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Non-pharmacological intervention on inhibitory control in adolescents with attention-deficit / hyperactivity disorder

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Abstract

One of the main neuropsychological features in Attention-Deficit / Hyperactivity Disorder (ADHD) are the failures in executive functioning, especially inhibitory control (IC), which is important for the stopping of an ongoing response, permits a delay in the decision to respond and protects this period of time. Due to these deficits, teenage population with ADHD are more susceptible to present behaviors such as substance abuse, high-risk sexual behavior and the presence of comorbidities. The aim of the present study was to conduct a review of the last 10 years about the non-pharmacological interventions on IC in adolescents with ADHD. An electronic search was made in *Scopus, PubMed and Web of Sciences* databases, combining the next keywords: "intervention", "inhibitory control", "adolescents", "teenagers" and "ADHD". Articles were selected from 2010 to 2020. Transcranial magnetic stimulation was the most reported non-pharmacological intervention for enhancing the IC in adolescents with ADHD, followed by physical exercise and neurofeedback. The lack of literature about this topic is a relevant issue to generate future research lines about the treatment of executive functions in adolescents with ADHD.

Keywords: *ADHD, executive functions, inhibitory control, non-pharmacological intervention*.

Introduction

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DMS-5)classifies attention deficit hyperactivity disorder (ADHD)within neurodevelopmental disorders, with a global prevalence of 2% to 7%[1], whereas for kids and adolescents it can reach 5-9% to 7.1%[2].

The main symptoms considered are the presence of a persistent pattern of inattention and hyperactivity/impulsiveness that interfere in the functioning or development, creating a bigger risk of maladaptive behaviors and the necessity to get immediate rewards, generating the inability to delay gratification[1].

Bandeira[3] states that ADHD symptoms appear before the age of 12 and are present in at least two contexts, which persistently creates difficulties throughout life, affecting the social, academic, and work spheres.

ADHD involves alterations to various neurotransmitters, such as serotonin, noradrenalin, and specially dopamine, which influences various processes, such as attention, concentration, motivation, interest, and learning new abilities[4]. Derived from neurobiological deficits that interact with some environmental factors, such as difficulties during pregnancy, drug use, childbirth complications, bad upbringing, and a low socioeconomic status; this makes it so the main difficulties that people with ADHD face manifest in a poor development of the executive functioning [5].

Executive functions are a set of control processes used when an action is set in motion or when it is not advisable to act on instinct or intuition, allowing for cognitive, social, and psychological success [7]. In this sense, these are crucial skills for learning since they allow the regulation of emotions under stress situations [8].

One of the main executive failures manifested in ADHD is inhibitory control (IC), which, according to Barkley [9], is the interrelation of the three following processes: a) the inhibition of the initial prepotent response to an event, b) stopping an ongoing response, which allows for a delay in the decision to respond, and c) the protection of this time period.

Successful inhibition has frequently been linked to areas such as the anterior cingulate cortex, dorsolateral prefrontal cortex, orbitofrontal cortex, and the inferior frontal cortex[10, 11], extending to the anterior insula, with the latter being found to activate more broadly and significantly in tasks related to IC[12]. Said areas are associated with decision-making, initiation of social behaviors, inhibition of inappropriate behaviors, as well as the risk-benefit processing[13].

The research is consistent when reporting that people with ADHC make more mistakes during inhibition tasks, have slower reaction times when a conflicting stimulus is presented, and their performance throughout the execution of these tasks is variable [14,15].

Because of this, it is considered that intervention in ADHD must mainly focus on executive functions to stimulate and train skills such as self-regulation, self-control, planning, and IC[16].

In general, the literature is expensive when reporting comprehensive intervention in children and adolescents with ADHD, mainly involving pharmacological treatment, which reduces the key symptoms in most children and young adults[17-19]. However, the literature that covers only the adolescent population is scarce, and there is even less literature addressing one of the main deficits that results in behavioral problems, such as IC , which is of great importance due to the fact that young people with untreated ADHD tend to get involved in high-risk behaviors, such as substance abuse, high-risk sexual behavior, and the presence of comorbidities (e.g., mood disorders and anxiety and personality disorders)[19].

The combined effects of methylphenidate with "response cost" techniques and cognitive training applied to children and adolescents with ADHD have been examined, also resulting beneficial for the decrease of long-term symptoms, primarily in attention, hyperactivity, and impulsivity [21,22]. Another study on this population reported the benefit of the same drug combined with neurofeedback (NFB), proving that they were able to increase the ability to inhibit prepotent responses to a similar degree, which suggests that both have a "braking" function [22].

Despite this, there are few experimental research and meta-analyses that only report the efficiency of non-pharmacological treatments on behavioral inhibition on young people with ADHD. To our knowledge, some recent reviews on the topic cover only one intervention, for example, mindfulness [23] and physical exercise [24]. However, they are not specific on the effects that they have on IC.

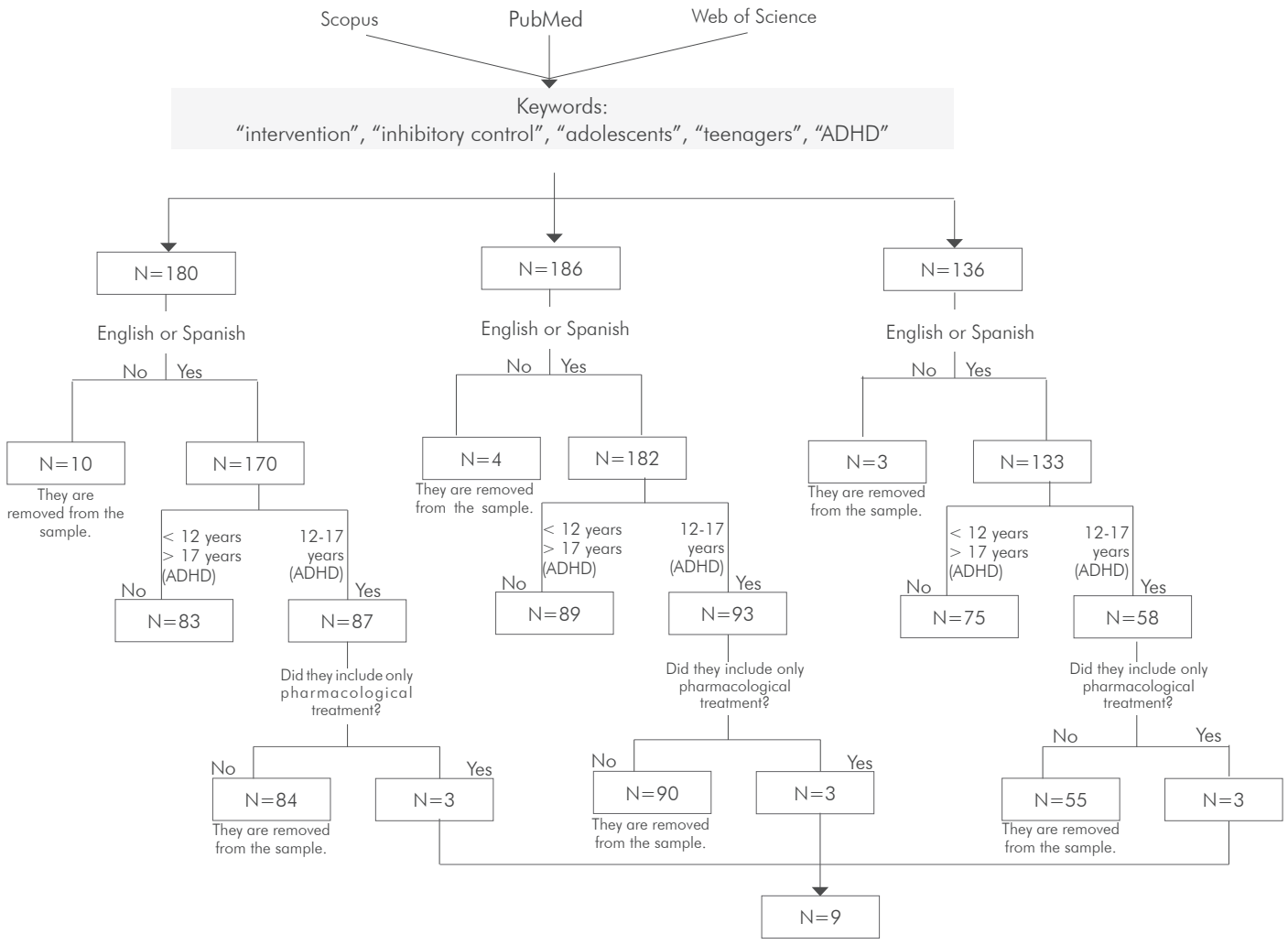
The objective of the present work is to review the non-pharmacological interventions on IC in adolescents with

ADHD to provide a general overview that outlines the strengths and weaknesses of this state of the art in question.

Methods

An electronic search in the Scopus, PubMed, and Web of Science databases was used, combining the following keywords: "intervention," "inhibitory control," "adolescents," "teenagers", and "ADHD". Articles from the last 10 years (2010 to 2020) reporting interventions in executive functions (specifically in IC) were selected, as well as those including adolescents (11 to 16 years of age) with ADHD among their sample. Articles analyzing these variables in children or adults, in other clinical populations, and that only reported pharmacological interventions were excluded, ultimately selecting 9 articles.

Figure 1. Flowchart of the procedure for selecting articles on non-pharmacological intervention in inhibitory control in adolescents with ADHD



Results

Of the studies reviewed for this work, four (44.4%) focused on transcranial magnetic stimulation (TMS); three (33.3%) on physical exercise, and two (22.2%) on neurofeedback (NFB). Regarding the studied ages, the nine articles evaluated adolescents of ages ranging between 11.11 to 14.5 years.

TMS

The analyzed studies (Table 1) reported that the values of the N100 amplitude between the clinically healthy group and the ADHD group were similar after TMS, which implies a better response to tasks that demand the use of IC [26]. Transcranial-direct current stimulation (tDCS) reduces the time needed to select new information through an improvement in inhibition and a decrease in the frequency of mistakes when alternating attention[4].

When adolescents with ADHD received TMS through only using the anode over the right inferior frontal gyrus, they showed a significant decrease in commission errors and a higher accuracy in reaction times [27]. Likewise, by using TMS and motor evoked potentials, a decrease in amplitude during the recording of the N100 component was observed, showing a reduction in motor disinhibition, which contributed to hyperactivity in adolescents of the clinical group [28].

The IC measures used in these studies were two continuous performance tests (Go/no-go and flankers), the Neuropsychological Development Assessment (NEPSY-II) IC subtest and a contingent negative variation task as a neurophysiological measure of IC. The three studies showed large effect sizes.

Table 1. Studies reporting intervention in inhibitory control through TMS in adolescents with ADHD.

Authors	Groups of participants and age in years (Mean and standard deviation)	Inhibitory control measures (IC)	Intervention technique used	Results
D'Agati E., et al., [25]	ADHD: 12.5 (1.0) n= 18 Control: 12.4 (1.3) n=19	*Go/no-go* paradigm	TMS over the left motor cortex. Electroencephalographic activity was recorded at 22 sites (using the 10-20 system without C3, e.g., the electrode under the TMS coil, Fpz, Oz, M1 and M2).	After TMS, during the *Go/no-go task*, participants with ADHD showed a smaller increase in N100 amplitude on go trials and a better response inhibition capacity.
Bandeira ID, et. al. [3]	ADHD: 11.11 (2.8) n= 9	NEPSY-II IC subtest	TMS over the left dorsolateral prefrontal cortex (anode at F3) and the right supraorbital area (cathode).	Se redujo el tiempo necesario de selección de información nueva mediante una mejoría en la inhibición y un decremento en la frecuencia de errores al alternar la atención
Breitling C., et. al. [26]	ADHD: 14.33a n = 21 Control: 14.24a n = 21	Eriksen Flanker Paradigm	TMS over the right inferior frontal gyrus with the stimulation electrode (anode) at F8 site and the reference electrode (cathode) at P7 site posterior to the left mastoid.	The anodal TMS over the right inferior frontal gyrus improved the IC in patients with ADHD.
Bruckmann S., et. al. [27]	ADHD: 11.4 (1.7) n= 20 Control: 12.2 (2.0)n=19	Negative contingent variation task	tDCS over the left motor cortex choosing C3 site for the electroencephalographic response.	A decrease in N100 amplitude was shown, indicating a qualitative difference with the control group regarding the typical motor inhibition of this disorder.

Note: TMS = Transcranial magnetic stimulation; NEPSY-II = Neuropsychological Development Assessment. a = Does not provide the standard deviation of age, only the mean; tDCS= Transcranial direct-current stimulation.

Physical Exercise

In two studies (Table 2) it was reported that, in adolescents with ADHD, doing moderate-intensity exercise on a recumbent bicycle (stationary) for 20 to 30 minutes can improve the performance on IC tasks, such as the Stroop test, even after only one exercise session [29], showing an increase in the P300 amplitude and a decrease in reaction times [30]. Finally, an intervention proved that two weekly 50-minute sessions for a year and a half has a favorable effect on IC of adolescents with ADHD, resulting in large effect sizes measured through the performance on all variables of the Stroop test [31].

Table 2. Studies reporting intervention in inhibitory control through physical exercise in adolescents with ADHD.

Authors	Groups of participants and age in years (Mean and standard deviation)	Inhibitory control measures (IC)	Intervention technique used	Results
Piepmeier A.T., et. al.[28]	ADHD: 11.32 (1.96) n = 14 Control: 11.22 (2.43) n = 18	Stroop test	30-minute acute exercise routines for 2 days	Patients with and without ADHD improved their processing speed and IC in response to a session of moderate exercise
Ludyga, et. al. [29]	ADHD: 12.8 (1.8) n = 5 Control: 13.5 (1.38) n = 7	Flanker task	Aerobic and coordination exercise for 20 minutes for 7-14 days	The results suggest that a single session of aerobic exercise improves the IC and attentional control. There were indications that aerobic exercise was more efficient than coordinated exercise in reducing deficits in inhibitory control in the ADHD group.
Kadri A., et. al. [30]	ADHD: 14.5 (3.5) n = 40	Stroop test	50-minute taekwondo exercises two times a week for a year and a half	Significant differences and large effect sizes were observed in the pre- and post-intervention assessments in the Stroop test, indicating an improvement in IC and in the selective attention of adolescents with ADHD.

NFB

The findings in the pair of articles found (Table 3) suggest that NFB is a technique that improves the performance of IC in children and adolescents with ADHD. Specifically, one of the studies with large effect sizes[32] claims that after 20 training sessions with this technique, the key symptoms of the ADHD group were reduced, improving IC measured through the performance in a combined flanker task/No-Go. In the second study, the use of NFB together with real-time functional magnetic resonance imaging is reported over the course of four 1.5-hour sessions for 2 weeks, during which ADHD symptoms decreased, the level of sustained attention and IC improved, and an increase in the activation of the superior frontal gyrus was found in response to IC tasks in adolescents with ADHD.

Table 3. Studies reporting intervention in inhibitory control through NFB in adolescents with ADHD.

Authors	Groups of participants and age in years (Mean and standard deviation)	Inhibitory control measures (IC)	Intervention technique used	Results
Baumeister S., et. al. [31]	ADHD: 11.81 (1.47) n =16	flanker/No-Go task (4 blocks of 40 trials)	20 60-minute NFB sessions	The group that received NFB showed a reduction in ADHD symptoms and an increase in the activation of areas associated with IC.
Alegria A.A., et. al. [47]	ADHD: 14.11 (1.53) n = 18 Control: 13.62 (1.66) n= 13	MARS battery and CPT Go/No-Go and Stop.	NFB through functional magnetic resonance imaging in 4 ½-hour sessions for 2 weeks	ADHD symptoms were reduced, the level of sustained attention improved, and there was an increase in the activation of the superior frontal gyrus during IC tasks.
Notes: NFB = Neurofeedback; MARS = Maudsley Attention and Response Suppresion task battery; CPT = Continuous Performance Test.				

Discussion

The obtained results based on the 9 studies indicated that the most used method was TMS, followed by physical exercise, and finally NFB.

Overall, when using NFB to stimulate some regions of the frontal lobe (mainly the primary motor cortex, the left dorsolateral prefrontal cortex, and the right inferior frontal gyrus)a decrease in disinhibition [26] better capacity to select new information[4], better interference control[27] and an improvement in motor inhibition [28] in adolescents with ADHD were observed. Despite the existence of studies that indicate that TMS is a non-pharmacological alternative for ADHD treatment, given the fact that it is non-invasive, effective [33-36], and allows for the activation of prefrontal circuits that enhance dopaminergic neurotransmission[37], the consulted research has reported side effects mainly related to headaches, neck pain, tingling at the site of the anode, itching, burning sensation, local redness, and mild drowsiness[4], which could be considered a short-term limitation for the long-term use of this intervention in some patients.

Regarding physical exercise, recent studies cover mainly two types of activities: acute exercise through the use of recumbent bicycles, and taekwondo. In the case of the former, the evidence is consistent regarding the beneficial effects of acute exercise on cognitive performance, particularly on executive functions [38-40]. However, the topic has not been studied much in populations with ADHD and focuses mainly on children.

The most used instrument in the articles that report interventions through physical exercise is the Stroop test, observing a higher speed and a lower number of mistakes prior to the intervention process, which is consistent with what Chang et al. report [40]. They observed a better performance on part C (interference) of the Stroop test in children with ADHD after moderate exercise sessions. On the other hand, the use of taekwondo has resulted in a recent interest in research due to the many benefits it entails in the cognition and behavior [41-44], as well as in executive functions such as working memory, cognitive flexibility, and IC[45], but not much has been studied on children and adolescents with ADHD.

Given the above, the limitations are noteworthy as other types of physical activities, such as tai chi, which has proven to be beneficial to young people with ADHD, as it decreases anxiety and improves behavior and emotions [46], have not been explored.

Finally, it has been reported that NFB, which is a type of electroencephalogram that trains self-regulation skills through computerized technology [47], has been associated with the decrease of ADHD-related symptoms[32,48].

In general, the pair of articles that were found about this type of intervention suggest that NFB is efficient for improving IC in adolescents with ADHD, mainly when they execute continuous performance tests such as go/no-go and stop, showing a significant increase in the activation of structures associated with IC (such as the bilateral insula, inferior frontal gyrus, and the anterior and medial cingulate cortex), regions that have also been associated with reward-based learning [49,50] and are hypoactive in patients with ADHD [51], suggesting that this type of intervention would not only improve IC, but also other executive functions, such as decision-making and cognitive flexibility.

Conclusions

The main objective of the present study was to conduct a literature review of the past 10 years about the different non-pharmacological interventions to improve the IC of adolescents with ADHD. Unlike previous studies, where the effects of interventions through physical exercise or NFB have been independently reviewed, there is no systematic review or meta-analysis (to our knowledge) that focuses only on the adolescent population and describes more than two non-pharmacological interventions to improve the executive function of the IC.

TMS turned out to be the most reported intervention of the past 10 years, which has shown that by stimulating the frontal cortex (mainly the dorsolateral prefrontal cortex), improvements in interference control, selection capacity, attention, and IC have been observed. On the other hand, physical exercise and NFB have also been beneficial for improving IC. However, the literature found about these last two types of intervention is still scarce.

The instruments used in most of the studies to evaluate the IC are some continuous performance tests such as go/no-go, stop, and the flanker task, as well as the Stroop test, which is important when designing a battery of standardized neuropsychological tests that evaluate the three processes involved in IC: (a) the inhibition of the initial prepotent response to an event, b) stopping an ongoing response, and c) the protection of a delay period, as said functions are compromised in ADHD patients.

Given the few reports found, it is important for future research to consider the behavioral responses and changes in different executive functions using measures that not only focus on experimental paradigms, but also on new standardized tests and ecological assessments through inventories or questionnaires in self-report and peer-report versions.

Finally, it is suggested that the research on executive functions convers the adolescent population and the way in which neurodevelopmental disorders such as ADHD impact the IC. This is because of the research into the topic in question being relatively new.

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