Cerebellar GABA-B receptors in essential tremor

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Background: Pathophysiology of essential tremor (ET) is unknown. Studies on ET show abnormal GABAergic system. That has led to “GABA hypothesis” in the pathophysiology of ET. It is unknown which subtype of GABA function may be altered in ET. This study measured the level of GABA-B receptors (GBR) in the cerebellar cortex of ET and control brains.

Material and Methods: ET cases seen at our clinic were autopsied within 24 hours of death. Frozen cerebellar cortex of 9 ET and 5 normal controls was studied by Western blot with GBR1 antibody (Novus Biologicals) and GBR2 antibody (Abcom Inc.).

Figure 1. GBR1 and GBR2 protein expression in the cerebellar cortex of control (C1–C5) and ET (ET1–ET9) brains. Representative Western blot showed the bands of GBR1 and GBR2 protein in the cerebellar cortex homogenates from control and ET brains. β-Actin was used as internal loading control and analyzed to demonstrate the normalization for equivalent protein loading per lane.

Results: Figure 1 shows Western blot GBR1 and GBR2 protein expressions in the ET and control brains. There was no significant difference in GBR1 protein level between ET and Control brains. However, mean GBR2 protein level was increased in the ET (Figure 2). There was no association between GBR1 or GBR2 levels with the onset age, tremor severity, family history of tremor or response to drug therapy.

Conclusion: GBR2 proteins are increased in ET. Further studies are needed to determine the significance of GBR2 receptor changes in ET.

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Recording pathological tremor with a smartphone

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Introduction: Follow-up of Parkinson’s disease symptoms represents a challenge for clinicians. Variations in the severity of symptoms makes it difficult to get a global picture of the disease’s state with isolated clinical consultations. Smart phones have become common devices within the past few years. Several of these smart phones are equipped with an accelerometer that is able to detect small movements.

Objective: Develop a smart phone application to assess the characteristics of pathological tremor.

Method: Tremor of 5 patient with Parkinson’s Disease, one patient with Essential Tremor, 6 healthy controls was assessed using a smart phone. Simulated pathological tremor was also assessed. Three tasks were performed: (i) Rest Tremor, (ii) Postural Tremor, (iii) Intention Tremor. Each condition was repeated 3 times and they lasted 10s. Tremor amplitude of each trial was also scored using a custom-designed clinical scale.

Results: Correlations between amplitudes obtained with the smart phone and clinical scores of patients were r = 0.88, r = 0.85 and r = 0.95 for the Rest, Postural and Intention Tremor conditions, respectively. Correlations were also high for the simulated pathological tremor, i.e.: r = 0.84, r = 0.91 and r = 0.96. Trials with different clinical scores were grouped. A significant difference in tremor amplitude obtained with the smart phone was found between trials that scored differently on the clinical scale. Moreover, the smart phone detected the smallest clinically visible tremor.

Conclusion: Smart phones are sensitive enough to detect and quantify pathological tremor. These devices could then be used to get a better global picture of disease state.

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Quantitative assessment of rest and action tremor and the effect of cueing in Parkinson’s patients treated with deep brain stimulation

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Introduction: In Parkinson’s disease rest and action tremor may occur. High frequency deep brain stimulation in basal ganglia nuclei has proved to be effective in the suppression of tremor. In addition, rhythmic auditory cues have shown to result in improved performance of repetitive movements, possibly by suppressing action tremor. The aim of this study was to investigate if deep brain stimulation has similar effects on rest and action tremor, and whether in case of action tremor, the effect of electrical stimulation is similar to or enhanced by auditory cueing.

Methods: Three exercises were carried out by 7 Parkinson’s disease patients treated with deep brain stimulation of the subthalamic nucleus: (1) sitting at rest; (2) performing a hand tapping movement as fast as possible; (3) performing hand movements on the rhythm of an auditory cueing signal. Inertial sensors registered the movement of the hands during the tests. The exercises were repeated for four different stimulation settings.
Results: Deep brain stimulation may either enhance or suppress rest and/or action tremor. Power spectral density analysis shows that tremor suppression is accompanied by an increase in relative power in the low frequency band for both rest and action tremor. Most patients could (temporarily) phase-lock their hand movements to the cueing signal of 1.6 Hz. Cueing signals at higher frequencies could result in (1:1 or n:m) phase-locking of tremor as well as movement.

Conclusion: Deep brain stimulation results in a re-scaling of tremor, while auditory cueing may lead to or enhance tremor suppression.

1.230 BOTULINUM TOXIN TREATMENT IN PATIENTS WITH ESSENTIAL TREMOR

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Objective: To evaluate the efficacy and safety of Botulinum toxin type A (BTXA) injections in patients with essential hand tremor (ET).

Methods: Twenty five patients with ET with an unsatisfactory medical therapy or with unacceptable side effects were treated during last 7 years using BTXA. Mean age in the time of the first injection was 71 years (51–84), 12 women and 13 men. Self-rating numeric scale and handwritten spiral analysis were used for evaluation. Overall 153 applications were done using EMG guidance. Repeated bilateral injections were used in 16 cases, 9 persons underwent the therapy of one extremity. The most frequently injected muscles were extensor digitorum communis, pronator teres, and flexor digitorum superficialis.

Results: The average improvement referred by patients was 59%, reduction of the tremor by spiral drawing was in most cases 1 point (maximal improvement 2 points in two cases). The mean time of the improvement was 11.5 weeks. The treatment was non-effective (equal or less than 20% during 2 consecutive applications) in 8 patients (32%). Adverse events (mostly transient mild weakness) were found in 22% of all injections. The weakness was more frequent in patients who did not answer sufficiently to the therapy. The long-term (more than one year) adherence to the treatment in the responders was 90%.

Conclusions: The treatment using BTXA could be considered in effectiveness of the therapy (in one third of patients) is accompanied more frequently with the muscle weakness.

1.231 SEVERITY OF HEMIFACIAL SPASM CORRELATES WITH THE USE OF COMPLEMENTARY THERAPIES

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Introduction: Hemifacial spasm (HFS) is a socially embarrassing condition to many patients. Complementary therapies (CT) are frequently sought after by patients with chronic neurological disorders. Our study determines the prevalence and the predictive factors associated with the use of complementary therapies (CT) in patients with hemifacial spasm (HFS).

Method: We recruited 96 patients with HFS and administered a structured questionnaire on the frequency of CT usage and investigate the factors influencing the usage. In addition, data on the demographics, HFS severity, and the use of botulinum toxin were systematically collected.

Results: 49 patients (51%) used one or more forms of CT. Only 2 (4%) of CT users reported the therapies as very helpful, forty-three percent reported the therapies as being sometimes helpful and the rest (53%) of CT users did not find the therapies useful. Median time to starting CT was significantly lower in patients of severity 4 (5.5 years (95% CI: 3.2–7.8 years) compared to patients of severity 2/3 (9 years (95% CI: 6.2–11.8 years); p = 0.042 by log rank test. Patients with a severity score of 4 or higher was 1.8 times more likely to start CT compared to a severity score of 3 or lower (95% CI for hazard ratio: 1.0–3.3).

Conclusion: The use of CT is high among HFS patients. Patients with higher severity of HFS were more likely to seek complementary therapies. However, only 4% reported significant improvement with CT.

1.232 TREMOR AND HIV INFECTION

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Symptoms associated with human immunodeficiency virus are very varied and very extensive neurological disorders due to injuries related exclusively to HIV and opportunistic pathologies that damage the nervous system. Here we present a man of 72 a, which debuted with a tremor of attitude in the hands and head, without other accompanying symptoms and was diagnosed with essential tremor. 18 months later revealed a single domain MCI am not, by pattern type Nesc subcortical and MMSE of 19/30. Cranial MRI showed diffuse cerebral atrophy. Infection VIH was confirmed by the severe immunodeficiency HIV starting antiretroviral treatment, resulting in a significant improvement in viral load in cognitive impairment with MMSE 27/30 actual and virtual disappearance of the tremor of attitude.

1.233 EXTRAPYRAMIDAL DISORDERS IN PATIENTS WITH SYMPTOMATIC EPILEPSY

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Background: The treatment of epilepsy requires the prolonged method of the anti-epileptic preparations, which have side effects. The frequency of the side effects of anti-convulsant composes 7–25%, which negatively influences the quality of the life of patients. Extrapyramidal symptoms (tremor, dystonia, chorea, myoclonia) are encountered in 6–45% of patients.

Purpose: To determine the frequency of the extrapyramidal side effects against the background of the method of antiepileptic drugs in the patients with symptomatic epilepsy.

Materials and Methods: Were observed 100 patients (58 men and 42 women) with symptomatic focal epilepsy. In 27 patients partial seizure were observed, in 8 – secondarily generalized, in 65 – partial seizure with the secondarily generalization. In the work the clinical, electrophysiological, laboratory, neuropsychological methods of study were used. 30 patients obtained valproid acid, 34 – carbamazepin, are 8 lamotridzhin, 9-topiramat, 3-okskarbazepin, to 2-levitiratsetam, 3-benzodiazepines; 6 patients obtained the combined therapy of valproid acid +topiramat, 5- valproid acid and carbamazepin.

Results and Consideration: In the structure of extrapyramidal symptoms most frequently is encountered the tremor – in 24% of patients, who obtained valproid acid, and in 2% of patients, who obtained Ohramazepin. Oramandibulyar dyskinesia is registered in 1% of patients, treated by carbamazepin. In patients, who assumed lamotridzhin in 2% is revealed the presence of akinetic-rigidity syndrome. These side effects bore the reversible nature, of drugs was required in 6% of patients.