

# Understanding clinical and neurodivergent conditions through the lens of social neuroscience

## WHAT IS A REWARD?

*“Any stimulus, object, event, activity, or situation that has the potential to make us approach and consume it is by definition a reward” (Schultz W. 2015)*



Rewards are strong drivers of our decisions and behavior



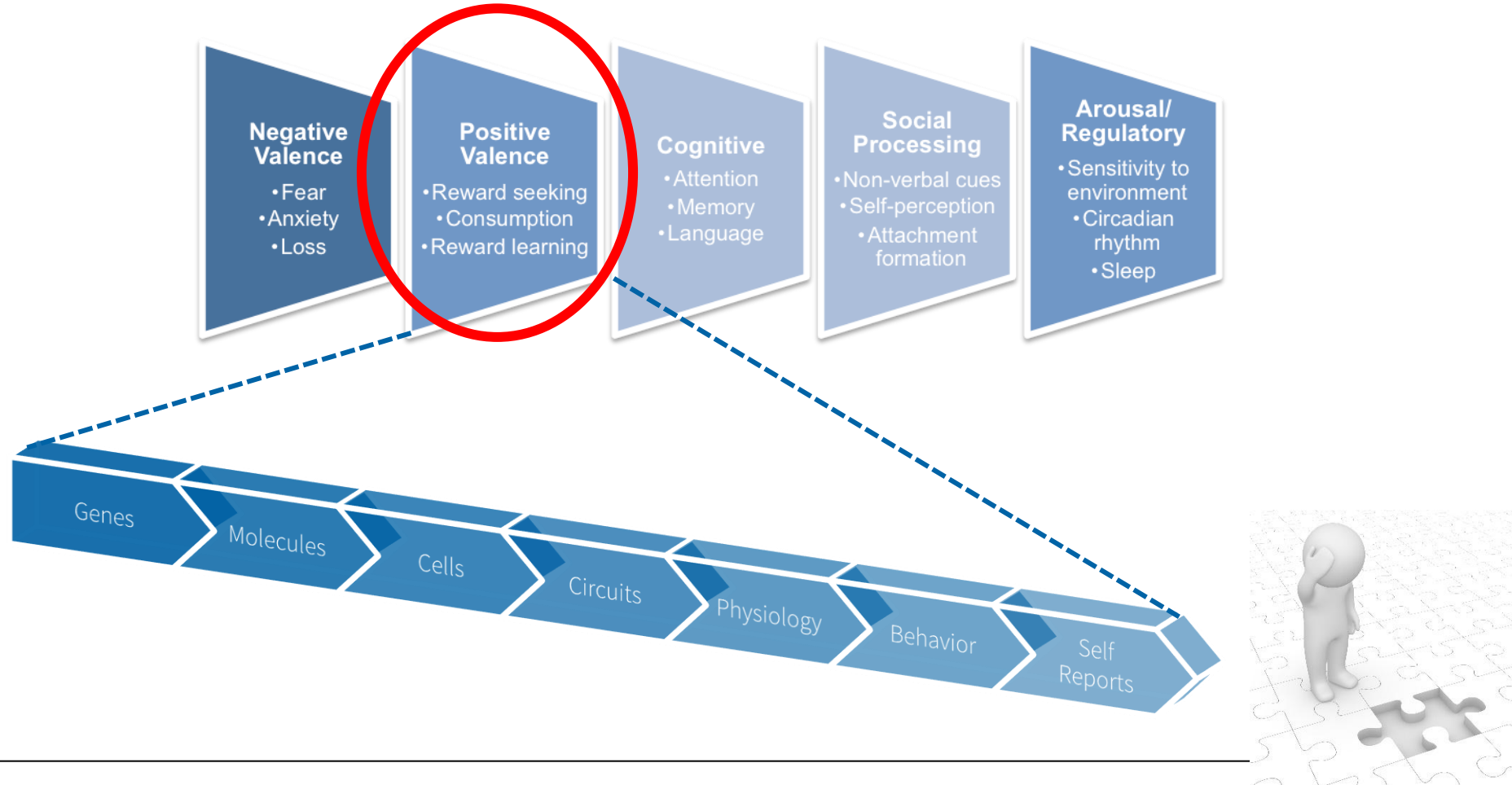
An intact reward system is fundamental for health and well-being



"We found the smiling face to be more of an incentive for him".

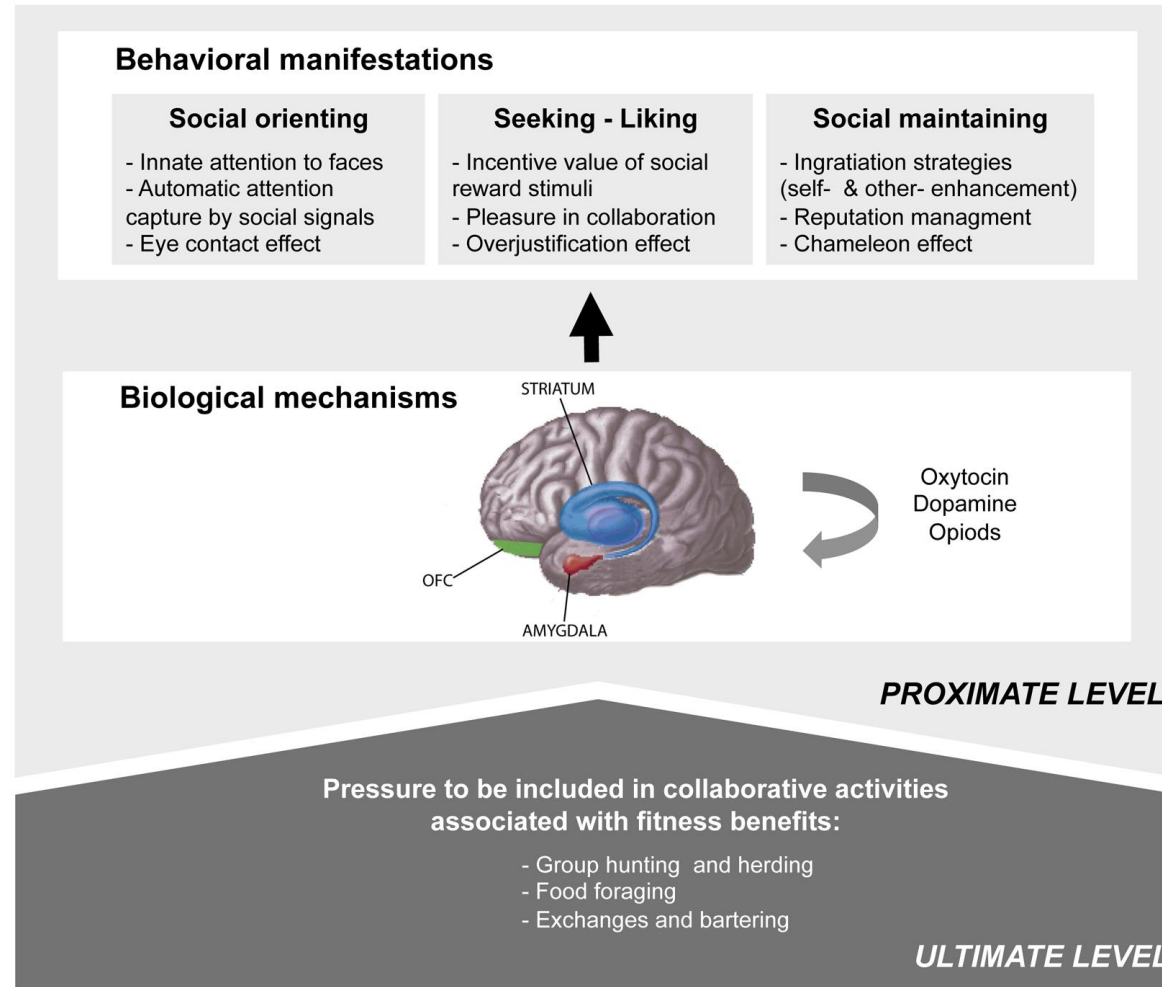


- Understanding how reward processing is functioning is fundamental as indicated by the recently proposed RDoC





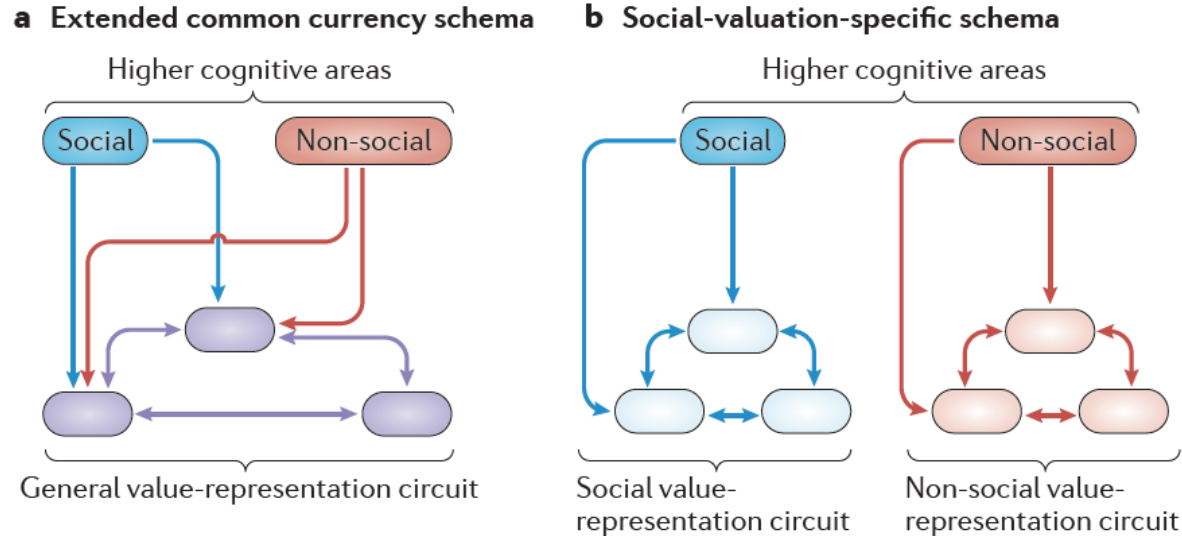
# SOCIAL REWARDS





# ARE REWARDS ALL THE SAME?

Different types of rewards (e.g. **social** and **nonsocial**) but **unclear** if rewards are processed by same brain circuitry and neurochemistry



RUFF & FEHR, 2014, NATURE REVIEWS NEUROSCIENCE





## OUTLINE OF THE TALK

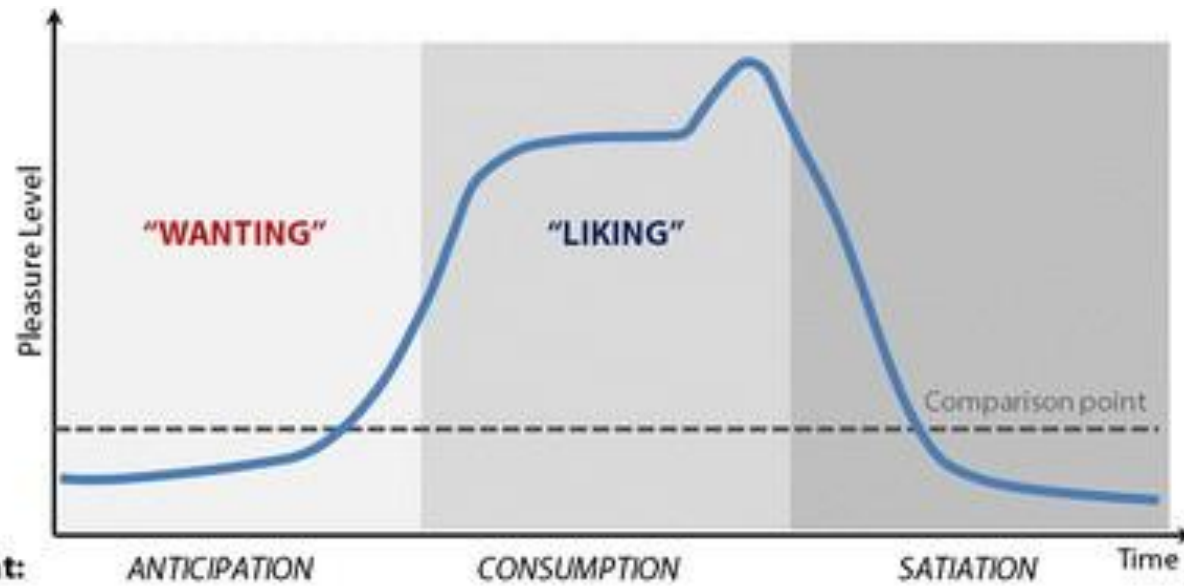
- Social and non social reward processing: translating animal research to humans
  - A state-depent account of social rewards: how different motivational states affect processing of social rewards
  - Reward processing in neurodiverse and clinical populations: lesson from autism and anorexia
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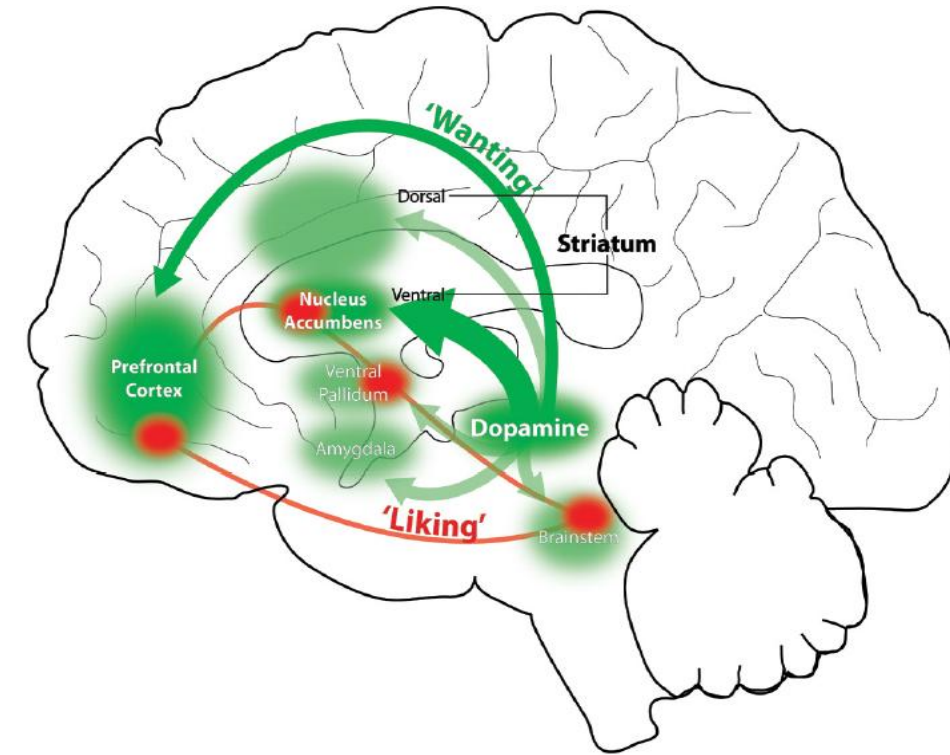
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# REWARD PROCESSING

- Wanting vs. liking



Reward component:



Methodological shortcomings :

- Comparing **secondary** (e.g. money) to **primary rewards** (e.g. faces/food)  
→ not ideal as different reward levels are involved
  - Did not provide **rewards at every trial**  
→ not ideal because measuring only anticipation
  - Few studies compared social and non-social rewards of **equal magnitude**  
→ problematic to infer if it is the «social» component that differs
  - Rarely used both **subjective** (ratings) and **objective** (effort & facial EMG) **measures**  
→ prone to differences in response biases
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# TRANSLATING ANIMAL RESEARCH TO HUMANS

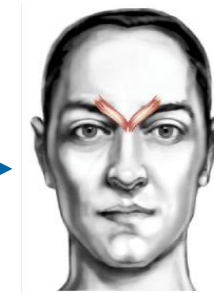
## Food rewards

- 2ml of Choco-milk in 3 concentrations (100, 25, 0 %)
- Delivered with computer-controlled pumps



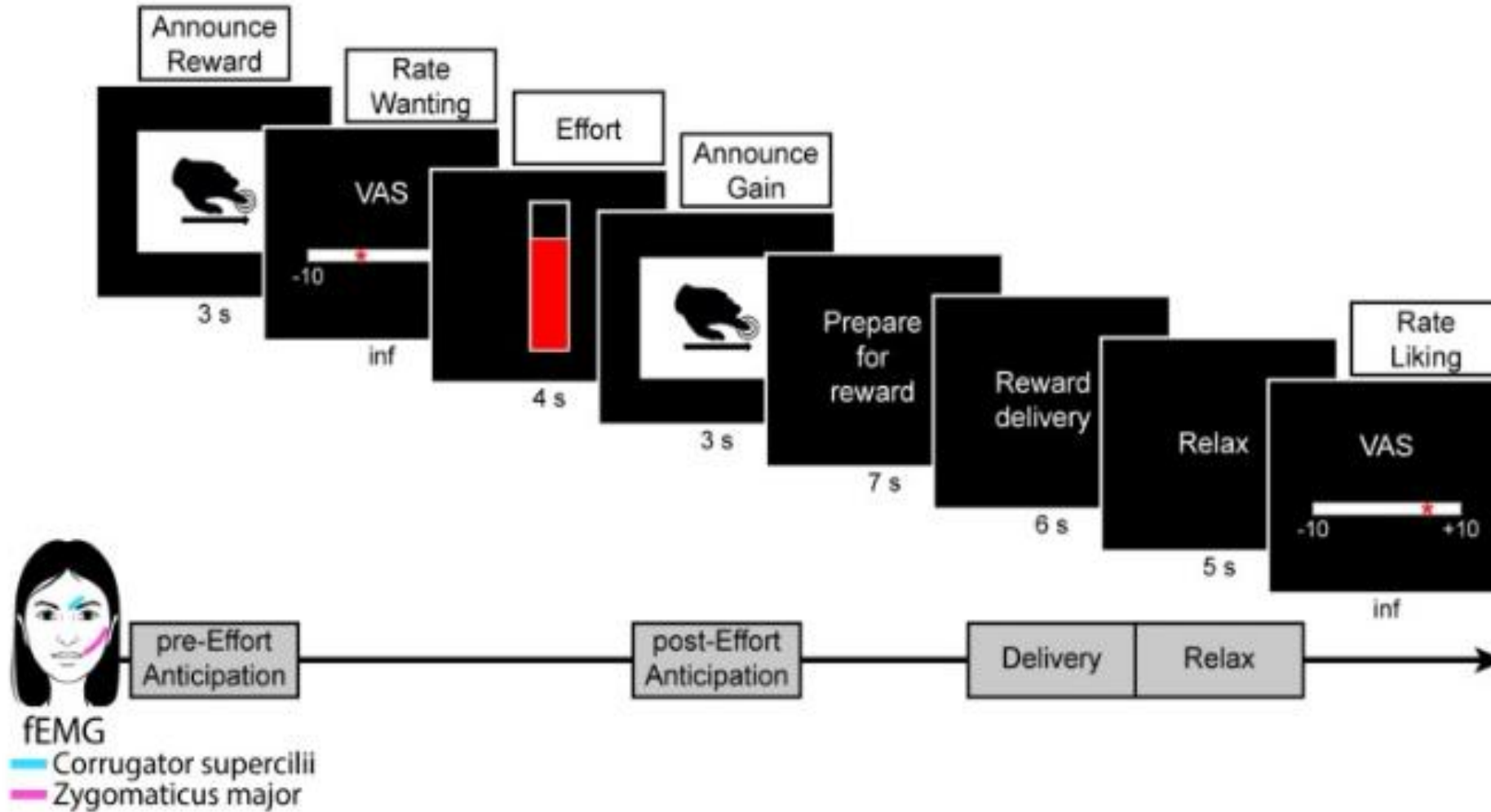
## Social rewards

- Forearm caresses at 3 speeds (6, 21, 27 cm/s) delivered by same-sex experimenter behind curtain.
- Speeds 1-10 cm/s are CT-optimal and perceived as more pleasant





## TRANSLATING ANIMAL RESEARCH TO HUMANS





## SOCIAL vs. NON SOCIAL REWARDS



Test for different neurobiological regulation of wanting and liking

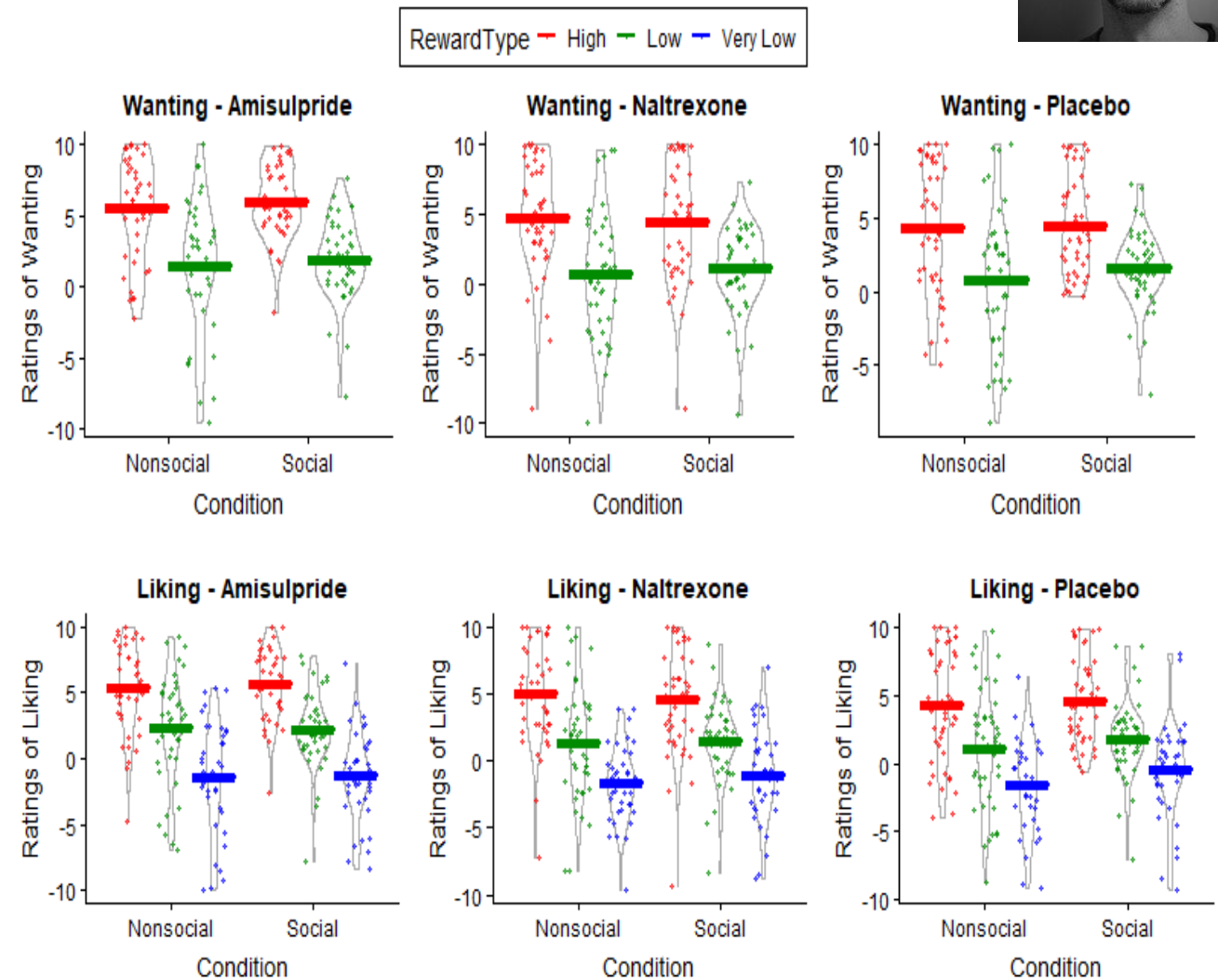


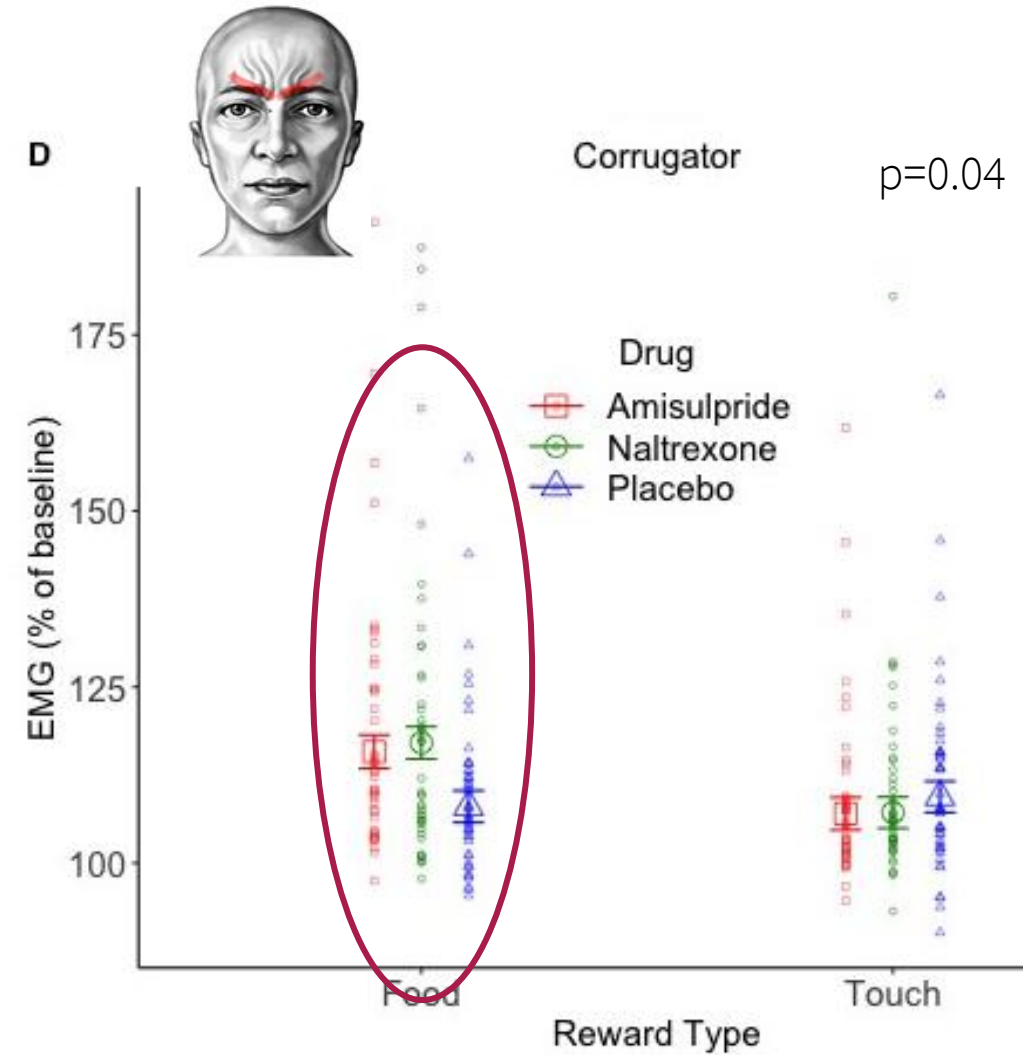
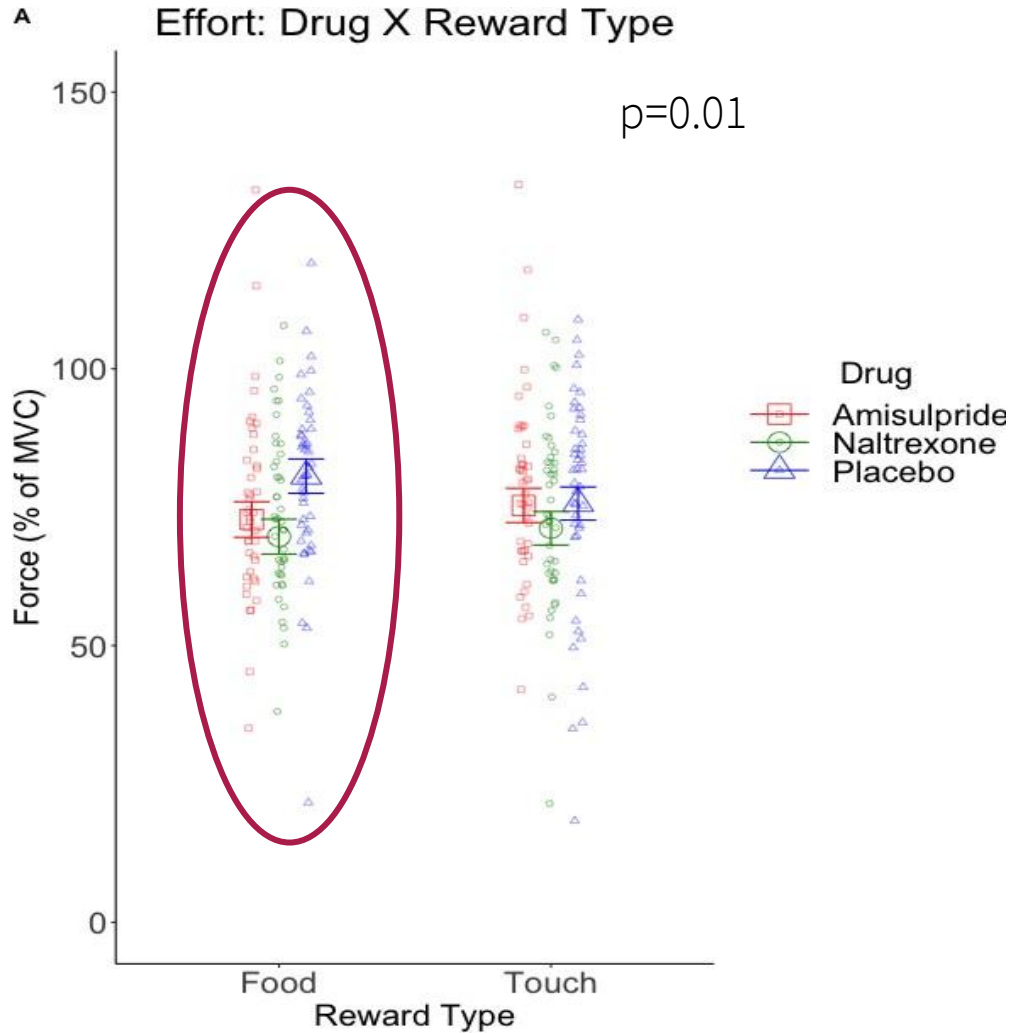
Test for different neurobiological regulation of social and non-social rewards

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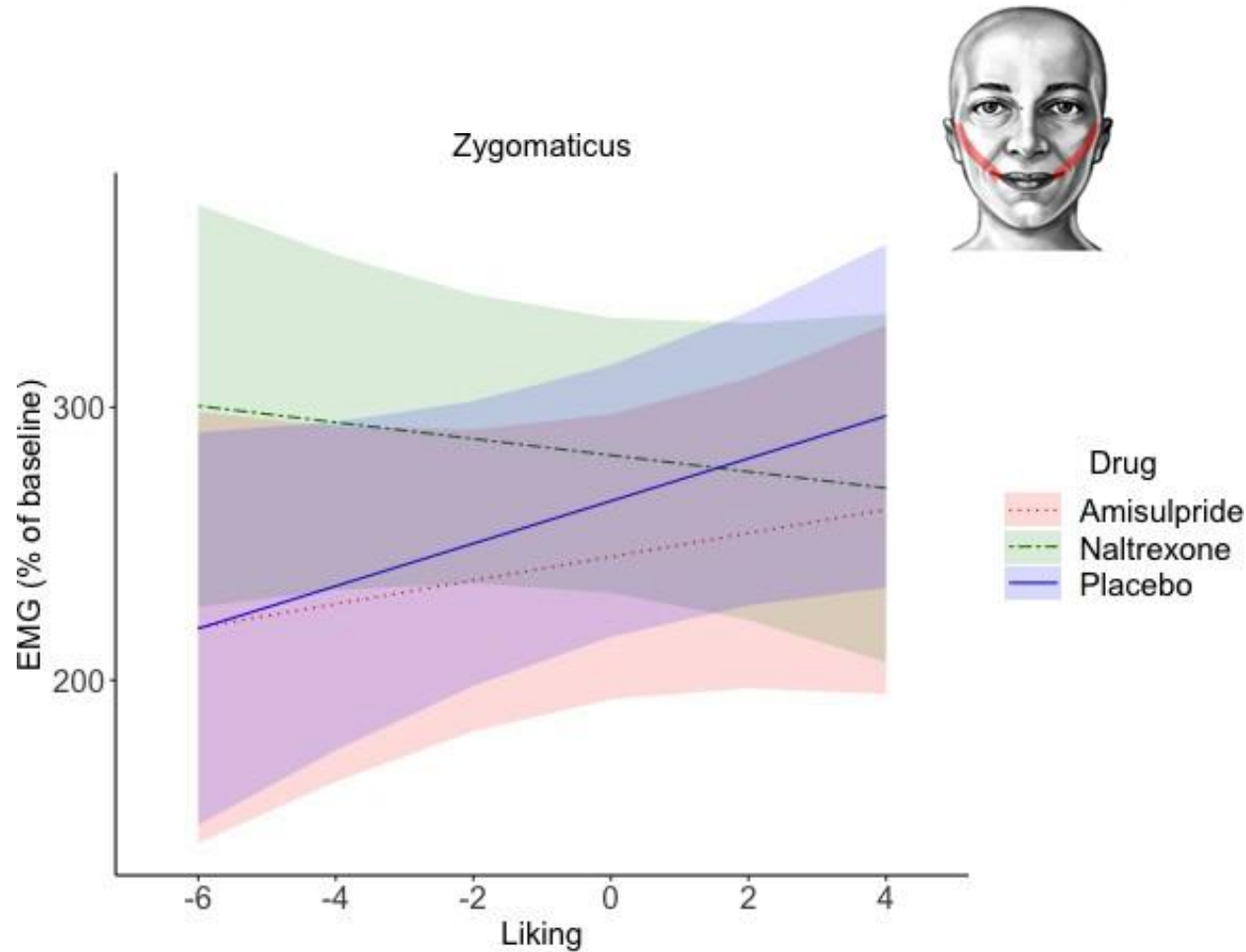


- 131 subjects ( 88 f, 43 m)
- age M = 23.36, SD = 3.6, range = 18-35
- Three groups:
  - Amisulpride 400mg (N=42, 28 f, 14 m)
  - Naltrexone 50mg (N=44 , 30 f, 14 m)
  - Placebo (N=45, 30 f, 15 m)





## PHARMACOLOGICAL STUDY



Partially different neurochemical regulation of wanting and liking of rewards

➡ In line with animal models of reward processing

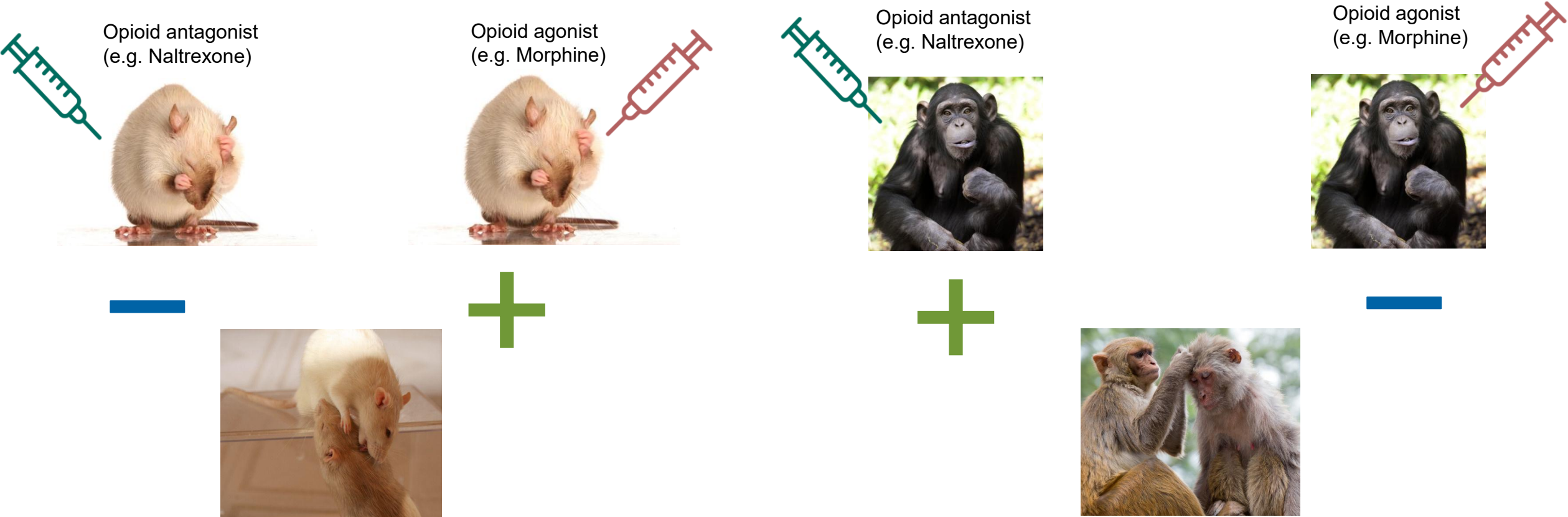
Partially different neurochemical regulation of social and nonsocial rewards

➡ Two separate systems that process different types of rewards?

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# STATE-DEPENDENT REGULATION OF REWARD



The State-dependent  $\mu$ -opioid Modulation of Social Motivation (SOMSOM) theory (Loseth et al. 2014)



## STATE-DEPENDENT REGULATION OF REWARD

### aversive motivation



### appetitive motivation



Reward

Negatively reinforced (reduction of negative state)

Positively reinforced (gain of pleasure) (Loseth et al., 2014)

# STATE-DEPENDENT REGULATION OF REWARD



101 participants (females)

- Aversive group (AV): n = 33
- Appetitive group (AP): n = 34
- Control group (CO): n = 34

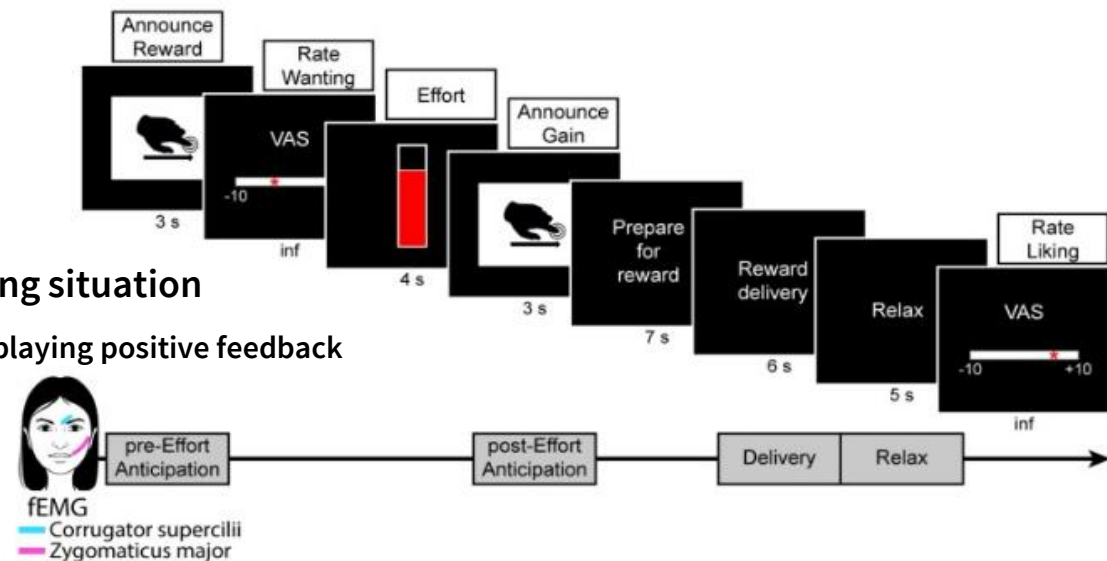


Participants come to the study with a same-gender close friend

① AV → TSST → induction of negative affect and stress  
speech and math task in front of a committee displaying negative feedback

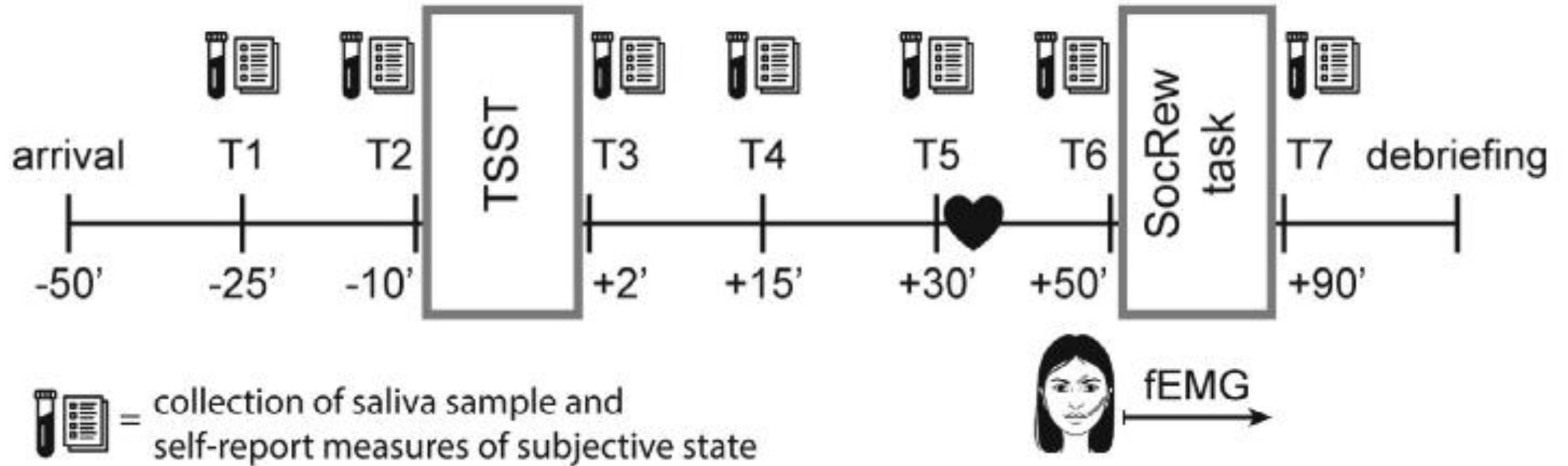
② AP → friendly TSST → induction of positive affect by means of a challenging situation  
speech and modified math task (increasing difficulty) in front of an engaged committee displaying positive feedback

③ CO → placebo TSST → control condition  
speech about favorite book and easy math task alone in the room



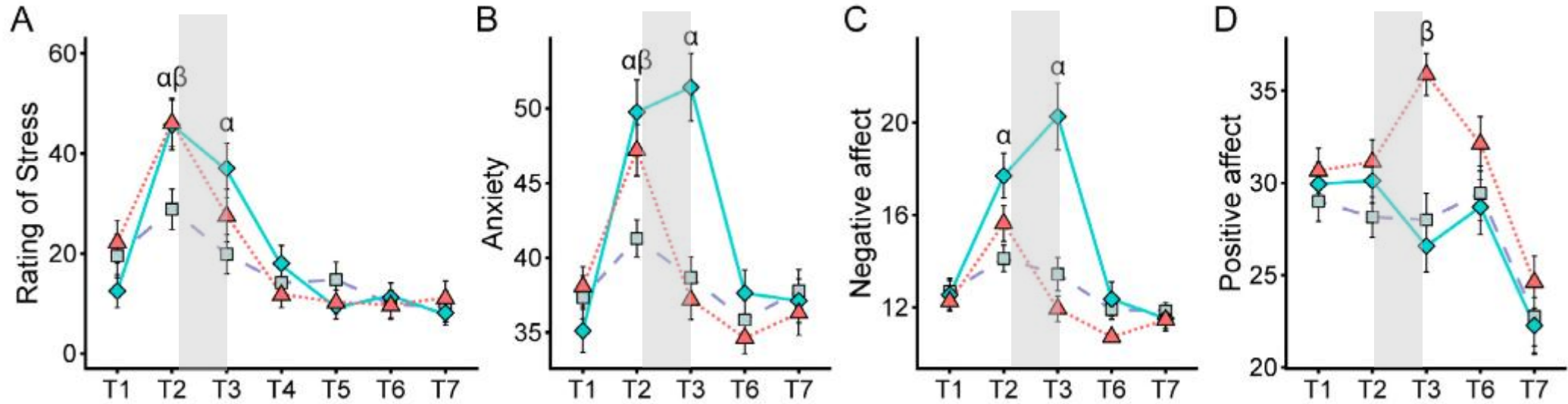


## STATE-DEPENDENT REGULATION OF REWARD



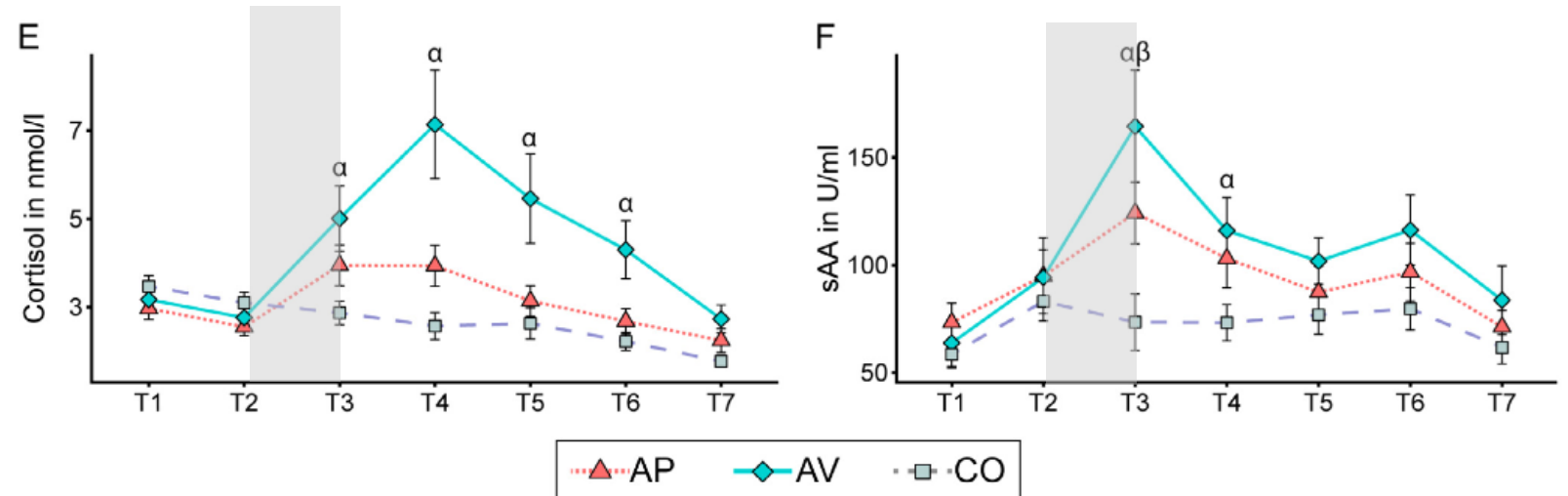


# RESULTS



Salivary Cortisol

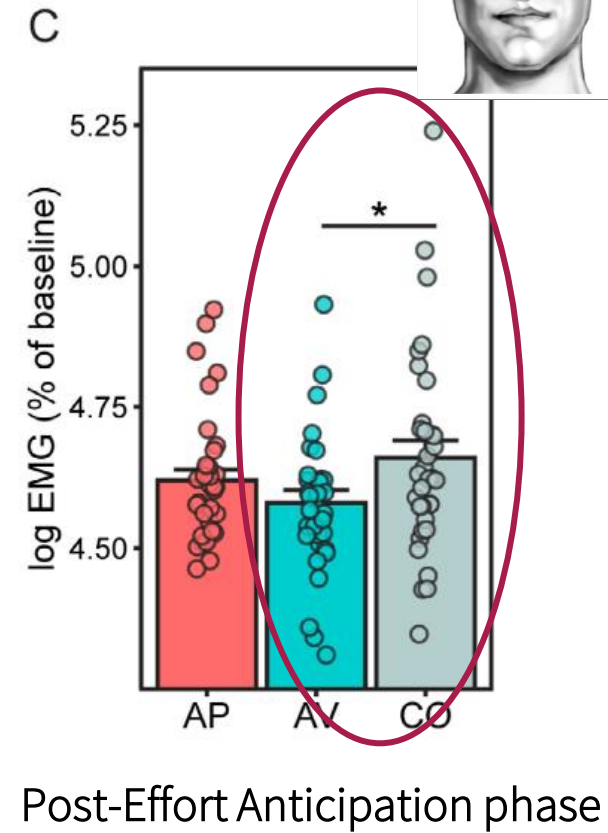
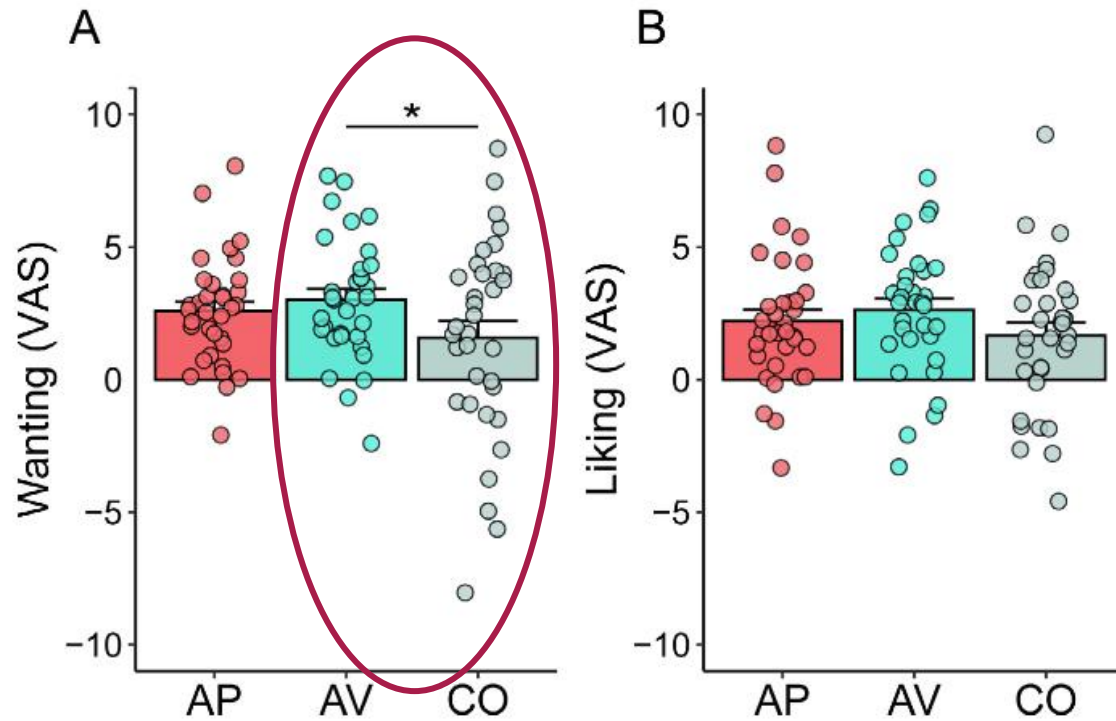
Salivary alpha amylase



$\alpha$  = sig. diff. AV vs. CO

$\beta$  = sig. diff. AP vs. CO

## RESULTS

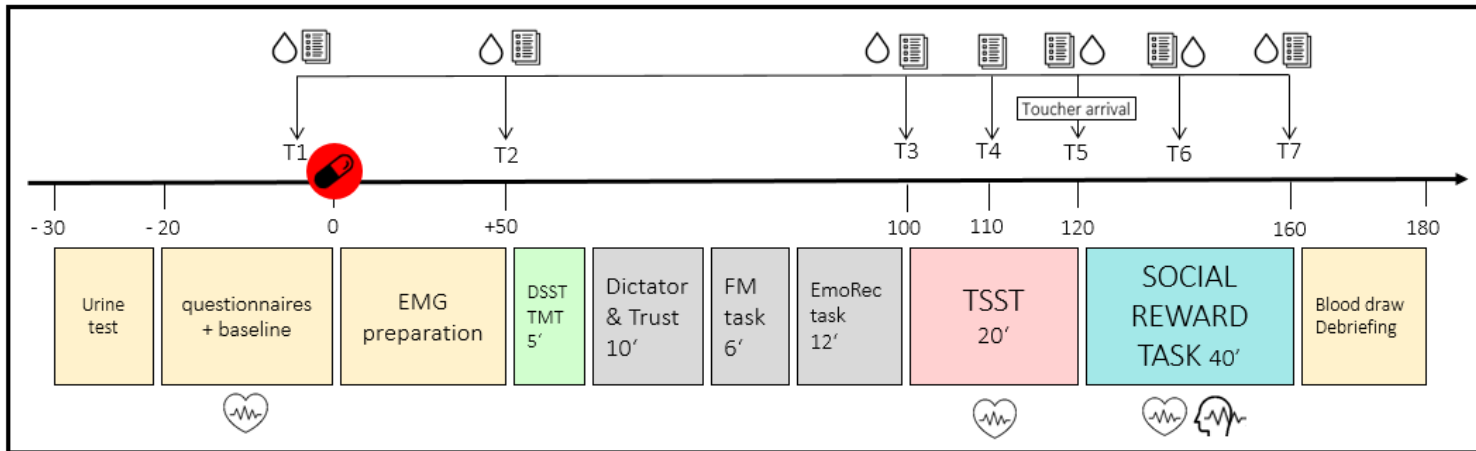
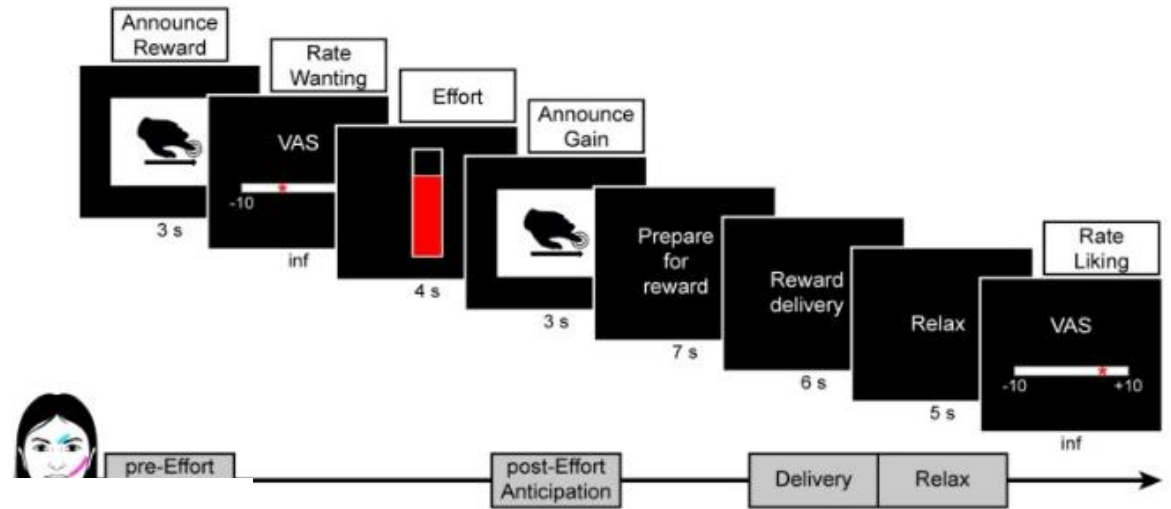




# STATE-DEPENDENT REGULATION OF REWARD

N = 82 healthy females (aimed sample size 80, 40/group)  
in luteal phase

- 40 administered with placebo (60mg mannitol)
- 42 administered with 10mg morphine (Morapid)



💧 = saliva sample collection

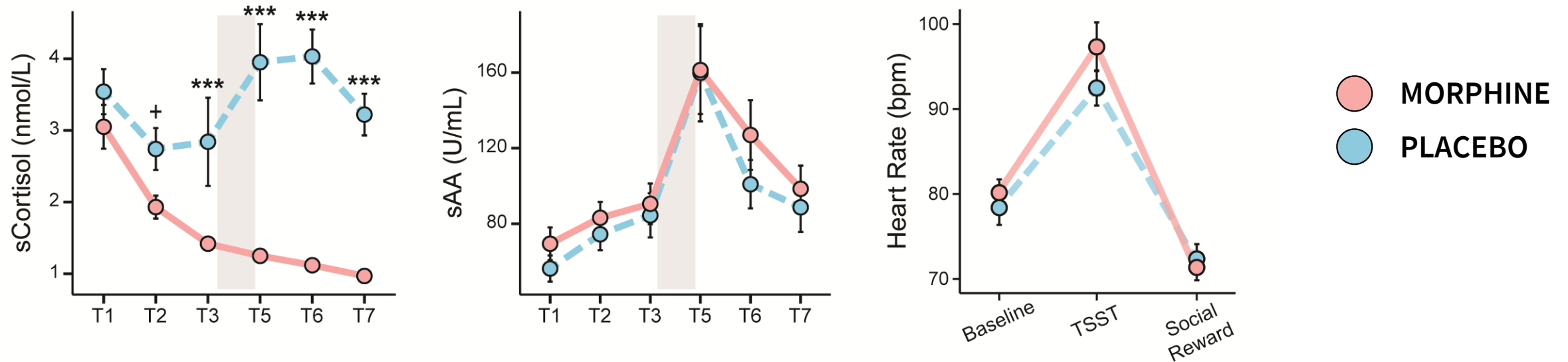
📄 = self-report subjective measures

💓 = heart rate recording

🧠 = facial EMG

## RESULTS

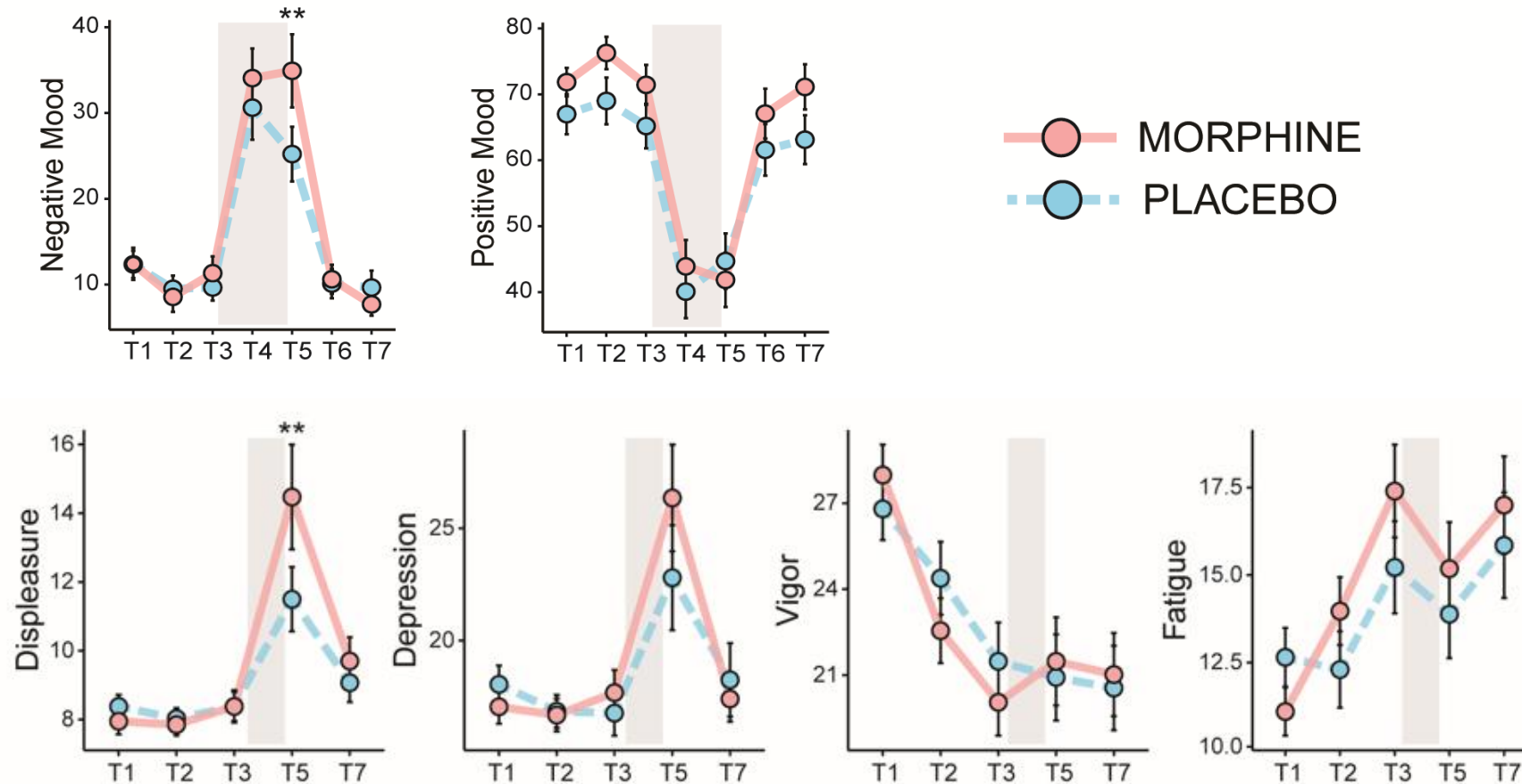
(\*  $p < .05$ ; \*\*\*  $p < .001$ ).



Morphine suppressed reactivity of the HPA axis (cortisol) to stress, but did not affect ANS (heart rate and alpha-amylase) response (*in line with Bershad et al., 2015; 2018*)

# RESULTS

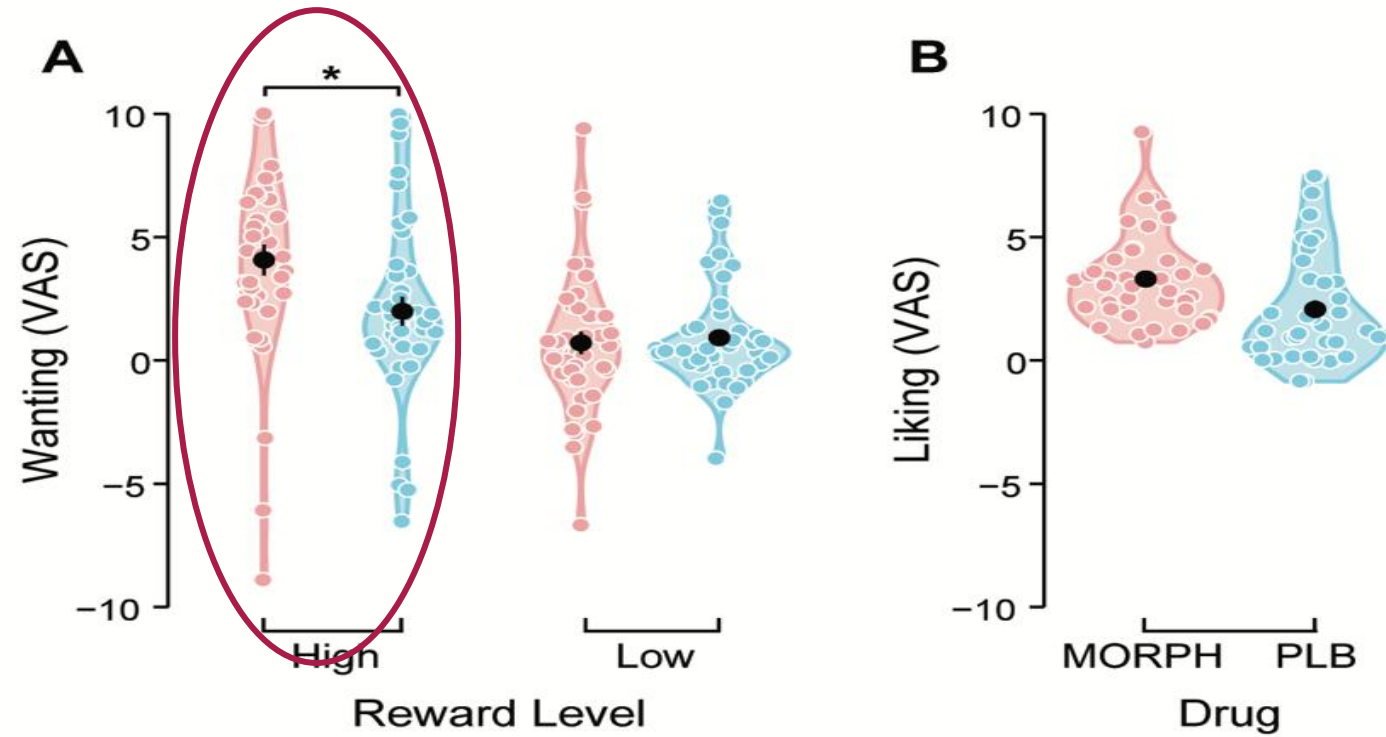
(\*\*  $p < .01$ ).



Morphine administration resulted in **greater negative response to stress** compared to placebo



## RESULTS



(\*  $p < .05$ ).

## CONCLUSION

Two main findings:

- 1) morphine increased the subjective negative response stress, possibly due to blockade of the normal physiological reaction
    - Previous studies found similar blocking of cortisol response after high dose of mu opioid agonist (hydromorphone and buprenorphine, *Bershad et al. 2015, 2018*) but no effects on subjective stress response
    - → There are quite some evidence showing that opioids not always make us feel better (*Wagner et al., 2010*: Remifentanyl increases dysphoria; *Lasagna et al., 1995*: morphine/heroin → feeling bad and dysphoria)
  - 2) The enhanced negative reaction following morphine administration, resulted in enhanced wanting of high social reward (CT optimal touch) → in line with previous research on stress (and with our previous study *Massaccesi et al., 2021*)
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An intact (social) motivational system is fundamental for typical development.

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*Trends Cogn Sci.* 2012 April ; 16(4): 231–239. doi:10.1016/j.tics.2012.02.007.

## The Social Motivation Theory of Autism

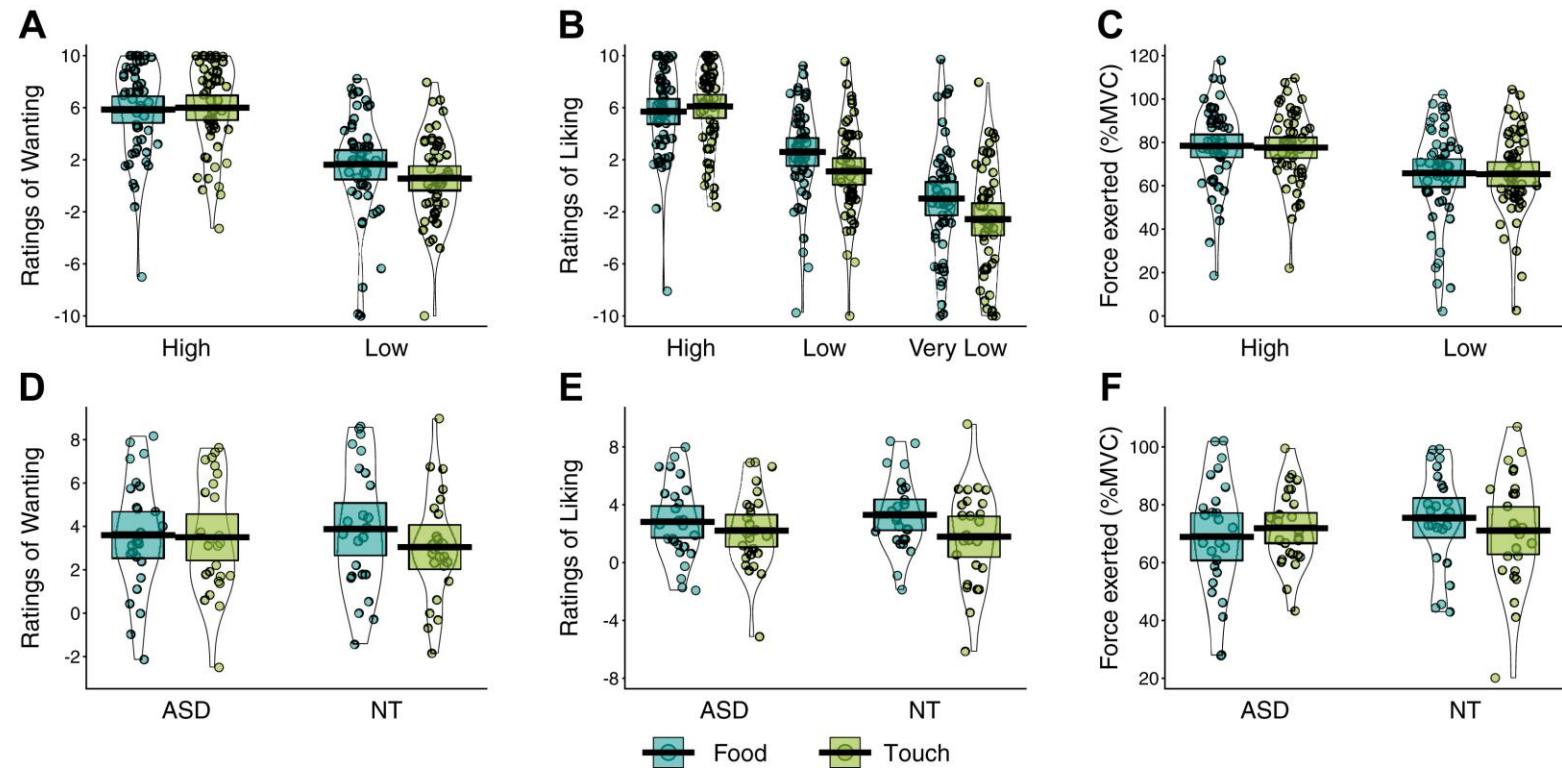
C. Chevallier<sup>1,\*</sup>, G. Kohls<sup>1</sup>, V. Troiani<sup>1,2</sup>, E.S. Brodtkin<sup>3</sup>, and R.T. Schultz<sup>1</sup>

<sup>1</sup>Center for Autism Research, Children's Hospital of Philadelphia, 3535 Market Street, Philadelphia, PA 19104, USA

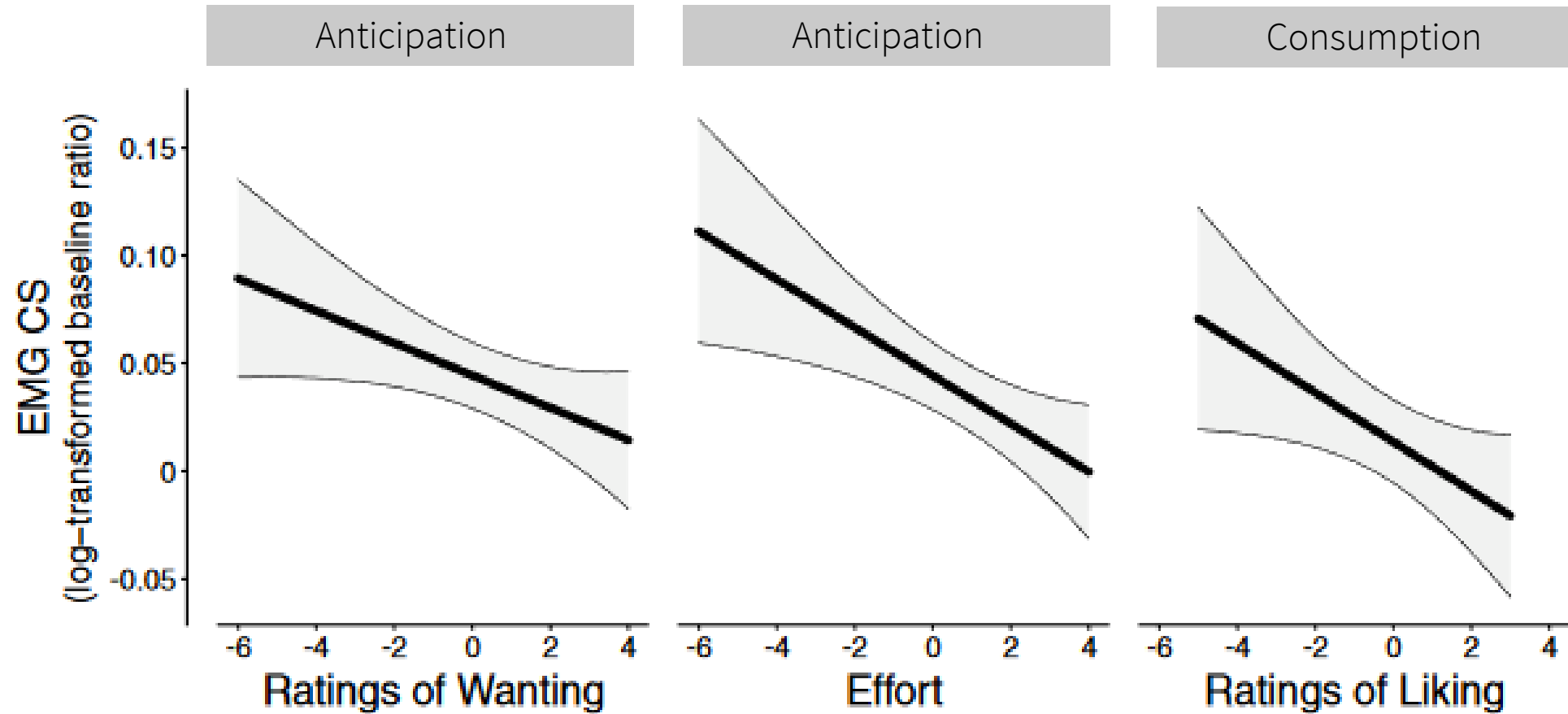




- 25 ASD subjects ( 12 f, 13 m)
  - age M = 33.2, SD = 12.19, range = 18-57
- 25 NT subjects ( 13 f, 12 m)
  - age M = 34.9, SD = 12.13, range = 20-60



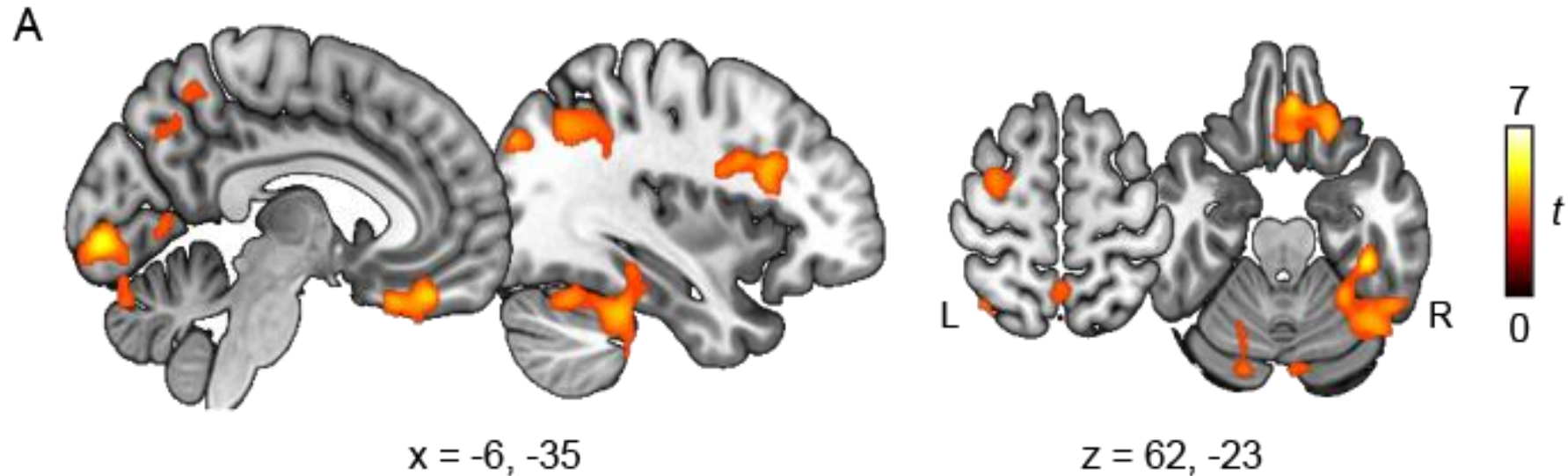
# CLINICAL fMRI STUDY



# CLINICAL fMRI STUDY: whole brain analysis

## ANTICIPATION

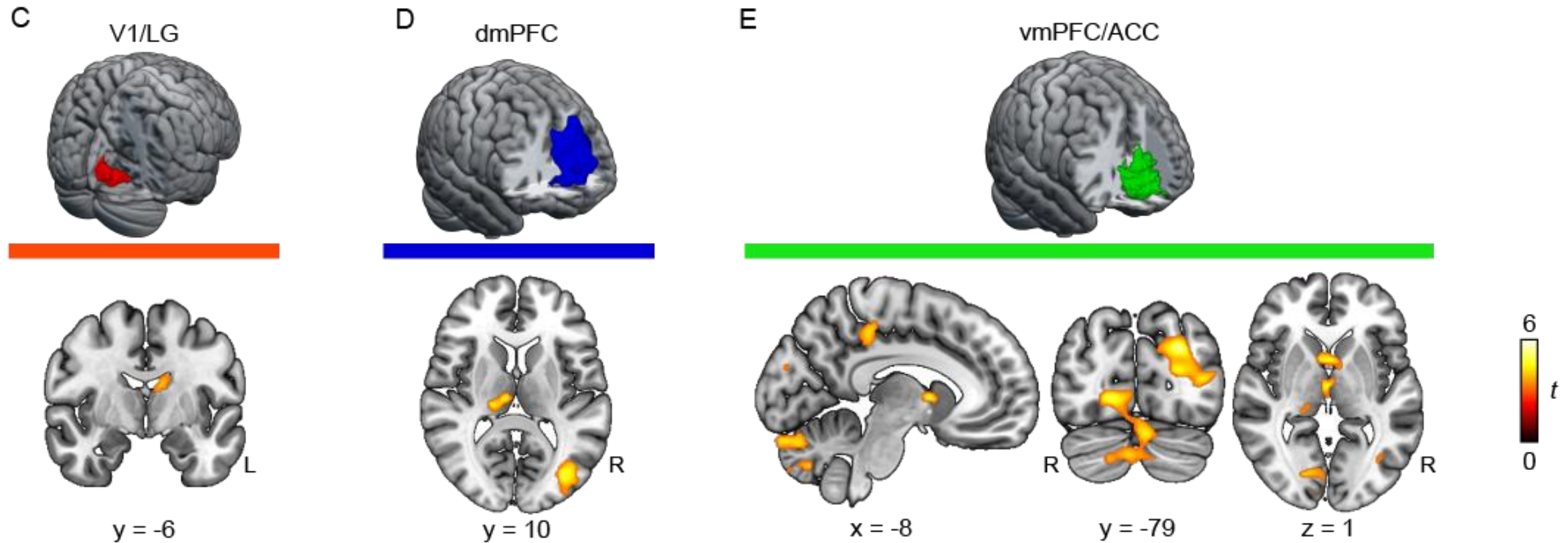
ASD > NT for High > Low rewards



# CLINICAL fMRI STUDY: PPI analysis

## ANTICIPATION

ASD > NT for High > Low rewards



# INTERIM DISCUSSION

1) No differences in subjective wanting, liking, effort and facial EMG to social and nonsocial rewards in ASD

- ➡ in line with recent findings suggesting intact subjective hedonic responses to touch (Perini et al. 21, Kaiser et al. 19)
- ➡ new evidence of intact motivation and facial reactions to interpersonal touch

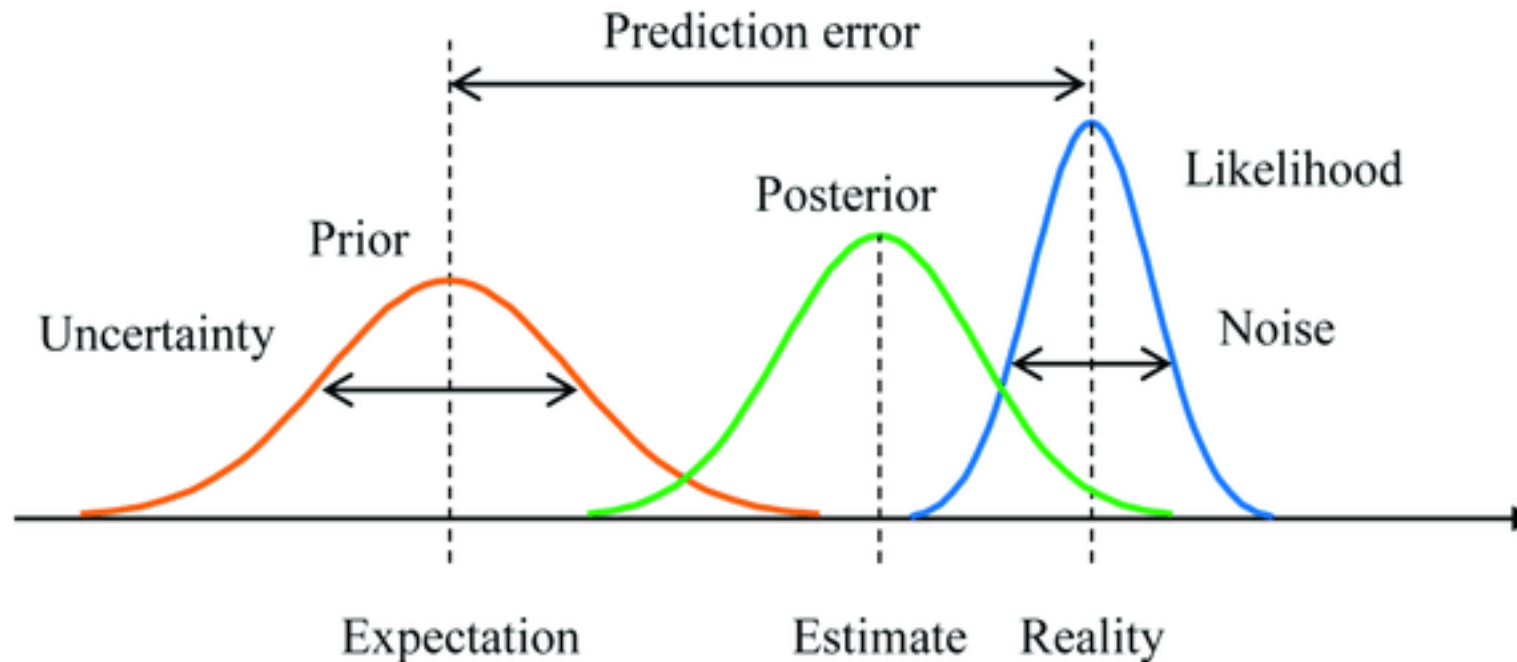
2) Different neural activity during reward anticipation in ASD

- ➡ widespread brain activations independently of reward type, and stronger connectivity between sensory and visual regions and prefrontal regions, possibly suggesting **over-processing** of such information



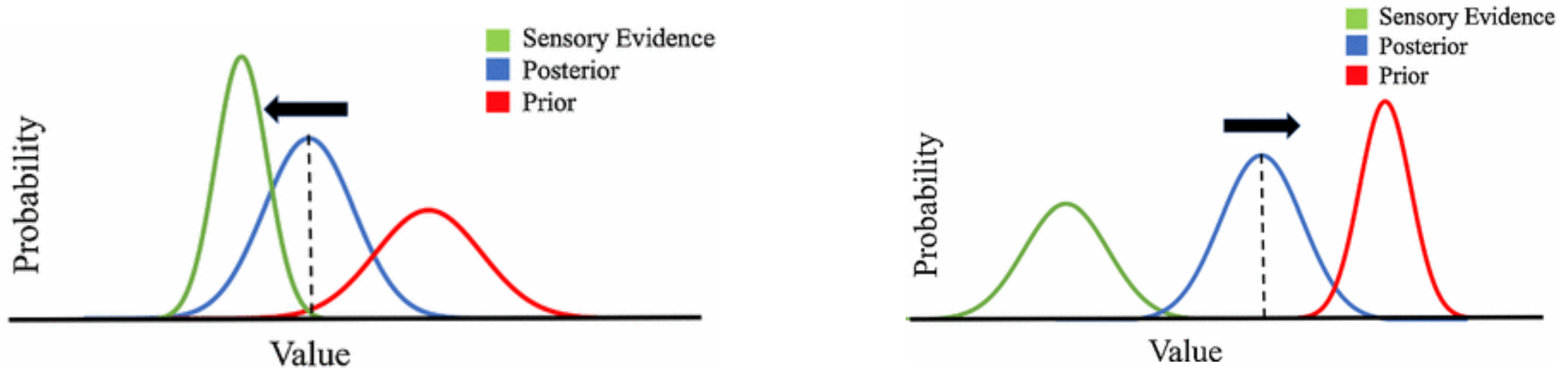
## PREDICTIVE PROCESSING IN AUTISM

Our brains generate a model of the world that predicts what we are going to see, hear, touch, smell and taste. The job of our senses is to check our predictions to make sure our inner model does not drift far from reality.



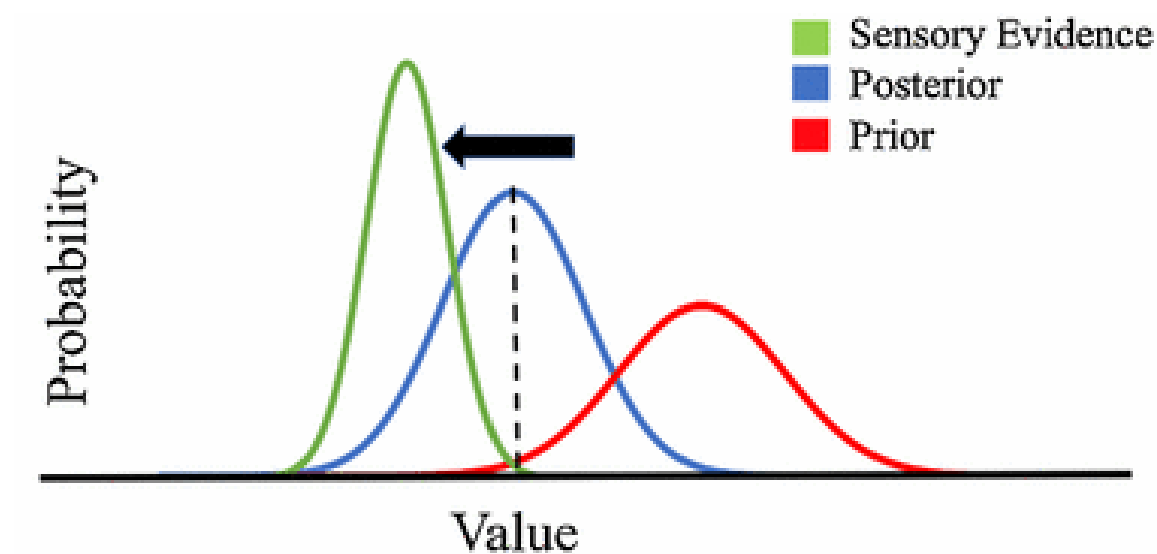
## PREDICTIVE PROCESSING IN AUTISM

‘Precision’ determines the weight the brain gives to discrepancies between sensory input and our expectations. When we learn something new, the brain dials up the precision and uses the input to form a model. When the brain judges that the model is complete, it dials down the precision, assuming that any further discrepancies are random variations that it can safely ignore.



## PREDICTIVE PROCESSING IN AUTISM

In autism, the brain may not form accurate predictions of imminent experiences, or even if it does, sensory input may override those predictions. The brain is slower to recalibrate precision. It remains attuned to details but finds it harder to generalize.



# Reward processing and anorexia nervosa

- In healthy humans and animals hunger leads to:
  - Increased reward sensitivity and approach motivation
- AN is characterized by dietary restriction despite reduced energy stores
  - Eating disorders reflect the discrepancy between one's physical need to eat and the motivational drive to eat
  - High level of social anhedonia, and preliminary evidence of interpersonal touch dysregulation





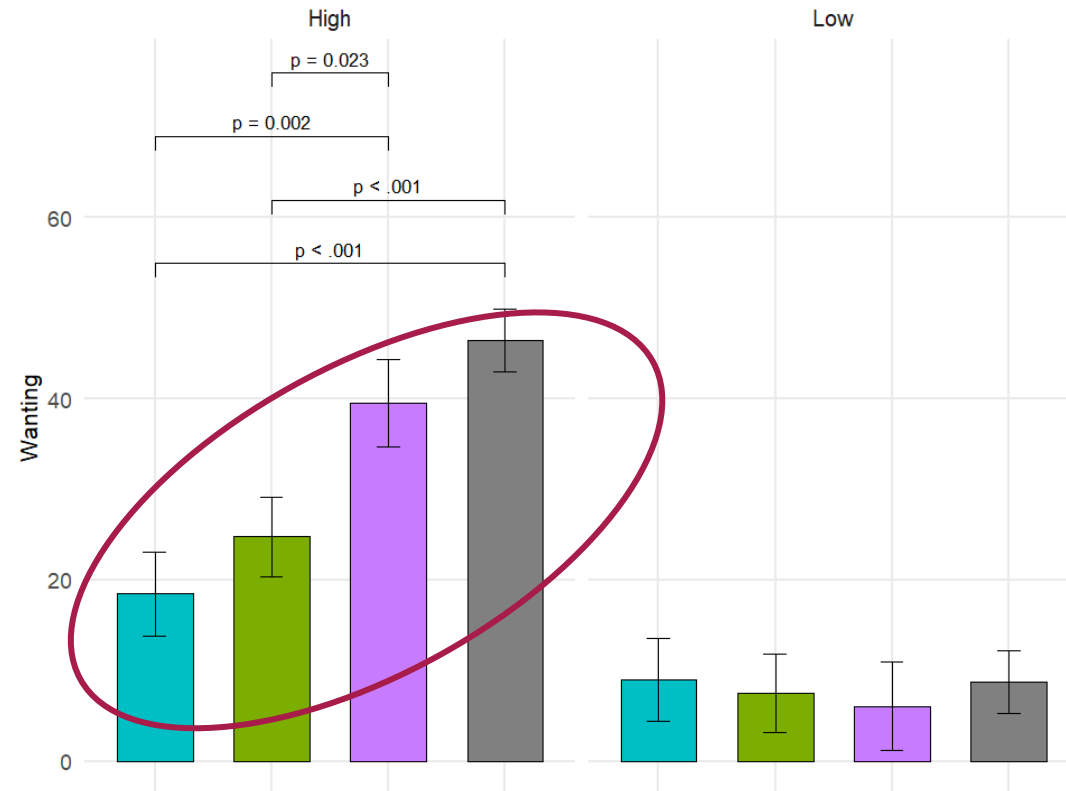
# Sample

- **AN group:** N = 99, 12-30 years (Age, y: 19.4 (SD: 3.7), BMI: 19.3 (SD: 2.5)), female, AN diagnosis
- **Control group:** N = 54, 12-30 (Age, y: 19.2 (SD: 3.8), BMI: 20.9 (SD: 2.5)), female, no psychiatric diagnosis

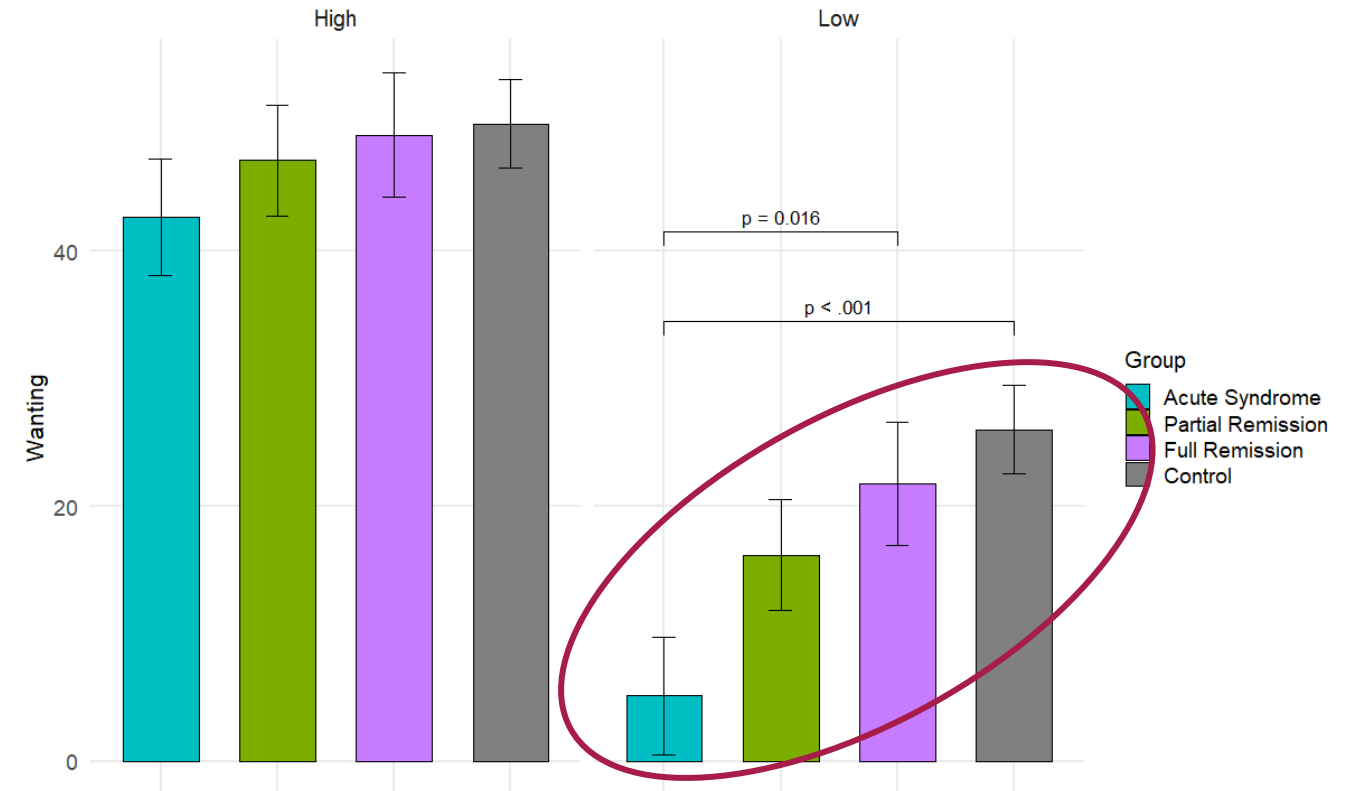
| Group             | Count | Mean BMI   | Mean Age   |
|-------------------|-------|------------|------------|
| Acute AN          | 34    | 16.4 ± 2.3 | 17.2 ± 3.0 |
| Partial Remission | 36    | 20.9 ± 2.6 | 20.6 ± 3.6 |
| Full Remission    | 29    | 21.0 ± 2.7 | 20.6 ± 3.4 |
| Control           | 54    | 20.9 ± 2.4 | 19.2 ± 3.8 |

# Behavioral Outcomes

## Wanting Food



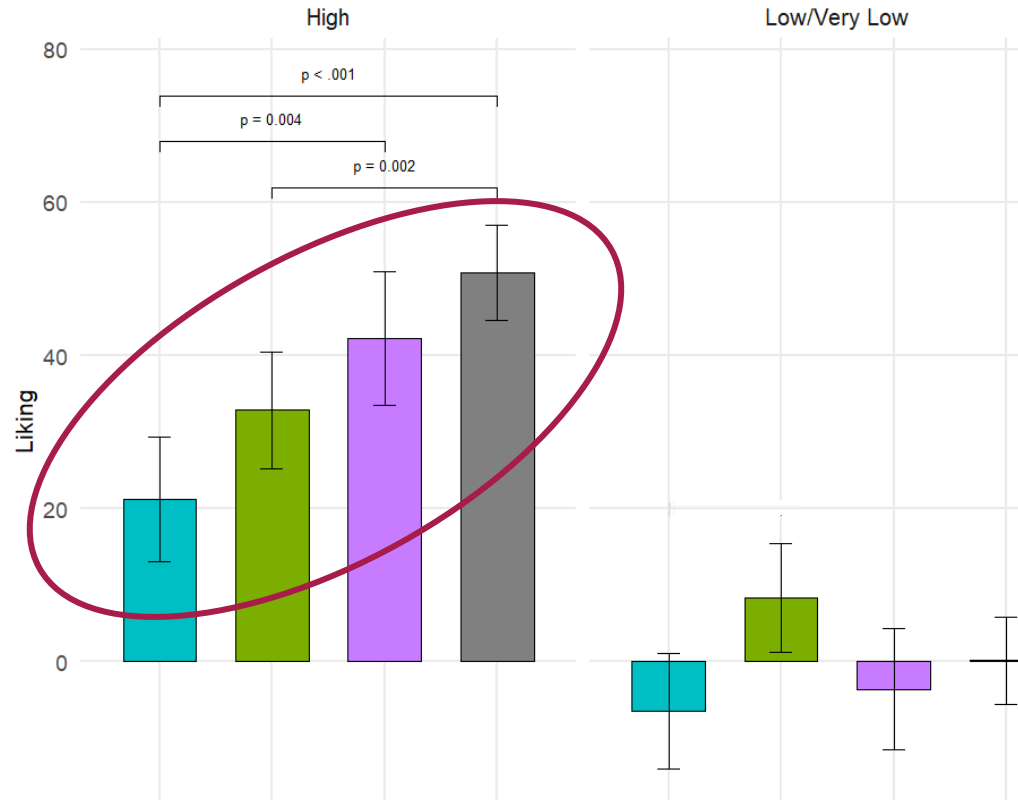
## Wanting Touch



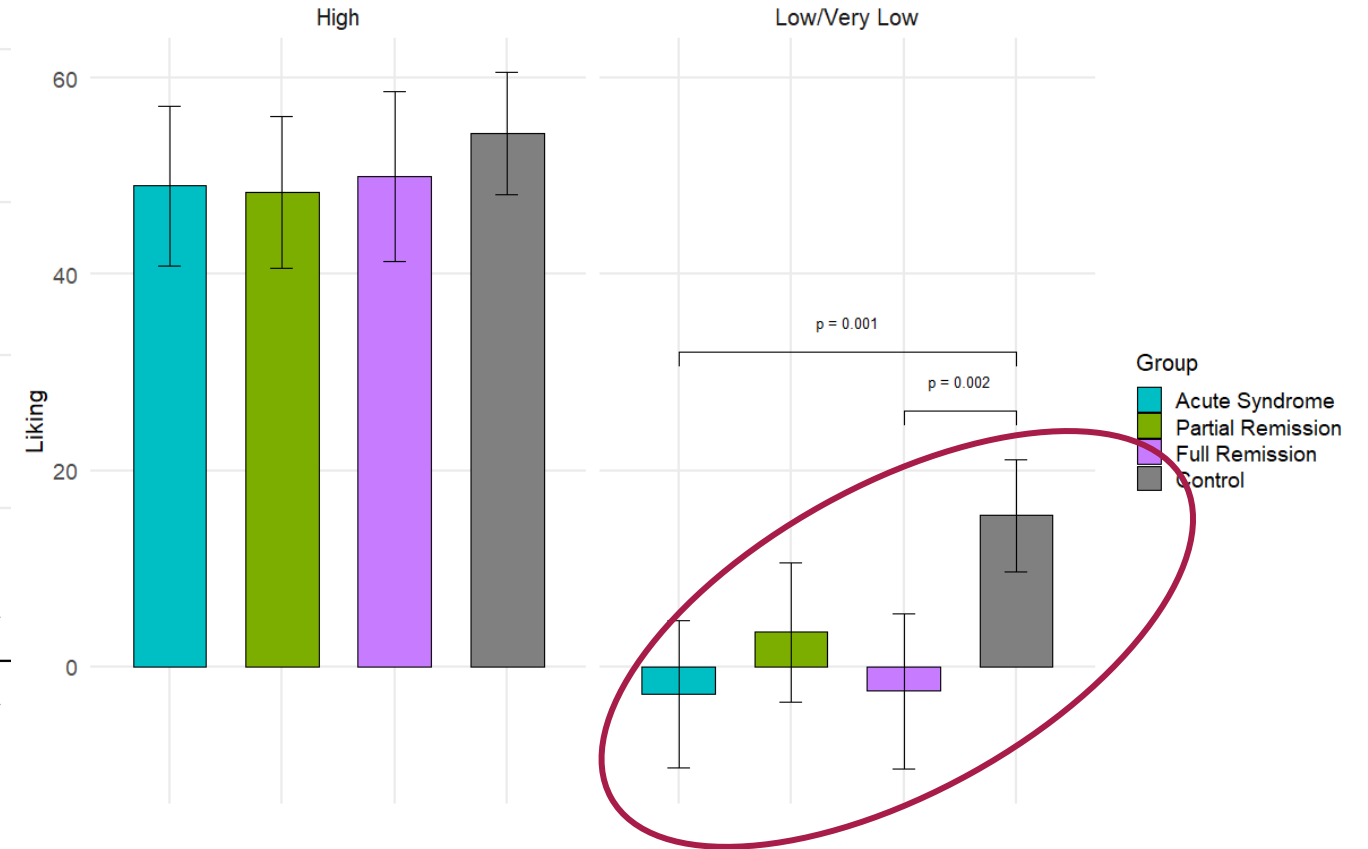
Three-way-interaction: Reward Type x Group x Announced Reward:  $F(3, 9272) = 38.3, p < .001$

# Behavioral Outcomes

Liking Food



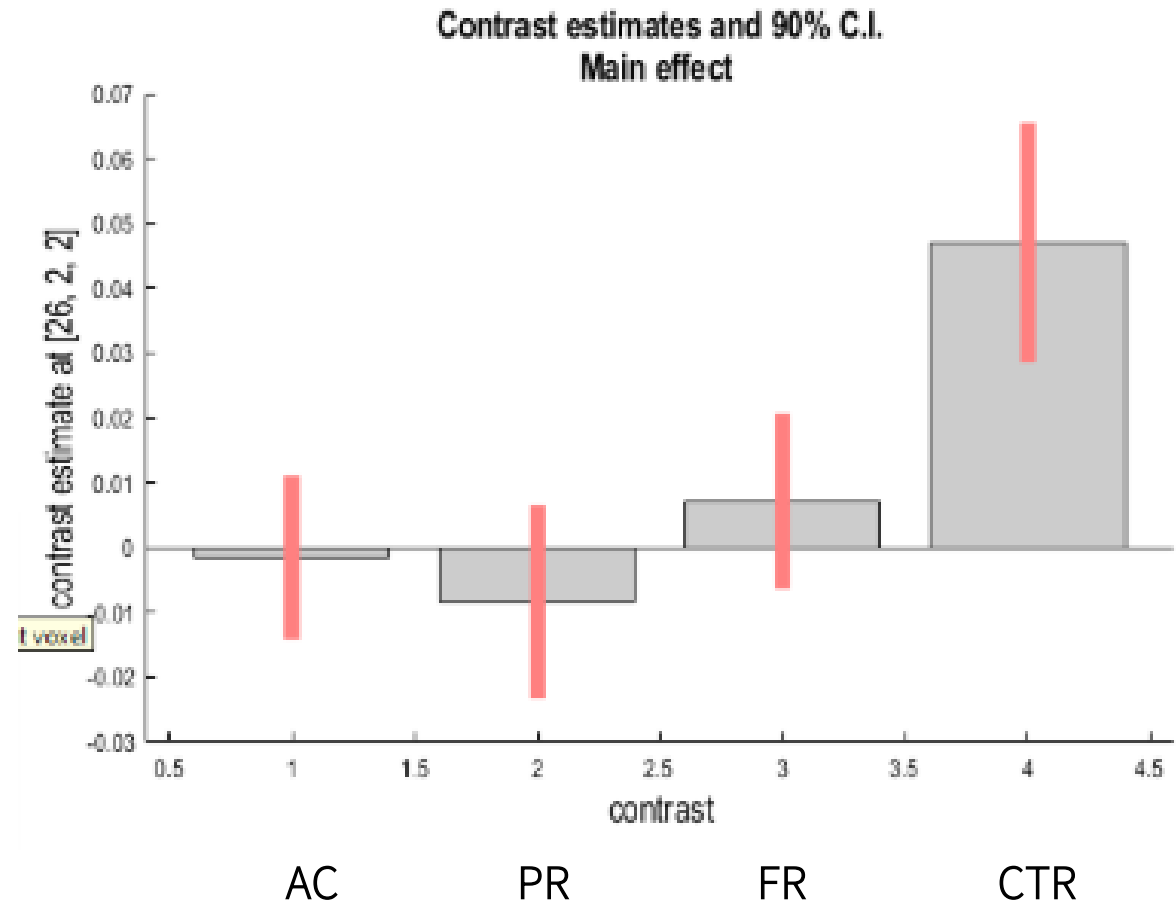
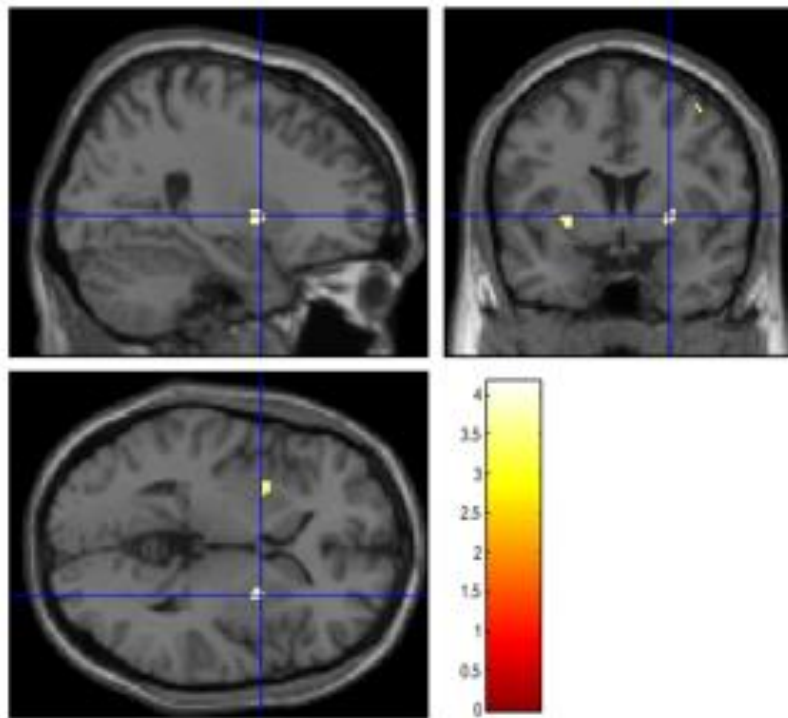
Liking Touch



Three-way-interaction: Reward Type x Group x Obtained Reward:  $F(3, 9289) = 24.1, p < .001$

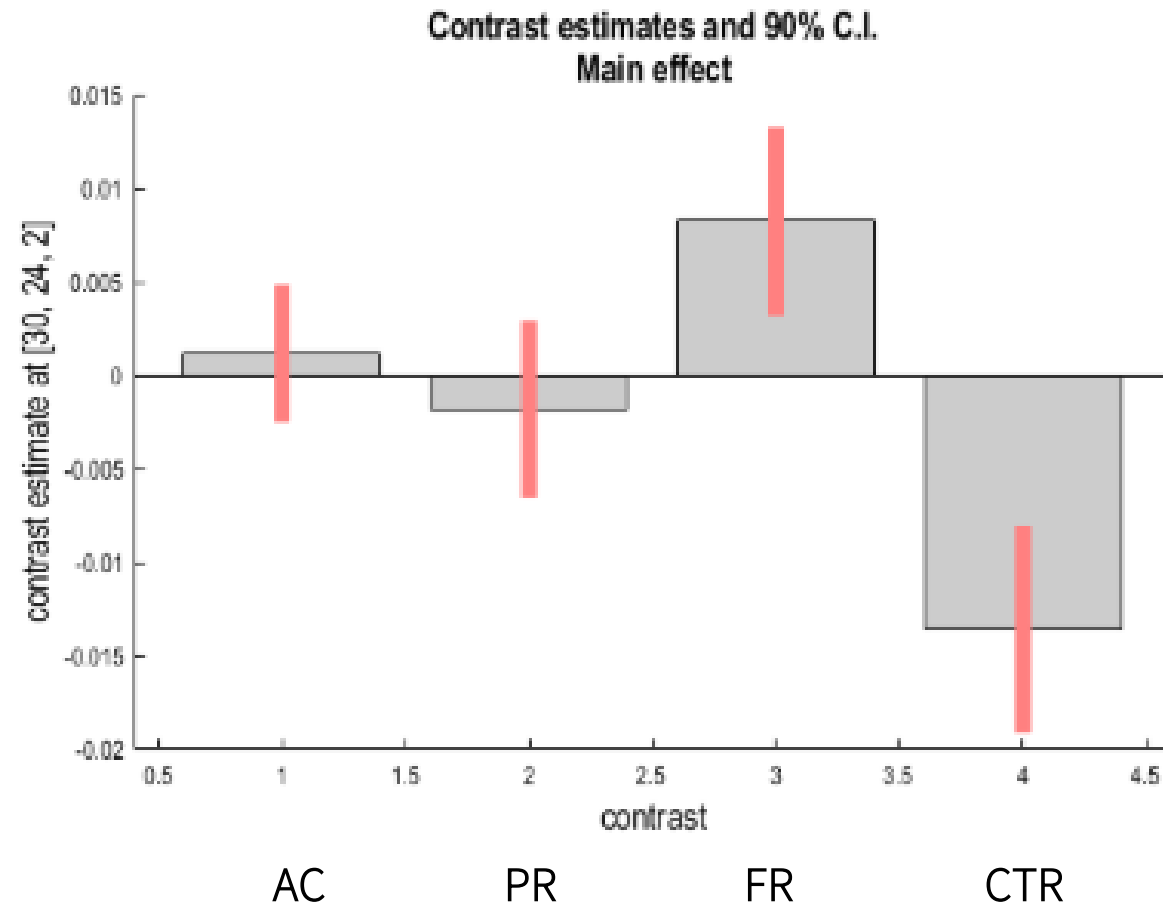
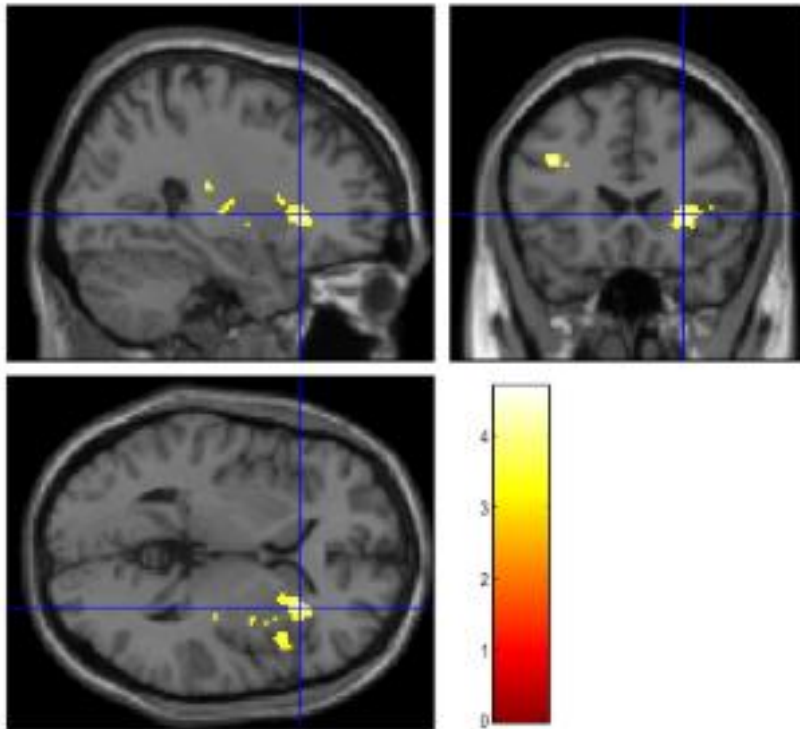
# fMRI Outcomes

Food anticipation High vs. Low rewards



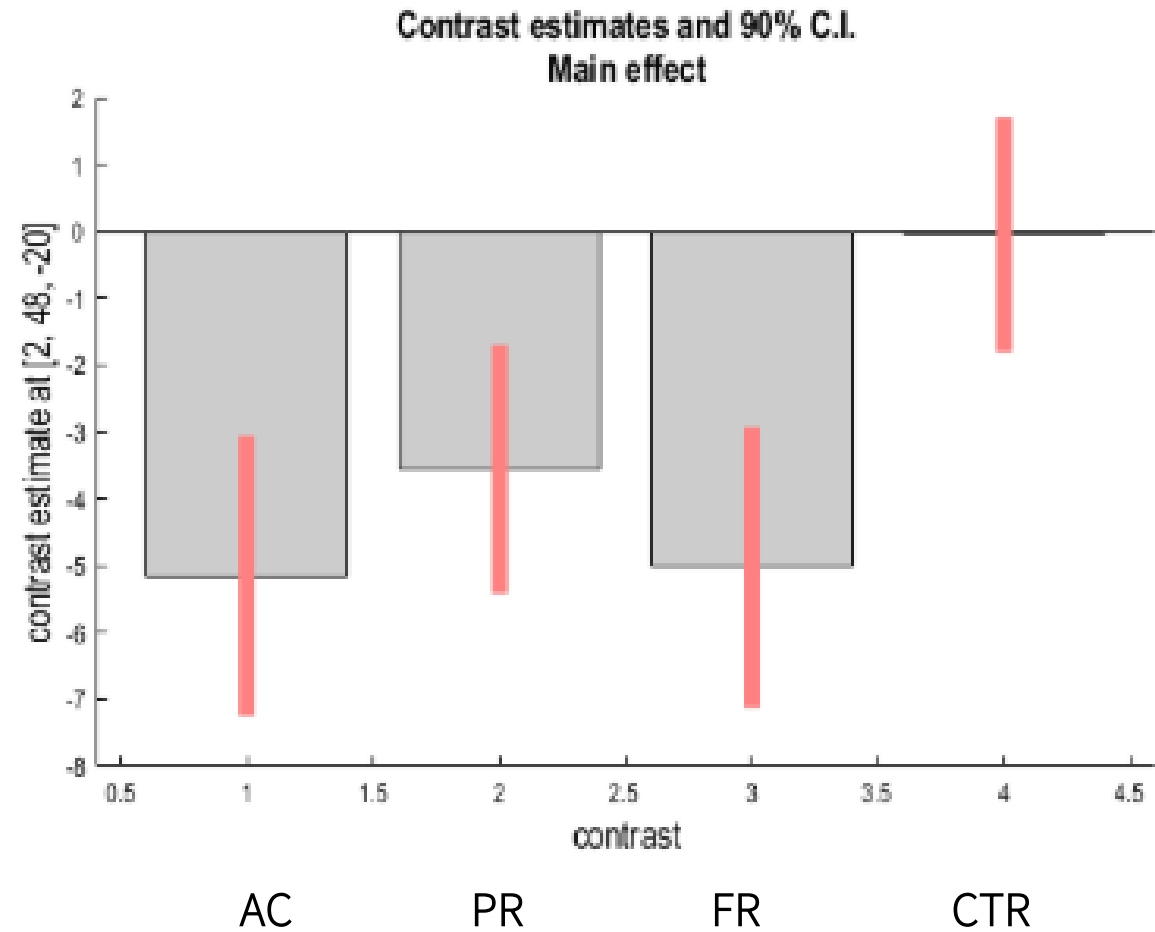
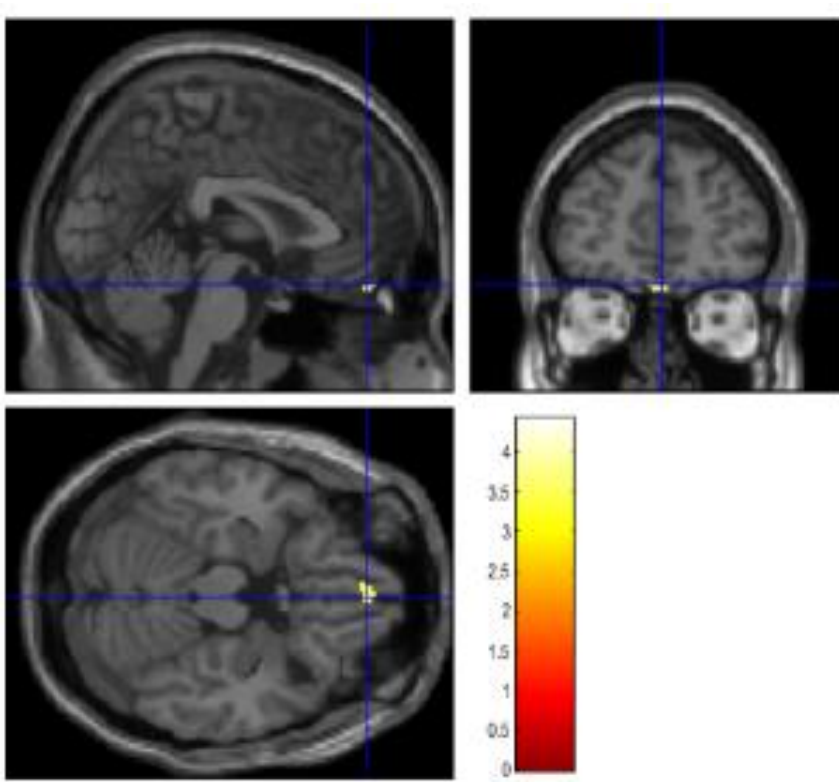
# fMRI Outcomes

Food consumption High vs. Low rewards



# fMRI Outcomes

Touch anticipation and consumption MAIN EFFECT



# Conclusion

- Participants with AN show **differences in the processing of social and non-social rewards** compared to controls, which means that alterations in reward processing may not be disorder specific
- Even fully remitted AN participants show significant differences in wanting and liking of social and non-social rewards compared to controls, suggesting that this may be a **chronic alteration** through the disorder
- These results point to the need for further research to better understand the relationship between stage of illness, and social and non-social rewards processing, to be able to create **individual treatment concepts**



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THANK YOU

