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# Tactile prediction errors in patients with Complex Regional Pain Syndrome (CRPS).

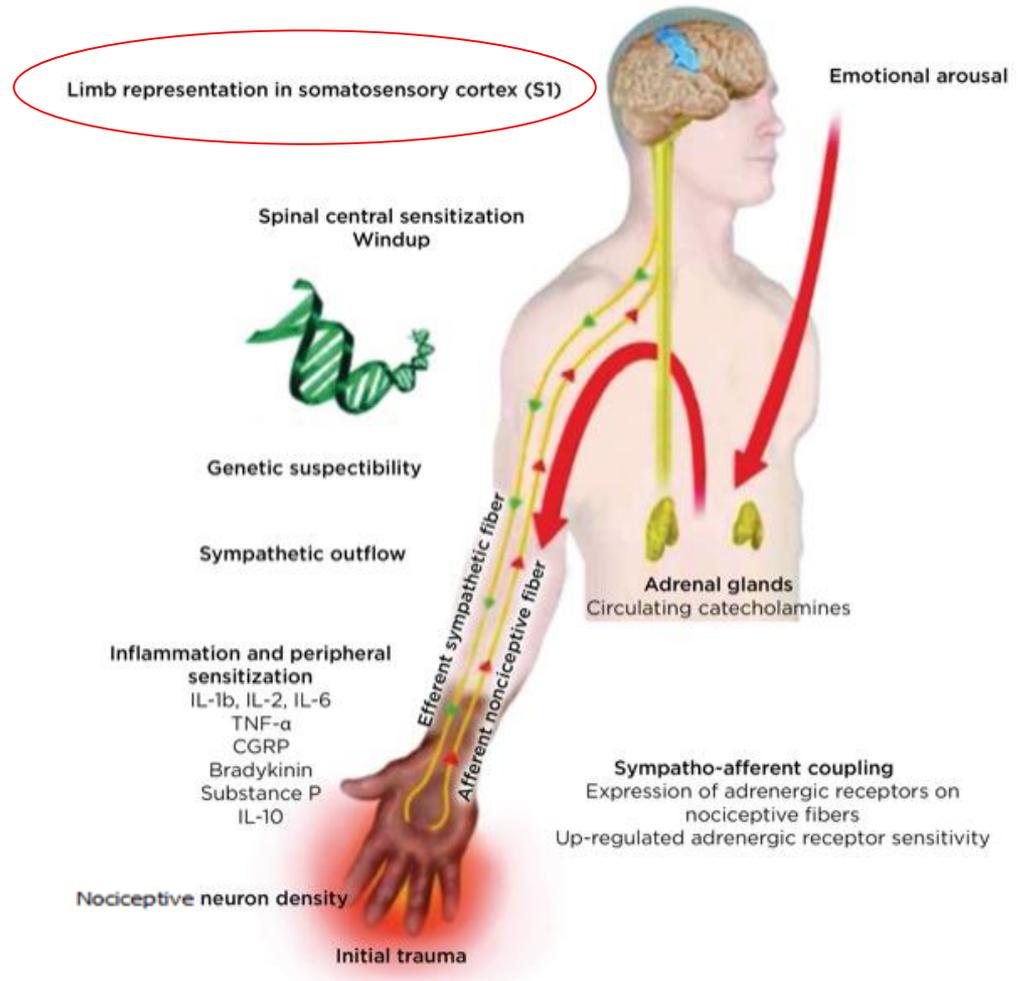
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# Complex Regional Pain Syndrome (CRPS)

- CRPS has variable signs and symptoms – a diagnosis of exclusion
- Pathophysiology is complex and variable between patients
- A range of biomarkers are needed to support patient stratification and improve diagnostic certainty

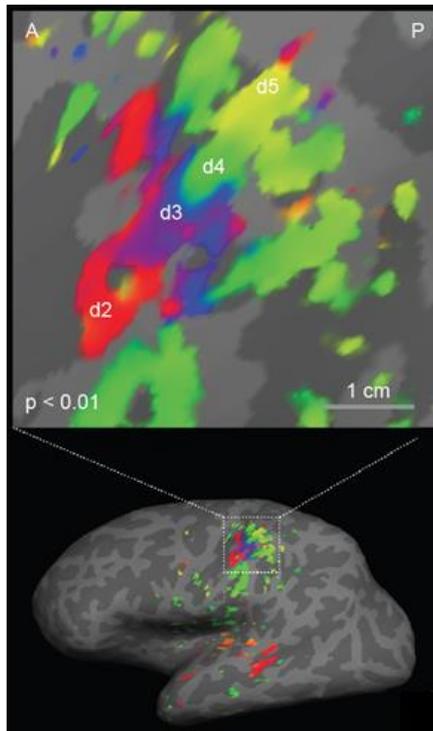


# Tactile-spatial processing in the brain

## Somatosensory homunculus

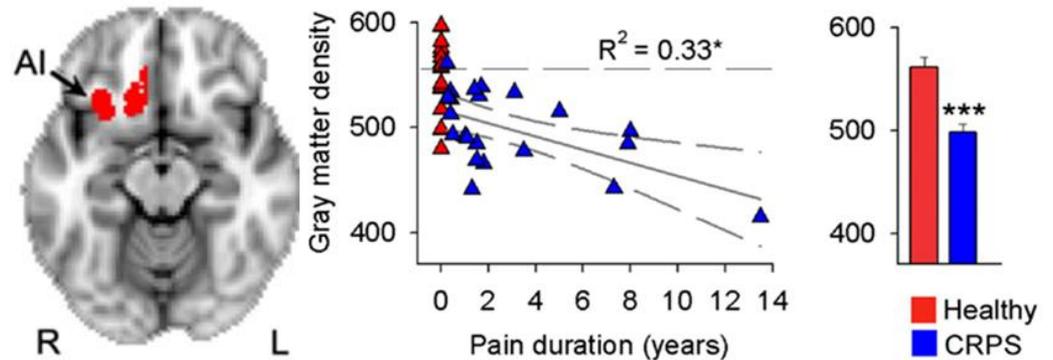
- fMRI studies find no difference

e.g. Mancini et al. 2018



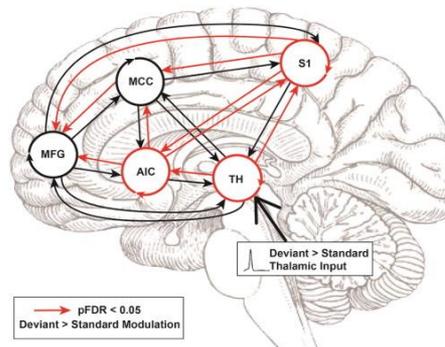
## Grey matter density (Geha et al., 2008)

- Smaller in CRPS > HC in anterior insula (AI) / vmPFC



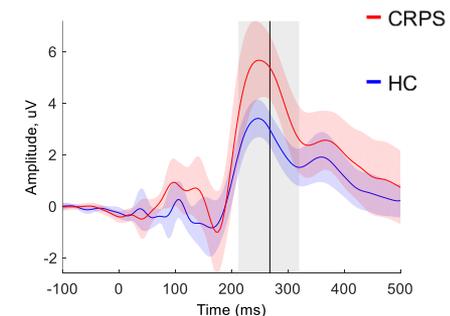
## Tactile “mismatch” responses

- Reciprocal insula-S1 connections (Allen et al., 2016)



## Late-latency somatosensory evoked potentials (SEPs)

- Larger in CRPS > HC when unexpected (Kuttikat et al., 2018)



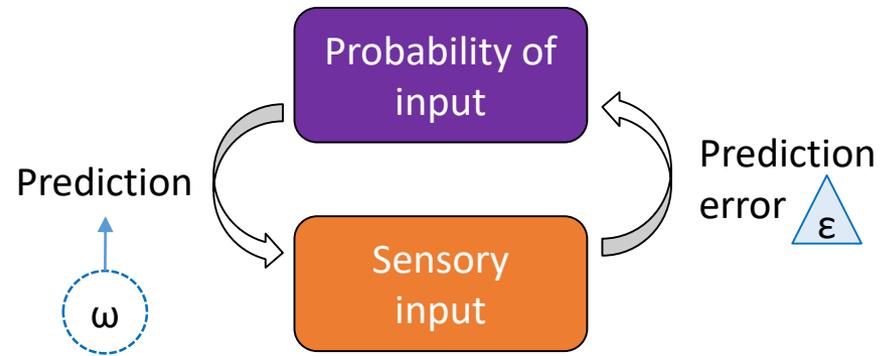
# The current study

## Aim

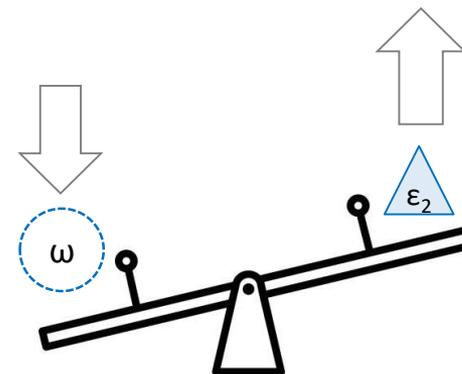
To identify *neural computations* underlying larger responses to unexpected tactile stimuli in patients with CRPS vs. healthy controls (HCs), using a *predictive coding model*

### Predicting coding model: simplified

- The brain tries to predict sensory inputs; must therefore contain representations of input *probabilities*
- Larger “mismatch” responses are thought to be *prediction errors*

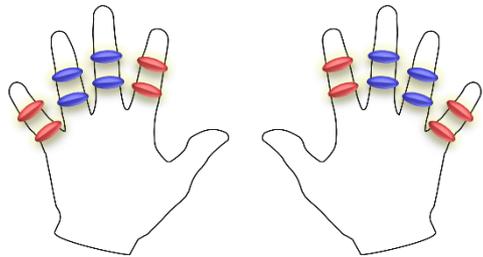


Greater *uncertainty in prediction* increases the *certainty (precision) of prediction error*



# Methods (CRPS n=22, HC n=22)

## Digit ring-electrode placement



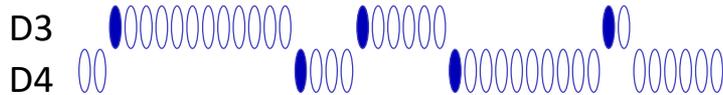
## Block types

		Change Distance (CD) →	
Change Probability (CP) ↓	CP = 10%	CP = 10% CD = 1	CP = 10% CD = 3
	CP = 30%	CP = 30% CD = 1	CP = 30% CD = 3
	CP = 50%	CP = 50% CD = 1	CP = 50% CD = 3

Behavioral response to digit change (response time)



## Example stimulus sequence

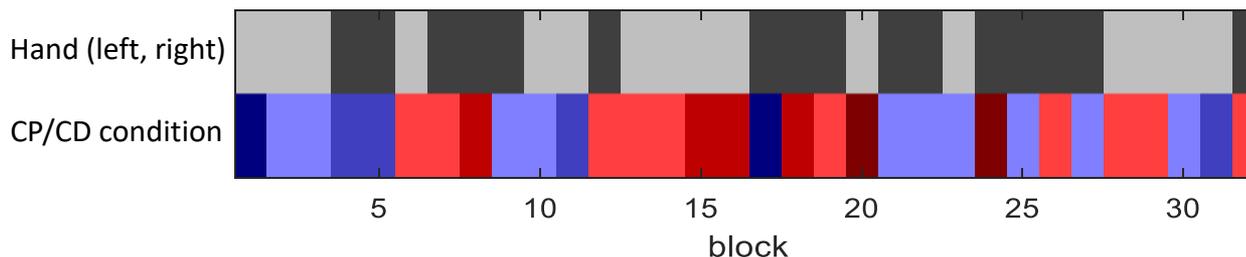


- Digit change (10%, 30% or 50% probability)
- No digit change (90%, 70% or 50% probability)

EEG (somatosensory-evoked potentials)

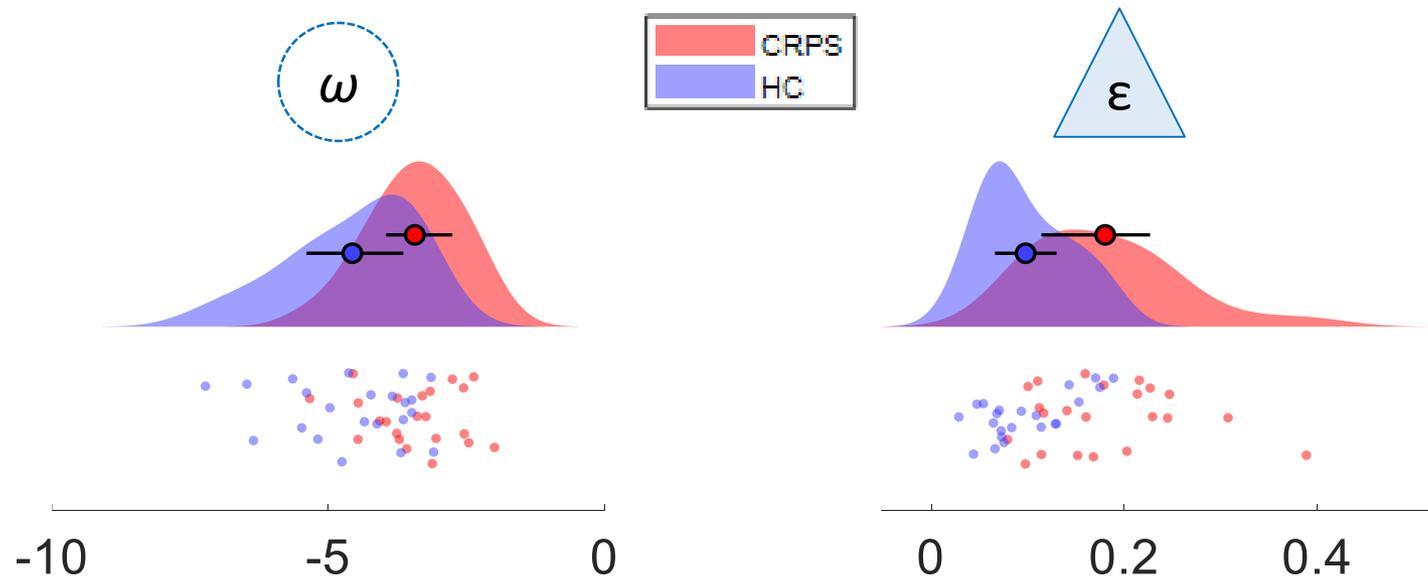


## Block order



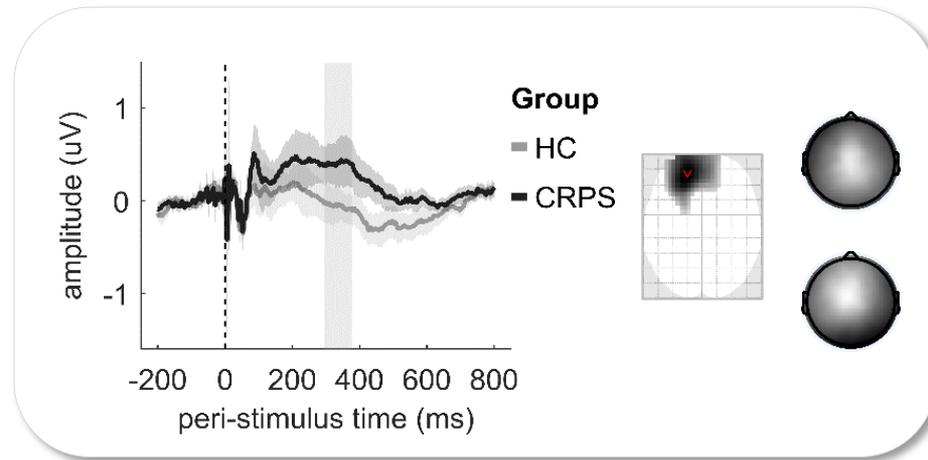
# Uncertain prediction drives more precise prediction error in CRPS > HC group

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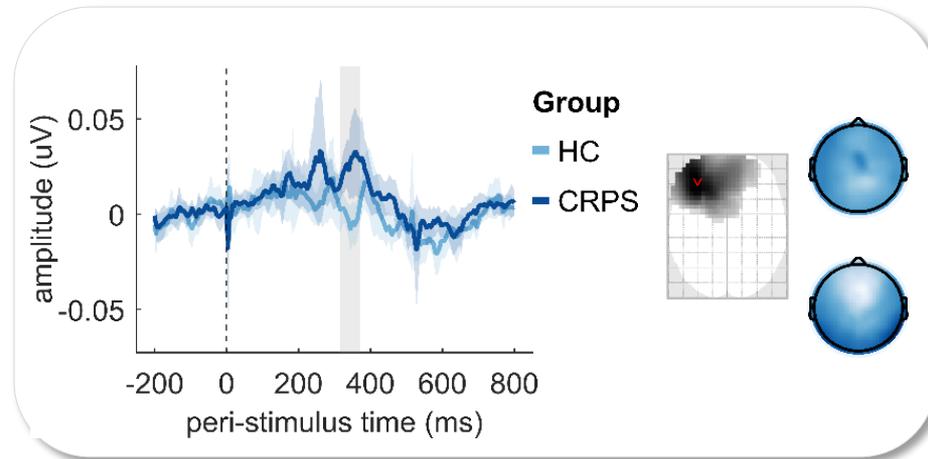


# Greater “mismatch” responses in CRPS partly explained by prediction error

Whole EEG



Partial EEG explained by prediction error  $\epsilon$



# Questions for further research

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1. Insula source of prediction error? Relation to insula atrophy?
2. Specificity to *somatosensory* spatial perception?
3. Specificity to patients with CRPS (vs. other chronic pain, fracture)?
4. Effects of medication?
5. Relation to peripheral symptoms/signs (e.g. autonomic, immune, inflammatory responses)?

# The study team

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Dr Mike Lee



Ingrid Scholtes



Dr Nick Shenker

