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Short Communication

Novel Mathematical Model may Provide Drug-Naïve Strategy to Relieve Postural Tremor in Multiple Sclerosis

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Abstract

Multiple Sclerosis (MS) is a progressive neurodegenerative condition. There isn't any effective strategy for the remission of MS signs and currently applied options have merely a relieving effect on the symptoms. Achieving new treatment strategies to overcome MS symptoms has always been among the researchers' priorities. The present paper aims to introduce a mathematical modeling of postural tremor in subjects with MS to study the effect of electric stimulations (Trans cranial Magnetic Stimulation and Deep Brain Stimulation) on MS motor symptoms.

Keywords: *Mathematical model, Postural tremor, Multiple sclerosis*

Introduction

Multiple Sclerosis (MS) is a complex chronic disease, mainly affecting young people and causing motor disabilities. The disease includes the destruction of myelin sheaths and eventually leads to the appearance of muscle weakness, fatigue, dizziness, and visual complications as well as marked postural tremor and instability [1]. As yet, there isn't much of an effective therapy for the remission of MS signs [2] and currently applied strategies have merely a relieving effect on the symptoms [3, 4]. It should be noted that the efficacy of current treatments is not everlasting and declines over the time. As a result, achieving new treatment options to cope with MS symptoms, such as developing high quality medicines and non-medicinal treatments, has always been among the researchers' priorities. Given this, it seems that non-medicinal treatments must be included in its treatment.

Some obstacles such as ethical considerations, the experimental limitations concerning human subjects and the lack of exact data about neural circuits involved in this disease makes it difficult to predict the proper target for electric stimulations. Therefore, it is of interest to undertake a mathematical modeling of MS neural disorders to study the influence of electric stimulations so as to ameliorate the motor symptoms and confirm appropriate anatomic and functional targets for the desired stimulations. To achieve this objective, the first step is to record an appropriate signal of the symptoms. In this connection, postural tremor was considered; its related behavior was recorded as the model response. The involved areas of the brain for producing the disorders were examined and the neural nuclei contributing to them were selected in the following order: vestibular nuclei, motor cortex, premotor cortex, pontine nuclei, ventrolateral thalamus, lateral reticular nucleus, spinal cord, cerebellar cortex, deep cerebellar nuclei (DCN) and somatomotor output [5]. The interconnection among these neural structures and their related entities (inhibitory or excitatory) were taken into account in presenting the relevant model structure. Then, model parameters for the healthy condition were obtained and altered according to physiological findings for the simulation of the diseased condition.

As a result, this model was able to successfully reconstruct both the disease and healthy (physiologic) conditions with acceptable accuracy. Consequently, it is possible to produce methods to restore the healthy condition for the diseased subjects through the study of model parameters. Because the aim of this model was to examine the effect of external stimulations on MS, we tried to apply a similar deep brain stimulation (DBS) electric signal in Parkinson's disease and Trans cranial Magnetic Stimulation (TMS) in patients with depression in each block as another input for neural structures. Studying the different neural blocks and applying electric signals revealed that stimulating the neural blocks of motor cortex and premotor cortex, cerebellar cortex as well as vestibular nuclei and DCN, can alter the behavior from diseased to healthy conditions. In other words, stimulation of these targets is able to improve postural tremor and reduce the severity of postural tremor in this model.

It seems that applying TMS on motor cortex can improve some non-motor symptoms of MS such as depression and fatigue [6]. As these disorders are frequently experienced in MS patients, it is thought that TMS stimulation in cerebellar cortex and DBS stimulation in DCN and vestibular nuclei may bring about positive effects on postural tremor. These mechanisms were also confirmed in our study.

In conclusion, exact mathematical, experimental and clinical trials should be designed to reveal the exact mechanisms involved in the stimulation of the proposed targets.

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