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Introduction:

According to clinical EEG and PET data botulin toxin therapy (BT) of generalized spasticity in disorder of consciousness in addition to reduction of spasticity improves functional state of the brain and higher brain functions (Vainshenker et al., 2015). However when these changes of functional state of the brain start and how develop remains unclear.

Methods:

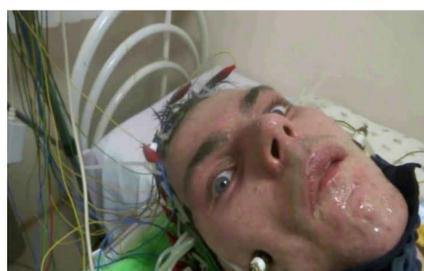
BT of generalized spasticity was carried out under EEG and clinical monitoring in 16 patients with disorder of consciousness. IncobotulinumtoxinA (Inco-A) was injected in all hypertonic muscles. The dose into each muscle did not exceed mean recommended dose (Jost, 2008). Additionally before BT pharmacological test was performed in two patients. The test consisted of the two consequent injections: 4.0 ml saline was injected into m. quadriceps femoris and in 30 minutes 25 units of Inco-A dissolved in 4.0 ml saline was injected.

Results:

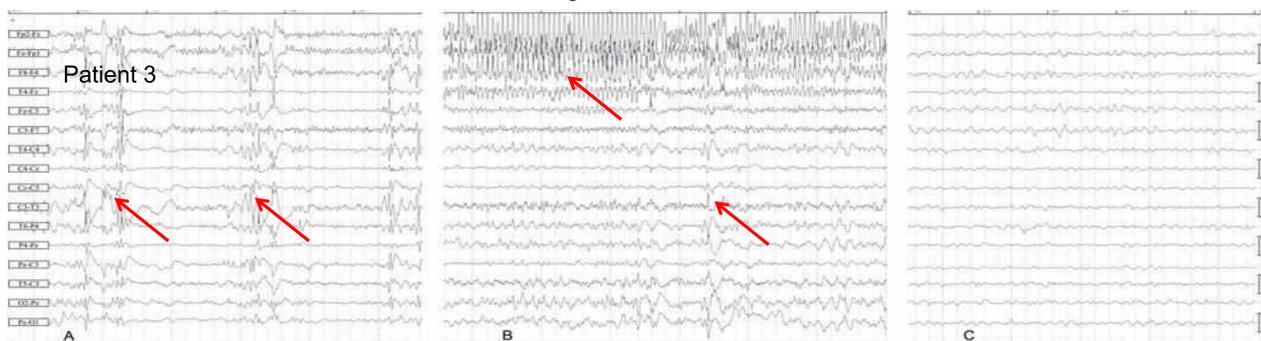
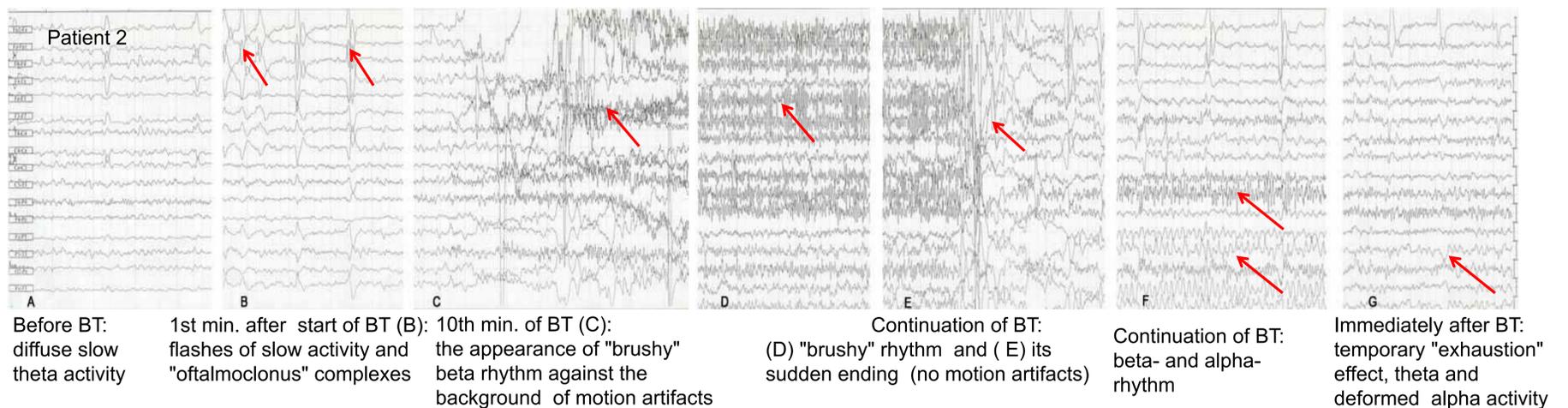
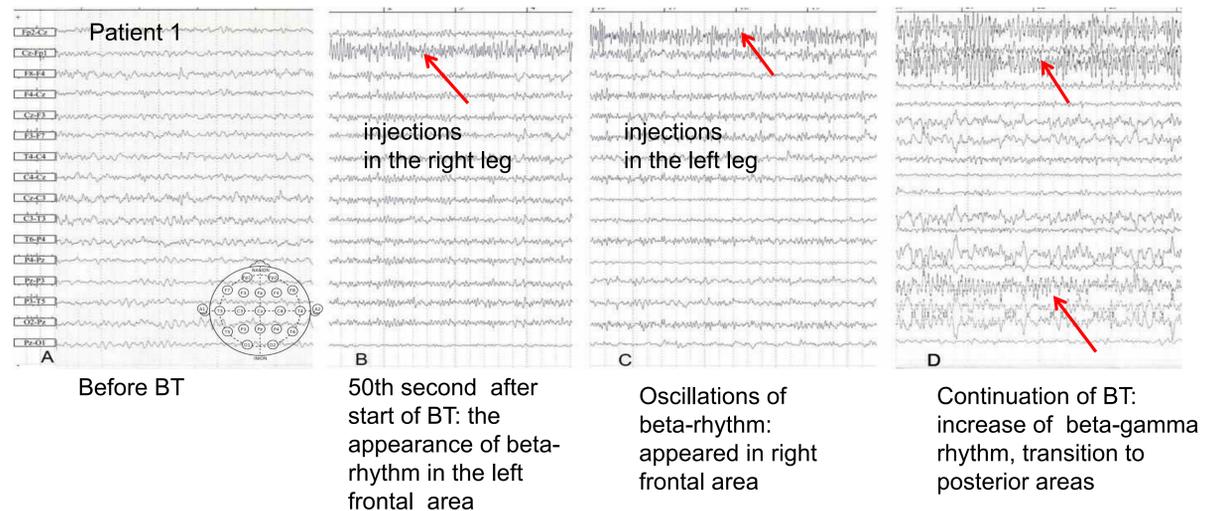
1. Changes of bioelectric activity of the brain (BEA) associated with injection itself (saline or Inco-A) appeared at the moment of the injection and were preserved up to 10 seconds.
2. Changes of BEA associated with the action of Inco-A appeared within 1 to 2 minutes after the first injection in all patients and initially caught the motor cortex in 15 patients. The more muscles were injected, the more widespread changes of BEA were registered with the appearance of beta and other rhythms ($P < 0.05$). Fewer oscillations of rhythms and a tendency to return to the initial background of BEA were observed.
3. Both initial transient decrease of muscle tone (in all patients) and improvement of consciousness (in 10 patients) appeared immediately after injections into all muscles when changes of BEA covered all parts of the brain and were preserved for 30-60 minutes.

Conclusions:

The central effect of BT of generalized spasticity (EEG) starts immediately with the beginning of the reduction of afferentation from the muscles. Taking into consideration the notion that abnormal sensorimotor integration covers many of brain regions in movement disorders (Patel et al. 2014), we suggest that the reorganization of BEA (EEG activity) we observed reflects disintegration of abnormal sensorimotor integration. We believe that the early transient clinical effect of BT of generalized spasticity reflects the appearance of the process of liberation of neurons for maintaining other functions, including awareness when the "normalizing disintegration" covers all areas relevant for abnormal sensorimotor integration. Further neuroimaging studies (PET, fMRI) are needed to explore the localization of changes of functional brain activity associated with effects of BT of generalized spasticity.



Before BT



Immediately after BT (after 1 hour from the start of BT) (video appended)

Referents:

- Vainshenker Yu., Korotkov A., Melucheva L., Ivchenko I., Medvedev S. Improvement of functional state of the brain as effect of treatment of generalized spasticity with high doses of incobotulinumtoxinA (Xeomin) in patients in a vegetative state. // *Toxicon*, 2015, 93S, a. 196.
- Jost W. Pictorial atlas of botulinum toxin injection: dosage, localization, application // New-Malden UK.: Quintessence Publishing Co Ltd., 2008, 264 p.
- Patel N., Jankovic J., Hallett M. Sensory aspects of movement disorders // *Lancet Neurol.*, 2014, 13(1), p.100–112.