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Reduced functional connectivity in resting-state EEG as a biomarker for chronic low back pain

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Background

- Chronic low back pain (CLBP) involves functional brain changes, highlighting the need for methods to visualize and study these changes.
- Electroencephalogram (EEG) is a suggested biomarker for chronic pain, providing non-invasive, cost-effective, and time-resolved neural assessments for diagnosis, monitoring, and prognosis.
- In a previous study, current source density (CSD) and functional connectivity (FC) were analyzed in addition to evoked potentials and power spectrum in chronic pain patients, and EEG characteristic of chronic pain was investigated.
- Few studies have used EEG to identify specific brain activity changes in CLBP.

The aim of this study was to compare CSD values and FC in resting EEG between patients with CLBP and healthy controls, and to examine the correlations between EEG indices and symptoms in patients with CLBP, using open EEG data.

Methods

Participants

- Open EEG data set (Technical University of Munich).
- 34 CLBP patients, and 34 healthy control (HC) (See the table on the right.)

Self-reported questionnaires to assess pain and mood status

- Current pain intensity (NRS)
- Average pain intensity (NRS)
- Pain quality (PainDETECT, Short Form McGill Pain Questionnaire; SF-MPQ)
- Depression (Beck Depression Inventory-Second edition; BDI-II)
- Anxiety (State-Trait Anxiety Inventory; STAI)

EEG recording and preprocessing

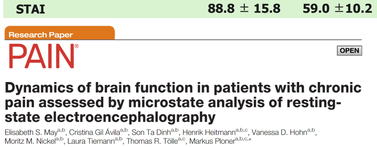
- 5-minute resting closed-eye EEG, 19 channels (reference: FCz) using the international 10-20 system
- Bandpass filter (1-50Hz)
- independent component analysis was performed to remove artifacts

EEG Analysis

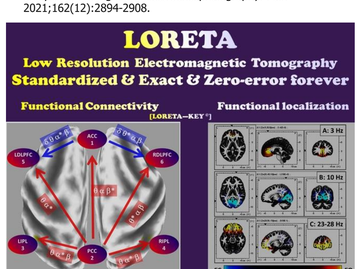
- CSD and FC values calculated using exact low-resolution electromagnetic tomography analysis (eLORETA) in δ, θ, α1, α2, β1, β2, and β3.
- The cortical gray matter was divided into 6239 voxels at a spatial resolution of 5 mm, and the CSD value for each was estimated.
- FC values between 24 regions of interest were calculated based on the phase lagged index.
- CSD and FC values compared between CLBP and HC using correspondence-free t-test by the statistical nonparametric mapping method (SnPM) in eLORETA.
- Correlation analysis between pain symptoms/mood status and EEG indices in the CLBP group was conducted using SnPM.

**footnote: Frequency bands
δ (1.5–6.0 Hz), θ (6.5–8.0 Hz), α1 (8.5–10.0 Hz), α2 (10.5–12.0 Hz), β1 (12.5–18.0 Hz), β2 (18.5–21.0 Hz), β3 (18.5–21.0 Hz)

	CLBP (n = 34)	HC (n =34)
	(Mean ± SD)	(Mean ± SD)
Age, years	56.6 ± 12.7	58.5 ± 13.3
Men / Women	16 / 18	14 / 20
Current pain intensity (0-10)	5.2 ± 1.7	-
Average pain intensity (0-10)	5.6 ± 1.6	-
Pain duration, months	140.2 ± 118.1	-
SF-MPQ-sensory	12.6 ± 4.8	-
SF-MPQ-affect	3.8 ± 2.7	-
SF-MPQ-total	24.8 ± 7.9	-
PainDETECT	16.0 ± 6.3	-
BDI-II	7.9 ± 12.7	2.4 ± 3.2
STAI	88.8 ± 15.8	59.0 ±10.2

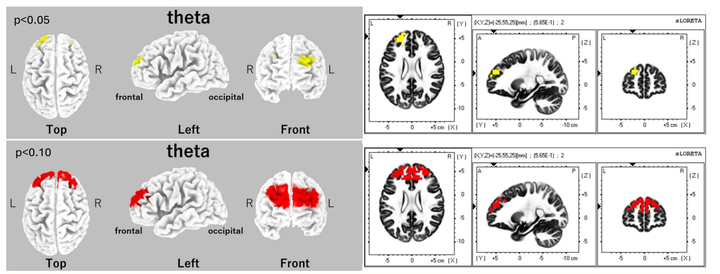


May ES, Gil Ávila C, Ta Dinh S, Heitmann H, Hohn VD, Nickel MM, Tiemann L, Tölle TR, Ploner M. Dynamics of brain function in patients with chronic pain assessed by microstate analysis of resting-state electroencephalography. Pain 2021;162(12):2894-2908.

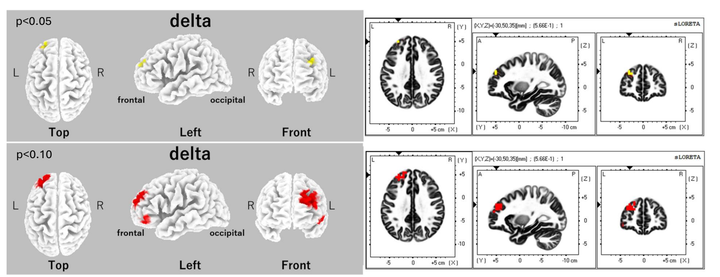


Results

CSD analysis



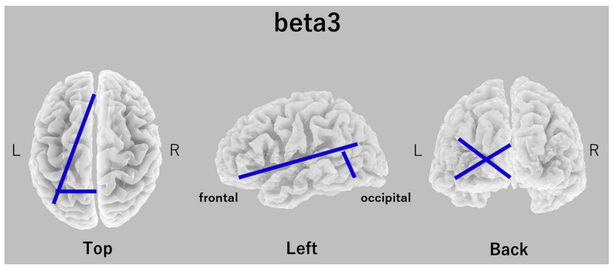
eLORETA maps showing cortical regions with significant correlation with SF-MPQ total score



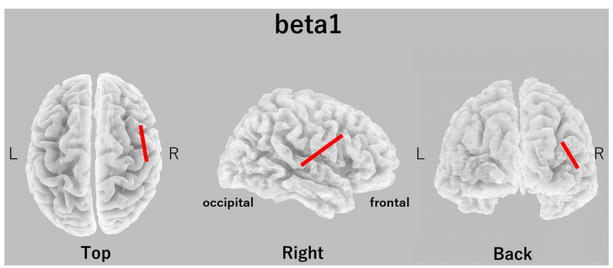
eLORETA maps showing cortical regions with significant correlations with current pain intensity

- No significant difference in CSD values between groups.
- **Upper figure:** Positive correlation between left dominant prefrontal cortex (PFC) θ band CSD value and SF-MPQ total score.
- **Lower figure:** Positive correlation between left PFC δ band CSD value and current pain intensity.

FC analysis



The eLORETA wire diagram indicating significantly reduced FC in the CLBP group



FC that showed significant correlations with current pain intensity.

β3 band FC (upper figure)
Reduced between the left middle temporal gyrus and the posterior cingulate cortex (PCC). Reduced between the ventral medial PFC and the left inferior parietal lobule in the CLBP.

β1 band FC (lower figure)
Positive correlation between the right dorsolateral prefrontal cortex (rDLPFC) and right auditory cortex with current pain intensity.

Discussion

- The role of the PFC in pain perception and regulation is underscored by the correlations between pain intensity and increased θ and δ activity in the PFC, which suggests that the PFC plays a crucial role in these processes. (Salomons TV et al. 2007, Fallon N et al. 2018)
- The significantly reduced FC in the CLBP group suggests that the PCC's connectivity with other pain-related brain regions is important in the experience of chronic pain. (Zhang S et al. 2014, Khoshnejad M et al. 2017)
- The significant increase in β1 band FC between the rDLPFC and the right auditory cortex may represent an adaptive mechanism in the brain to manage or reduce increased pain intensity, involving both sensory and emotional regulation components (Grachev ID et al 2003, Sevel LS et al. 2016)

The results of this study may lead to the discovery of promising biomarkers for noninvasive brain stimulation and neurofeedback

Acknowledgments
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