Study of Available Intervention Techniques to Improve Cognitive Function in Cerebral Palsy Patients

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Abstract

The brain is inherently plastic in nature; hence, it is moldable, malleable, changes with experience and is never quiet. There are many factors that influence the brain’s capacity and plasticity throughout the lifespan of an individual. Damage or injury to any part of the brain leads to neurological disorder that affects normal development and cognition. Cognitive impairment is predominantly seen in cerebral palsy (CP) patients with some other associated problems such as poor physical development, low vision, hearing impairment and poor social skills. In CP, cognitive impairment is one of the major issue due to which normal development is not achieved with respect to the age of the child. Cognitive impairment may be defined as poor amplification of core capacities of the mind due to which person has difficulties in remembering, making decisions and learning of new things that poorly affects their day to day activities of living. This review tries to study the various interventions and techniques available that could help in improving cognitive ability in CP patients. The study encompasses the present conventional and unconventional treatment approaches available for cognitive enhancement and the results open viable possibility of exploring new interventions for cognitive development in CP patients.

Keywords: Cerebral palsy, Cognitive impairment, Cognitive enhancement.

Introduction

The term Cerebral Palsy (CP) was first described by Dr. William John Little in 1861 who was an orthopedic surgeon. According to him, CP is a wide range of disorders related to movement and posture that affects development of cognitive abilities [1]. CP can be classified in various forms; according to clinical features, level of muscle tone, topographical classification and affected body part. According to muscle tone, CP can be hypotonic (decrease muscle tone) and hypertonic (increase muscle tone); according to topography, CP can be hemiplegic (half body part involved), monoplegic (only one limb involved), diplegic (lower limb involved more than upper limb) and quadriplegic (all four limb involved) [2]. If CP is classified according to clinical features, it can be ataxic, athetoid, mixed and dystonic. CP is frequently seen as one of the major developmental disability in children and the incidence is rising day by day due to increased rate of survival of premature infants. CP is the major permanent physical disability caused by cerebral dysfunction of the brain. This cerebral dysfunction occurs before, during or after birth [3]. The major region of damage is seen in the white matter composition of brain material near the lateral ventricle area called periventricular area [4]. CP is associated with other problem such as nystagmus, poor intelligence, hearing problem, drooling of saliva, impaired speech and developmental delay [5]. The impairments include sensory, poor socialization, poor communication, limited visual perception and cognition [6]. Out of these associated problems cognitive impairment is most important issue in CP that is responsible for poor overall development. According to statistical data of 2014 [7] every 2-3 children have CP out of thousand live births and 25-80% of these patients have additional posture, motor and other disabilities.

Cognitive ability is a mental process of acquiring knowledge and understanding through acquired knowledge and experience [8]. It encompasses many processes such as knowledge [9], attention [10], memory, judgment [11], evaluation [12], reasoning, decision making and problem solving [13]. Cognitive ability can be affected congenitally in some neurological conditions such as autism, cerebral palsy, Down’s syndrome and mental retardation or it can also be affected by some acquired diseases such as dementia, old age factor, poor exposure, traumatic brain injuries and neurodegenerative diseases. These disabilities can appear at any age. The level of cognitive disability depends either on the structure of the brain or the chemical component of the brain. Lesion or damage in
these structures affect the cognitive ability in an individual. Since CP is caused due to an insult to a developing brain, henceforth the causes of cognitive impairment in these patients can be well understood. In order to increase the level of cognitive ability in CP patients several interventional tools are employed such as brain gym, cognitive exercise, neurofeedback and Transcranial magnetic stimulation. This review projects commonly used interventional tools for improving cognitive abilities in CP patients.

**Stages of cognitive development**

According to the Piaget’s theory, the cognitive development is a progressive development that matures in stage wise manner. The cognitive development occurs in four stages (figure 1) [14-15]. Stage-I is the period of sensorimotor development, it starts from birth to the second year of life. During this period child learns coordination of sensory and motor inputs. Stage-II is a preoperational period which start from second year of life to seven years. In this stage, children learn development of symbolic thought marked by irreversible centration and egocentrism. In stage-III, a child learns mental operations applied to concrete events. This stage is known as concrete operational stage, which spans from seven to eleven years. The last stage of cognitive development is formal operation period which starts from the age of eleven years through adulthood and during this period a child learns mental operation applied to abstract ideas and logical systematic thinking.

**Cognitive disability**

The human brain is a live machine which is highly complicated to understand and any disorders associated with its functioning are even more difficult to interpret. One such disorder is cognitive disability, this is an inability of an individual to perform higher level of brain functions such as planning, problem solving, maintaining and performing tasks in meaningful manner. Cognitive disability interferes with daily needs and functioning of an individual which is not only seen in CP but it also in various other conditions such as traumatic brain injury, autistic spectrum disorder, attention deficit hyperactive disorder, congenital disease and malformation of brain structure [16]. In CP, grey and white matters are the most common type of damage observed using Magnetic Resonance Images (MRIs) studies [17]. Hypoxic Ischemic Encephalitis (HIE) in the frontal lobe of CP patients results in global hypoxia which causes severe damage in several cases manifested by muscle tone abnormality and cognitive impairment. In such cases, the internal capsule gets less blood supply in the brain, the brunt of HIE falls on the internal capsule involving cognitive impairment. If the level of cognitive impairment increases it leads to mental retardation and learning disability. The prevalence of moderate, severe and profound mental retardation is about 30% to 65% in all cases of CP [18].

**Physiology and Causes of cognitive impairment**

Acquisition of cognitive functions in human brain is accomplished by various sequences of neurodevelopmental events during brain growth comprising of cell differentiation and migration followed by morphogenesis [19]. These cellular changes include extension and branching of neuritis and formation of synapses to assemble the proper neural circuit during brain development [20]. The integrity of white matter and dopaminergic pathways is considered an important component for normal brain function with respect to cognitive ability [21]. In general, there are eight dopaminergic pathways in which nigrastral pathway is related to cognitive ability, associated learning and reward related cognition [22]. It transmits dopamine through substantia nigra to the putamen and caudate nucleus if there is any damage in dopamine transmission it results in the cognitive disability. Cognitive impairment may occur due to several reasons some causes are reversible while other are not. The potential causes of cognitive impairment are acquired brain injury, progressive neurodegenerative disease, and others as mentioned in Figure 2.

**Available intervention for cognitive enhancement**

In CP patients, components such as physical therapy, oromotor, fine motor and gross motor skills are paid due attention in society as well as by different rehabilitation professionals. On the other hand, the domain of cognitive impairment which is equally important for an overall development of a CP child is always neglected. Currently there are many techniques for cognitive skill enhancement for related disorders such as brain computer interface [23], Transcranial magnetic stimulation [24], brain training through neurofeedback [25] and high-pressure oxygen therapy (hyperbaric oxygen therapy) [26]. These therapies have demonstrated good results in improvement of cognitive domain of injured as well as normal brain.

**Brain Computer Interface (BCI)**

Brain computer interface also known as mind machine
interface (MMI), direct neural interface (DNI) or brain machine interface (BMI) [27]. BCI is a direct pathway for communication between the wired brain and an external device. BCI has been one of the most outstanding biomedical engineering researches for decades. BCI allows an individual to control external devices by modulating their brain waves. In BCI, device control and their modulation are performed using electroencephalography (EEG) [26]. EEG is used directly in research, mapping, assisting augmenting and repairing human cognitive or sensory motor functions. The interaction between brain and machine is an old concept; however, BCI is increasingly becoming popular in medical field as well as in clinical practice. In BCI, some physical devices (electrodes) are implanted into the brain for either brain signal acquisition or stimulation to treat some neurological disorders [28]. BCI is beginning to be seen as a potentially valuable technique to restore lost neurological functions such as speech, motor leaning and cognitive skills. It works on phenomena of neuroplasticity that allows the brain to store new set of information either by enabling creation of new connections between neurons or by deletion of older connection due to damaged neurons. In BCI, computer generated visual stimulation and sophisticated signal processing provides a communication channel between brain and machine [29]. These acquired signals are processed through digitization technique which helps to extract the feature and translates it into algorithm for the understanding of computing devices. Most BCI uses EEG signals originated mainly in somatosensory or motor areas of the cortex along with various brain waves such as alpha, beta, gamma and delta through the scalp in a close packed manner for signal acquisition (figure 3). A BCI interface utilizes the brain electrical activity which communicates brain signals. In one of the study by Emanuel Donchin et al. (2000) suggested that the exogenous components of sensory functions are largely independent of the role that stimuli play. The endogenous components, on the other hand, are manifestation of processing activities that depend on the role of the stimuli within the task the subject is performing, and on the interaction between any given event and the context in which it is presented. This process helps in perceptual leaning which helps in improved cognition through neuroplasticity. These process of work helps in enhancement of cognition in BCI [30].

Neurofeedback Training

Neurofeedback (NFB) has been employed in research and clinical settings for the investigation and treatment of a growing number of psychological illnesses [31]. This technique involves detection of EEG signal from the scalp and its frequency decomposition into its component waveform (alpha, beta, theta, gamma and delta) thereby making them visible as polygraphic traces on a computer screen. Neurofeedback is being considered as a promising new method for restoring brain function in mental disorders [32]. It takes into account behavioral, cognitive, and subjective
aspects as well as brain activity. The working process of NFB based on phenomena of neuroplasticity [33] in which NFB device measures the different brain waves such as alpha, beta, gamma and theta that help in teaching the brain to make healthier patterns by rewarding the brain when it does so. Once the healthier brain wave patterns are practiced it helps the brain to learn and improve its own regulation. NFB helps in the improvement of concentration, attention, perception working memory and cognition [34-35]. NFB uses real time displays of electroencephalography (EEG) to illustrate brain activity, often with a goal of training brain activity. Sensors are placed on the scalp for monitoring the brain waves. The brain's electrical activity, which is the language that the brain uses to communicate within its complex neural networks, is recorded on a Quantitative electroencephalography (QEEG). The QEEG shows the patterns of electrical activity in different areas of brain. NFB is based on specific aspects of cortical activity. It requires the individual to learn to modify some aspect of his/her cortical activity. The procedure is based on operant conditioning whereby an individual modifies the amplitude, frequency or coherence of the electrical activity and learn to influence the electrical activity of their brain. QEEG is a tool for evaluating encephalopathies associated with diverse causes such as hypoxic ischemic [36], hepatic [37] and methamphetamine abstinence [38]. Nowadays, NFB have gained much attention for research in field of cognitive
enhancement because it is an approach based on operant conditioning in which brain activity, decoding or identifying the brain pattern of interest and then providing the user with feedback stimuli depends on the desired working level. NFB training have therapeutic effect on neurological as well as psychological conditions such as CP, autism, attention deficit, dementia, schizophrenia and senile memory loss [39]. In a study by Efthymios et al. (2007) found that NFB helps in enhancement of non-disordered cognition and the same study also suggested that EEG peak alpha frequency (PAF) has positive correlation with cognitive performance and is correlated negatively with age after childhood [40].

**Transcranial magnetic stimulation**

Trancranial magnetic stimulation (TMS) is a technique for noninvasive stimulation of the human brain by magnetic pulse through a coil put on the scalp [41]. It is widely used in the field of human motor and cognitive functions. Anthony Barker was the first person who developed this technique of brain stimulation in 1985 and ever since then it had been researched thoroughly both as an investigational and therapeutic tool. TMS is an approved tool by the Food and Drug Administration, USA for various neurological and psychiatric disorders. Depending upon various parameters such as frequency, intensity, number of pulses and number of sessions, TMS helps in the inhibition or excitation of neural pathways and neurons [42]. The working mechanism of TMS depends on Faraday’s law of electromagnetic induction which states that the magnetic pulses situated near the conductors are transformed into electrical current and results in the depolarization and hyperpolarization of underlying nerve cells [43]. In TMS, the targeted part is not only stimulated by this stimulation technique, it also stimulates the surrounding areas. Various therapeutic applications of TMS were demonstrated in vision [44], language [45] and cognitive [46] enhancement. TMS enhances the cognitive ability by cortical modulation and increases communication efficiency within the neural networks of the brain for a cognitive level enhancement [47]. Administration of TMS appears to prevent excess neural excitability and correct frontal dysfunction thereby improving cognitive performance [48]. TMS is one of the effective modality for regional activation that activates the underutilized neural pathways, neurons, and neurotransmission.

TMS has established itself as investigation tool for cognitive neurosciences [49]. In 1997, Ashbridge et al. used single pulses TMS for investigation of visuo-cognitive function in human samples [50]. Bohning and colleagues in 1998 measured bold response induced by TMS [51]. In 1997, Paus et al. reported successful combination of TMS and positron emission tomography (PET) to study neural connectivity [52] related work. TMS have range of application in cognitive domain some are mentioned in Figure 6. According to Grafmen et al. (1994) TMS improve working memory and implicate learning which was further demonstrated by Pascaul Leone et al. (2007) by applying TMS on prefrontal cortex for linguistic processing. In another study by Barsani et al. (2013), it was found that TMS was able to modulate cortical excitability up to a maximum depth of 6 cm which not only modulated the activity of the cerebral cortex but also the activity of deeper neural circuits [53] that were responsible for cognitive functions.

**Hyperbaric oxygen therapy (HBOT)**

Hyperbaric oxygen therapy (HBOT) is the use of 100% oxygen in a pressurized chamber to treat wounds in the brain of any duration in any location. In cerebral palsy, hypoxic brain injury is major cause of brain damage and impaired cognitive functions. In HBOT, oxygen is used from a medicinal point of view at an ambient pressure higher than atmospheric pressure, allowing therapeutic recompression for the decompression illness intended to reduce the injurious effects of brain damage [54]. HBOT significantly improves the tissue oxygen concentration and affects both oxygen and pressure sensitive genes. It also helps in initiating the vascular repair and improves cerebral vascular flow, regeneration of axons, white matter, promotes blood brain barrier integrity and reduces inflammation reaction [55]. In cellular level, HBOT helps to improve cellular metabolism, reduce apoptosis, alleviate oxidative stress and increase neurotophins and nitric oxide by enhancement of mitochondrial function in neurons and glial cells. These improved factors promote the neurogenesis of endogenous neural stem cell and helps in cognitive enhancement in cognitive disabilities such as CP, Autism, dementia [56]. According to Jain et al. (1996) HBOT reactivates the metabolic potential in recoverable brain tissue [57]. In 1994, Neubauer and colleagues suggested metabolic
reactivation to support the cognitive enhancement in CP. They also suggested this HBOT therapy in CP improves more muscular flexibility in spastic CP patients [58]. In HBOT, due to vasoconstriction the microorganisms are killed which enhances the antibiotic activity that leads to the enhancement of immune system. When the body immune system improves it increases the rate of tissue proliferation and ultimately helps in healing of damage nerve tissue (figure 7).

### Pharmacological Approaches

In various neurological and psychological disorders such as schizophrenia, CP, autism, etc; cognitive impairment is a core feature. According to studies on schizophrenia by the National Institute of Mental Health (NIMH), India in the year 2015 it was found that new drugs namely galantamine, glutamine and anticholinergic can be used for the treatment of cognitive impairment. In their study, they found that the use of single drug is not much effective for cognitive enhancement; instead they suggested combination of an acetyl cholinesterase inhibitor (AChEI) and memantine [59]. In human body, cholinergic system is associated with attention, memory, processing and sensory inputs [60] but in schizophrenia these inputs are impaired. The alteration in muscarinic receptor and nicotinic receptor improves the cholinergic activities that help to improve level of cognition in schizophrenic patients. Similarly, glutamine is not only anticholinergic drug but it also has property of allosteric modulator of the α4β2 and α7 nicotinic receptors [61]. Galantamine increase dopamine release in the hippocampus and this effect was associated with improvement in cognition [62]. Galantamine with combination of resperidine drug have good result for cognitive changes in autism and CP patients.

In case of cerebral palsy, omega-3 fatty acids to certain extent may help to improve cognitive ability. Omega-3 fatty acids are mainly present in fish, vegetable oils, nuts (especially walnuts), flax seeds, flaxseed oil, and leafy vegetables. Omega-3 fatty acids are the long chain of polyunsaturated fatty acids (PUFA) which during desaturation and elongation reaction produces neurobehavioral responses. It is one of the essential fatty acid which is not synthesized in the body so it is derived from dietary source. It plays a major role in cognitive development, learning ability, neuroplasticity and neurogenesis [63].

### Physical exercise for cognitive development

The brain has a capacity to learn through experiences. It is moldable, malleable and changeable with experience and is never quiet. There are many factors that influence the brain capacity, potential and plasticity throughout the lifespan of an individual and this is where physical exercise merges with neurosciences for cognitive enhancement. Exercises are the developmental approach to the rehabilitation that facilitates social cognition. Physical exercises have positive effects on brain development, according to researchers from Duke University; they report that exercise have antidepressant properties [64] that improves the brain functions by producing the endrotropin responsible for boosting the activity of hippocampus and the frontal lobe. Physical activities or exercises have widespread effects on central nervous system (CNS) as well as peripheral nervous system (PNS). Physical activities improve cognitive function by involving different neuronal pathways which results the neuroplasticity [65]. According to Trejo et al. (2001), physical exercise affects production of the neurotransmitters by releasing serotonin and acetylcholine which helps to enhance cortical choline uptake and dopamine receptors. This factor helps to play important role in neuroplasticity [66].

### Challenges and future works

Development of an effective treatment for cognitive impairments in cerebral palsy is a major public health concern because conventional methods for cognitive enhancement such as education, brain games, social interaction, and mental activities techniques are widely accepted till date while unconventional methods such as drugs, implants, BCI and HBOT tend to evoke more of moral and social concerns. The demarcation between conventional and unconventional methods is problematic. These conventional methods are easily absorbed by the society for cognitive development as ordinary category of human tools but the use of unconventional
techniques is controversial. Ericsson et al. (1980) suggested that the use of biomedical techniques for cognitive enhancement produces modest improvement but more dramatic result can be obtained with use of conventional methods such as brain activity games, puzzles solving, and educational methods [67]. The use of drugs for cognitive enhancement is task specific and their results are often quite general. In future multidisciplinary approaches such as standard therapies that include brain exercise, play therapy, physical activity, virtual reality sessions and educational surrounding along with other available unconventional intervention may help in cognitive enhancement in cerebral palsy.

**Conclusion**

Cerebral palsy is one of the lifelong diseases and life span of CP patient is more than 40 years. There is need of development of significant protocols for enhancement of cognitive ability. In these days where medical and research field are at an advanced stage; many interventional tools for cognitive development for neurodegenerative and psychiatric disorders are emerging. If we talk about cerebral palsy, autism and mental retardation there is lack of treatment protocol for cognitive development in these children. In case of pediatric population where the chance of cognitive improvement is fast due to developing age, we have very few interventional tools especially for CP. There is need to develop improved protocols for any given technique according to the mental status and level of brain injury of a CP patient, which could enhance their intellectual ability and improve cognitive functions for day to day life.

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