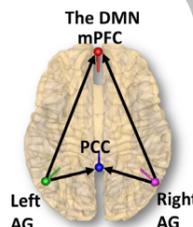


## INTRODUCTION

- Neuroplastic mechanisms associated with the transition from acute to persistent pain are still not fully understood.
- Resting state functional connectivity (rsFC) is a method shown to reflect neuroplasticity [1].
- Most studies investigating the effect of tonic pain on rsFC rely on models employing short painful stimulation [2].
- To better model chronic pain, pain models relying on longer pain stimulation are needed [2].
- The default mode network (DMN) is shown to be consistently altered during chronic pain [3].

## AIM

To examine the effects of 1-hour capsaicin-induced pain on the rsFC of the DMN :connections from the bilateral angular gyrus (AG) to the posterior cingulate cortex (PCC) and medial prefrontal cortex (mPFC) at alpha oscillations during eyes closed (EC) and eyes open (EO).



## METHODS

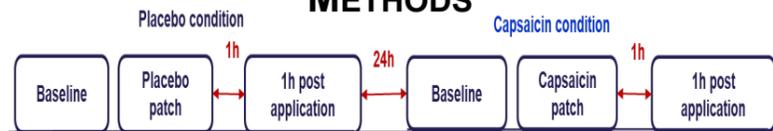


Figure 1. Experimental procedure

- 28 healthy right-handed volunteers (age:25.1±4 years) participated in the experiment.
- The experiment consisted of 2 sessions/conditions (placebo followed by capsaicin) separated by 24 hours.
- **Baseline measurements:**
  - Questionnaires
  - EEG 10 min (5min EC, 5min EO)
- **1 hour post app. measurements:**
  - EEG 10 min (5min EC, 5min EO)



## METHODS (CONT.)

### EEG acquisition

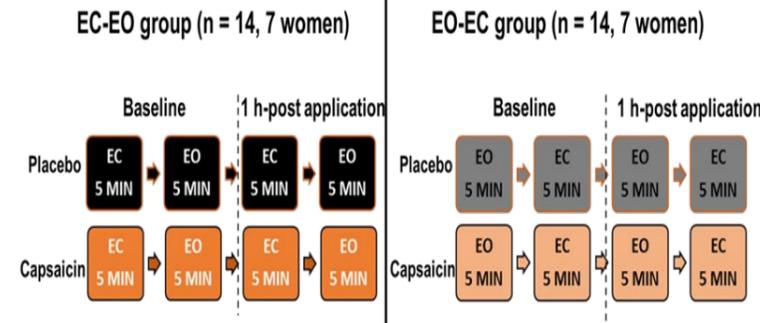


Figure 2. EEG recording and eye-sequence randomization. Depending on the eye-sequence, subjects were randomly and balanced assigned to one of 2 groups: EC-EO group and EO-EC group. The same eye sequence for each group was maintained for placebo and capsaicin sessions.

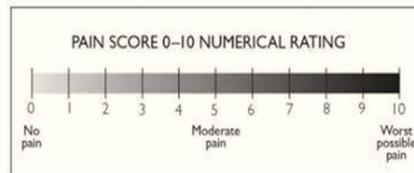


Figure 3. EEG was measured using 64-electrode cap. EEG based rsFC was assessed using Granger causality. Subjective pain ratings was assessed using numerical rating scale (NRS).

## RESULTS

### High subjective pain intensity after 1-hour capsaicin

- Subjective pain intensity scores after 1-hour application for EC-EO and EO-EC groups ( $7.8 \pm 0.5$  and  $7.0 \pm 0.6$ , respectively) were higher in capsaicin than placebo ( $0 \pm 0$  and  $0.2 \pm 0.2$ ,  $p < 0.001$ ).

## RESULTS (CONT.)

### DMN rsFC at baseline differed between eyes closed and eyes open

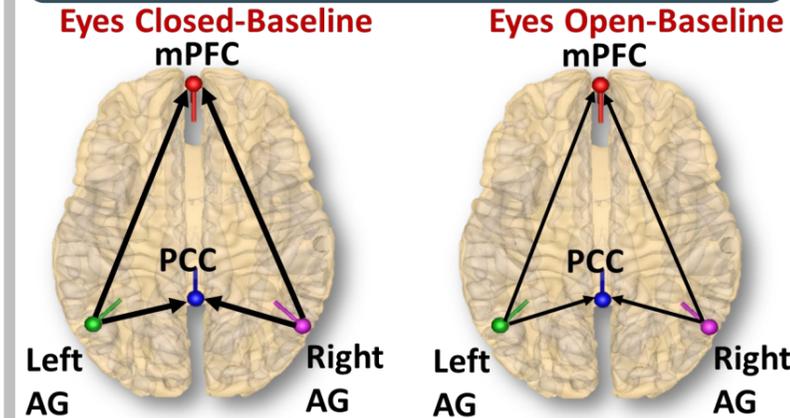


Figure 4. rsFC at four DMN connections: (right AG-PCC, right AG-mPFC, left AG-PCC, left AG-mPFC) at baseline during EC and EO. rsFC was **higher** during EC (thicker arrows) compared to EO. No significant difference in rsFC between the groups or conditions at baseline.

### Contralateral effect of tonic pain during eyes open

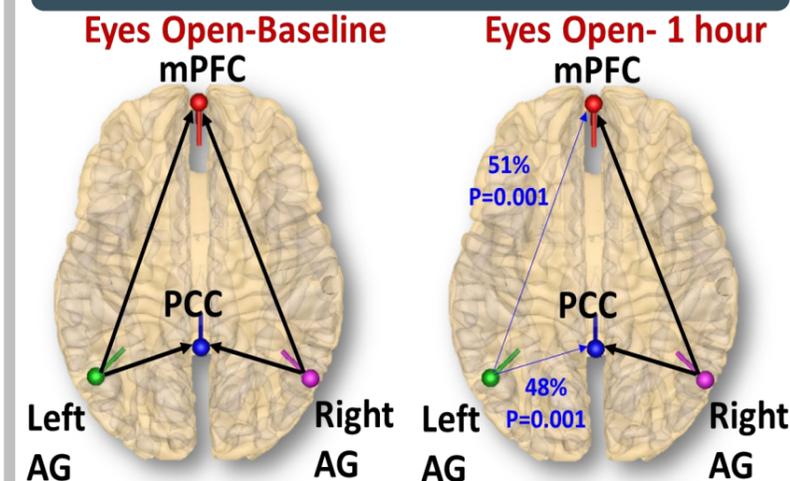


Figure 5. rsFC at four DMN connections after 1-h capsaicin compared to baseline during EO. rsFC was **reduced** at the **Left connections only** (left AG-mPFC and left AG-PCC). **Both groups showed this reduction. No significant change in placebo condition.**

## RESULTS (CONT.)

### Ipsilateral effect of tonic pain during eyes closed

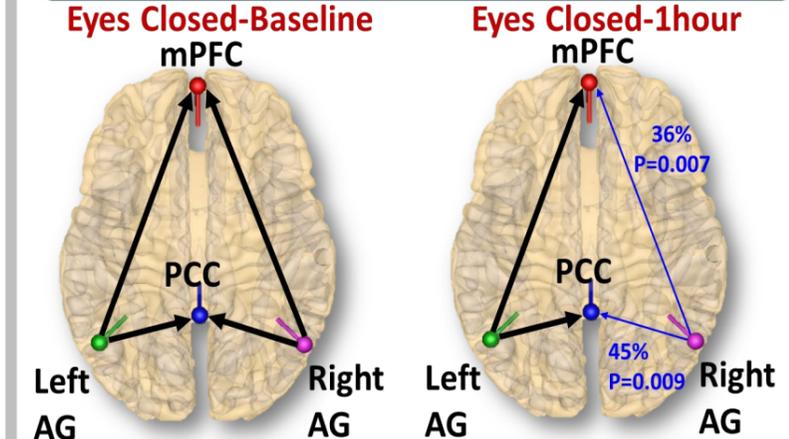


Figure 6. rsFC at four DMN connections after 1-h capsaicin compared to baseline during EC. rsFC was **reduced** at the **right connections only** (right AG-mPFC and right AG-PCC). Only **EC-EO group** showed this reduction. No significant change among EO-EC group or in placebo condition.

## CONCLUSIONS

- Tonic pain differentially altered the rsFC of the DMN during eyes closed and eyes open.
- Possible pain-specific modulation of DMN connectivity.
- Eyes-closed-eyes-open sequence is crucial for assessing DMN connectivity during tonic pain.
- The results provide insight into resting-state functional connectivity changes in the cortical DMN that may precipitate persistent pain.

## REFERENCES

- [1] Guerra-Carrillo, B., Mackey, A.P., Bunge, S. A., 2014. Resting-state fMRI: a window into human brain plasticity. *Neuroscientist*. 20, 522-33.
- [2] Kim, J.A., Davis, K.D., 2020. Neural oscillations: understanding a neural code of pain. *Neuroscientist*.
- [3] Baliki, M.N., Mansour, A.R., Baria, A.T., Apkarian, A.V., 2014. Functional reorganization of the default mode network across chronic pain conditions. *PLoS One* 9.