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Cognitive Neuroscience 2020: Dynamic resting state functional connectivity differences between ictal and the pre or postictal phase of migraine- Noboru Ima- Japanese Red Cross Shizuoka Hospital, Japan

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Introduction:
Migraine headache is an episodic phenomenon, and patients with episodic migraine have ictal (headache), peri-ictal (premonitory, aura, and postdrome), and interictal (asymptomatic) phases. We aimed to find the functional characteristics of the migraine brain regardless of headache phase using dynamic functional connectivity analysis. We prospectively recruited 50 patients with migraine and 50 age- and sex-matched controls. All subjects underwent a resting-state functional magnetic resonance imaging. Significant networks were defined in a data-driven fashion from the interictal (>48 hours apart from headache phases) patients and matched controls (interictal data set) and tested to ictal or peri-ictal patients and controls (ictal/peri-ictal data set). Both static and dynamic analyses were used for the between-group comparison. A false discovery rate correction was performed. As a result, the static analysis did not reveal a network which was significant in both interictal and ictal/peri-ictal data sets. Dynamic analysis revealed significant between-group differences in 7 brain networks in the interictal data set, among which a frontoparietal network (controls > patients, P = 0.0467), 2 brainstem networks (patients > controls, P = 0.0467 and <0.001), and a cerebellar network (controls > patients, P = 0.0408 and <0.001 in 2 states) remained significant in the ictal/peri-ictal data set. Using these networks, migraine was classified with a sensitivity of 0.70 and specificity of 0.76 in the ictal/peri-ictal data set. In conclusion, the dynamic connectivity analysis revealed more functional networks related to migraine than the conventional static analysis, suggesting a substantial temporal fluctuation in functional characteristics. Our data also revealed migraine-related networks which show significant difference regardless of headache phases between patients and controls.

Objectives: Migraine is characterized by a series of phases (inter-ictal, pre-ictal, ictal, and post-ictal). It is of great interest whether resting-state electroencephalography (EEG) is differentiable between these phases. The imaging method is based on blood-oxygen-level dependent (BOLD) recordings of the resting brain (i.e. the person lying in the MRI scanner is relaxing with closed eyes, but not sleeping). Every voxel in the obtained image of the brain emits a signal with a specific frequency. The higher the degree of synchronization of signal frequency between two different voxels, the more functional connected are these voxels, and vice versa. Brain areas displaying a particular level of similarity represent a functional connectivity network. Thus, all areas in the brain are more or less functionally connected to each other. The use of this method depends on the change in the functional connectivity between areas in a network, when measured in two different conditions or population samples.

Results: Fifty patients with episodic migraine (1–5 headache days/month) and 20 HCs completed the study. Patients were classified into inter-ictal, pre-ictal, ictal, and post-ictal phases (n = 22, 12, 8, 8, respectively), using 36-h criteria. Compared to HCs, inter-ictal and ictal patients, but not pre- or post-ictal patients, had lower EEG power and coherence, except for a higher effective connectivity in fronto-occipital network in inter-ictal patients ($p < .05$). Compared to data obtained from the inter-ictal group, EEG power and coherence were increased in the pre-ictal group, with the exception of a lower effective connectivity in fronto-occipital network ($p < .05$). Inter-ictal and ictal patients had decreased EEG power and coherence relative to HCs, which were “normalized” in the pre-ictal or post-ictal groups.

Conclusions: Resting-state EEG power density and effective connectivity differ between migraine phases and provide an insight into the complex neurophysiology of migraine. Our findings may provide new insights into the characterization of migraine as a condition affecting brain activity in intrinsic connectivity networks. Moreover, the abnormalities may be the consequence of a persistent central neural system dysfunction, reflecting cumulative brain insults due to frequent ongoing migraine attacks.