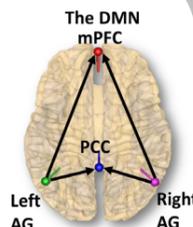


INTRODUCTION

- 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

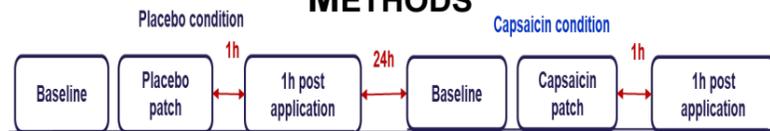


Figure 1. Experimental procedure

- 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

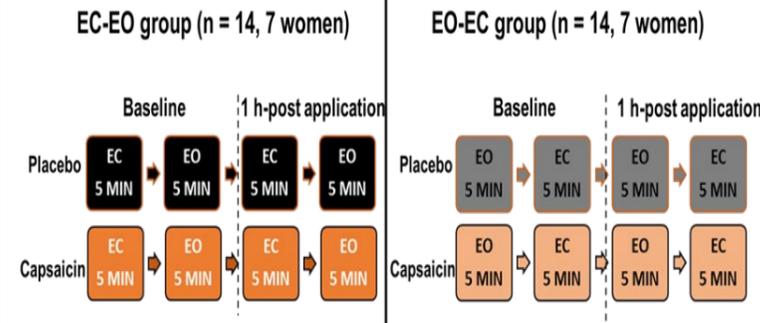


Figure 2. EEG recording and eye-sequence randomization. Depending on the eye-sequence, subjects were randomly and balanced assigned to one of 2 groups: EC-EO group and EO-EC group. The same eye sequence for each group was maintained for placebo and capsaicin sessions.

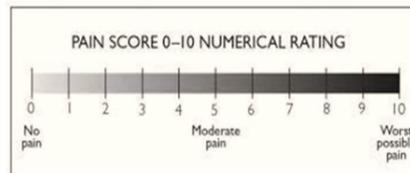


Figure 3. EEG was measured using 64-electrode cap. EEG based rsFC was assessed using Granger causality. Subjective pain ratings was assessed using numerical rating scale (NRS).

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 ± 0.5 and 7.0 ± 0.6 , respectively) were higher in capsaicin than placebo (0 ± 0 and 0.2 ± 0.2 , $p < 0.001$).

RESULTS (CONT.)

DMN rsFC at baseline differed between eyes closed and eyes open

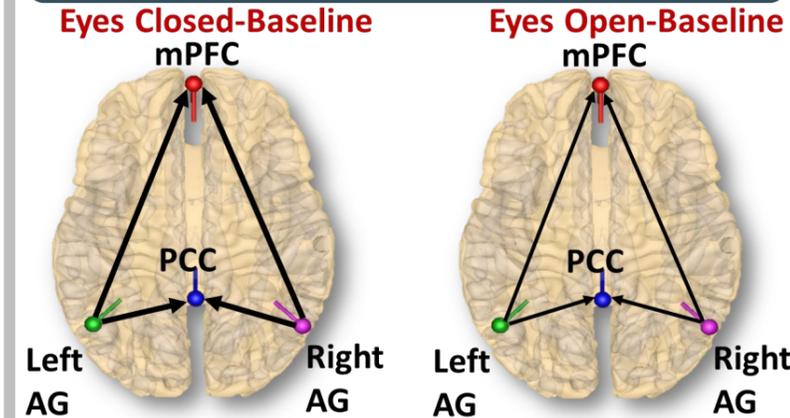


Figure 4. rsFC at four DMN connections: (right AG-PCC, right AG-mPFC, left AG-PCC, left AG-mPFC) at baseline during EC and EO. rsFC was **higher** during EC (thicker arrows) compared to EO. No significant difference in rsFC between the groups or conditions at baseline.

Contralateral effect of tonic pain during eyes open

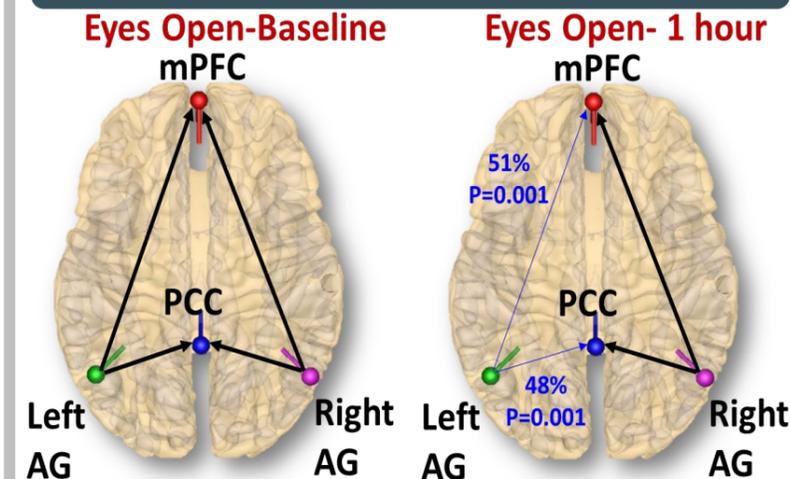


Figure 5. rsFC at four DMN connections after 1-h capsaicin compared to baseline during EO. rsFC was **reduced** at the **Left connections only** (left AG-mPFC and left AG-PCC). **Both groups showed this reduction. No significant change in placebo condition.**

RESULTS (CONT.)

Ipsilateral effect of tonic pain during eyes closed

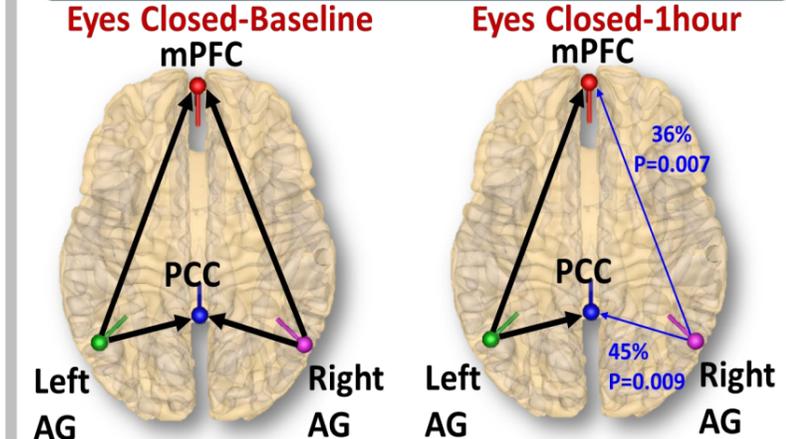


Figure 6. rsFC at four DMN connections after 1-h capsaicin compared to baseline during EC. rsFC was **reduced** at the **right connections only** (right AG-mPFC and right AG-PCC). Only **EC-EO group** showed this reduction. No significant change among EO-EC group or in placebo condition.

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.