



Review Article

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A New Look at Stimulation Therapy with Complex-Structured Stimuli in Traumatic Brain Injuries



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Abstract

Neurorehabilitation, based on the principles of neuroplasticity, is considered to be the promising way to mitigate the adverse consequences of traumatic brain injury (TBI) to cognitive functions. The ability of the brain to restore and to create the neural connections makes it essential to search for methods that could stimulate the restoration of disturbed networks and also can help building the new ways to compensate the deficit of the cognitive functions. Technologies of cognitive rehabilitation relying on the structural and functional plasticity of the brain include programs of mental and physical training and various techniques of stimulation therapy, including transcranial magnetic and electrical stimulation, and noninvasive sensory stimulation exploiting the BWE phenomenon.

Currently, the stimulation therapy applies a periodic rhythm of audio, visual and other signals which can provide the local improvement of the cortical activity in the particular range of oscillations. But it is unable to restore the complex dynamics of the activity of the brain characteristic of a healthy person and therefore, cognitive performance of the person. We suppose that in patients after brain injuries, the fractal flicker stimulation, as well as the stimulation by complex-structured sound tones and signals of other modalities will promote activating the structural-functional plasticity and improving the memory and other cognitive functions. The changes of the cortical activity evoked by complex-structured stimuli can mediate the impact of fractal stimulation on cognitive performance.

Keywords: Fractal stimulation; Traumatic brain injury; Cognitive deficit; Neurorehabilitation

Abbreviations: BWE : Brainwave Entrainment; EE: Environmental Enrichment; NIBS: Noninvasive Brain Stimulation; TBI: Traumatic Brain Injury; MRI: Magnetic Resonance Imaging

Introduction

Every year, around ten million people worldwide are known to undergo traumatic brain injury (TBI) [1]. Acquired traumatic brain injury (TBI) is often the cause of the disability and lead to a weakening of cognitive abilities [2]. In the persons undergone the severe TBI, cognitive decline with the memory impairment is observed in 40-84% of cases [3]. Depending on the severity of a closed trauma and the time after the injury, symptoms of memory impairment were found in 20% to 79% of the injured (cited from [4]) and can remain up to one year after the TBI in 4-25% of patients [5]. Besides, the chronic TBI exacerbate the cognitive decline in the distant post-traumatic period [6,7], and in many cases, rehabilitation activities became to be necessary to carry out for a long time. Therefore, it is significant to understand better the recovering and compensatory mechanisms occurring after the TBI [8] and to elaborate new approaches that might be efficient in an improvement of the brain's functions.

Strategies for assisting for persons with the memory weakening due to the TBI currently include methods related to external compensation strategies and techniques of internal restorative approach [9]. The external strategy comprises, for example, such means as using electronic organizers and keeping diaries for compensation of memory disorder, while the internal strategy deals with the repetitive training and learning to cognitive ways of preserving information [10]. The recent achievements in the studies of neuroplasticity led an enhanced attention to internal restorative strategies [4,11]. Neurorehabilitation, based on the principles of neuroplasticity, is considered to be the promising way to mitigate the adverse consequences of TBI to cognitive functions [12]. The ability of the brain to restore and to create the neural connections makes it essential to search for methods that could stimulate the restoration of disturbed networks and also can help building the new ways to compensate the deficit of the cognitive functions.

That is, the most significance can be those internal strategies that would be aimed at restoring a lost function rather than tissue. Negative neuroplastic changes according to the concept put forward by Mahncke and co-authors are a mediator of the physiological mental aging [13,14] and this idea was recently extrapolated to the TBI-related cognitive decline [15]. While the activity-dependent plasticity according to Hebbian rules [16] reinforces the most active neuronal pathways, with the aging and traumatic injury to the brain, the simple processes of sensory processing become stronger due to a decrease in the activity of competing complex cognitive processes. This non-use of the complex processes in information processing leads to even more weakening of the basal synaptic contacts. Thus, a “self-reinforcing, downward spiral” of negative plasticity develops [13,14]. Mahncke et al. [13,14] noted that negative learning associated with the dependency on simple processes of sensory processing due to non-use of more complex processes leads to negative neuroplastic changes that serve as the physiological basis for cognitive decline. Besides the decrease in the complex cognitive activity, other factors contributing the negative learning they assume to be the increasing noise in the sensory processing and reduced control from neuromodulatory systems.

Tomaszczyk and colleagues [15] assume that related with disuse negative neuroplastic changes underlie the progressive cognitive decline in chronic TBI and should be taken into account for the elaboration of rehabilitation methods aimed at alleviating cognitive deficits and improving long-term clinical outcomes. The cognitive training is known to help improving memory [17] and contributes to recruiting the distinct intact brain regions for encoding information [18,19]. Daily, in an adult brain, thousands of neurons are formed [5]. Physical exercise can lead to a significant increase in the production of new cells in the hippocampus [20] but near half of the new-born cells were shown to be dead within one to two weeks, and therefore they are not able to integrate functionally into neural networks [21]. Moreover, it has been demonstrated that an intensive cognitive learning can significantly enhance the survival of newly generated neurons in the hippocampus [22].

These facts were taken into account in the concept of a combined applying of the cognitive and physical training to reinforce neurogenesis in the hippocampus [22,23]. Results from animal studies testify that in the combined training, the majority of surviving new cells can differentiate into neurons, to form synaptic contacts and integrate into the neural networks of the brain [22,23]. The combination of mental and physical training programs (the MAP training), is expected to be more efficient for the recovery of cognitive functions, than separately the exercises or cognitive training. Some studies on the neurorehabilitation of patients with acquired TBI support the conclusion that methods based on virtual reality, the computer cognitive “retraining” methods are useful in improving working memory after TBI [17,19]. However, the most researchers suppose that despite the evidence for definite memory improvement via cognitive

training, there is the need of a more thorough study of the internal strategies in cognitive rehabilitation and the creation of new approaches and technologies for more significant neurocognitive effects [4,17].

The structural and functional neuroplastic changes in the brain arising in patients with the chronic TBI during the cognitive rehabilitation activity can significantly alter brain activity in the trauma of any severity [12,24]. Neuroplasticity is an inherent feature of the brain that makes possible its experience-dependent changes throughout life [25,26]. Mechanisms of the structural-functional plasticity of the neocortex chains allow the brain to adjust neural networks to a changing environment by selective regulation of numerous synapses enhancing the representation of significant sensory signals [27]. The critical periods in the brain development, during which the input sensory information is especially necessary for the proper forming of neural networks [28] are closed a few later in ontogenesis, after a balance of excitatory and inhibitory processes is reached [27].

The adult brain retains the potential of structural-functional plasticity [29] that allows the adaptation and training throughout life but it this potential is much lower than in the early development. The neuroplasticity was shown reduced in both the process of the human aging and the brain damage including TBI [28]. Consequently, the ability to adapt to variable environmental conditions and to restore the structure and dynamics of brain activity after the acquired injuries must be sharply limited and it is difficult to expect a proper clinical effect for rehabilitation technologies. For an enhancement of the efficiency of any neurorehabilitation activities, it seems to be significant to activate beforehand the potential of the plasticity of the brain to reach the level sufficient for the experience-related creation of new connections. Technologies, which will be able to reactivate the neuroplasticity in the TBI and other pathological conditions, should be considered as a promising tool providing the more efficiency of the existing and new methods of neurorehabilitation.

The potential of the plasticity of the brain may be partly activated through the technologies of physical and cognitive training, which one can refer to the strategy of “environmental enrichment” (EE) (see, for example [30,31]). The EE paradigm includes different conditions of multimodal learning, an enriching the environment with sensory information, mental and motor activity. From numerous animal studies, it follows that the EE can have effects on various levels including behavioral, structural, cellular and molecular levels. The EE was shown to lead to morphological changes in the dentate gyrus, cingulate cortex and corpus callosum [32], an increase in the neurotrophic factors, the enhancement of the expression of genes controlling the proteins synthesis and neuronal signaling [33], the accumulation of neuronal processes in the cortex [34]. The benefit of EE methods was demonstrated in particular for the brain injuries cases [35].

It is assumed that in the TBI patients, the EE can break the “downward spiral of negative neuroplastic changes” through the gain of the activity, which can prevent the negative learning [15]. The hypothesis of negative neuroplasticity is noted to underline the relationship that exists between the behavioral problems, alterations in sensory perception, and the influences of the environmental cues, which is significant to keep in mind when using the EE methods in neurorehabilitation [15]. Currently, different methods of noninvasive brain stimulation (NIBS) are intensively studied, the most well-known of which are various regimes of transcranial magnetic and electrical stimulations [18,36]. In after TBI patients, the repeated transcranial magnetic stimulation (cited from [37]) and the continuous theta-burst stimulation improved symptoms of visual-spatial neglect, confirmed in resting-state functional MRI [38].

A link was recently noted between the evoked by NIBS changes in temporal characteristics of brain activity, an axonal sprouting, and behavior of the person [36]. The mechanisms of TMS and TES impacts the brain are studied as a possible tool to treat some neurological and psychiatric disorders. Also, it was found that noninvasive stimulation therapy can be useful for optimizing the cognitive functions in healthy persons by the impact on cortical plasticity [39]. Another promising approach is related to the low-intensity sensory stimulation with audio, visual and some other signals and is based on the phenomenon of “brainwave entrainment” (BWE). The BWE refers to a well-known high ability of the brain to follow the temp of external influences and synchronize with them its activity [40-42]. The stimulation therapy with sound and light stimuli has been studied in some pathological disorders [41,42]. Flicker stimulation was demonstrated to can modify the cortical activity and improve episodic memory in adults [43]. We should note, however, that in stimulation therapy technologies a periodic rhythm of sound or light signals with deterministic dynamics of oscillations at the preset frequency is commonly applying.

For instance, to support cognitive functions, relaxation, and meditation, rhythms in the alpha, beta, gamma or theta ranges can be used (see, for example, [44,45]). However, according to present notions, the periodic rhythms can improve the activity of the brain in the local, selected EEG range but is unable to restore the complex fractal dynamics of the activity characteristic of the healthy brain. Healthy physiological rhythms including cortical electrical activity have been shown to have the deterministic-chaotic dynamics also known as a fractal dynamics (for review see [46]). The fractal complexity of the healthy physiological processes is well documented for rhythms of breathing [47], the heart-beats [48], steps intervals [49], and the brain activity [50]. On the other hand, during the aging and in diseases, under psychological stress and other conditions, the simplification in the rhythms’ dynamics and the emergence of entirely random stochastic behavior or a deterministic process (harmonic or quasi-harmonic fluctuations) [51] have been revealed.

Thus, the stimulation therapy applying rhythms with deterministic or random (stochastic) dynamics cannot recover the fractal dynamics of physiological rhythms characteristic of healthy physiological systems properly. Moreover, it cannot be ruled out that the applying the regular stimuli can exacerbate the structural and functional disturbances in the brain in the TBI patients. It was demonstrated the possibility of synchronization of the rhythm of physiological activity by an external fractal stimuli (the phenomenon of fractal entrainment). For example, the rhythm of steps while walking can be synchronized with a fractal rhythm of external audio signals [52,53]. However, the therapeutic effects of the stimulation therapy with complex-structured signals have not been studied to date and should be tested in animal and clinical research as a new promising approach to reinforce the efficiency of neurorehabilitation.

Recently we put forward the hypothesis that the normal development and maintenance of the complexity of neural networks and functional activity typical for a healthy brain are intimately linked with the fractal complexity of sensory signals in the environment that affect a person throughout his life [46]. From this hypothesis, it follows that the reduction in the temporal and spatial complexity of environmental cues can promote the progression of an existent or hidden pathology, or can provoke its development. On the other hand, the applying of fractal sensory stimulation or complex-structured stimuli of other modalities can help enhance the efficiency of different therapeutic strategies aimed to a restoration of the brain through the activation of neuroplasticity [31,46]. A little earlier [54], we have noted particularly to the perspectives of using technologies of the fractal flicker stimulation for the elaboration of new approaches in the diagnosis and treatment of the visual system and the brain through the affecting the neuroplasticity.

One can suggest that in patients after brain injuries, the fractal flicker stimulation, as well as the stimulation by complex-structured sound tones and signals of other modalities can promote activating the structural-functional plasticity and improving the memory and other cognitive functions. The changes of the cortical oscillatory activity evoked by a complex-structured signal can serve as a mediator of the impact of fractal stimulation on cognitive performance. In the persons undergone the TBI the potential of neuroplasticity is significantly reduced due to the negative plastic changes developing and it seems to be an objective reason restricted the efficiency of the mental and physical training programs and other technologies of neurorehabilitation, which are relying on the brain’s plasticity mechanisms.

Therefore, the use of new approaches to neurorehabilitation, which can increase the potential of neuroplasticity, must theoretically also improve the therapeutic effects of other known methods of the training the brain. We would like to note that the period of enhanced plasticity reached with the help of fractal stimulation, can present that therapeutic temporal

window, during which an increase in the efficiency of different neurorehabilitation measures should be expected.

Conclusion

The TBI is known to lead to a significant weakening of cognitive functions including an impairment of the memory, making it difficult for the person to be professionally and socially adapted. The ability of the brain to restore and to create the neural connections makes it essential to search for methods that could stimulate the restoration of disturbed networks and also can help building the new ways to compensate the deficit of the cognitive functions. Technologies of cognitive rehabilitation relying on the structural and functional plasticity of the brain include programs of mental and physical training and various techniques of stimulation therapy, including transcranial magnetic and electrical stimulation, and noninvasive sensory stimulation exploiting the BWE phenomenon.

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