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Aim: To investigate the neuronal networks in children with tuberous sclerosis complex (TS) undergoing treatment with Everolimus.

Methods: Sleep and wake electroencephalography (EEG) before and one year after the start of the treatment with Everolimus were investigated in 13 patients with TS. To investigate functional and effective connectivity within the network generating the delta and theta activity in the background sleep and wake EEG, the methods of dynamic imaging of coherent sources (DICS) and renormalized partial directed coherence (RPDC) were applied.

Results: Sources before the treatment. Independent of location of the tubera and severity of epilepsy, delta activity in the background EEG pattern in patients with TS was associated with the sources in the medial prefrontal cortex, the supplementary motor area and the putamen during sleep. Theta waves during sleep were associated with sources in the prefrontal cortex, sensory cortex, hippocampus and the thalamus. The sources of delta frequency during wakefulness were identified at the posterior parietal cortex, the parahippocampal gyrus and the Broca area. Sources at theta frequency were found at the sensorymotor cortex, the prefrontal cortex, the primary visual cortex and the thalamus at awake state.

Sources after the treatment. The sources one year after the start of the therapy, for both delta and delta frequencies were located in the same areas as before, however with a significantly weaker strength of coherence.

The RPDC analysis at baseline showed strong bidirectional connections between described sources. The RPDC analyses after the one year of treatment showed significantly weaker unidirectional connections within the described network.

At the follow up patients were grouped in two groups; group 1: five patients with >50% reduction of seizures and spike wave index, group 2: eight patients with <50% reduction of seizures and spike wave index. Interestingly, at follow up patients from the group 1 had decreased values in absolute power of the sources, coherence values and strength of connections. Whereas, patients from the group 2 had increased values in all above mentioned parameters.

Conclusion: The current study described the neuronal network in children with severe epilepsies due to TS. Regardless of the locations of the tubera the DICS analyses showed a complex network of cortical and subcortical sources with strong bidirectional connections. The described network was significantly weaker after one year under the treatment with Everolimus and appears to be characteristic for the children with TS and severe epilepsy.