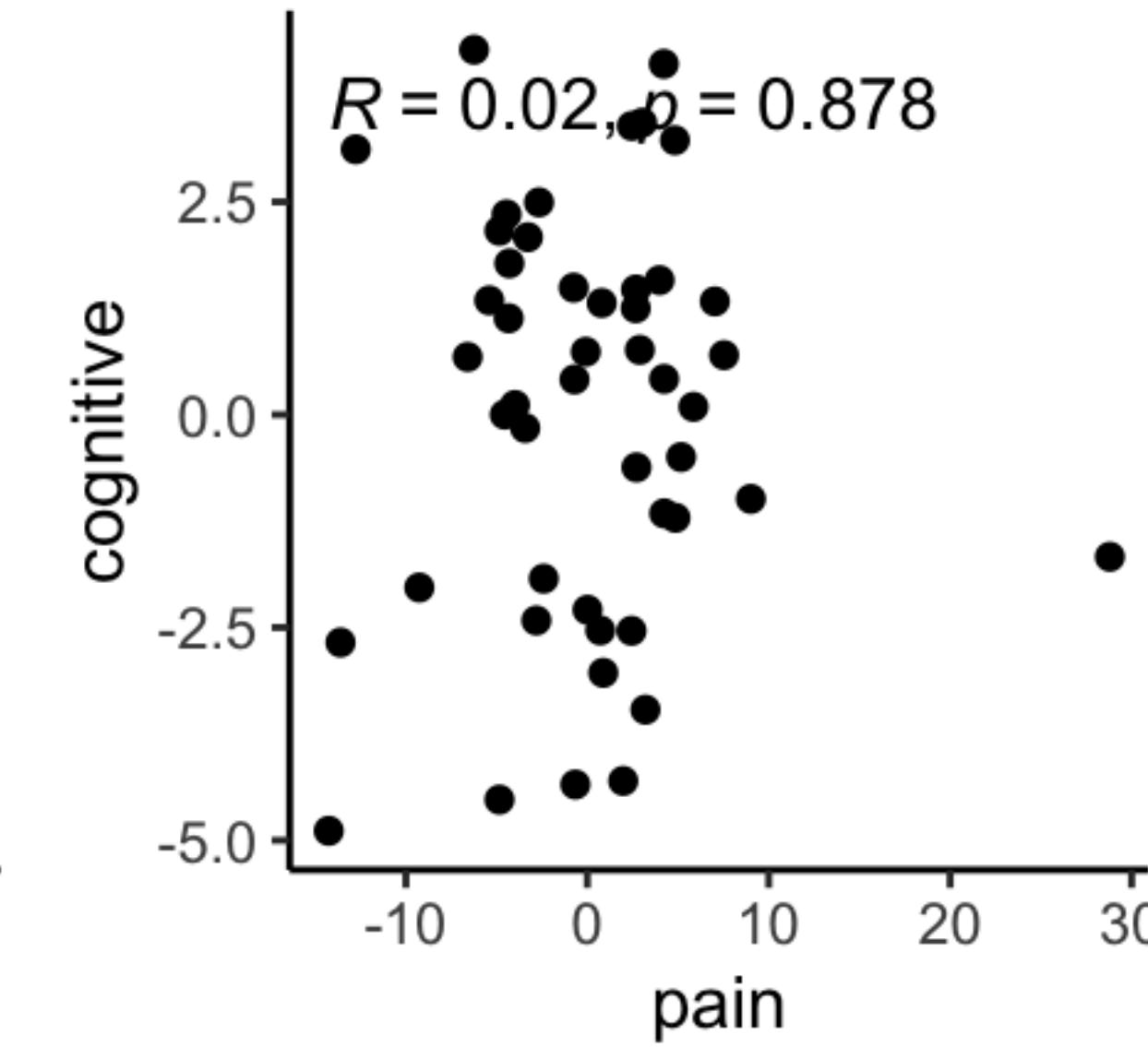
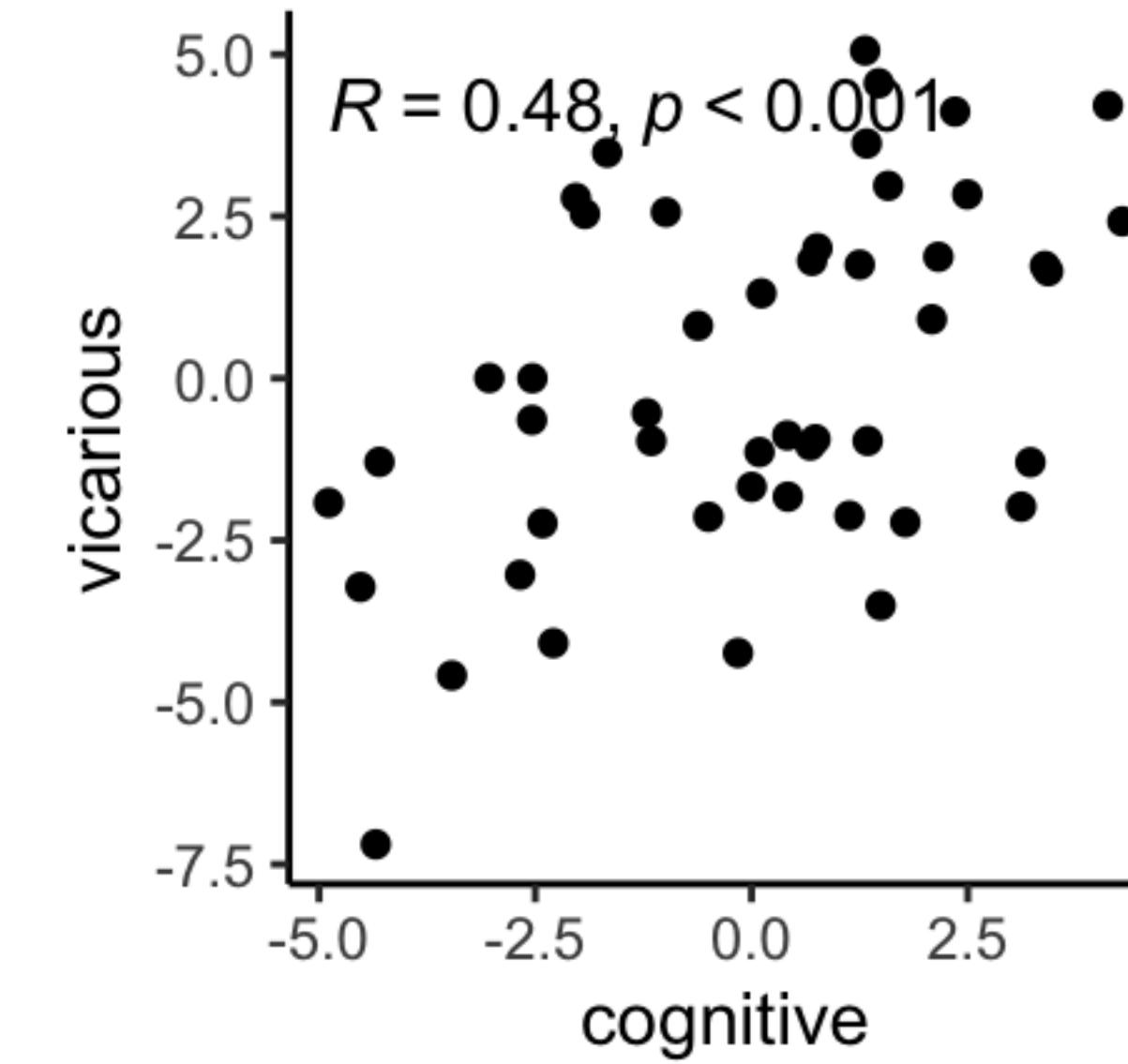
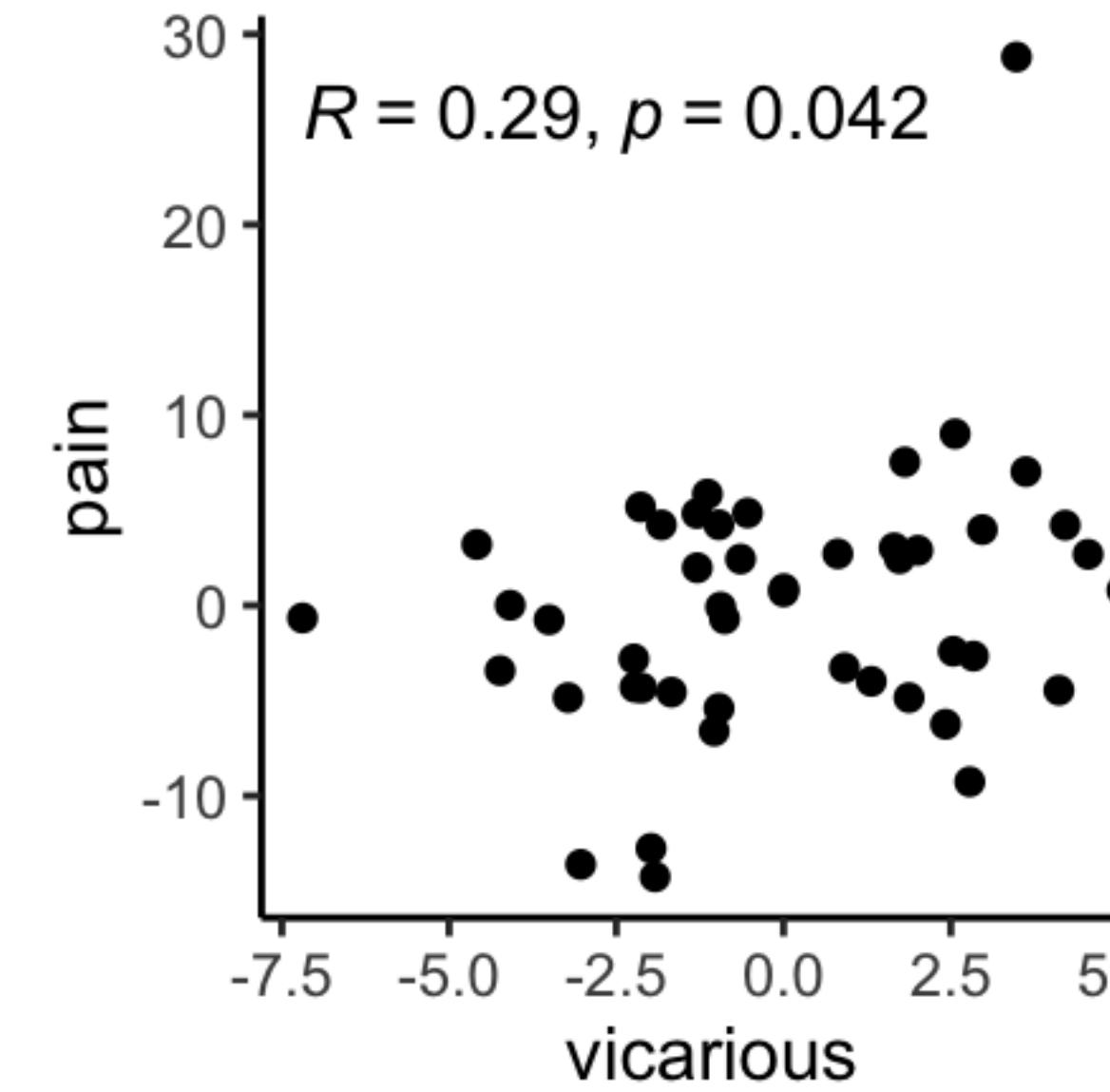
N = 21



Are individual differences in cue effects domain-general?

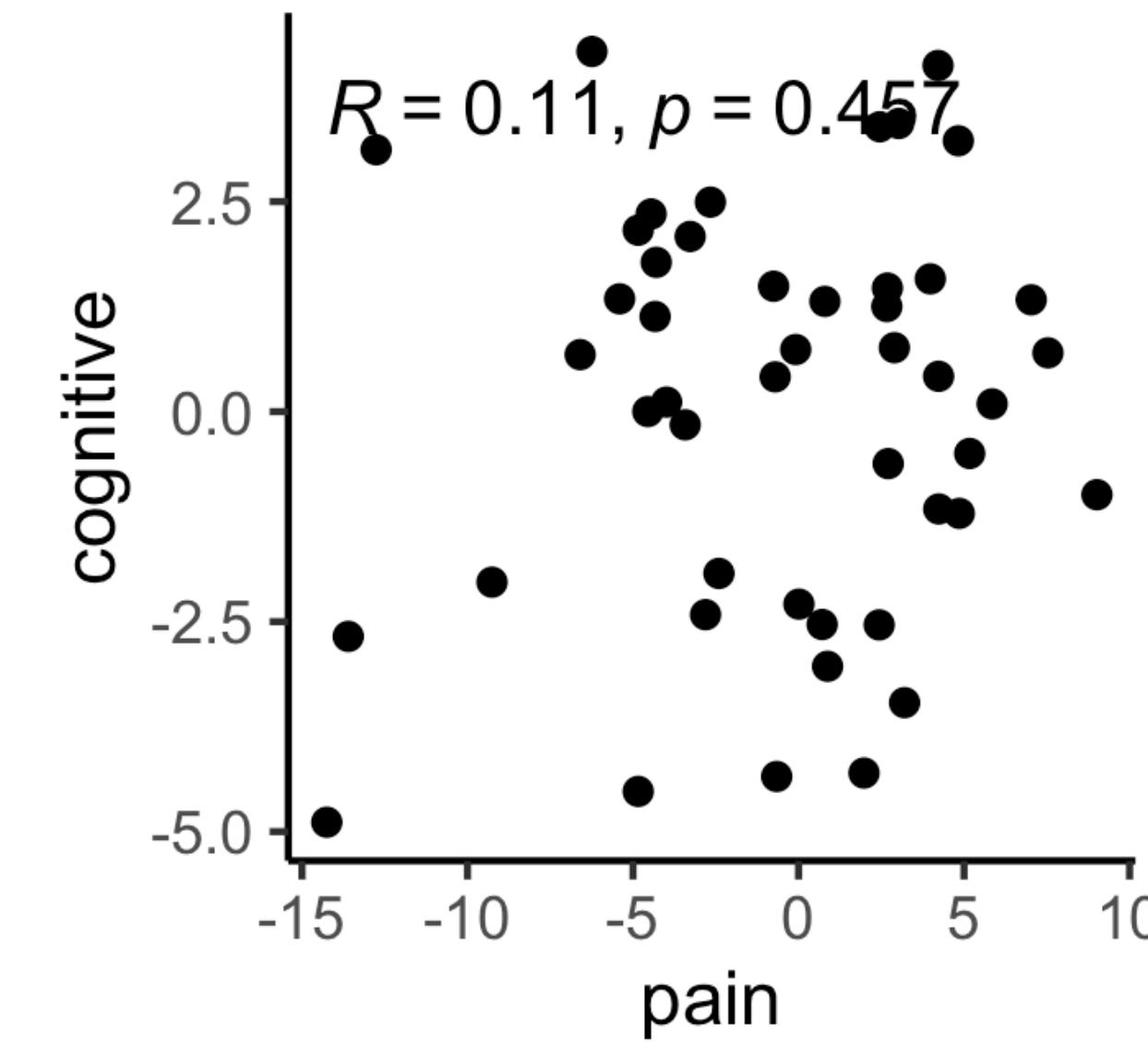
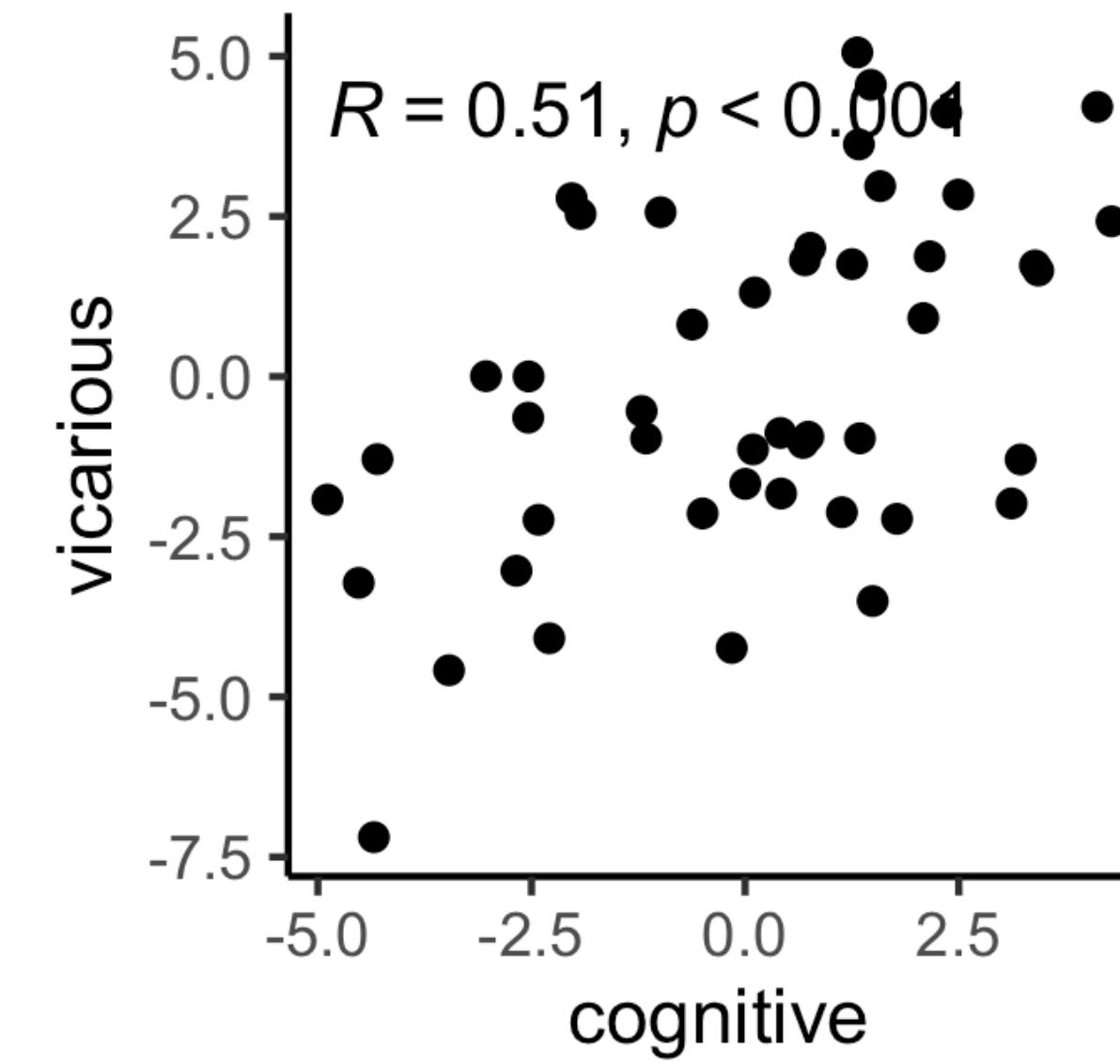
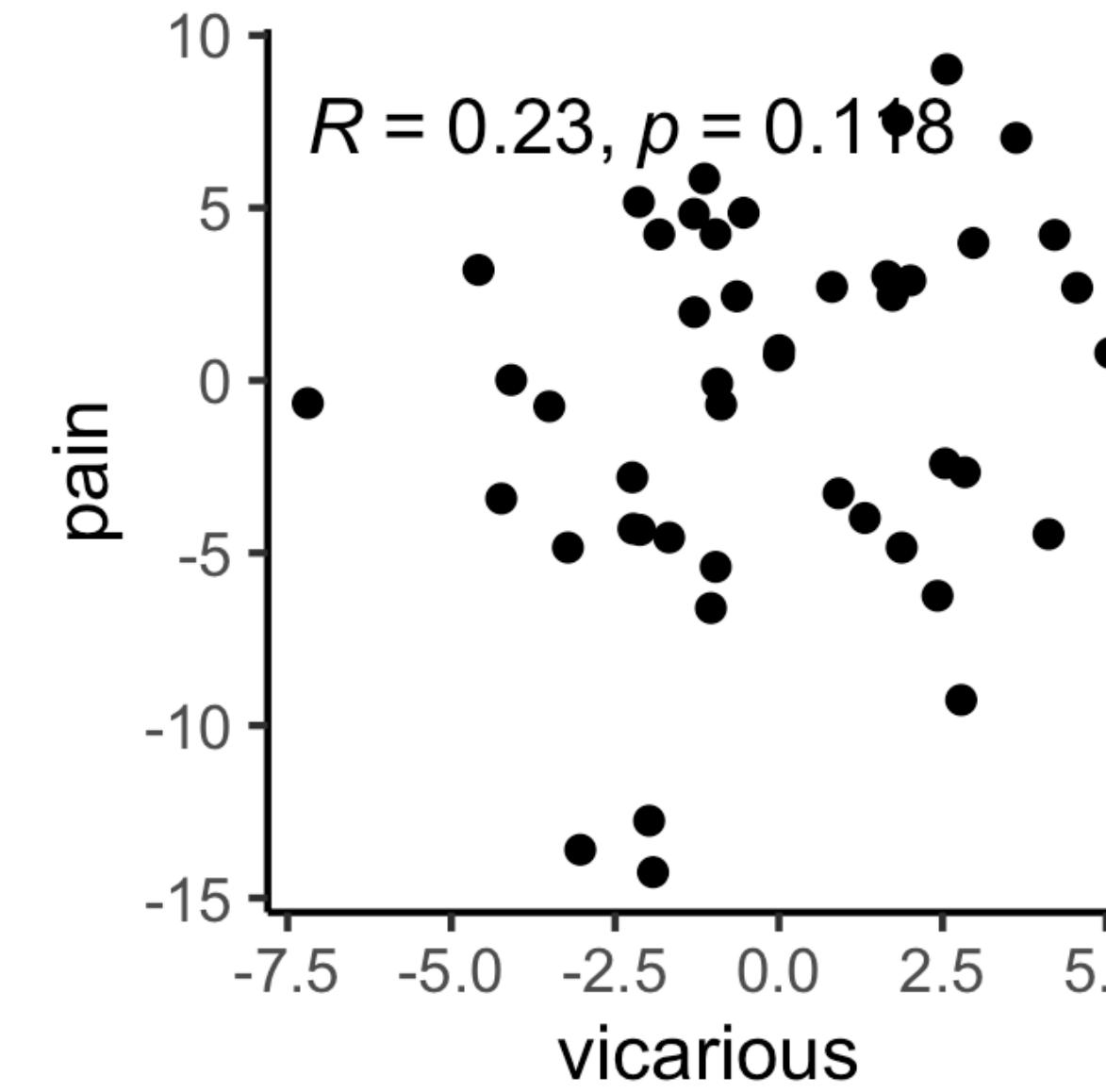
N = 48 Plot random slopes of “cue effect on actual ratings”

N = 48

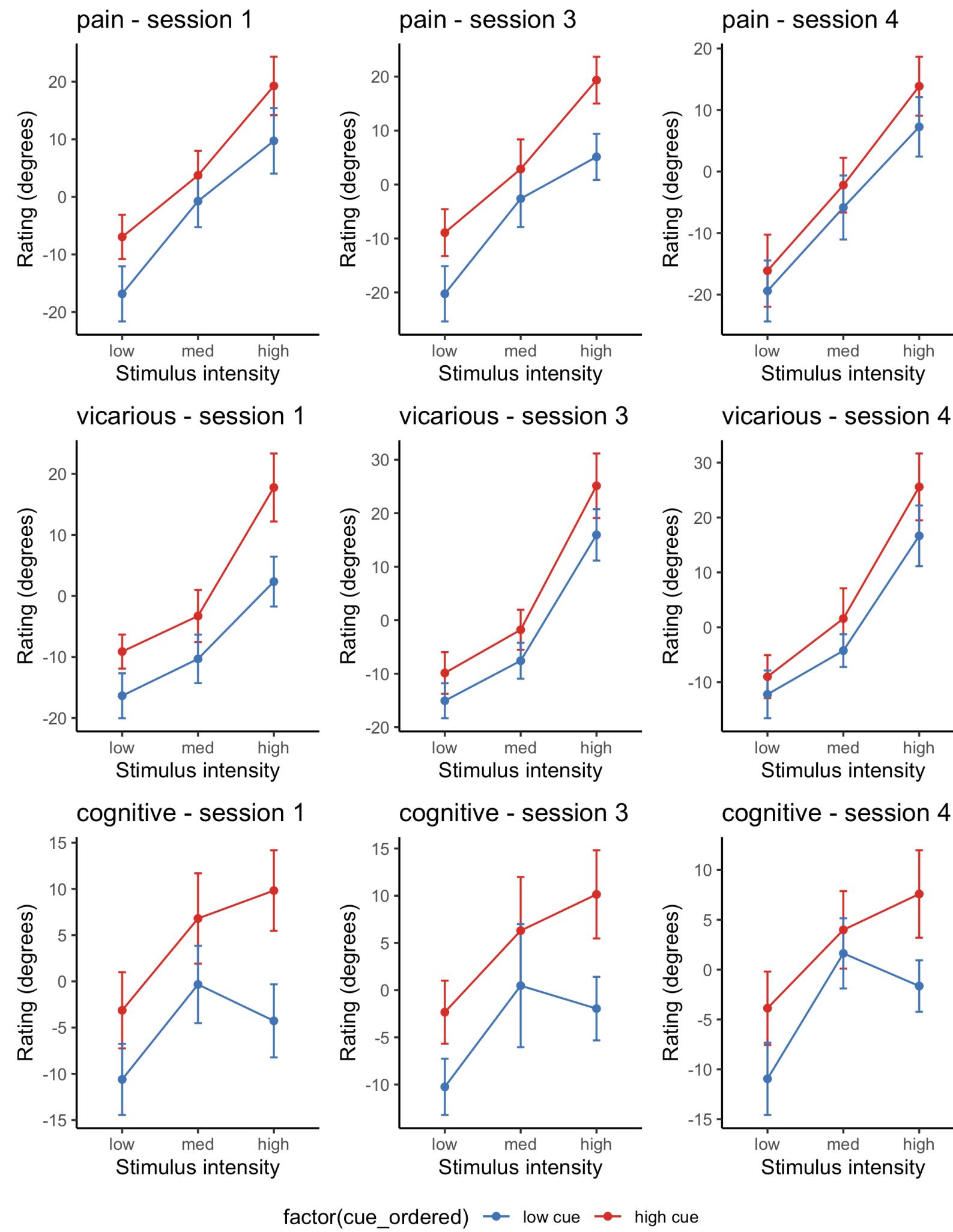


Are individual differences in cue effects domain-general?

N = 47 (Outlier removed) Plot random slopes of “cue effect on actual ratings”



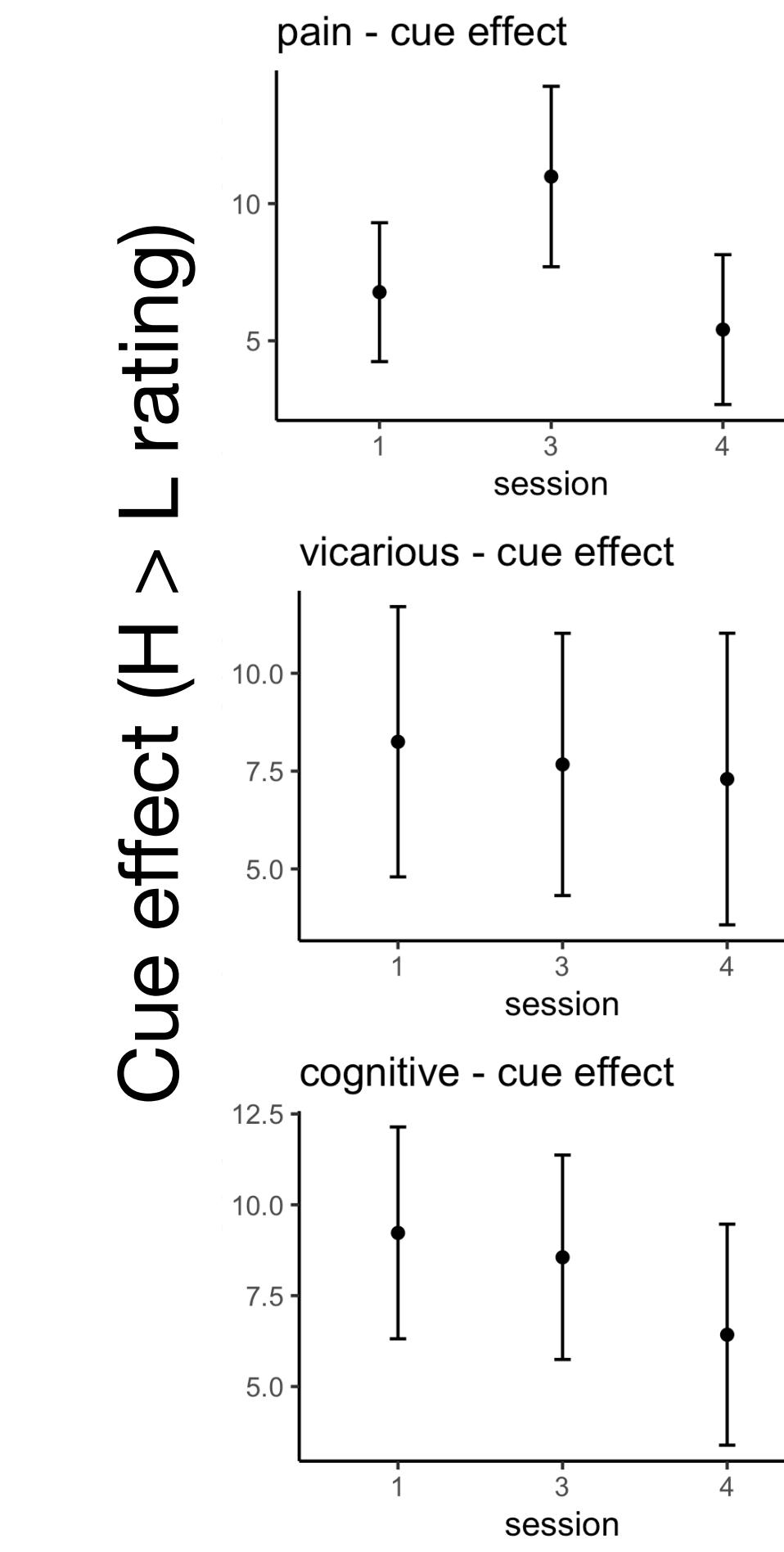
Is the cue effect different across sessions?



Main effect of SESSION: Marginal
Interaction CUE x SESSION: N.S.

Main effect of SESSION: Marginal
Interaction CUE x SESSION: N.S.

Main effect of SESSION: N.S.
Interaction CUE x SESSION: N.S.

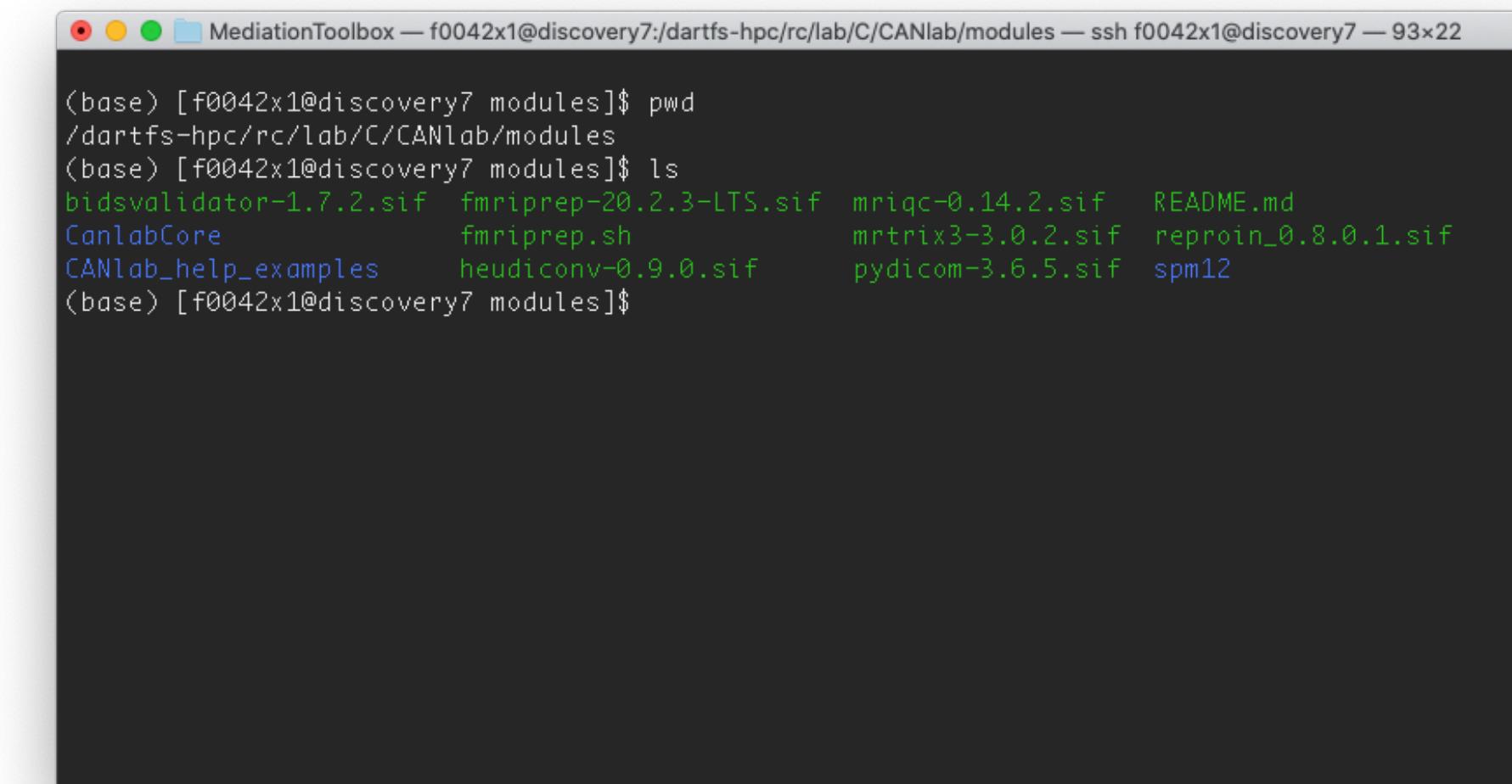


Discovery modules

/dartfs-hpc/rc/lab/C/CANlab/modules

Lab common modules

bidsvalidator-1.7.2.sif
mriqc-0.14.2.sif
pydicom-3.6.5.sif
reproin_0.8.0.1.sif
fmriprep-20.2.3-LTS.sif
heudiconv-0.9.0.sif
mrtrix3-3.0.2.sif
README.md
CANlab_help_examples
spm12
CanlabCore

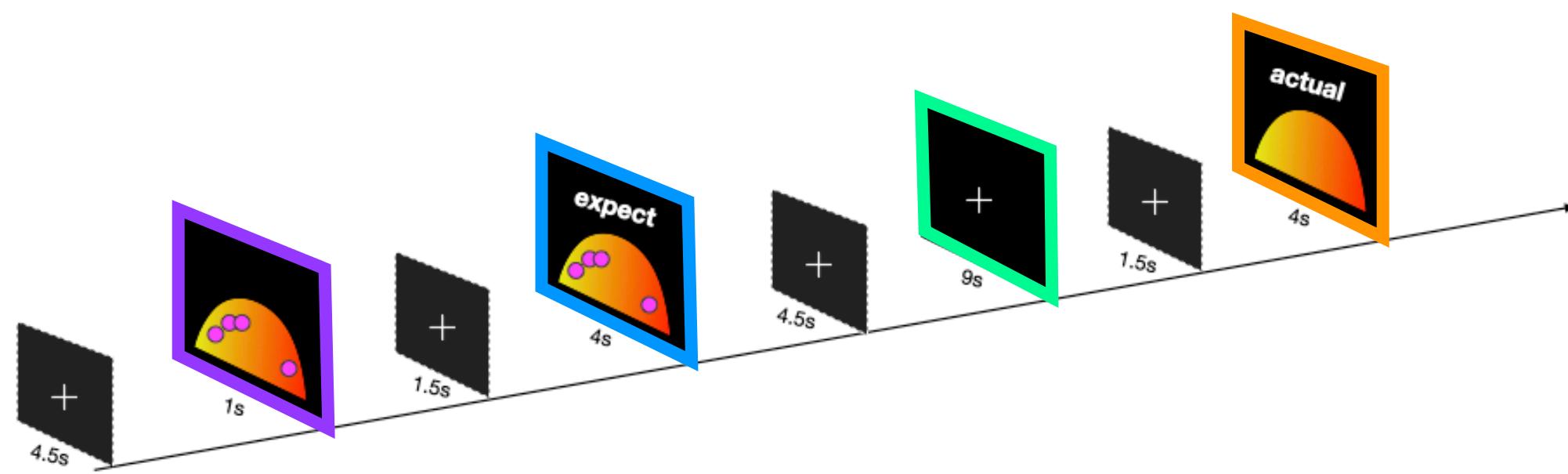


```
(base) [f0042x1@discovery7 modules]$ pwd
/dartfs-hpc/rc/lab/C/CANlab/modules
(base) [f0042x1@discovery7 modules]$ ls
bidsvalidator-1.7.2.sif  fmriprep-20.2.3-LTS.sif  mriqc-0.14.2.sif  README.md
CanlabCore               fmriprep.sh                mrtrix3-3.0.2.sif   reproin_0.8.0.1.sif
CANlab_help_examples     heudiconv-0.9.0.sif      pydicom-3.6.5.sif  spm12
(base) [f0042x1@discovery7 modules]$
```

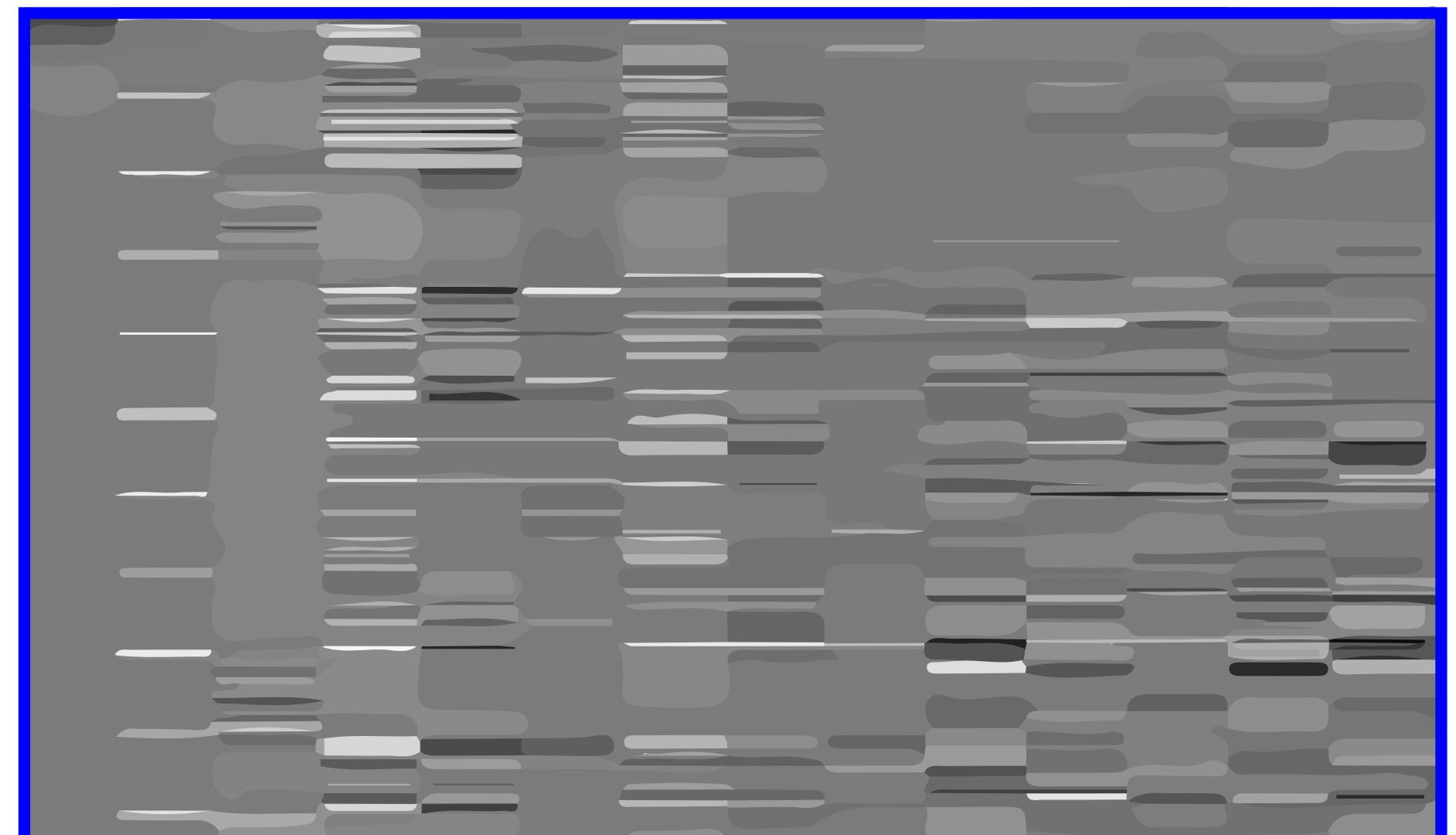
Group permissions

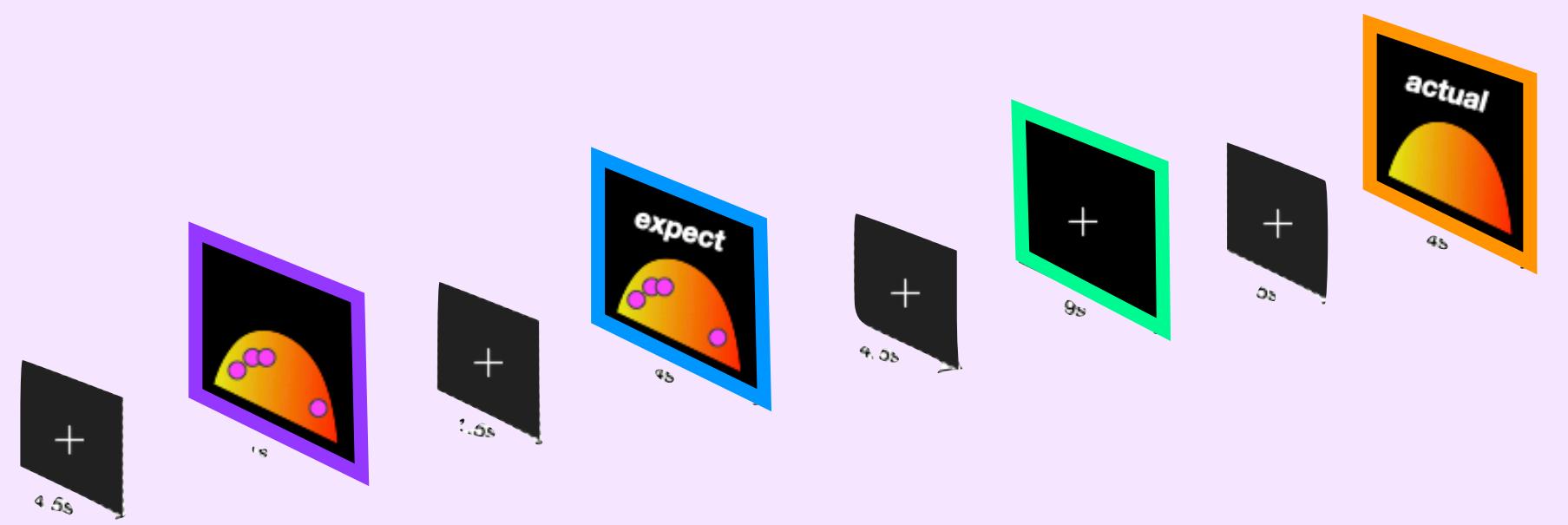
- Scenario 1: you started a new study
- Scenario 2: you have a new member on your project

Univariate glm

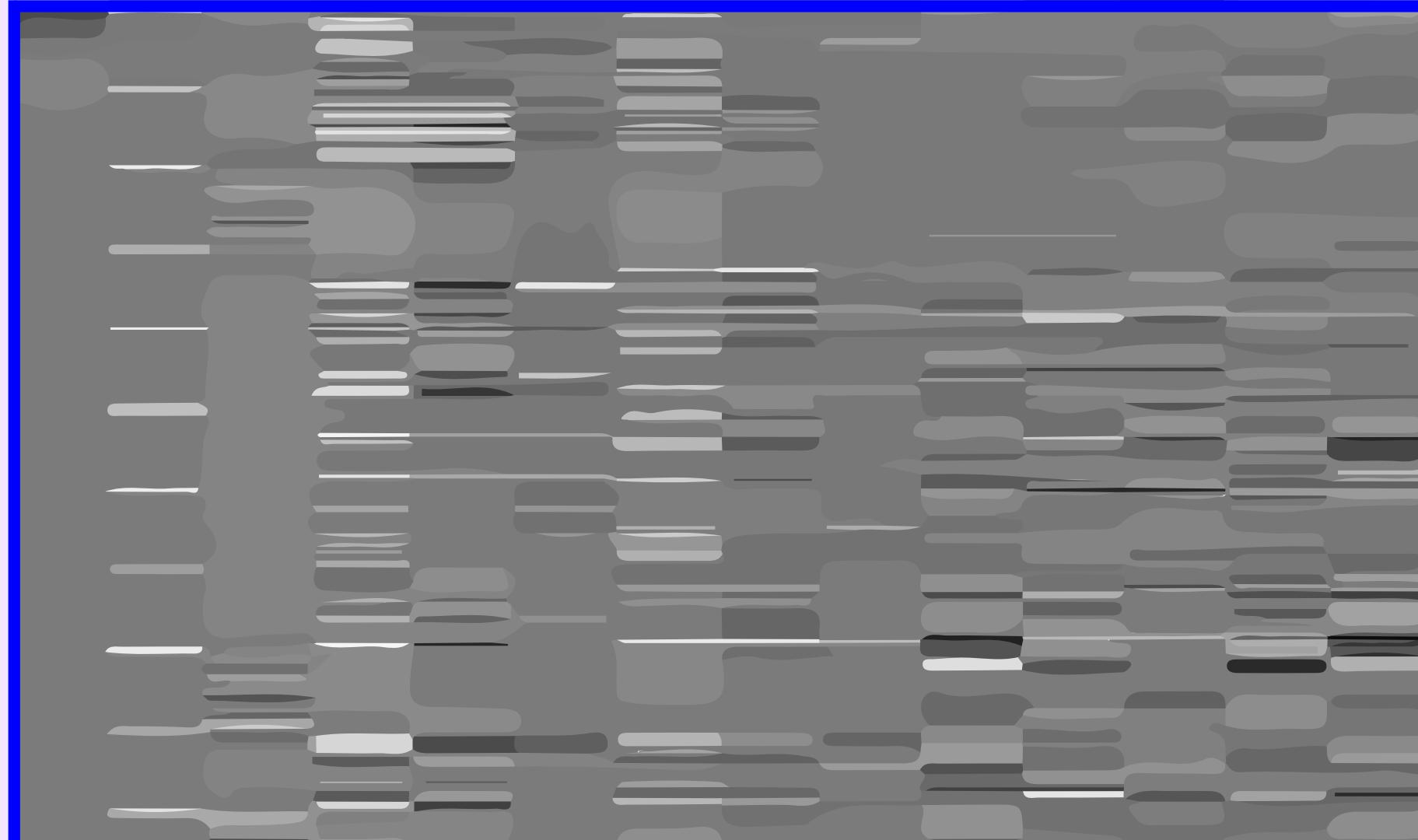


CUE
CUE \times CUE
EXPECT
STIM
STIM \times CUE
ACTUAL \times actual





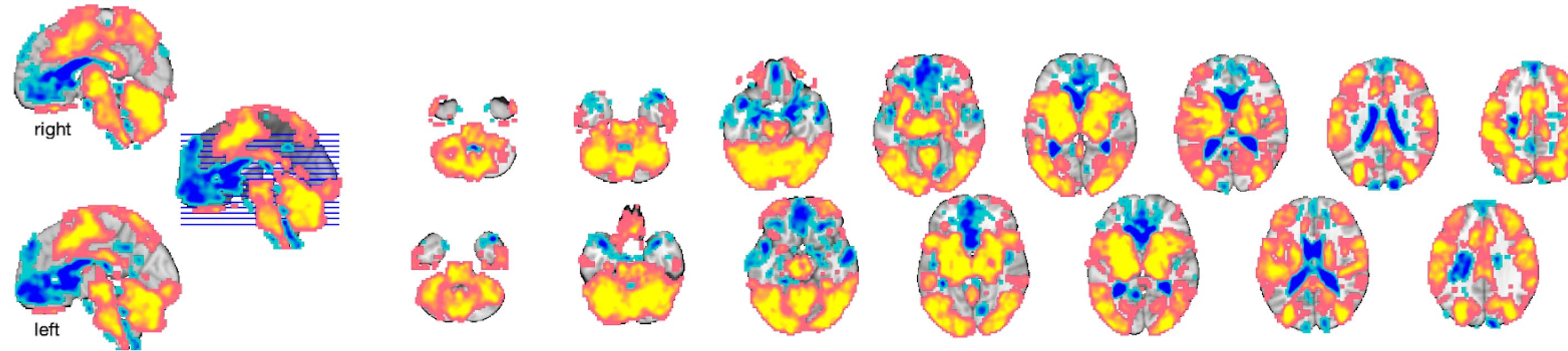
CUE
CUE \times cue
EXPECT ●
STIM
STIM \times cue
ACTUAL ●



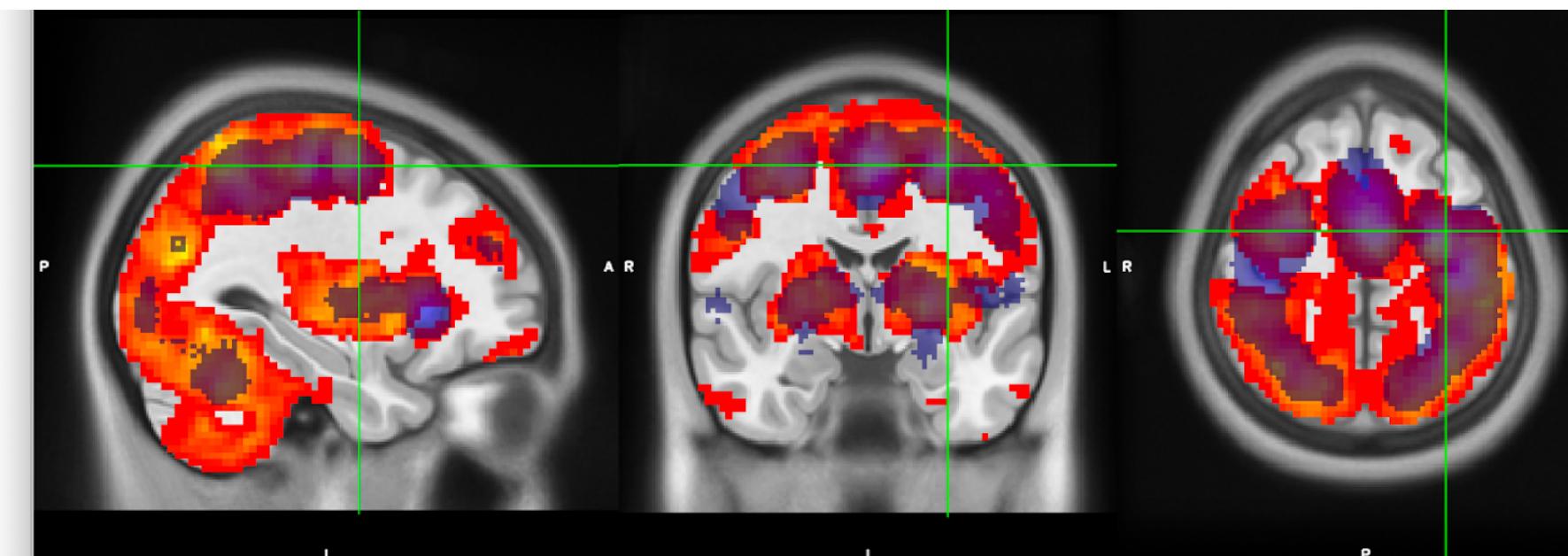
Q1. Sanity Check:
Do we see motor responses
during button presses?

Sanity Check: Do we see motor responses during button presses

Motor ($q < .05$, FDR adjusted)

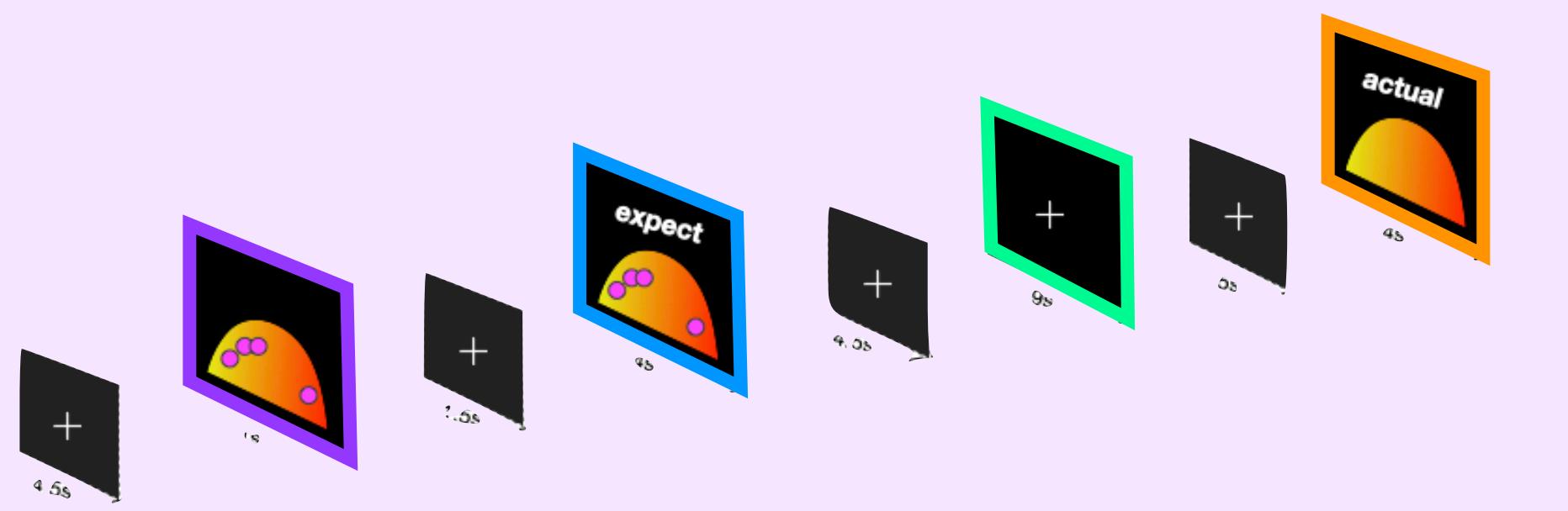


Overlay with neurosynth

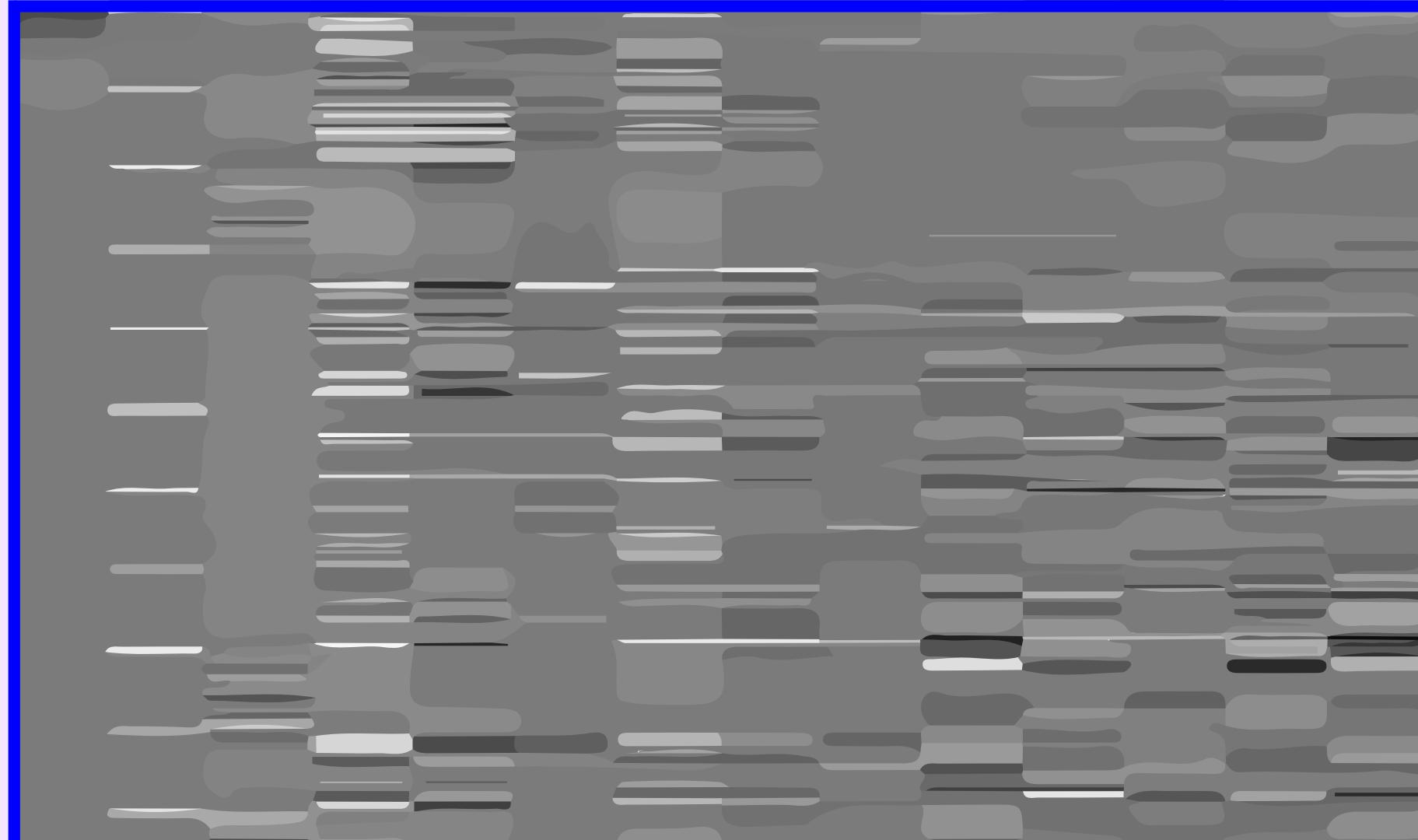


■ Social influence button press

■ Neurosynth "motor" $Z > 3$



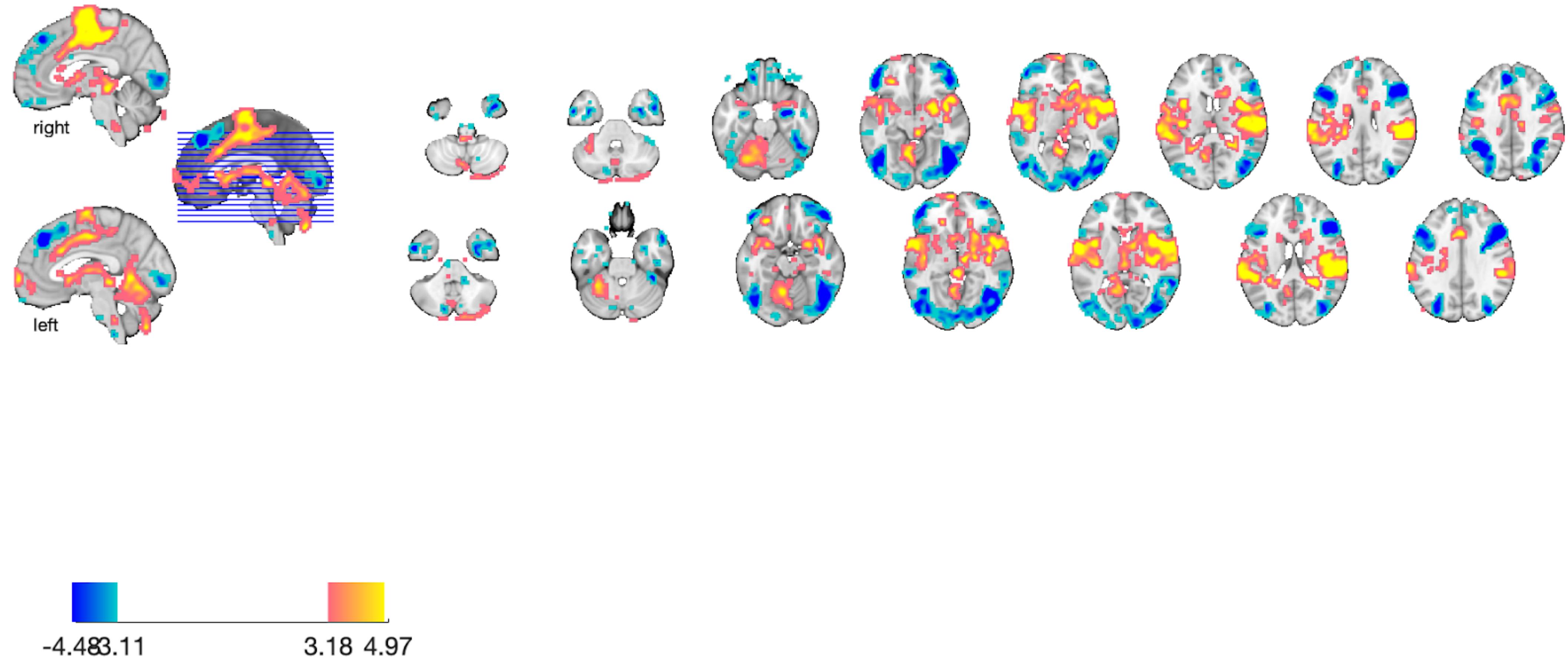
CUE
CUE × *cue*
EXPECT
STIM ●
STIM × *cue*
STIM × *actual*
ACTUAL



**Q2. Stimulus effects:
What are the neural correlates
of stimulus intensity?**

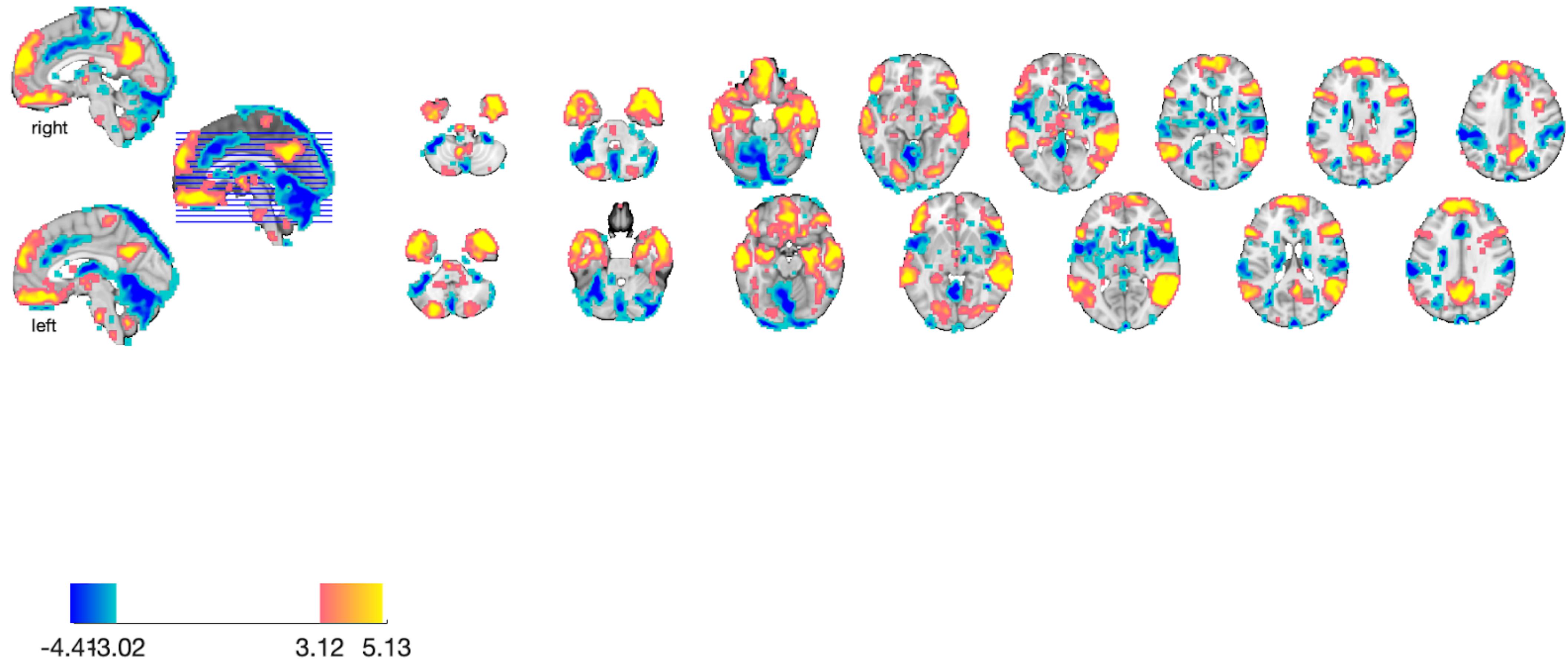
What are the neural correlates of stimulus intensity?

Pain > VC ($q < .05$, FDR adjusted)



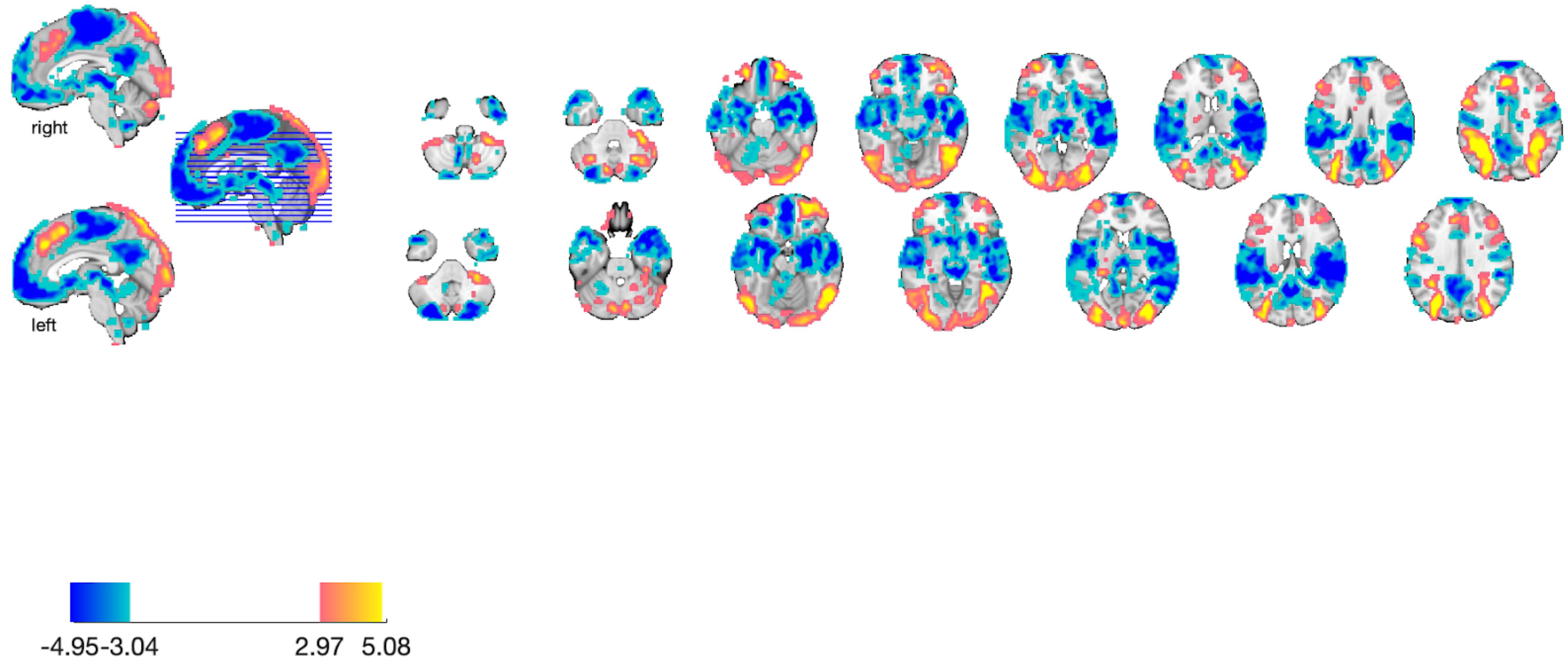
What are the neural correlates of stimulus intensity?

Vicarious > PC ($q < .05$, FDR adjusted)



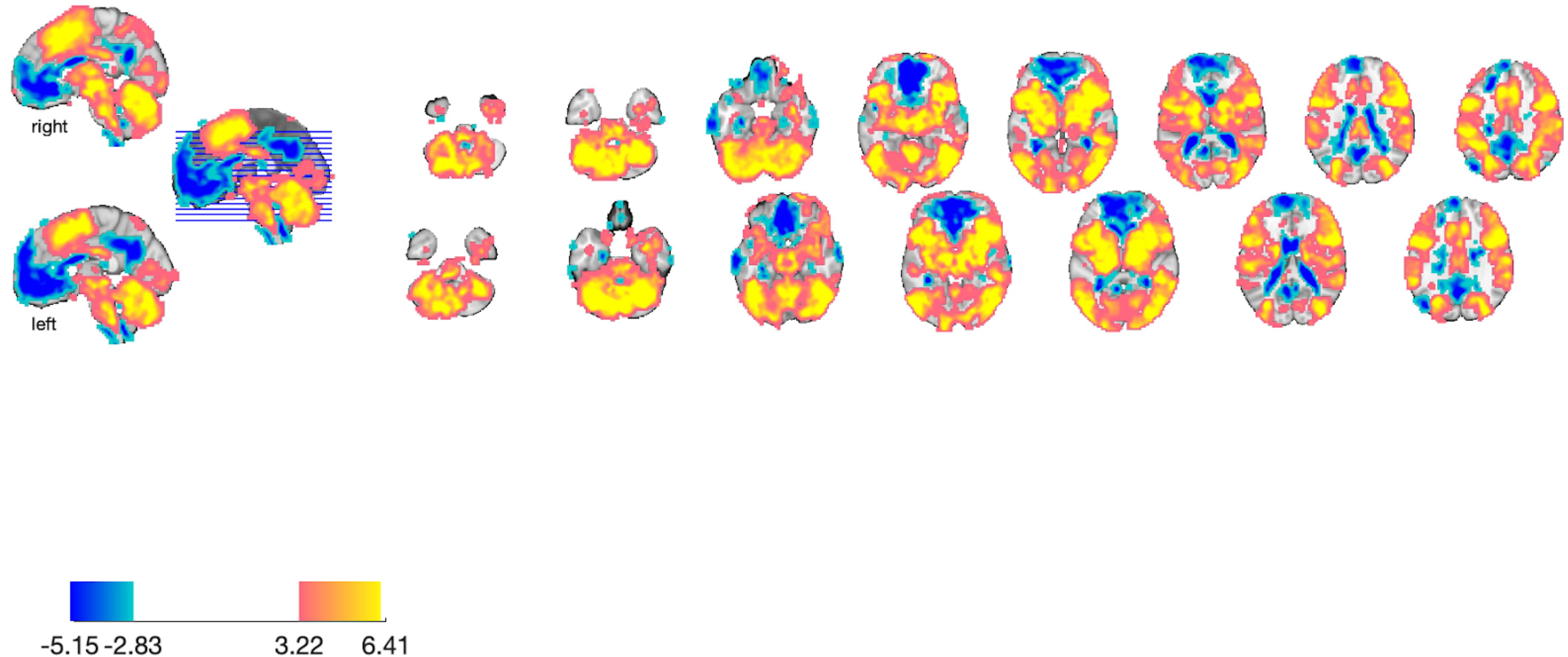
What are the neural correlates of stimulus intensity?

Cognitive > PV ($q < .05$, FDR adjusted)

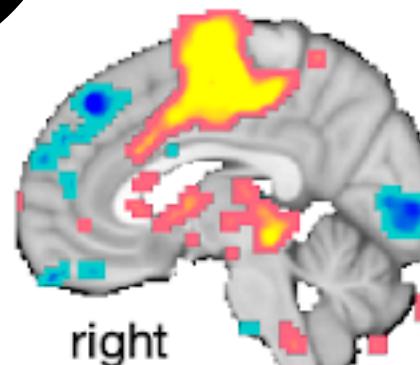


What are the neural correlates of stimulus intensity?

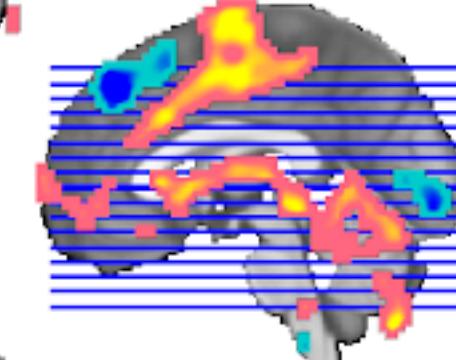
Domain general ($q < .05$, FDR adjusted)



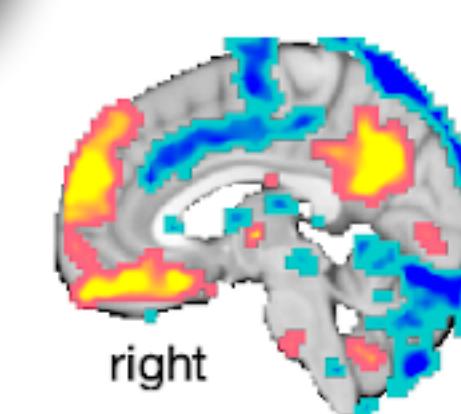
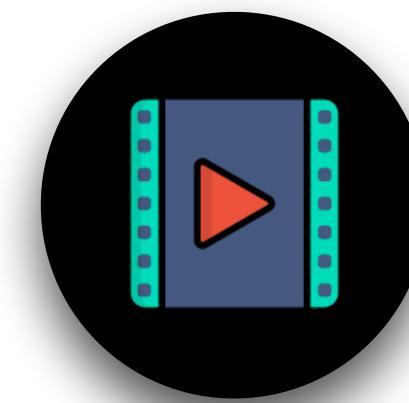
What are the neural correlates of stimulus intensity?



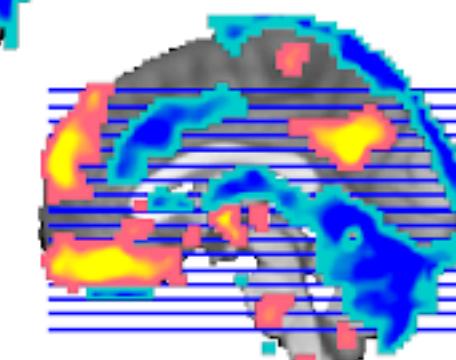
right



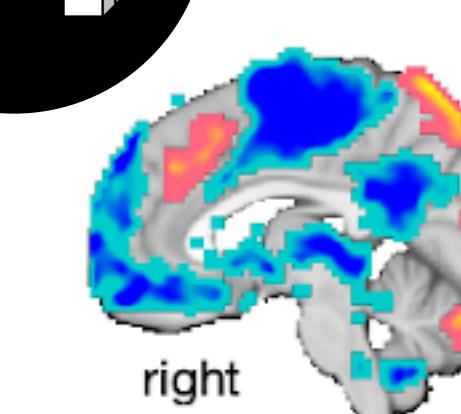
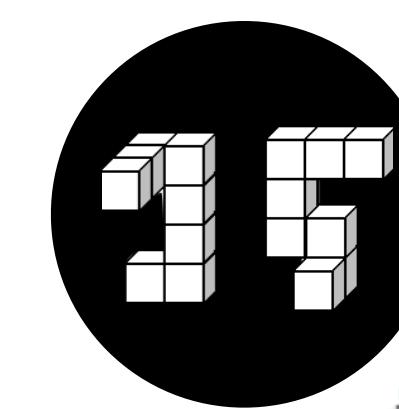
left



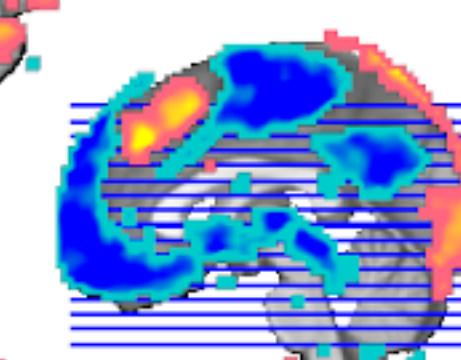
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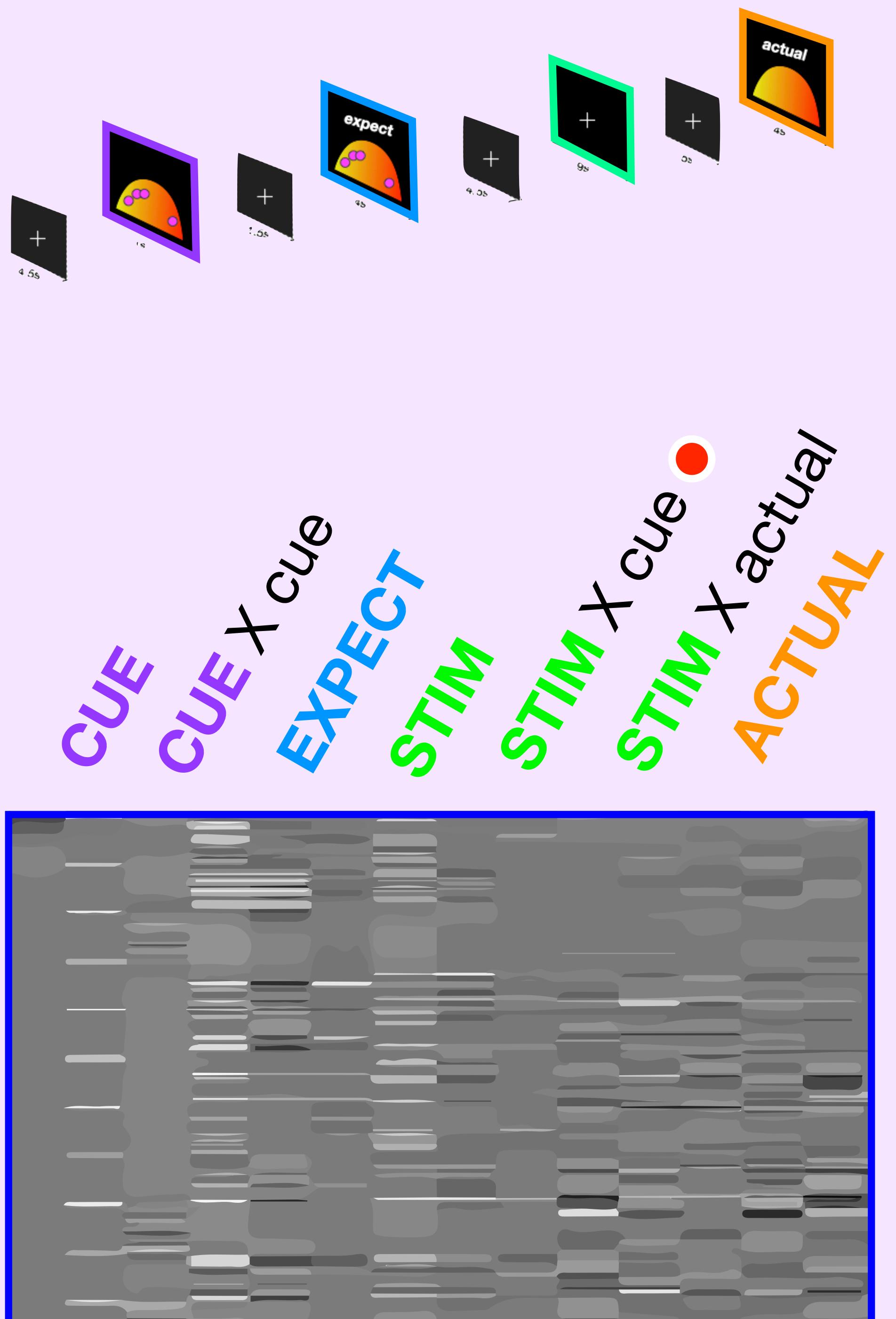
left



right



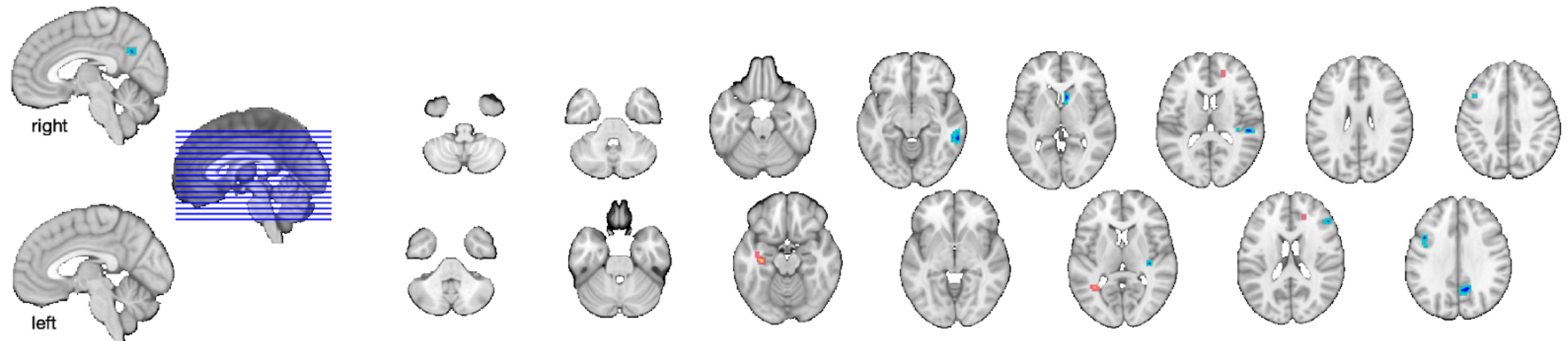
left



Q2. Cue effects:
What are the neural correlates
of cue modulated stimulus
effects?

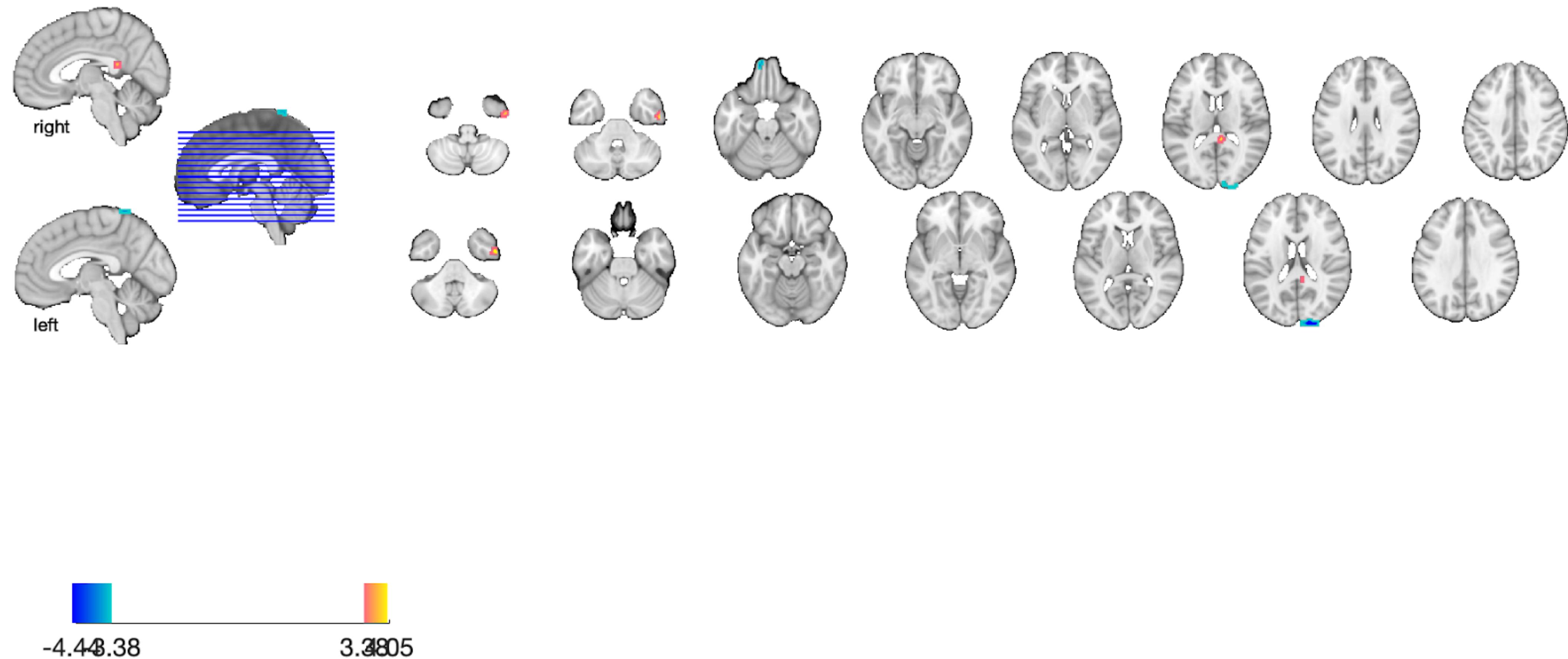
Cue-modulated stimulus intensity effects

Pain > VC ($p < .001$, uncorrected)



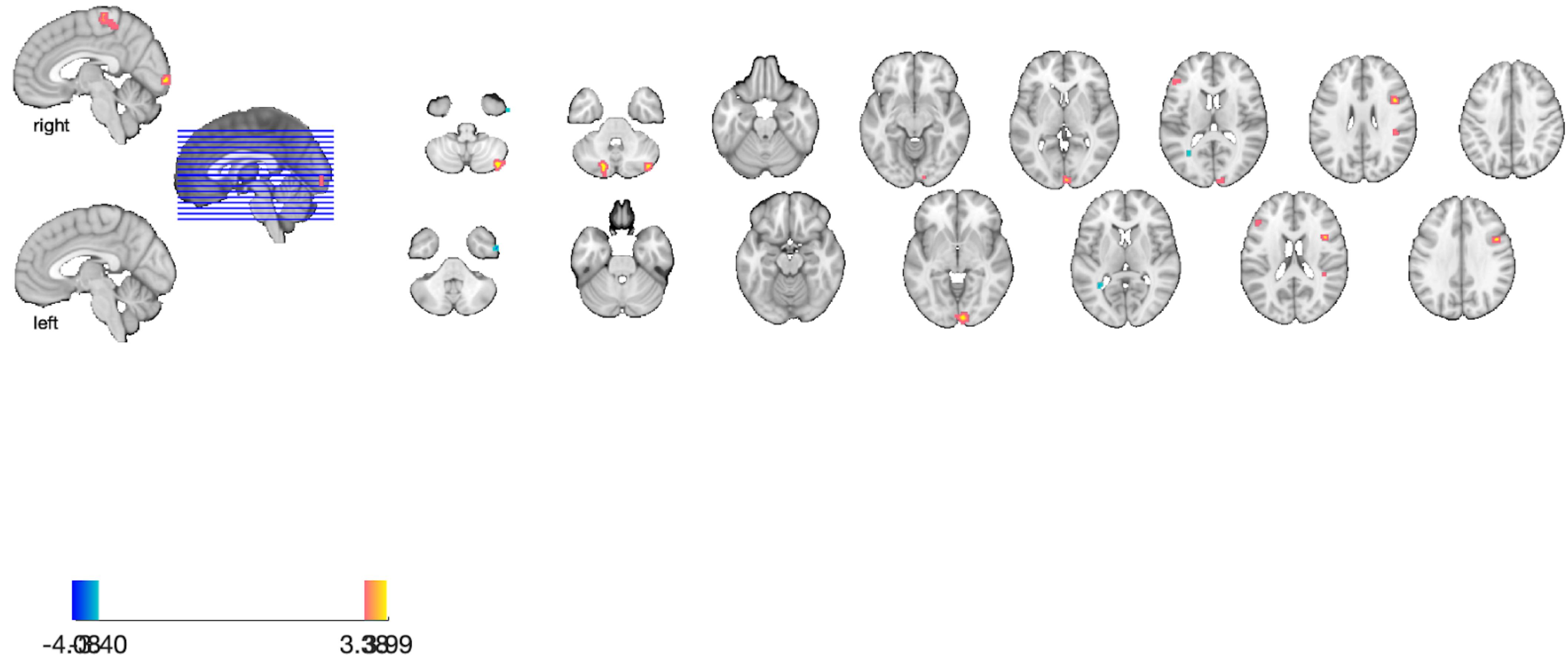
Cue-modulated stimulus intensity effects

Vicarious > PC ($p < .001$, uncorrected)



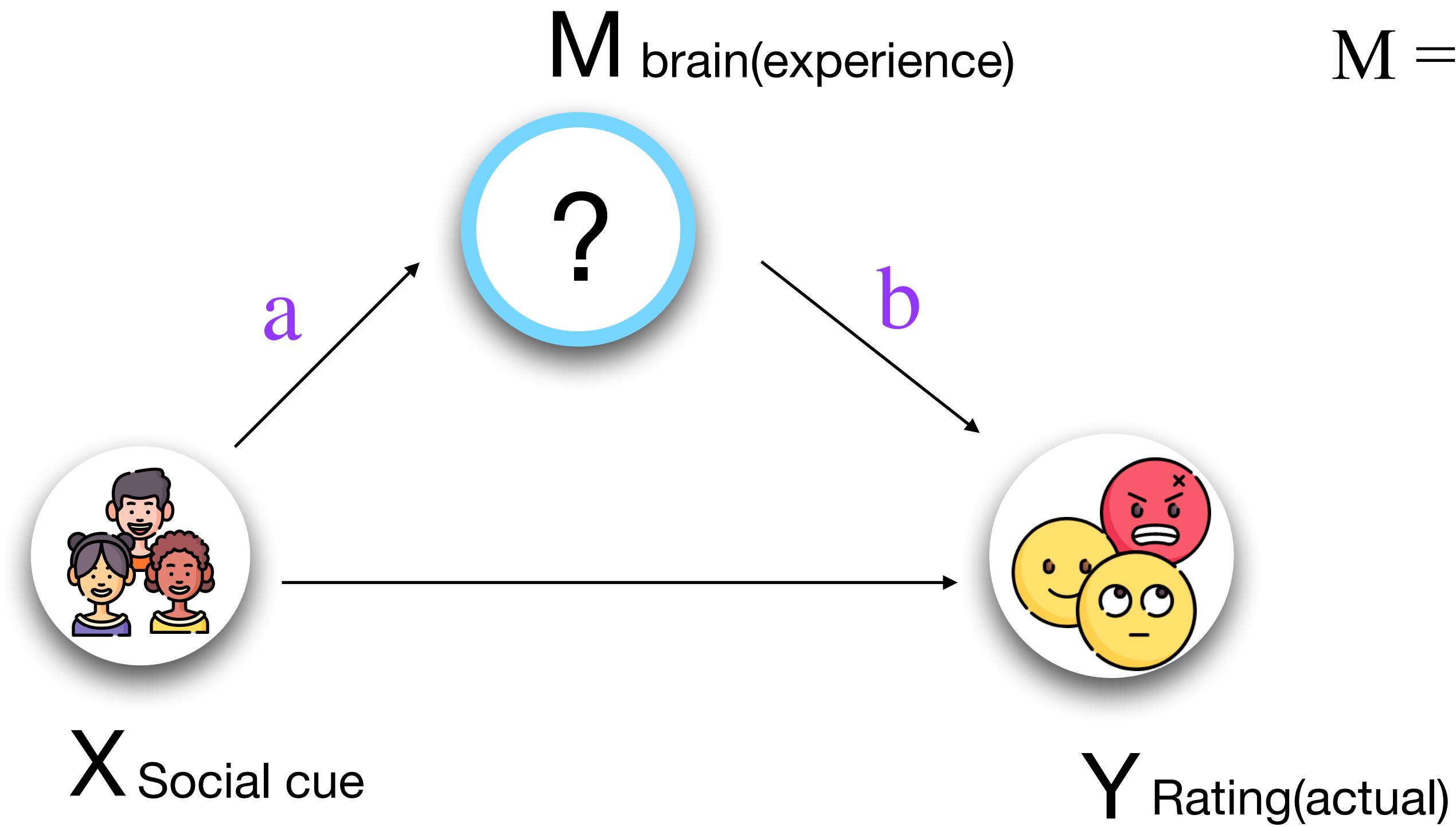
Cue-modulated stimulus intensity effects

Cognitive > PV ($p < .001$, uncorrected)



Mediation

Two-path mediation

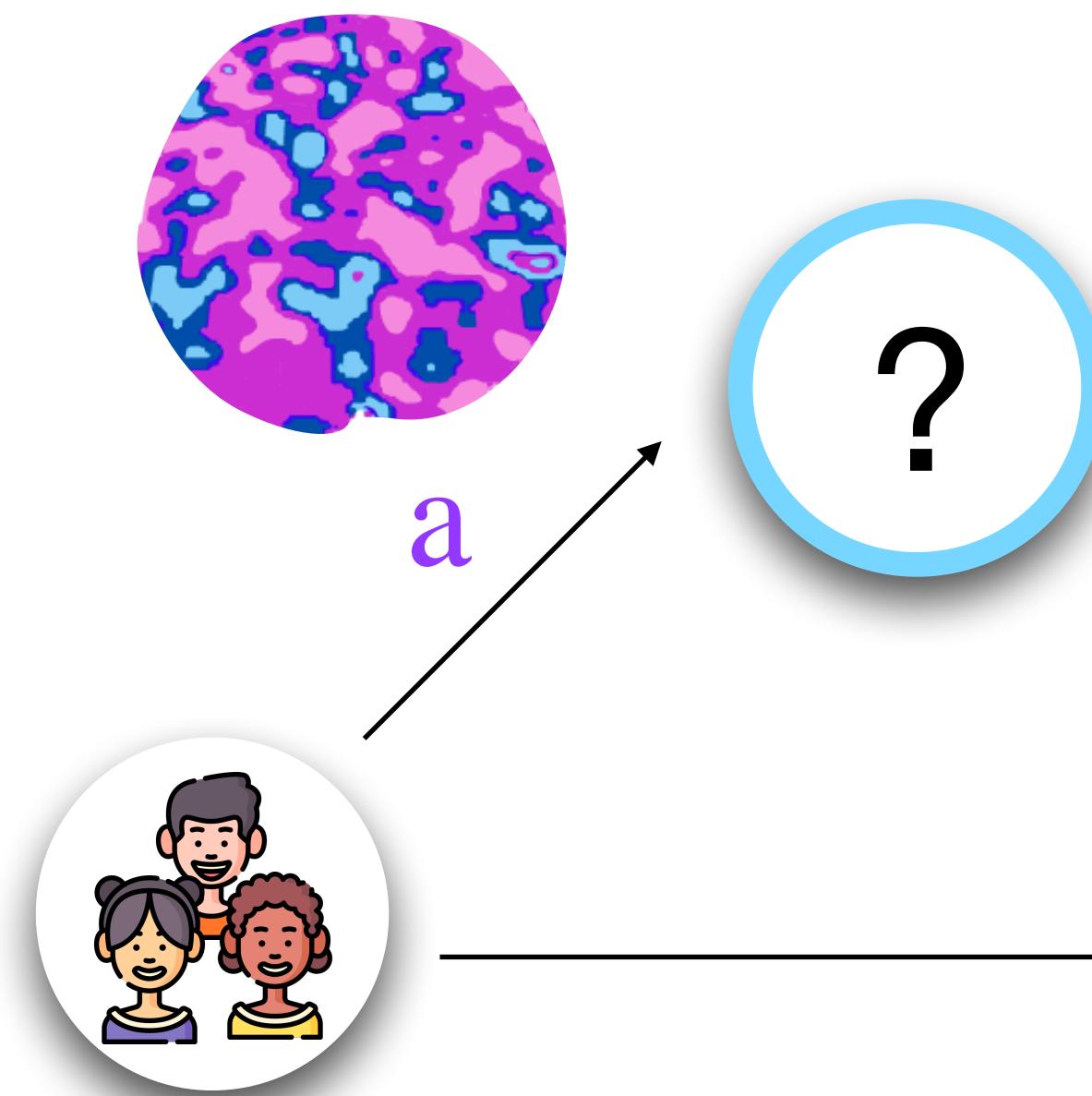


$$Y = \beta_0 + cX$$

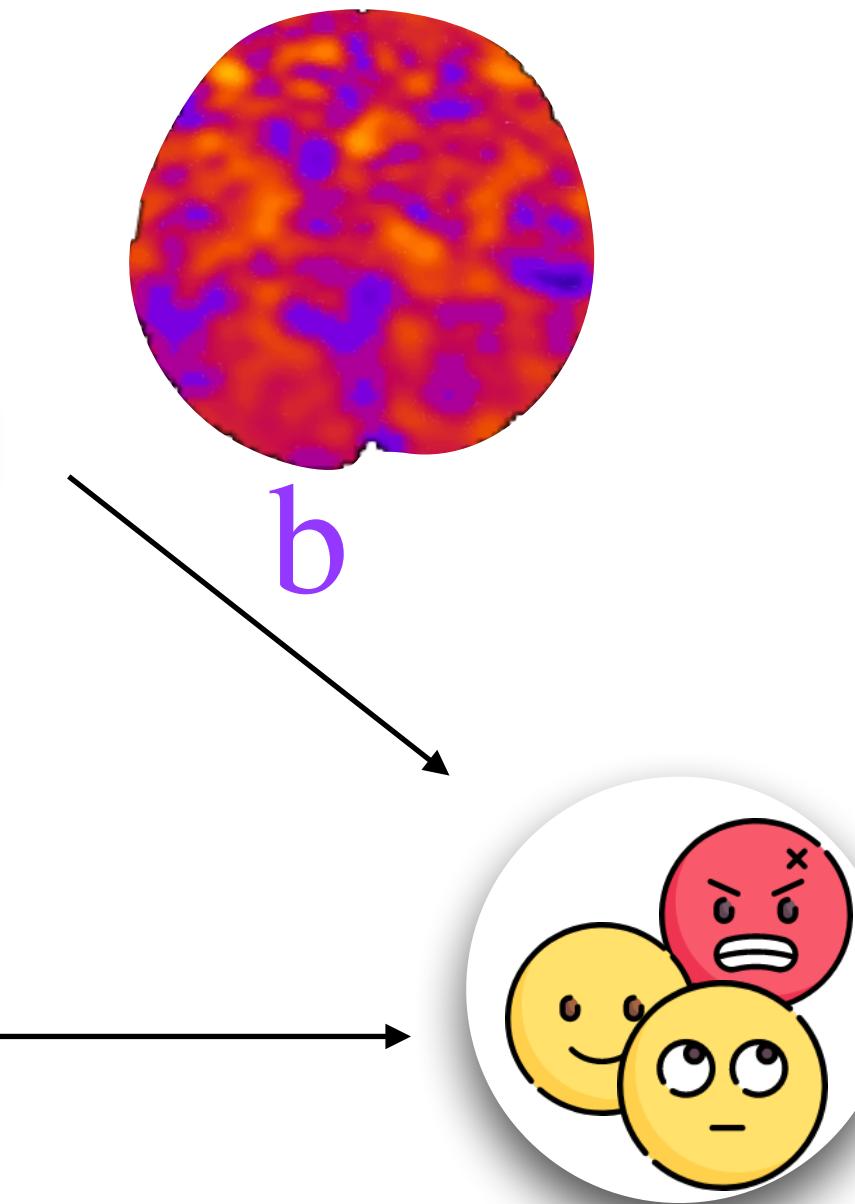
$$Y = \beta_0 + c'X + bM$$

$$M = \beta_0 + aX$$

STIM * cue



STIM * cue actual

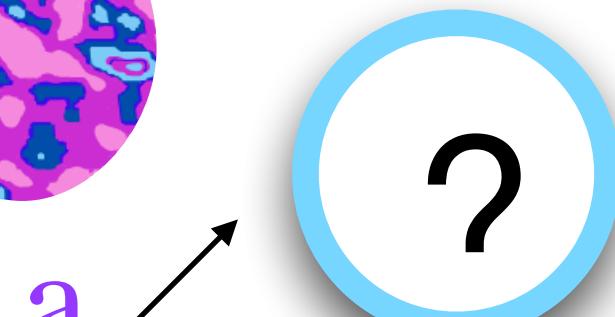
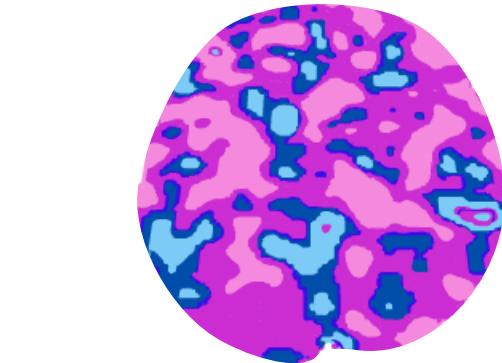


X Social cue

Y Rating(actual)

$\therefore ab = \text{indirect effect (mediation)}$

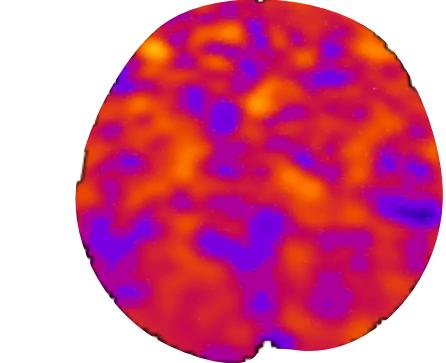
STIM * cue



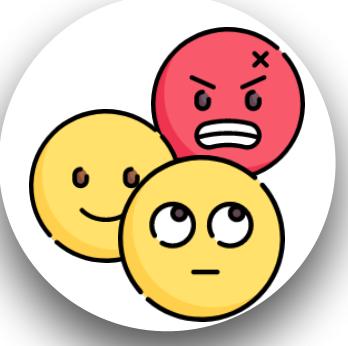
a



STIM * cue actual



b



$$Y_{(\text{Rating})} = \beta_0 + c' \text{CUE} + b \text{BRAIN}$$

$$M_{(\text{brain})} = \beta_0 + a \text{CUE}$$

X_{Social}

Y_{Rating(actual)}

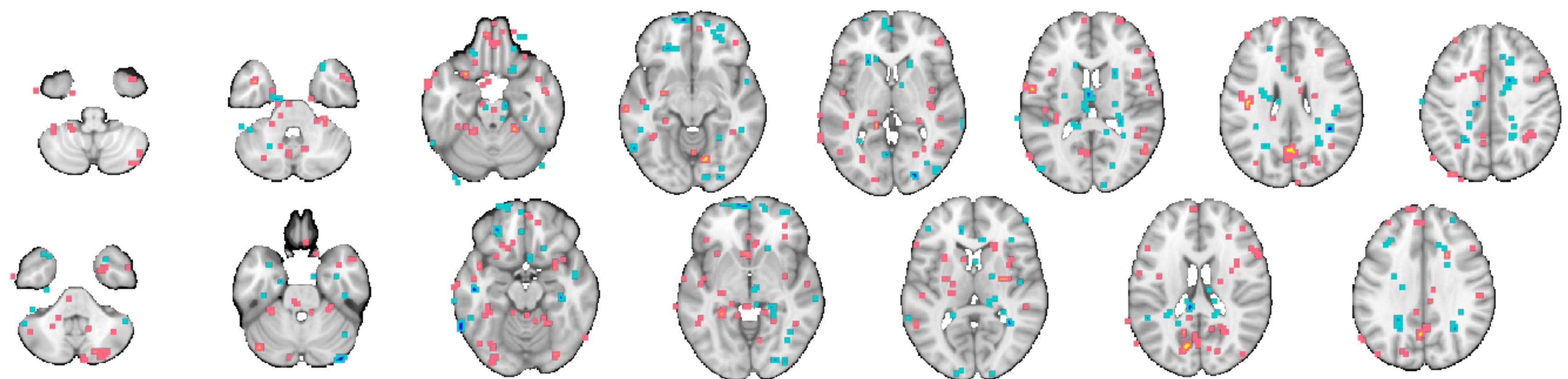
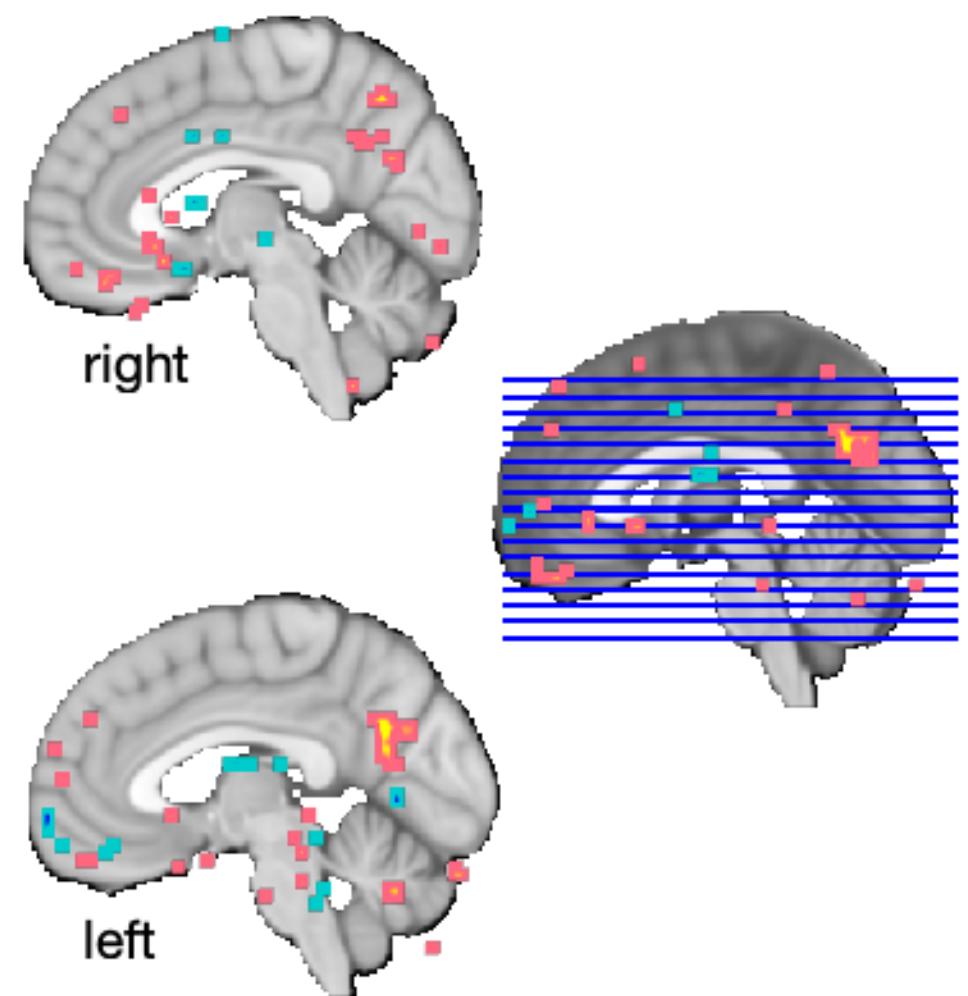
$\therefore ab = \text{indirect effect}$

$$M_{(\text{brain})} = \beta_0 + c' \text{CUE} + b \text{ACTUAL}$$

$$M_{(\text{brain})} = \beta_0 + a \text{CUE}$$

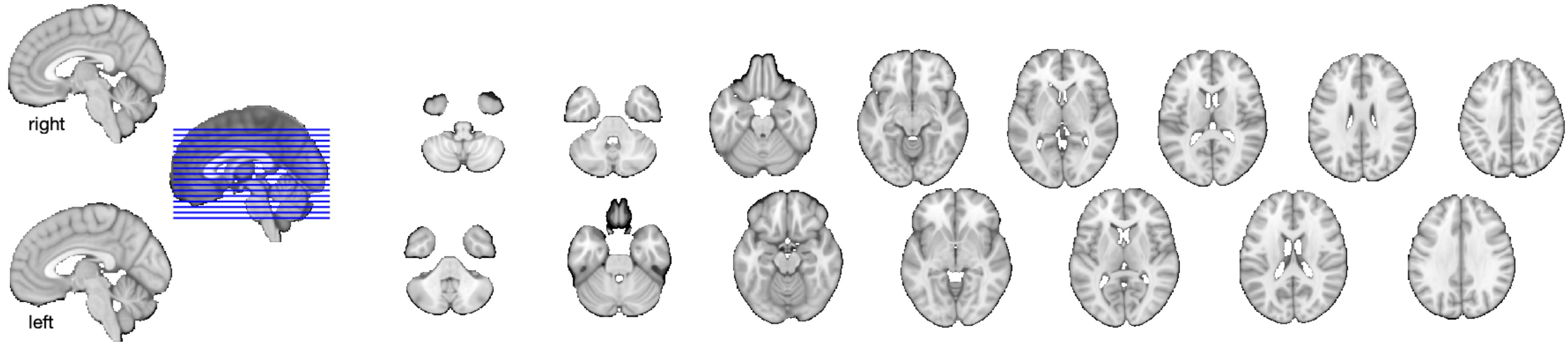
Mediation ab map

Pain stimXcue * stimXactual ($p < .001$, uncorrected)



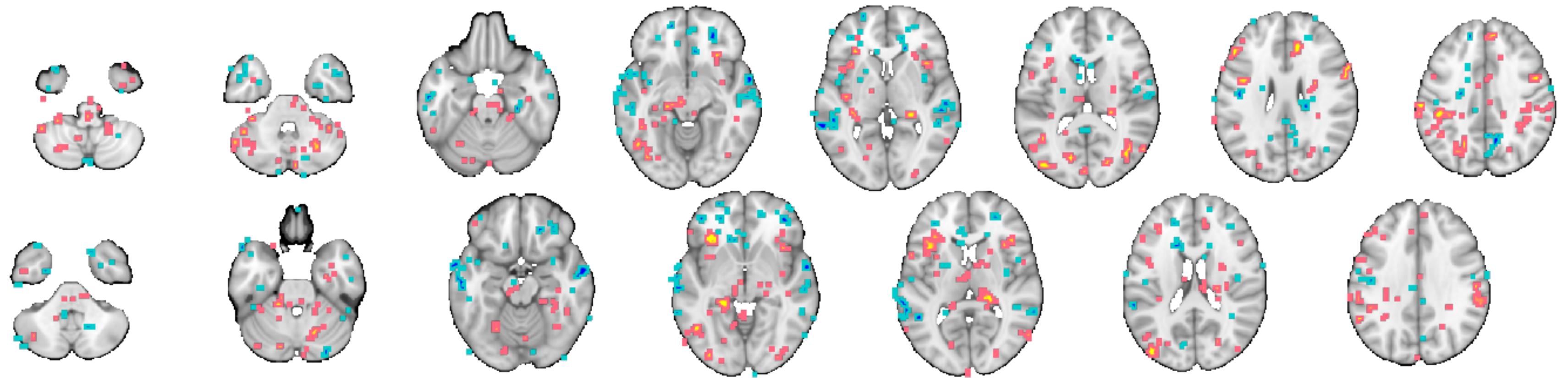
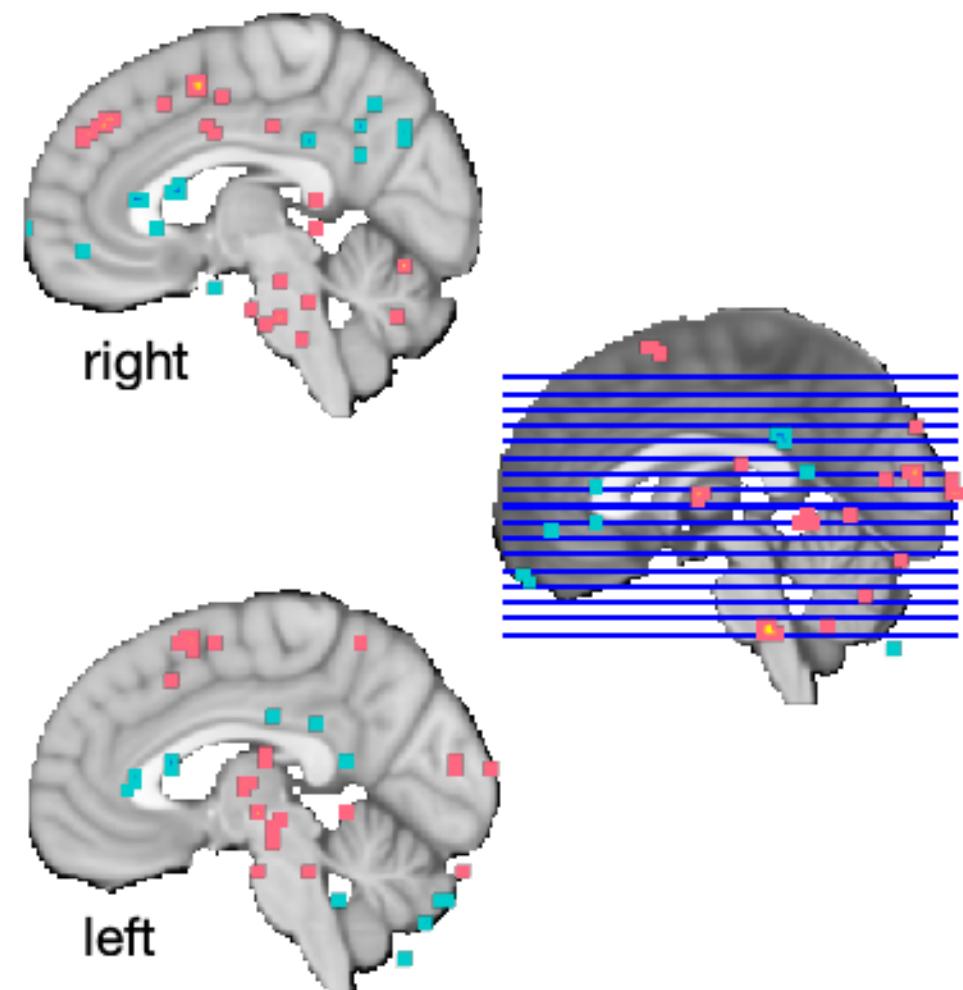
Mediation ab map

Vicarious stimXcue * stimXactual ($p < .001$, uncorrected)



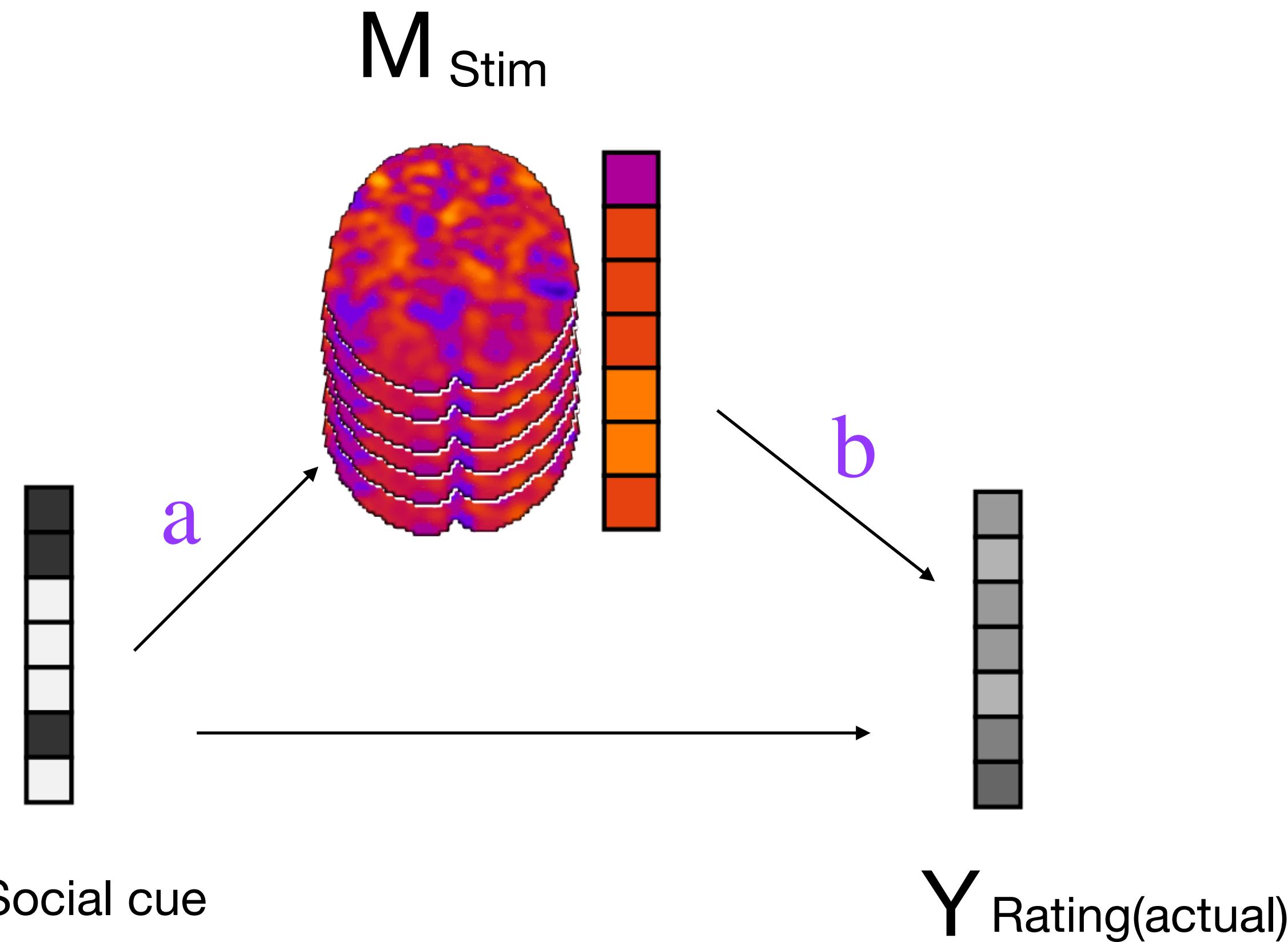
Mediation ab map

Cognitive stimXcue * stimXactual ($p < .001$, uncorrected)



What's next?

Single trial analyses and multi-level mediation



Single trial analysis

Least Squares Single

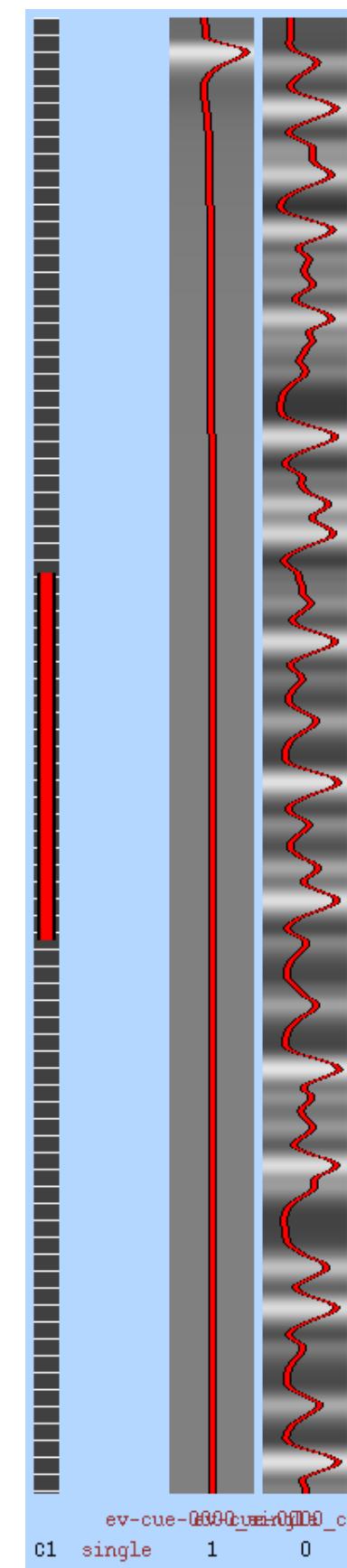
When you have short inter-stimulus interval (ISI)

$$X_{LSA} \beta = \begin{pmatrix} \text{wavy lines} \end{pmatrix} \begin{pmatrix} \beta_1 \\ \beta_2 \\ \vdots \\ \beta_{10} \end{pmatrix}$$

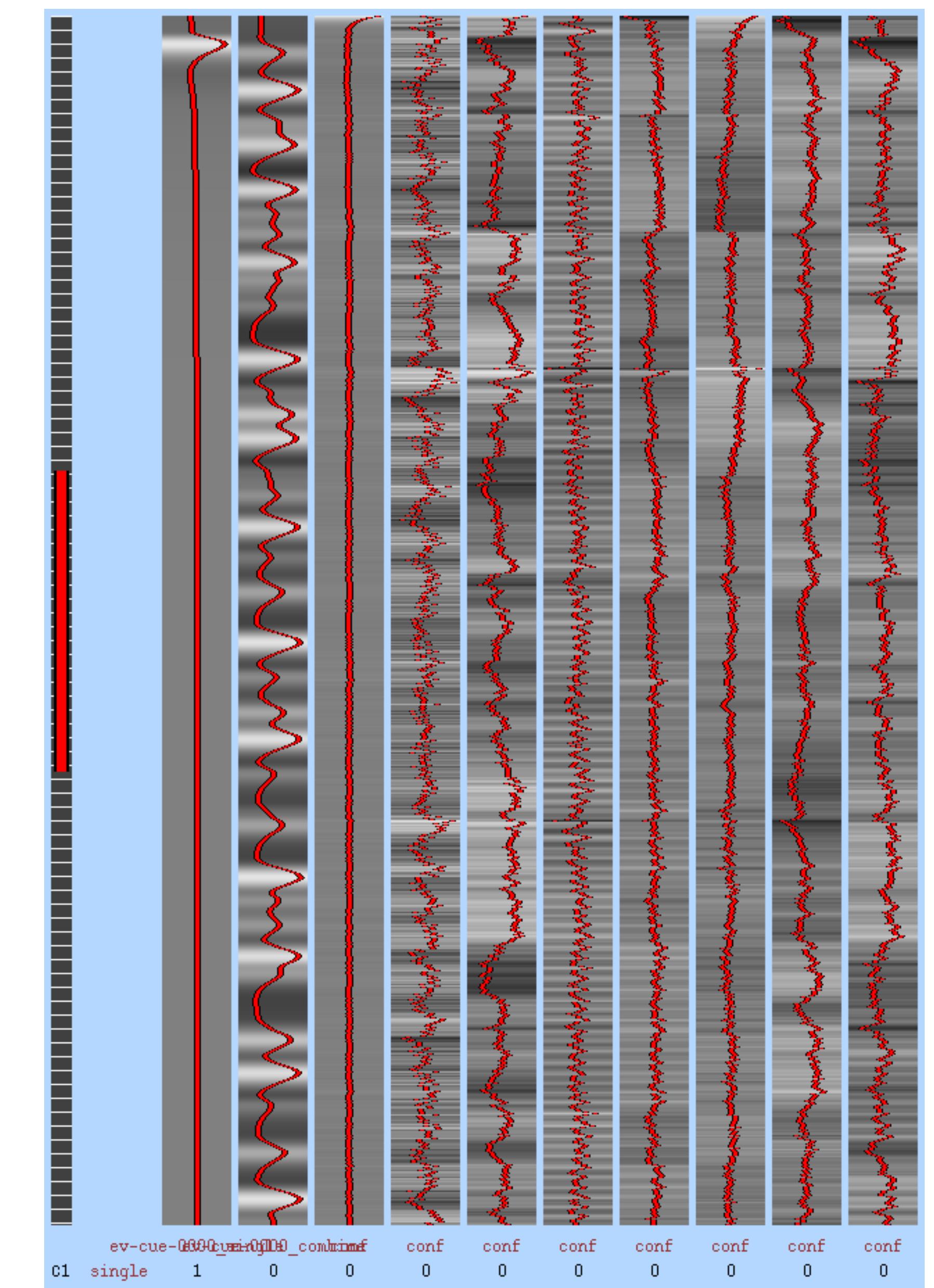
Least Squares All
(LSA)

$$\begin{array}{ll} X_{LSS_1} \beta & \dots \\ \begin{pmatrix} \text{wavy lines} \end{pmatrix} \begin{pmatrix} \beta_1 \\ \beta_{\text{Trial1}} \\ \beta_{\text{Trial2}} \end{pmatrix} & \dots \\ \text{Trial 1} & \text{Trial N} \\ & \end{array} \quad \begin{pmatrix} \text{wavy lines} \end{pmatrix} \begin{pmatrix} \beta_{10} \\ \beta_{\text{Trial1}} \\ \beta_{\text{Trial2}} \end{pmatrix}$$

Least Squares Single
(LSS)

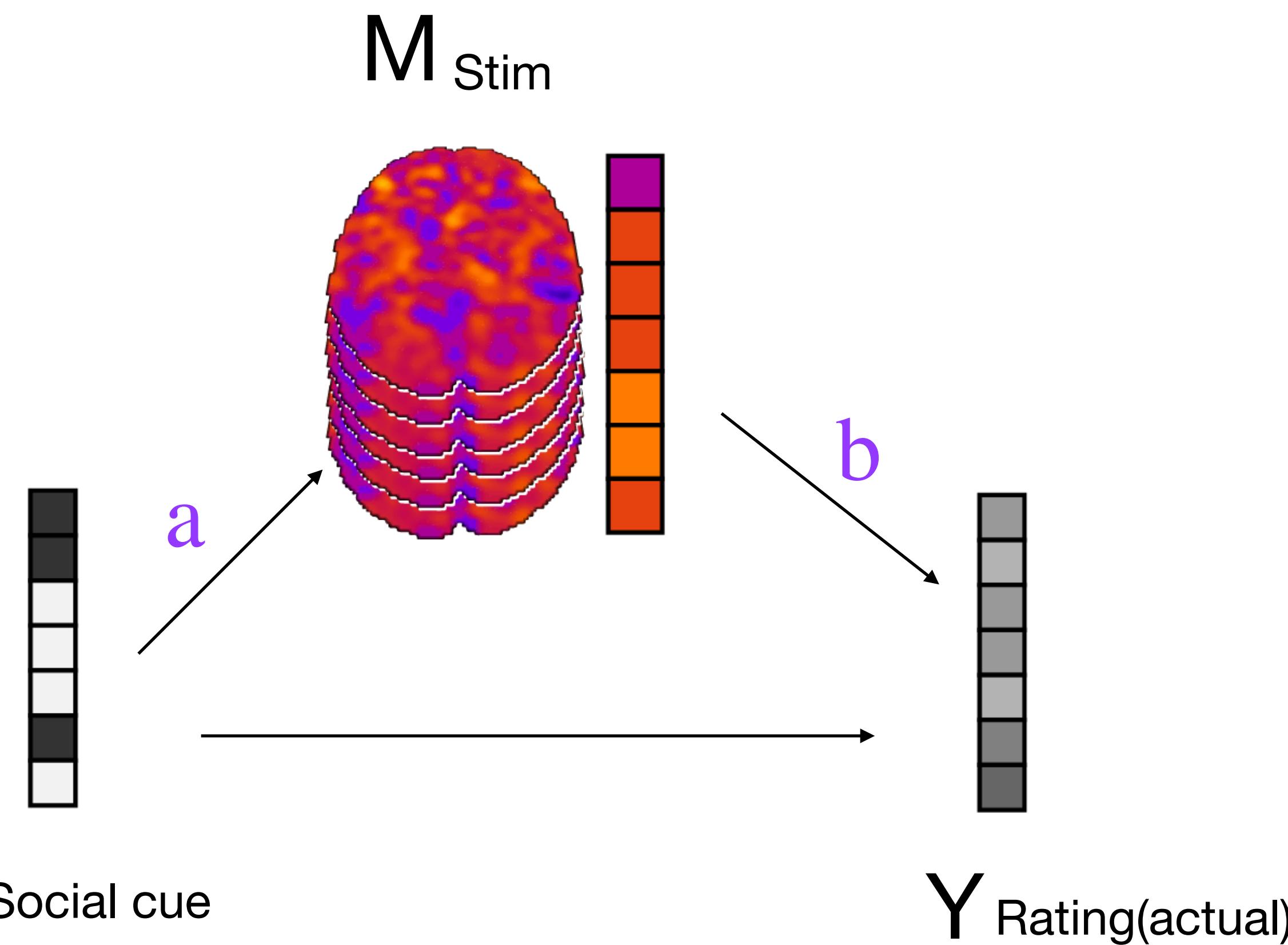


Example trial of my pipeline

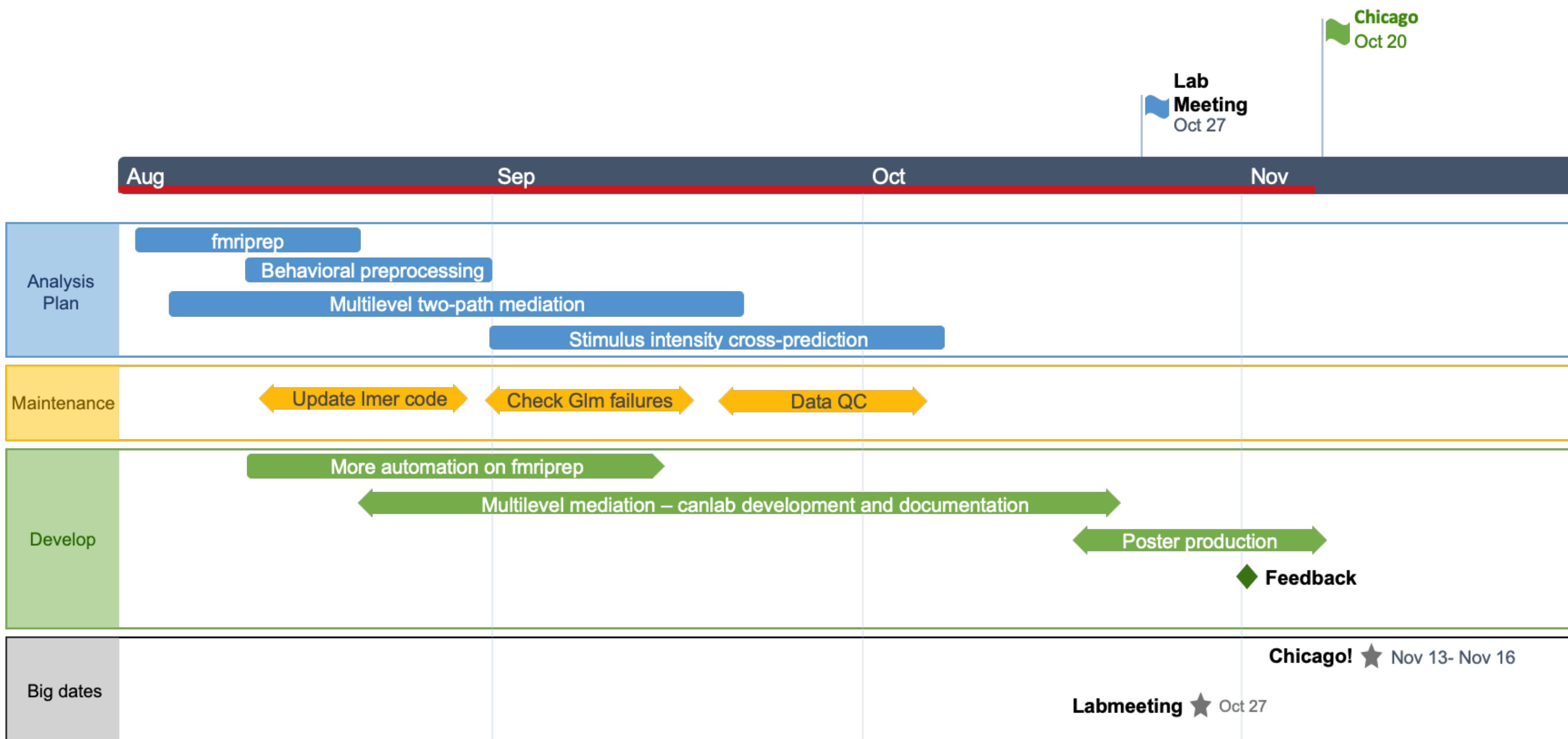


What's next?

Single trial analyses and multi-level mediation

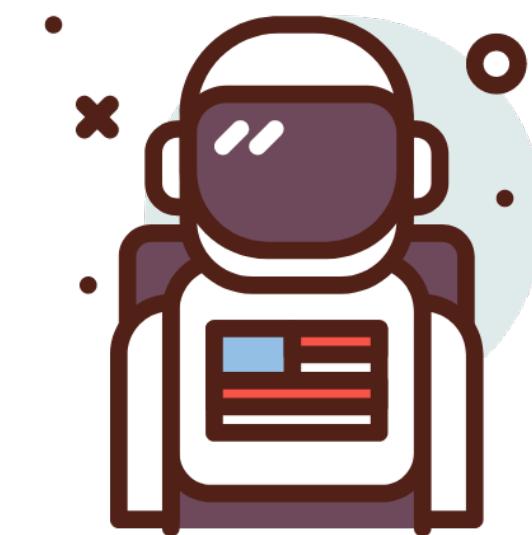


Social influence analysis roadmap

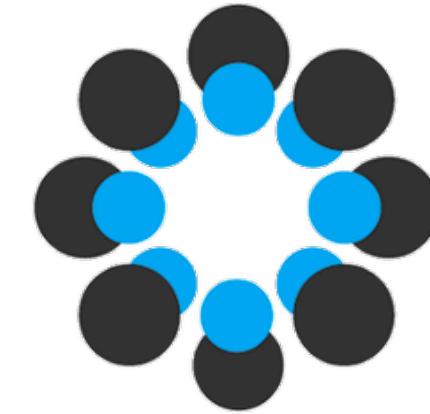


Feedback & Questions

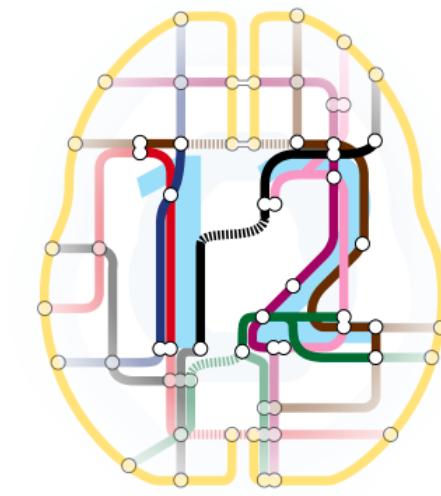
Thank you!



- Maryam
- Courtney Rodgers
- Bethany
- Terry Sackett
- Eilis
- Luke



- Rotem
- Michael
- Ke

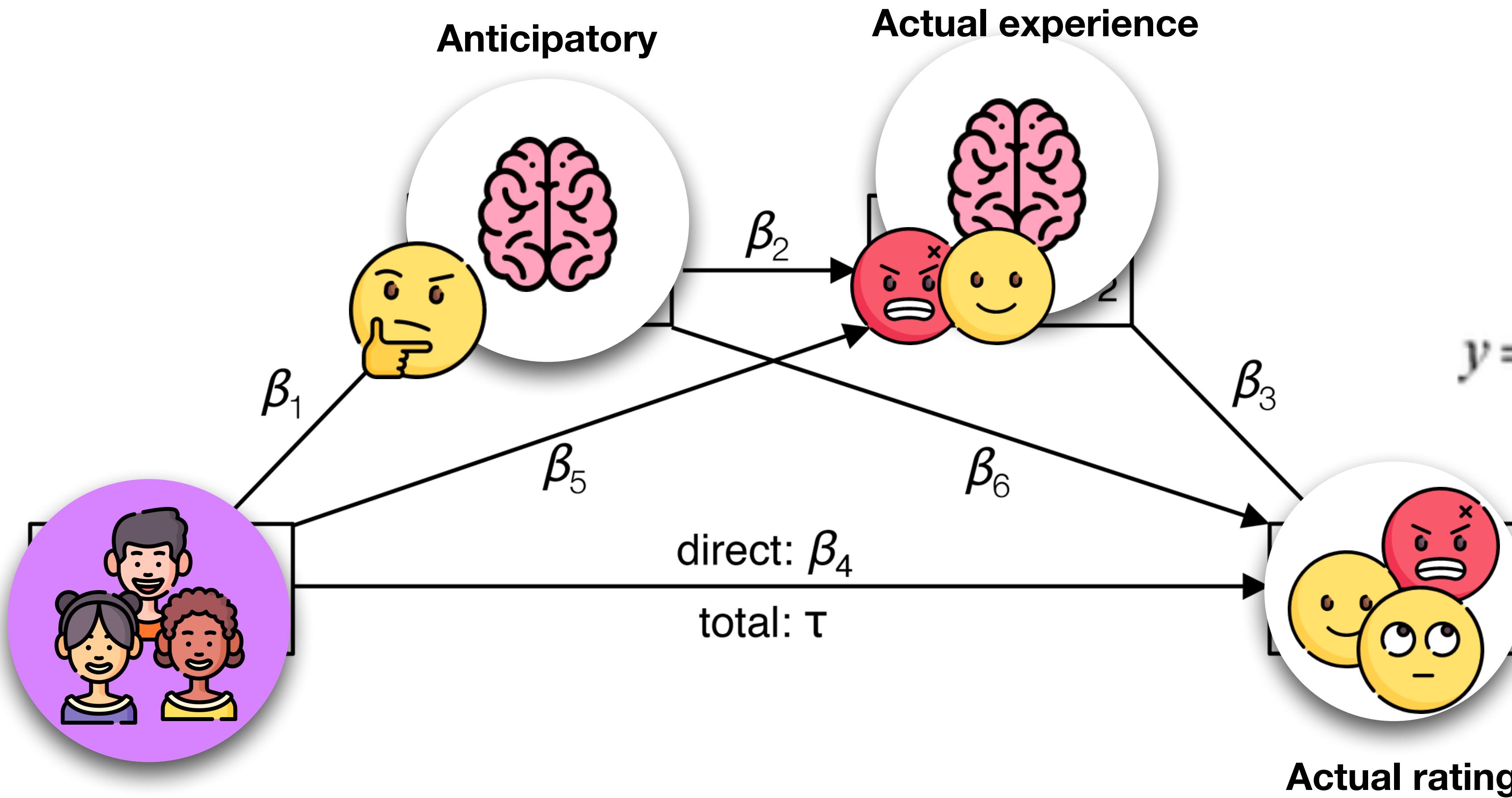


Tor!

Appendix

What is the relationship (in the brain) between expectation & actual experiences? “multilevel mediation analysis”

$$y = \tau x + e_y$$



$$m_1 = \beta_1 x + e_{m_1}$$

$$m_2 = \beta_2 m_1 + \beta_5 x + e_{m_2}$$

$$y = \beta_4 x + \beta_3 m_2 + \beta_6 m_1 + e'_y$$

Behavioral/Systems/Cognitive

Isolating the Modulatory Effect of Expectation on Pain Transmission: A Functional Magnetic Resonance Imaging Study

John R. Keltner,¹ Ansgar Furst,² Catherine Fan,² Rick Redfern,² Ben Inglis,² and Howard L. Fields³

¹Pain Management Center, Department of Anesthesia and Perioperative Care, University of California San Francisco, San Francisco, California 94143,

²Henry H. Wheeler, Jr. Brain Imaging Center, Helen Wills Neuroscience Institute, University of California Berkeley, Berkeley, California 94608, and

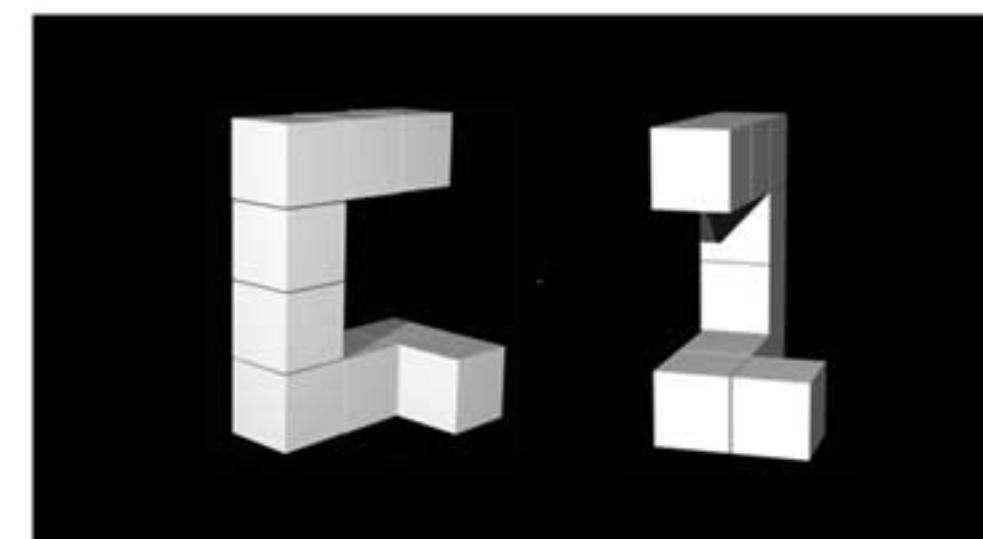
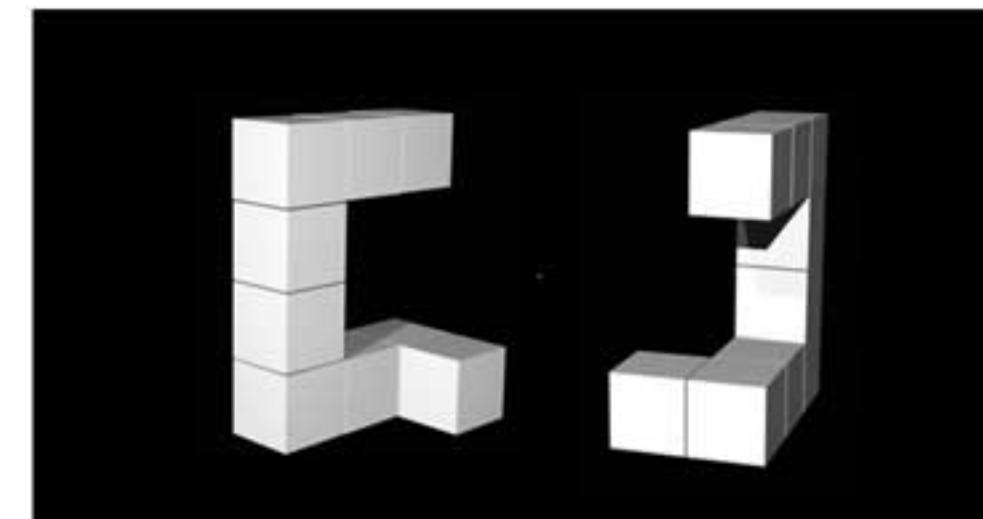
³Wheeler Center for the Neurobiology of Addiction, Department of Neurology, University of California San Francisco, Emeryville, California 94608

We use a novel balanced experimental design to specifically investigate brain mechanisms underlying the modulating effect of expected pain intensity on afferent nociceptive processing and pain perception. We used two visual cues, each conditioned to one of two noxious thermal stimuli [$\sim 48^\circ\text{C}$ (high) or 47°C (low)]. The visual cues were presented just before and during application of the noxious thermal stimulus. Subjects reported significantly higher pain when the noxious stimulus was preceded by the high-intensity visual cue. To control for expectancy effects, for one-half of the runs, the noxious thermal stimuli were accompanied by the cue conditioned to the other stimulus. Comparing functional magnetic resonance imaging blood oxygenation level-dependent activations produced by the high and

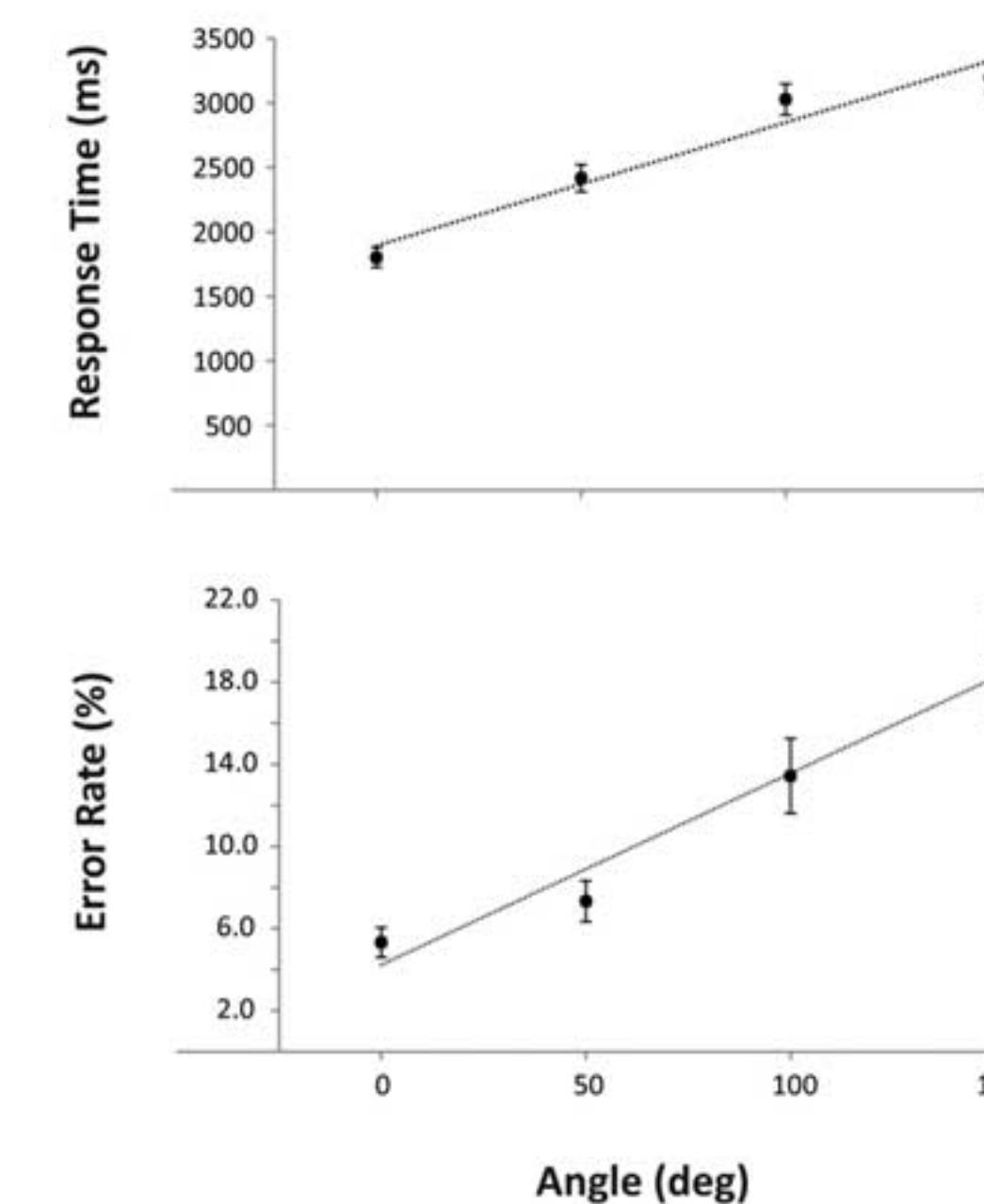
We use datasets with normed ratings

Cognitive - mental rotation dataset (Ganis & Kievit, 2015)

Example



Normed results from Ganis & Kievity (2015)

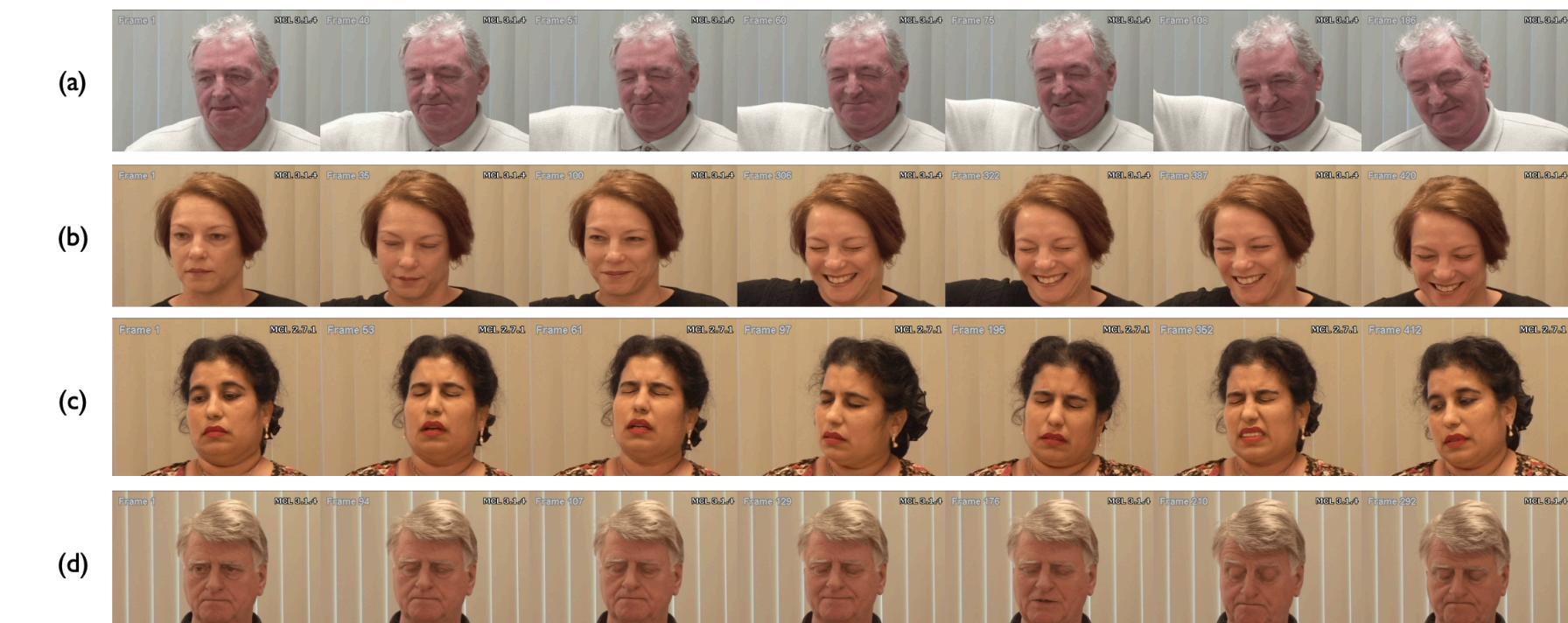


We use datasets with normed ratings

Vicarious - McMaster shoulder pain dataset

What McMaster pain dataset offers

- 1) Temporal Spontaneous Expressions:
- 2) Manual FACS codes:
- 3) Self-Report and Observer Ratings
- 4) Tracked Landmarks: 66 point Active Appearance Model (AAM) landmarks.



High



Med

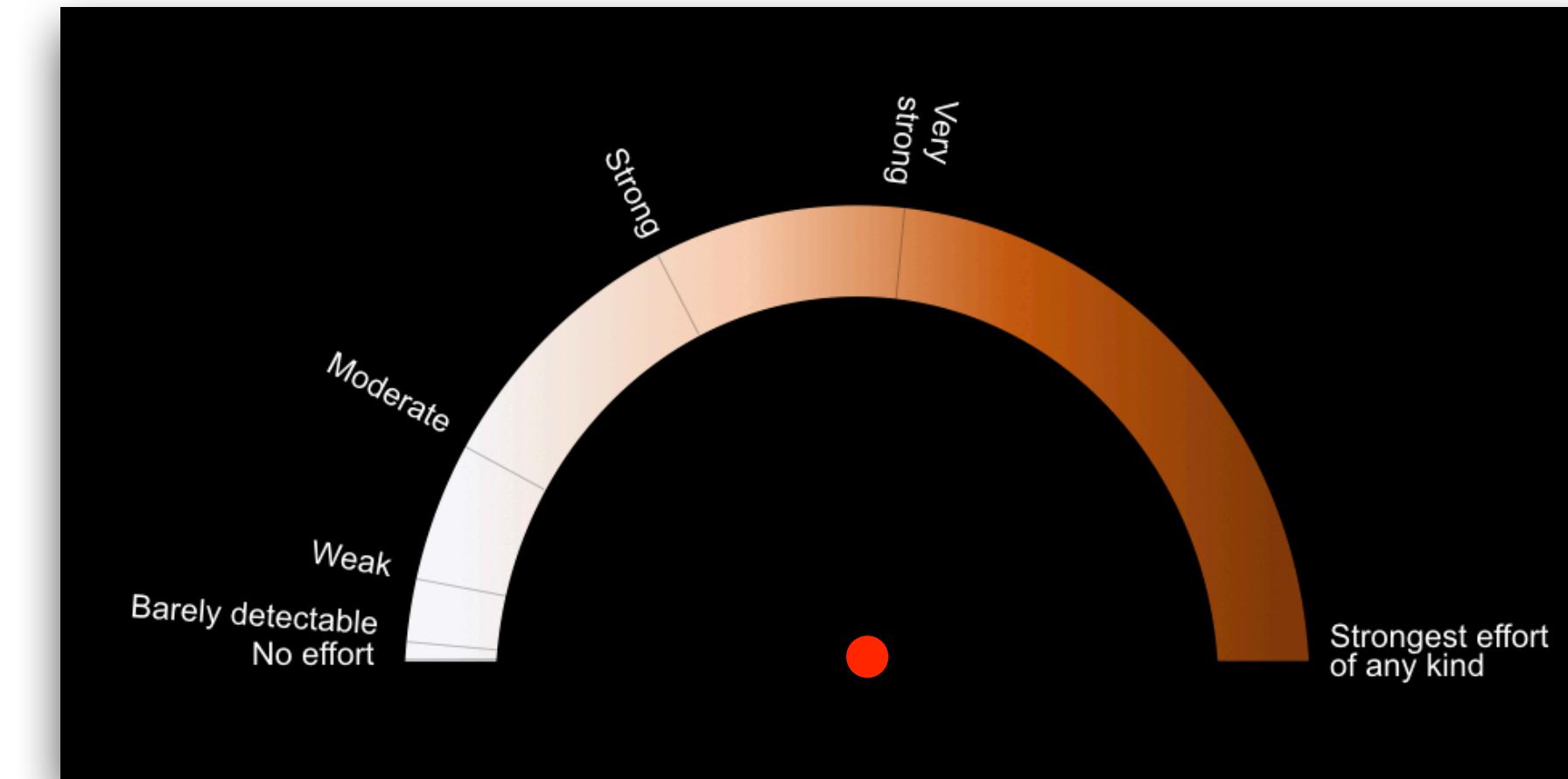
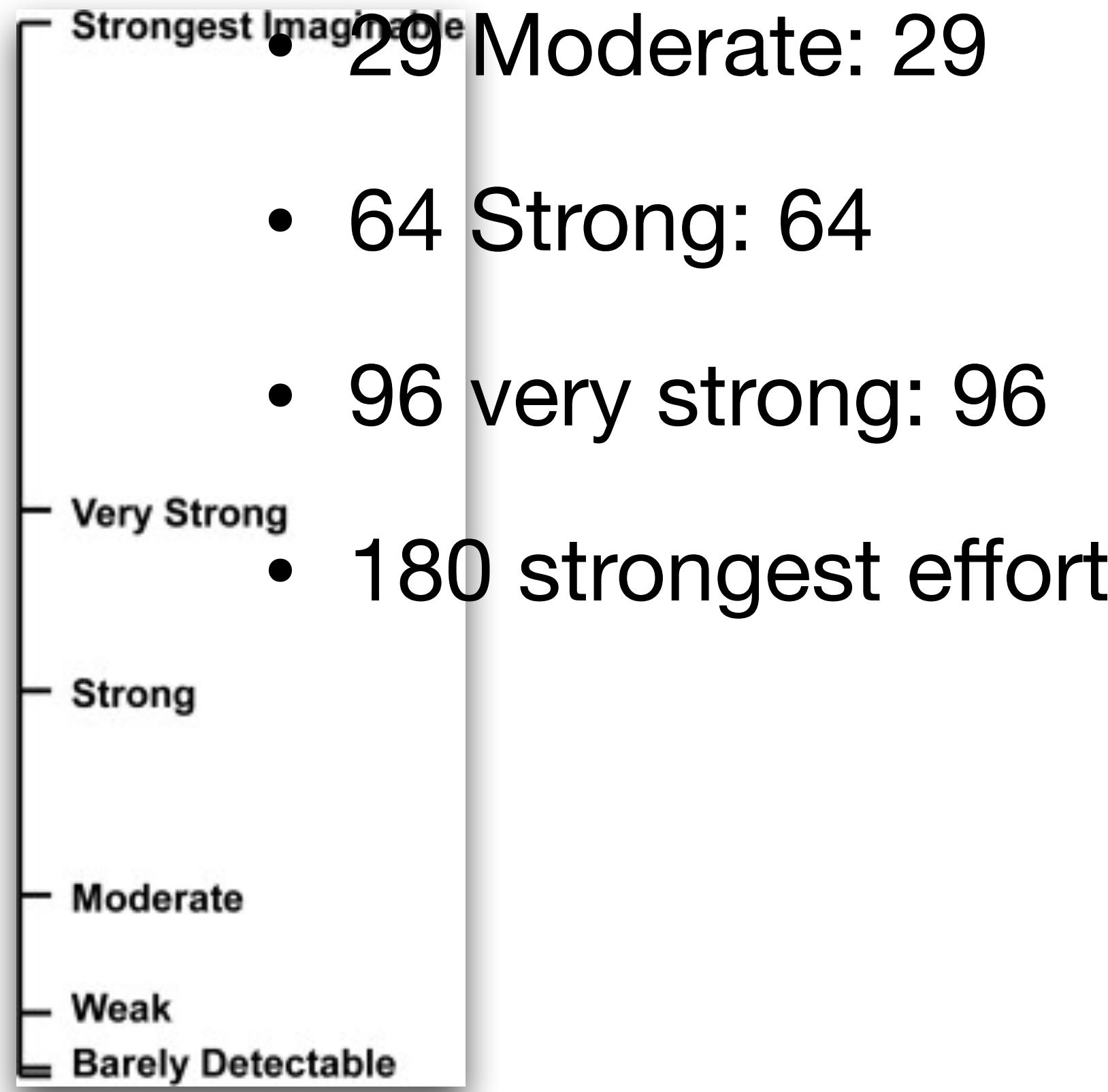


Low



gLMS

General Labeled Magnitude scale + semi-circular



- ### Benefits of circular rating
- Equidistant
 - Mouse trajectory

(e.g., [Bartoshuk et al., 2002](#), [Green et al., 1993](#), [Green et al., 1996](#))