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Hypothesis Study

The Possibility of Improvement in Balance and Function Following Conjunct Effects of Transcranial Direct Current Stimulation and Whole-Body Vibration Therapy in Spastic Cerebral Palsy Patients: A Hypothesis Study

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ABSTRACT

Cerebral palsy (CP) results from developmental brain injury, affecting posture and muscular coordination. Traditional treatments offer varying effectiveness, among them the most recent therapies are whole-body vibration therapy (WBVT) and transcranial direct current stimulation (tDCS). WBV enhances proprioceptive function, muscle mass, bone density, and joint stability by stimulating muscle spindle fibers and activating dormant motor units. It also modulates spastic reflexes through mechanoreceptors, proving more effective than traditional physiotherapy. tDCS, a non-invasive neuromodulation, reshapes cortical excitability and modulates synaptic plasticity by altering neuronal activity. It affects long-term potentiation and depression, crucial in learning and adaptive functions. tDCS's interaction with neurotransmitters, especially dopamine and GABA, and its effect on NMDA and dopaminergic receptors make it promising for CP rehabilitation. Both therapies offer novel insights into CP rehabilitation through their influence on central and peripheral neural system.

This hypothesis study tends to explore the conjunct effects of transcranial direct current stimulation (tDCS) and whole-body vibration therapy (WBVT) on improving balance and function in children with spastic cerebral palsy. The hypothesis suggests that WBVT's vibratory input, alongside tDCS's central stimulation, enhances function by modulating neuronal excitability and sensory information. The tonic vibration reflex (TVR) from WBV is believed to amplify muscle strength and modulate spinal excitability. When integrated with tDCS, it might accelerate excitability in the motor cortex, essential for brain-injured patient rehabilitation. Despite evidence of individual benefits from both therapies, conjunct effects remain under-researched. Preliminary results show improvements in balance, gait velocity, and motor functions. Validating this combined approach could revolutionize treatment for children with spastic cerebral palsy.

Keywords: Balance, Cerebral Palsy, Cortical excitability, Non-invasive brain stimulation, Spasticity, Transcranial Direct Current stimulation, Whole-Body Vibration Therapy.

INTRODUCTION

Cerebral palsy is classified as a non-degenerative condition that affects posture, muscular coordination, physical movement that results from developmental brain injury. One or more specific brain regions may be affected by this damage, which often occurs just before, during, or shortly after birth, in infancy, or early childhood (1). The symptoms of cerebral palsy include spasticity, involuntary movements, difficulty in mobility, difficulties in swallowing, speaking, feeding, cognitive impairments, issues with vision, hearing, or speech, learning difficulties, unusual sensory experiences, and breathing difficulties brought on by poor muscular control (2). Based on muscle tone and movement patterns, cerebral palsy is characterized as spastic, ataxic, or dyskinetic (3).

The fundamental biological ideas of neuroplasticity, regeneration, and recovery serve as the foundation for rehabilitation. A growing number of small-scale experimental studies, such as functional magnetic resonance imaging studies and animal models, have shown that plastic phenomena occur within damaged neural networks, the cerebral cortex, and subcortical structures, both at the synaptic

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and cellular levels (4). Traditional treatment for CP in children includes physiotherapy and neurodevelopmental techniques, which can be used in varied degrees of intensity. (5).

One of the most important clinical features of CP is spasticity which is defined by abnormal muscle tone caused by damage to the pyramidal area of brain (6). Muscular spasticity and contractures in people with cerebral palsy can cause changes in joints and bones, particularly in the spinal and lower extremity. Walking, staying in bed, sitting, adjusting seat heights, transitioning between positions, and even standing up all be affected by lower limb spasticity. Spasticity management is one of the basic goal of any therapy for CP children (7).

Numerous rehabilitation treatments have recently been shown to be successful in managing spasticity, motor dysfunction, and balance impairments in people with a variety of neurological diseases such as Cerebral palsy, Parkinsonism, stroke and multiple sclerosis etc. Techniques such as mental practice, focal muscle vibration, functional electrical stimulation (FES), task-oriented therapy, non-invasive brain stimulation, and whole-body vibration therapy are examples of the most known approaches used in the above mentioned diseases. (8) It is believed that when applying peripheral stimulation several body members with low motor function may have and increase in corticomotor excitability, whereas with the application of central stimulation over the motor cortical area, response can be modulated and cortical reorganization can occur. Therefore the conjunct effects of both tDCS and WBV can be of potentially beneficial for the neurological disorders.(9)

Whole-body vibration elicits tonic vibration reflex causing oscillatory vibrations that further progress towards alterations in the length of the muscles. This causes the stimulation of primary sensory receptors of involved muscle spindles, which in turn give rise to more reflexive contractions. (10).

The transference of oscillations and vibrations to the body is recognized by its ability to activate skin receptors, the vestibular system, and muscle spindles. This occurrence is intricately tied to biomechanical attributes of mechanical vibration such as acceleration, frequency, and peak-to-peak displacement. In the context of resonance, each tissue and area possess its biomechanical characteristics. (11). This whole process leads to transformation and various adjustments in brain activity. These changes in brain activity impact the somatosensory area, cortex, and amygdala. This also modulates the dopamine and serotonin that act as communication agents for nerve cells (12).

WBV AND ITS FACILITATION OF VARIOUS SYSTEMS

Whole body vibrations facilitate proprioceptive function at the level of the neural system, reducing the intensity of pain symptoms. On the musculoskeletal front, WBV causes improved muscle mass and strength that in turn improves performance and diminishes muscle wasting. Furthermore, the Vibratory training supplements bone mineral density and elevate joint stability. Taking into consideration the combined positive outcomes, Whole body vibration therapy improve the brain health by increasing the neuronal activity, cognitive function and synaptic plasticity. It may also be consider as the valuable preventive strategy for the neurodegenerative diseases and musculoskeletal disorders(13).

H-REFLEX AND STIMULATION OF IA NERVES DURING WBV

The motor neuron excitability in response to whole-body vibrations could be gauged by a method that involves the measurement of Hoffman Reflex or H-reflex. Based on the results of studies conducted on the muscle-tendon unit it has been shown that vibration is a strong proprioceptive stimulus that reaches both primary somatosensory and motor cortices directly, and different frequencies have a different effect on the firing rate of Ia afferents and also group II that can be observed in differential frequency-dependent effects in the excitability of the motor neurons in the corticospinal tract (13). Vibrotactile stimulus enhances physiological changes in the brain and its enhancement causes rapid activation of the contralateral sensorimotor areas of the brain and stronger cortical lateralization while leading to a richer causal brain network. It also causes the repair and development of cortical neural pathways (14). Neurophysiological observations suggest that balance and proprioception can be improved with training that incorporates tactile, vibratory, proprioceptive, and vestibular stimulation concurrently (15).

WHOLE BODY VIBRATION AND SPINAL EXCITABILITY

Whole-body vibration therapy platforms have variable and fixed parameters. Frequency and time are variable while the side to side amplitude is fixed parameter. Most commonly used frequency range falls within 5 to 40 Hz. The duration of vibration exposure may span from 3 to 20 minutes. However, the number of total sessions and duration of the entire rehabilitation protocol may vary from

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patient to patient (16). There can be horizontal or vertical oscillations (17). These vibrations have the potential to enhance neural drive to the muscles, this augmented response enables the activation of motor units that are previously inactive thus increasing muscle mass and strength in CP (18)

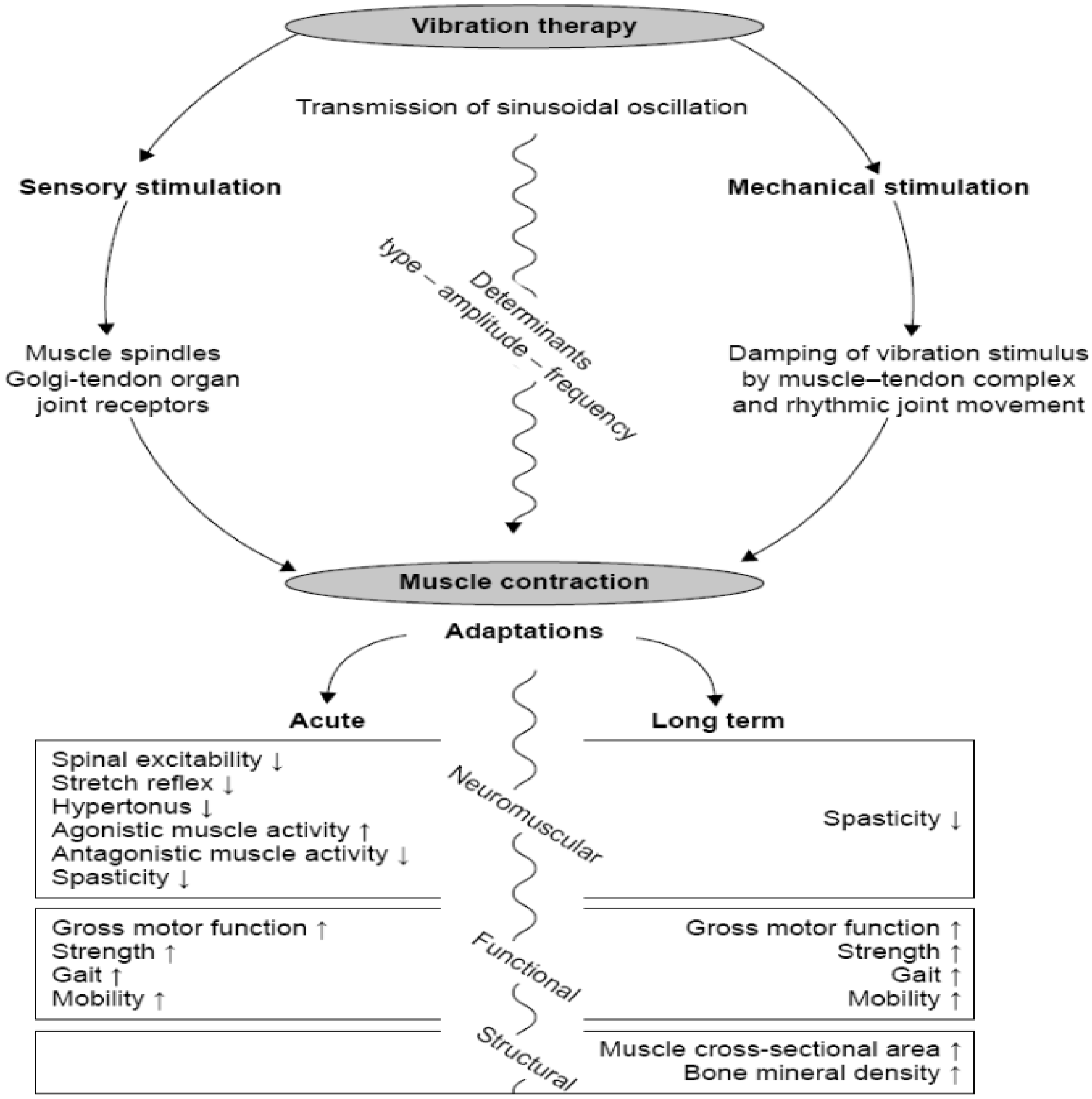


Figure 1 Overview of mechanisms underlying vibration therapy and resulting short- and long-term effects.(19)

The mechanoreceptors are responsible for the detection of certain types of vibrations. The initiation of vibration is detected and the information is transferred through signals that pass from the spinal cord to the somatosensory cortex. The main mechanoreceptors are the Pacinian corpuscles which are also termed pressure receptors. The Pacinian receptors are located deep in the skin and are lesser in other parts of the body. Pacinian receptors can recognize and sense vibrations that are within the range of 20-1000Hz. Apart from there, other touch receptors are known as Meissner corpuscles. Meissner's are located near the surface of the skin; they usually function when there is a formation of skin deformities. Meissner corpuscles detect vibrations that are within the range of 5-150Hz (20).

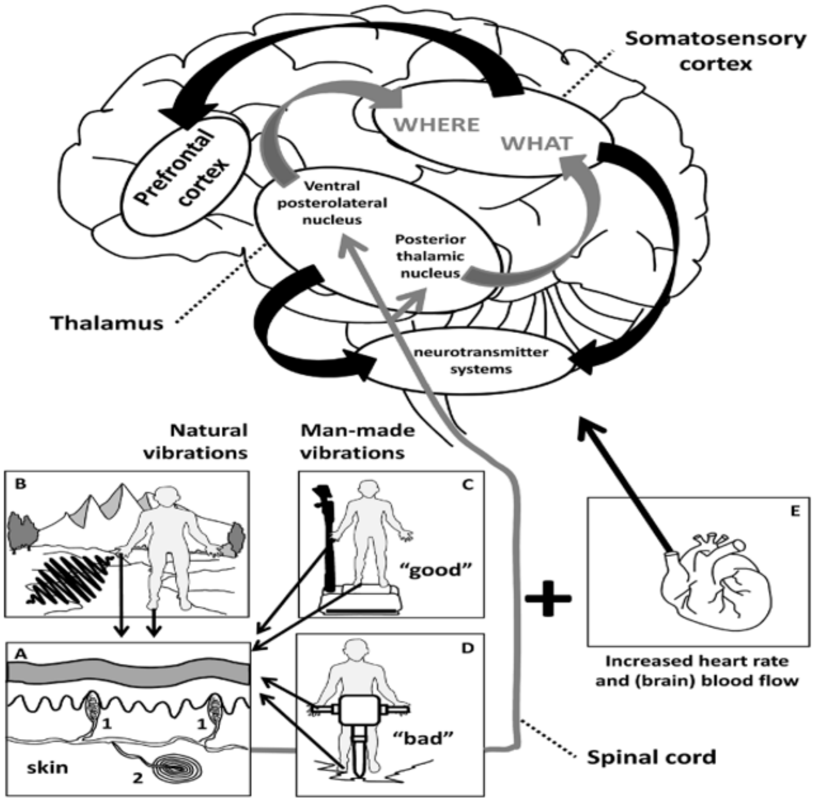


Figure 2: The sensory (skin) component of whole-body vibration (WBV).

A schematic and simplified overview of vibration detection influencing the brain. Mechanoreceptors in the skin (Panel A: 1. Meissner corpuscles, 2. Pacinian corpuscles) detect the (naturally caused) vibrations (depicted in Panel B) and relay the signal to the brain via the spinal cord. In the thalamus, the signal reaches the ventral posterolateral nucleus and the posterior thalamic nucleus.(21)

According to a Meta-analysis by Xiaoye Cai et al, WBV showed a positive impact on gross motor function and increased ankle joint range of motion in children with lower extremity cerebral palsy. They also reported that WBVT can decrease timed up and go test results, leading to decreased risk of fall. They concluded that whole-body vibration therapy proves to be more efficacious and superior to traditional forms of physiotherapy as it enhances the lower limb motor skills of children with cerebral palsy (22).

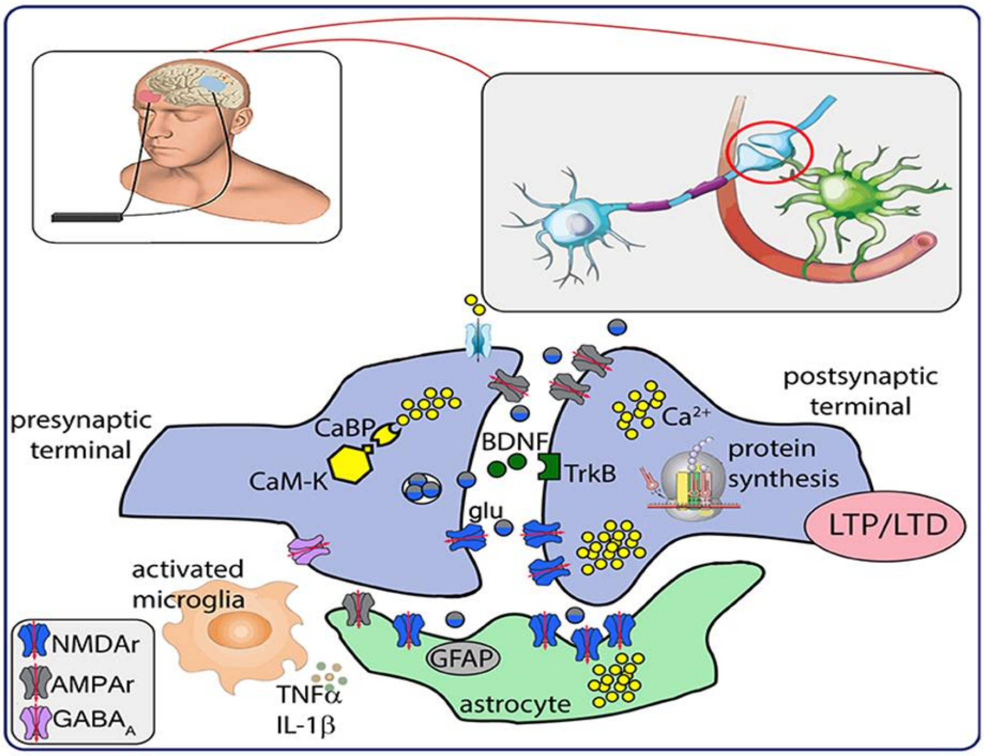
TRANSCRANIAL DIRECT CURRENT STIMULATION AND ITS ROLE IN SYNAPTIC PLASTICITY

Transcranial direct current stimulation is a non-intrusive and innovative approach to enhance the functioning of the brain. It consists of a device and dual electrodes; anode and cathode which work as a channel for generating low electrical current. The subtle electrical flow helps in reshaping the cortical excitability thus enhancing the clinical outcomes. Emerging evidence about transcranial direct stimulation indicates that it could be a useful therapeutic tool for neuropsychiatric disorders (23).

The mechanism of tDCS is fascinating as it can influence the synaptic plasticity. Synaptic plasticity is a phenomenon that carries out adjustments in the speed and intensity of neuronal signals as a response to individuals' activities accordingly. The synaptic connections are deeply affected by the Long-term potentiation (LTP) that leads to an increase in synaptic strengths. In contrast to this, long-term depression (LTD) causes a decrease in synaptic strength. (24).

The core concept of tDCS is operating on a simple principle i.e. the positive terminal of the battery also referred to as the anode is connected to one specific location on the head and the negative terminal or cathode is attached at the other end of the head. An electromotive force is generated between these two contact points on the head that creates a potential difference. This difference pushes positively charged ions that are potassium, sodium, and calcium away from the anode i-e. towards the cathode. This way neurons that are located under the anode get a boost for excitation and at the same time inhibition occurs at the cathode end. That's how whole brain activity is modulated. (25)

Multiple neurotransmitters including amphetamines which are catecholamine reuptake blockers, dopamine, and GABA can increase the state of cortical hyperexcitability that is induced by anodal tDCS. A remarkable decrease in GABA levels occurs with the increase in the concentration of glutamine and glutamate. Looking at the broader picture, it is manifested that the neuroplastic effects of tDCS are in connection with the calcium-dependent synaptic plasticity of glutamatergic neurons (26).



tES induces intracellular Ca^{2+} increase and activation of Ca^{2+}-dependent enzymes (CaM-K). Presynaptic mechanisms result in glutamate release that activates AMPA/NMDA receptors, modulates BDNF release and interaction with TrkB receptor, responsible for a cascade of intracellular events that lead to protein synthesis. Electrical stimulation also modulates activation of astrocytes and neuroinflammatory response. Altogether, these mechanisms may underlie the establishment of LTP/LTD.(27)

Figure 4 Schematic representation of neurobiological after-effects of transcranial electrical stimulation (tES)

MECHANISM AND EFFECTS OF TDCS DURING AND AFTER STIMULATION ON NMDA RECEPTORS: -

Spontaneous neural activity was noted when the anode was placed above the cortex but the reduction in spontaneous discharges was observed during cathodal polarity. When employing a pharmacological route, it becomes evident that the effects of transcranial direct current stimulation are contingent on cell membrane polarization. It is to be noted that when sodium and calcium channel blocker is administered, it nullifies the enduring effects of tDCS. The lasting effects triggered by tDCS are because of the alterations in NMDA receptor sensitivity. In this context, it is to be taken into consideration that dopaminergic receptors play a vital role in the neuroplasticity that depends on NMDA receptor activity (28).

APPLICATION OF TDCS TO TARGET SPASTICITY

Addressing spasticity, which is one of the most common and challenging symptoms in cerebral palsy and a key component targeted by tDCS intervention. Spasticity is characterized by an increase in muscle tone, exaggerated tendon jerks, and stretch reflexes due to heightened reflex activity. The association of spasticity with cerebral palsy is a fatal combination as it damages the motor cortex and inhibits the cortical input to the corticospinal tract. In return, spinal excitability escalates in speed and induction which directly affects the muscle tone (29).

To evaluate the effectiveness of transcranial direct current stimulation on spastic cerebral palsy Aree-Uea et al, conducted research that was based on 46 CP children between the age of 8 and 18 years. The intervention specifically planned was a combined anodal tDCS applied over the left primary motor cortex. The dosage for tDCS was 1mA for 20 minutes and over 5 sessions. The results and findings of the study suggested that there was a promising decrease in spasticity in the elbow and wrist immediately after 24 hours of post-treatment sessions. This highlights the potential of transcranial direct current stimulation as a promising therapeutic tool in managing spasticity and other symptoms related to cerebral palsy (30)

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HYPOTHESIS

1. The conjunct effects of transcranial direct current stimulation and whole-body vibration therapy might improve the balance and function in spastic cerebral palsy children more as compared to either modality applied alone.
2. If peripheral stimulation such as mechanical input like vibration is applied to the lower extremity with the conjunct application of central stimulation as transcranial direct current stimulation applied to the primary motor cortex area, it can improve the function via vibratory inputs to the receptors together interacting with the neuronal excitability through central inputs. more as compared to either modality applied alone.

EFFECTS OF INTERVENTION: -

The whole-body vibration therapy is a distinctive technique due to its oscillatory movement which mimics the pattern of human gait. This triggers the activation of proprioceptive spinal circuits that induce rhythmic muscle contractions in the lower limbs and trunk as a compensatory response. (31).

The effect of transcranial direct current stimulation is influenced by the timing and sequence in which it is paired with rehabilitation. Implementing tDCS influences the activity of the brain at specific areas where the electrodes are positioned. It is applied to the motor cortex to affect the motor activity of the brain. The reduced cortical input into the corticospinal tract leads to spasticity in cerebral palsy children; here anodal tDCS plays an essential role. The neurophysiological effects of anodal stimulation enhance motor learning by augmenting cortical excitability. These benefits translate into functional improvements in gait and spasticity. This also helps in improving static balance in CP (32).

EVALUATION OF HYPOTHESIS: -

For populations with frailty and medical issues, WBV has drawn more attention, presumably because of its safety, efficacy, and efficiency.(33) Whole-body vibration (WBV) therapy has positive neuromuscular effects on muscle strength, it is becoming more popular as a modality for sports, exercise, and physical rehabilitation. The spinal segmental reflex is the most frequently suggested mechanism for the benefits of muscle strengthening. Still, the spinal reflex pathway's neural architecture and receptors are not fully understood. The tonic vibration reflex (TVR) is said to account for the neuromuscular action of WBV. When 100–150 Hz vibrations are given to a muscle's tendon or belly, Ia afferent activation occurs, resulting in the TVR, a polysynaptic spinal response based on muscle spindles.(34)

Based on the existing hypothesis, the mechanism underlying the effect of neuromuscular training on sensorimotor deficits may be related to both spinal (e.g., altered H-reflex) and supraspinal adaptation (e.g., feed-forward reflexive mechanism) (35). The central nervous system's reflexive activation at the spinal and supraspinal levels may be facilitated by WBV, which could explain its potential benefits.(36). Specifically, it has been demonstrated that WBV can modify spinal excitability in a human trial and animal brain synaptic plasticity and neurogenesis (37)

Focusing on the evaluation of the hypothesis the repetitive electrical peripheral nerve or muscle stimulation can induce a lasting increase in the excitability of the corticomotor projection. Combining peripheral stimulation such as vibration therapy with transcranial direct current stimulation as central stimulation possibly shorten the duration of stimulation needed to induce the effect. This capacity to cause alterations in motor cortex excitability may be important for brain injury patients' rehabilitation. The motor and sensory cortex can undergo organizational changes as a result of changes in afferent input. Larger motor evoked potentials (MEPs) after Non-invasive brain stimulation such as transcranial magnetic nerve stimulation or transcranial direct current stimulation have been used as evidence that temporary deafferentation of a limb causes a swift increase in the excitability of the cortical projection to muscles proximal to the block. (38)

It is proposed that central stimulation used in conjunction with ischemic block enhances the increase in MEP size and specifies the role of NMDA receptors and long-term potentiation-like mechanisms. (39) By combining peripheral nerve stimulation with central stimulation, it is possible to shorten the time required to induce robust excitability increases. Little is known about the mechanisms responsible for the increases in excitability seen following peripheral, or dual peripheral and central, stimulation. However, given the nature of the changes induced by these different protocols, it would seem plausible that similar mechanisms may be responsible. From the time course of effects, parallels have been drawn with the changes associated with long-term potentiation reported in the animal literature (40).

Consequently, we hypothesize that there may be changes and improvements in the function, balance, and gross motor function of spastic cerebral palsy patients due to the conjunct effects of the whole-body vibration therapy and transcranial direct current stimulation. As previously up to our knowledge no evidence has been found that focuses on the conjunct effect of the central and peripheral stimulation using mechanical stimuli and low-intensity electrical stimuli. Thus, it

is suggested that, by combining central stimulation with peripheral stimuli, it would be possible to enhance the effects of each intervention individually and, as a consequence, achieve faster and long-lasting results.(41) Additionally, as it has been proposed that tDCS is able to alter sodium and calcium channels as well as NDMA-receptor's activity while peripheral stimulation exerts more influence over GABAergic interneurons and less modulations of NDMA-receptor.

Therefore, it is possible to suggest that central and peripheral stimulation have synergistic effects in neuromodulations tasks and cortical excitability.(9)

DISCUSSION AND CONSEQUENCES OF THE HYPOTHESIS: -

Most studies reported the positive effects of Whole-body vibration therapy on balance, strength, gait, walking speed, standing function, spasticity, flexibility, proprioception, and range of motion. Furthermore, there is no evidence found of whole-body vibration stimulation in conjunct with transcranial direct current stimulation for the patients with spastic cerebral palsy patients. We hypothesize that conjunct effects of transcranial direct current stimulation and whole-body vibration therapy will have pronounced effects on balance and function in spastic cerebral palsy patients. By applying mechanical vibration, a stimulus to the mechanoreceptors in combination with the central stimulus of low-intensity current as in TDCS results in modulation of the neuronal excitability as well as alternates the sensory information from the skin receptors and musculoskeletal system that is transmitted and processed by all the peripheral and central components of the somatosensory system. If the abovementioned hypothesis is verified, perhaps it can be of significant importance for CP children to improve their functional status. Regular whole-body vibration therapy can serve as an alternative, safe, and efficient treatment for children with cerebral palsy in both clinical and home settings.(42)

Similarly, tDCS appears to be safe and highly tolerable in several neuro-disorders(43)In adults with neuromotor disorders, tDCS is safe and moderately effective in improving performance and participation(44). A study reported that 3- week whole-body vibration training was effective in improving ankle Joint position sense, balance, and gait variables in children with CP. (45)

Another study reported that a 12-week intervention of WBVT can improve the strength of knee extensors and also decrease spasticity with positive effects on motor development as well as walking speed in Diplegic CP children (46).

Therefore, if it is proved that the WBV therapy in combination with transcranial direct current stimulation can have positive results on the neural plasticity of the brain. Therefore, it might help provide some strong scientific evidence and clinical approach considering its availability and ease of accessibility for spastic cerebral palsy children.

CONCLUSION: -

Based on the presented data, we hypothesize that there may be a promising potential in the conjunct application of transcranial direct current stimulation (tDCS) and whole-body vibration therapy (WBVT) for enhancing balance and function in children with spastic cerebral palsy. Independently, each intervention of WBVT and tDCS has demonstrated efficacy in improving various parameters related to mobility and motor function. WBVT, through its mimicry of human gait, offers benefits in reducing immobility and augmenting lower limb functionality. Similarly, tDCS, when targeted at the motor cortex, can ameliorate the challenges of spasticity by modulating cortical excitability. The underlying mechanisms, such as the tonic vibration reflex induced by WBV and the increased cortical excitability due to tDCS, suggest potential synergistic effects when both interventions are applied concurrently. While preliminary studies support the individual efficacies of WBVT and tDCS, comprehensive research on their conjunct effects remains scant. If the hypothesized conjunctive benefits are validated through rigorous study, this combination could revolutionize therapeutic approaches for children with spastic cerebral palsy, offering a safe, accessible, and effective treatment regimen.

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