INFLUENCE OF AEROBIC EXERCISE ON INHIBITORY CONTROL OF EXECUTIVE FUNCTION IN SPASTIC HEMIPLEGIC CEREBRAL PALSY: A Randomized Controlled Trail

Document Date: - 01/08/2019.

Human Subjects protection review board approval date: - 31/03/2019
INFLUENCE OF AEROBIC EXERCISE ON INHIBITORY CONTROL OF EXECUTIVE FUNCTION IN SPASTIC HEMIPLEGIC CEREBRAL PALSY: A Randomized Controlled Trail

Abstract

Background: Inhibitory control of executive functions (EF) is one of the main specific cognitive impairments that affect children with cerebral palsy, cognitive skills begin to develop in infancy and continuing through the pre-school years, childhood and into adolescence it changes across the lifespan of an individual and has great effect on their participation and quality of life. Aim: The aim of study was to assess the influence of aerobic exercise on inhibitory control of executive functions in spastic hemiplegic cerebral palsy. Methods: Sixty children with spastic hemiplegic cerebral palsy were enrolled in this study and were assessed for eligibility. Their aged ranged from seven and eleven years. They were assigned randomly into two equal groups. Group (A) the study group received aerobic exercise in addition to selected physical therapy program. And group (B) the control group received the same selected physical therapy program only. The treatment was conducted for one hour, three times / week for three successful months. Eriksen flanker test and Stroop Color-Word test were used to assess inhibitory control of EF pre and post treatment. Results: Post treatment there was significant increase in accuracy in Eriksen flanker test and Stroop Color-Word test and decrease in reaction time (congruant and incongruant) only in study group, P< 0.05. Conclusion: Aerobic exercise has significant effect on inhibitory control of executive functions in spastic hemiplegic cerebral palsy. Key words: Hemiplegic cerebral palsy, inhibitory control of executive functions and aerobic exercise.

Introduction:

Cerebral palsy (CP) is a group of permanent disorders of the development of movement and posture causing activity limitation. It is the most common cause of physical disability that attributed to non-progressive neurological condition that occur in the developing fetal or infant brain.[1] Motor impairment has frequently been associated with secondary disturbances as communication, sensation, perception, behavior and cognition, as well as the presence of epilepsy, disequilibrium[2], and secondary musculoskeletal problems[3]. Hemiplegic CP is a subtype in which one side of the body is involved. It affects about 1 in 1,300 live births[4]. It is characterized by a clinical pattern of unilateral motor impairment[5]. The severity of motor impairment varies widely, depending on the site and severity of brain lesion[6, 7]. Early brain injury impacts concomitantly on motor, function and cognitive development[8]. Cognitive ability is a mental process of acquiring
knowledge and understanding through acquired knowledge and experience[9].

Executive function (EF) constitutes a set of cognitive processes that comprise distinct yet highly interrelated components such as cognitive flexibility, inhibitory control, and working memory [10]. Because EF is involved in the regulation of both thought and action, the behavioral manifestations of EF can be assessed [11], including difficulty switching between tasks, difficulty initiating new nonroutine actions, and a lack of impulse control [12]. EF have received considerable interest and are strong predictors of children’s early school success and it includes intentional shifting/flexibility, working memory, and inhibitory control[13].

Inhibitory control referred to as response inhibition, is one of the separable cognitive processes thought to comprise the construct of executive function. In the past, inhibitory control was thought to emerge only in middle to late childhood, corresponding with improvements in the child’s ability to execute complex, higher-order integrative tasks [14].

Aerobic exercise refers to exercise that involves or improves oxygen consumption by the body. It is the type of activity that uses large muscle groups. Its performance is in a continuous and rhythmic way with a main goal to make the heart and lungs work harder than they do when the person at rest [15]. Aerobic exercise produces vascular changes, including an increase in oxygen saturation, promotes angiogenesis, and increases cerebral blood flow (CBF) in areas related to cognitive function [16]. Aerobic exercise training improves cerebral perfusion[17] and metabolism [18], resulting in the reduction in Aβ load [19], up-regulation of neurotrophins[18], and hippocampal neurogenesis and volume [20]. Exercise increases serum calcium levels, which can then be transported to the brain to activate the rate limiting enzyme for catecholamine (dopamine and norepinephrine) synthesis. Both norepinephrine and dopamine are neurotransmitters [21]. Aerobic exercise is an efficient strategy to positively influence executive control during [22] and after exercise [23].

**Subjects and methods:**

A pretest-posttest randomized controlled study was conducted in outpatient clinic in faculty of physical therapy, Cairo university. Informed consent was provided for each child from their parents. The procedures followed were in accordance with the Institutional Ethical Committee Clearance No:P.T.REC/012/002278.
Subjects: Sixty children with spastic hemiplegic cerebral palsy were enrolled in this study and were assessed for eligibility. Their aged ranged from seven and eleven years, they were from both sexes, they have left side hemiplegic cerebral palsy and they were able to walk independently. We excluded children with visual or auditory problems, children with history of drug intake that may affect the cognitive function, medically unstable children especially with cardiovascular disorders and uncooperative children.

They were assigned randomly into two equal groups. Group (A) the study group received aerobic exercise in addition to selected physical therapy program. And group (B) the control group received the same selected physical therapy program only. The treatment was conducted one hour / week for three successful months.

Materials for evaluation:

Eriksen Flanker test and Stroop Color-Word test were used to assess inhibitory control of EF pre and after treatment.

1) Eriksen Flanker Test: Modified Eriksen Flanker task that has been widely employed to examine the inhibitory aspect of executive function [24]. The Flanker task consisted of 20 trials consisted of two trial types, with either congruent reaction time (CRT) or incongruent reaction time (iCRT) to certain visual stimuli. The congruent trial was a horizontally arranged array of arrows presented in the same direction. The incongruent trial had a similar array of arrows, but the middle arrow, the target, was displayed in the opposite direction. Participants were asked to respond to the direction of the target arrow within the array of arrows by pressing the corresponding right or left finger button as quickly and accurately as possible. The accuracy percentage and reaction times of correct responses on both congruent and incongruent trials were identified as metrics of behavioral cognitive performance.

2) Stroop Color-Word Test: One measure of executive function is the color word Stroop Test, originally developed in 1935 by Stroop to measure selective attention and cognitive flexibility. It is most often described as measuring the individual’s ability to shift cognitive set [25]; it is believed to provide a measure of cognitive inhibition[26], or the ability to inhibit an over learned (i.e., dominant response) in favor of an unusual one [25]. The Color–Word task on which the individual is shown the names of colors printed in conflicting ink colors (e.g., the word “blue” in red ink) and the
participants were asked to respond to is asked to name the color of the ink rather than the word by pressing the corresponding first letter of the color if red press (r) button if yellow press (y) button if orang press (o) button if purple press (p) button if green press (g) button if blue press (b) button as quickly and accurately as possible [27]. The Stroop test consisted of 20 trials consisted of two trial types, with either normal congruent reaction time (CRT) or incongruent reaction time (iCRT) to certain visual. The normal trial was when color of the ink is the same color of the word and The interfere trial the color of the ink not the same as the color of word. The accuracy percentage and reaction times of correct responses on both congruent and incongruent trials were identified as metrics of behavioral cognitive performance.

**Flow chart**

![Flow chart image]

**Fig 1, flow chart**
**Methods of Treatment**

Group (A) which is the study group received 20 min. selected physical therapy program which contain strengthening exercises for upper limb and lower limb muscles, stretching exercises for elbow extensors, hand supinator, wrist extensors, knee extensors and ankle dorsiflexors, balancing exercises, coordination exercises and gait training exercises in open environment. In addition to aerobic exercise on a bicycle ergometer for 40 min. Bicycle ergometer (**Monark Rehab trainer model 88E**) was used to train children in study group. It is a stationary bicycle with an ergometer (electronically braked) to measure the work done by the exerciser. It is equipped with an electronic meter showing pedal revolutions per minute, total pedal revolutions and time function. It provides low-impact, safe, and effective cardiovascular exercise. This low-impact movement does not put much stress on joints.

Before starting the training procedure each child was instructed to wear comfortable training suit and shoes and to sit vertically on the bicycle ergometer seat with erect back. Extra strap was placed on child's feet to provide complete fixation on ergometer pedal. The exercise on bicycle was done under supervision of researcher to ensure correct and accurate application.

In the first week, children bicycled to tolerance at 40% to 50% max HR, and then progressed to the 70% max HR in the second week. Intensity of aerobic exercise was systematically progressed for each child by increasing resistance to maintain conditioning at 70% of max HR. Maximum HR calculated from the following equation: \( \text{max HR} = 220 - \text{age} \) [28]. The first five minutes of each session were dedicated to warming up exercise on the bicycle in the form of slow progression exercise (to decrease the risk of musculoskeletal injury and cardiovascular complications), followed by the active phase of exercise for 30 min., and finally cooling down phase for five min. with intensity and speed decreased gradually until reaching the resting heart rate (RHR) [29].

Group (B): which is the control group received the same selected physical therapy program only for one hour. The treatment was conducted one hour, three times / week for three successful months.
**Statistical analysis**

For analysis of data in the present study, SPSS software version 21 was used for data analysis. Descriptive statistics was used to identify the mean and standard deviation for each variable. Paired t-test was used to test pre and post changes in each group of the study.

**Results:**

The mean values of age and grade in study group (A) were 9.77±1.135 and 4.77±1.135 respectively and in control group (B) were 9.2±1.243 and 4.2±1.243 respectively. There was no significant difference between the two groups in their mean values of ages and grades (P > 0.05).

In the study group (A) the number of boys was 21 (70%) and the number of girls was 9 (30%), while in the control group (B) the number of boys was 17 (56.7%) and the number of girls was 13 (43.3%); there was no significant difference between the two groups in gender distribution.

There was no significant difference in pre-treatment values Flanker test accuracy, CRT and iCRT and Stroop test accuracy, CRT and iCRT between two groups P > 0.05. While there was significant difference in post-treatment values Flanker test accuracy, CRT and iCRT and Stroop test accuracy, CRT and iCRT between two groups P < 0.05 in favor of the study group (A).

The mean values of the Flanker test accuracy, CRT and iCRT post treatment in study group (A) were 90±10.91, 1161±291.7 and 1417±588.1 respectively, and in control group (B) were 82±10.88, 1489±509 and 1792±755.7 respectively. Comparison of the mean value of each test in study group (A) with the corresponding mean value in control group (B) revealed significant difference of all variables (p < 0.05) in favor of study group (A).

The mean values of the Stroop test accuracy, CRT and iCRT post treatment in study group (A) were 83.5±11.15, 2240±947.7 and 2647±729.9 respectively, and in control group (B) were 75.67±12.37, 2752±911.1 and 2990±558.4 respectively. Comparison of the mean value of each test in study group (A) with the corresponding mean value in control group revealed significant difference of all variables (p < 0.05) in favor of study group (A).
There was a significant increase in post treatment values of Flanker test accuracy 16.17 and Stroop test accuracy 13.33 while P-value was 0.0001 and the percentage of improvement was 21.9% and 18.9% respectively. While there was a significant decrease in post treatment values of Flanker test CRT 406, iCRT410 and the percentage of improvement was 25.91% and 22.44% respectively and also there was a significant decrease in post treatment values of Stroop test CRT 741 iCRT 360 and the percentage of improvement was 24.88% and 11.97% respectively while P-value was 0.0001.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study Group (A)</th>
<th>Control Group (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre treatment</td>
<td>Post treatment</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td>Mean±SD</td>
</tr>
<tr>
<td>Flanker test accuracy</td>
<td>73.83±10.4</td>
<td>90±10.91</td>
</tr>
<tr>
<td></td>
<td>(21%)</td>
<td></td>
</tr>
<tr>
<td>Flanker test CRT</td>
<td>1567±369.2</td>
<td>1161±291.7</td>
</tr>
<tr>
<td></td>
<td>(25.91%)</td>
<td></td>
</tr>
<tr>
<td>Flanker test iCRT</td>
<td>1827±779.6</td>
<td>1417±588.1</td>
</tr>
<tr>
<td></td>
<td>(22.44%)</td>
<td></td>
</tr>
<tr>
<td>Stroop test accuracy</td>
<td>70.17±8.758</td>
<td>83.5±11.15</td>
</tr>
<tr>
<td></td>
<td>(18.9%)</td>
<td></td>
</tr>
<tr>
<td>Stroop test CRT</td>
<td>2982±992</td>
<td>2240±947.7</td>
</tr>
<tr>
<td></td>
<td>(24.88%)</td>
<td></td>
</tr>
<tr>
<td>Stroop test iCrt</td>
<td>3007±885.1</td>
<td>2647±729.9</td>
</tr>
<tr>
<td></td>
<td>(11.97%)</td>
<td></td>
</tr>
</tbody>
</table>

Non-significant: p> 0.05*Significant: p<0.05
Discussion:

This study was conducted to assess the influence of aerobic exercise on inhibitory control of EF in spastic hemiplegic cerebral palsy. The children that was selected in this study have left side hemiplegic cerebral palsy that agreed with Godefroy & Bogousslauksy 2007[30] who concluded that damage in right hemisphere, hemi-spatial neglect is the most frequent deficit where there is impaired or lost ability to react to or to process sensory stimuli in the hemispace opposite to the lesion side. This visuospatial perceptual deficits can affect different cognitive activities which show up as difficulty copying designs, making constructions, discriminating pattern of faces, selecting the correct sleeve and self-monitoring left side or covering the paretic shoulder.

In the current study, selection of hemiplegic cerebral palsied children comes in agreement with Bodimeade et al.[31] who concluded that although disruptions in motor functioning are often the most recognizable feature of CP, executive function impairment is also a central feature of CP when compared EF in children with CP (mean age 11 y/o) to typically developing controls.

The choice of using a bicycle ergometer for aerobic exercise training instead of a treadmill was because safety was our foremost concern for the participants. The bicycles were powered by participants and easy for them to get on and off, which reduced fall risk, a prevalent problem in the study population.

The present study was revealed significant improvement of all measured variables of inhibitory control of EF after three successful months that agreed with Renaud, et al. 2010[32] who observed that only 3 months of well-structured and supervised exercise is associated with a significant improvement in attention and executive functions.

The results of the present study revealed significant improvement of all measured variables in study group (A) as there was significant increase in accuracy and decrease reaction time congruant and incongruant that mean improvement of inhibitory control of EF this was attributed to aerobic exercise.

The results of the present study proved that there was no significant improvement in all measured variables of Flanker test accuracy, CRT and iCRT in the control group (B), while there was significant improvement in all measured variables of Flanker test accuracy, CRT and iCRT in the control group (A). This improvement may be attributed to the
physiological effect of aerobic exercise on brain as it increases the cerebral tissue oxygenation, blood flow velocity and cerebral metabolism and homeostasis which in turn improve the speed of information processing, motor learning, implicit memory and executive function. This result agreed with McAuley et al., 2004[33], Kluding et al., 2011[34], Barbara et al., 2009[35] and Rand et al., 2010[36]. Improvement in cognitive flexibility was proportional to the degree of exercise Masley et al., 2009[37].

The improvement of EF after aerobic exercises may be due to increases activity in cortical areas associated with cognition, including the right medial frontal gyrus (BA 46), superior frontal gyrus (BA 8), and superior parietal lobe (BA 40). It increases the number of interconnections (synapses) in frontal and parietal gray matter, allowing for greater systematic recruitment of these areas under higher cognitive load and also increases prefrontal and anterior cingulate plasticity in the aging brain to a level more consistent with neurologically intact young adults This results agreed with (Colcombe and Kramer, 2004).[38].

The results of this study showed that there was significant changes in all measured variables Stroop test accuracy, CRT and iCRT when comparing pre and post treatment variables between two groups in favor of the study group (A) this improvement comes in agreement with Pottet et al., (1996) [39], and Ainslie et al., (2008)[40] who reported that aerobic exercise increases oxygen consumption, reduces blood pressure and resting heart rate, strengthens and enlarges the heart muscle which reflects on its pumping efficiency leading to increase in global & regional cerebral blood flow. Plus aerobic exercise was proved to promote angiogenesis and increase in capillary density.

Gapin et al., 2011[41] also supports the beneficial effects of physical activity on EF and suggests that effects might be particularly large for children.

Most studies supported greater improvements of EF after moderate to vigorous aerobic exercise in typically developing (TD) children (Crova et al., 2014[42]; Diamond and Lee, 2011[43]; Verburgh et al., 2014)[44].

The improvements of EF after sustained aerobic exercises is (over months) is required for cognitive improvement this comes in agreement with Masley 2009.[37].

Previous studies have reported improved performance on a variety of cognitive task categories, including attention, information processing, memory, and executive function, after a single bout of aerobic exercise
(Audiffren, Tomporowski, & Zagrodnik, 2008[45]; Coles & Tomporowski, 2008[46]; Hillman et al., 2009[47]).

The significant improvement in post treatment Stroop test accuracy, reaction time congruancy and reaction time incongruancy supported by Etnier and Chang 2009[48] that found a significant improvement in the Stroop Test after an acute moderate-intensity strength exercise (10 sets of 10 repetitions for six exercises) session in healthy middle-aged (49 ± 9 years) adults. Altogether, these findings reveal the potential of both aerobic and strength exercise alone in improving executive function.

The potential benefits of physical exercise in promoting increased EF in our study are consistent with the findings reported in recent empirical studies on regular aerobic activity and open-skill exercise in children with and without disabilities (Chang et al., 2014[49]; Guiney and Machado, 2013[50]; Hilton et al., 2014[51]; Pan et al., 2015[52]; Tsai et al., 2012[53]).

The results of the present study contradicted with the finding of Ploughman et al., (2008)[54] who reported that treadmill exercise did not cause improvement in cognitive function (including the Trail Making Test A and B, Symbol Digit Substitution Test, and Paced Auditory Serial). The discrepancy between the present and Ploughman et al.[54] study may be attributed to the small sample size and the short duration of the physical therapy intervention of Ploughman et al.[54] study. It was assumed that sustained aerobic exercise (over months) is required for cognitive improvement (Masley, 2009)[37].

The results of the present study also contradicted with the finding of Correia et al., (2010)[55] who demonstrated that acute strengthening exercises do not induce significant alterations in the levels of brain-derived neurotrophic factor plasma concentrations in healthy individuals. The discrepancy of results between two studies may be attributed to the type of exercise program that may be a decisive factor in altering peripheral brain-derived neurotrophic factor level.

Conclusion: It can be concluded that aerobic exercise has significant effect on inhibitory control of executive functions in spastic hemiplegic cerebral palsy children.
References


48. Etnier J. L., & Chang Y. K. The effect of physical activity on executive function: A brief commentary on definitions, measurement issues, and
the current state of the literature. *Journal of Sport & Exercise Psychology*, 2009;31(4), 469–483.


