Transcranial Direct Current Stimulation in Children and Adolescents With Attention-Deficit/Hyperactivity Disorder (ADHD): A Pilot Study

Article *in* Journal of Child Neurology · February 2016

DOI: 10.1177/0883073816630083

Igor Dórea Bandeira
The University of Sydney

Original Article

Journal of Child Neurology
2016, Vol. 31(7) 918-924

DOI: 10.1177/0883073816630083
jcn.sagepub.com
SAGE

Transcranial Direct Current Stimulation in Children and Adolescents With Attention-Deficit/Hyperactivity Disorder (ADHD): A Pilot Study

Igor Dórea Bandeira, MD[1], Rachel Silvany Quadros Guimarães, MD[1], João Gabriel Jagersbacher, MD[1], Thiago Lima Barretto, MD[1], Jéssica Regina de Jesus-Silva, BScPsy[1], Samantha Nunes Santos, MSc[2], Nayara Argollo, MD, PhD[3], and Rita Lucena, MD, PhD[1]

Abstract

Studies investigating the possible benefits of transcranial direct current stimulation on left dorsolateral prefrontal cortex in children and adolescents with attention-deficit hyperactivity disorder (ADHD) have not been performed. This study assesses the effect of transcranial direct current stimulation in children and adolescents with ADHD on neuropsychological tests of visual attention, visual and verbal working memory, and inhibitory control. An auto-matched clinical trial was performed involving transcranial direct current stimulation in children and adolescents with ADHD, using SNAP-IV and subtests Vocabulary and Cubes of the Wechsler Intelligence Scale for Children III (WISC-III). Subjects were assessed before and after transcranial direct current stimulation sessions with the Digit Span subtest of the WISC-III, inhibitory control subtest of the NEPSY-II, Corsi cubes, and the Visual Attention Test (TAVIS-3). There were 9 individuals with ADHD according to *Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition)* criteria. There was statistically significant difference in some aspects of TAVIS-3 tests and the inhibitory control subtest of NEPSY-II. Transcranial direct current stimulation can be related to a more efficient processing speed, improved detection of stimuli, and improved ability to switch between an ongoing activity and a new one.

Keywords

attention-deficit hyperactivity disorder (ADHD), transcranial direct current stimulation, dorsolateral prefrontal cortex, noninvasive brain stimulation, neuromodulation

Received July 23, 2015. Received revised November 13, 2015. Accepted for publication December 29, 2015.

Attention-deficit hyperactivity disorder (ADHD) is characterized by a persistent pattern of inattentive symptoms (always present) and/or hyperactivity-impulsivity, has a heterogeneous nature and impacts in different domains of cognitive skills such as motivation and executive functions. Symptoms appear before age 12 years and are present in at least 2 different environments, leading to interference in social, academic, or occupational areas,[1-4] and many individuals continue to be persistently affected by this disorder throughout life.[5-9]

The prevalence of ADHD ranges from 5.29% to 7.1%[10] in children and adolescents and from 1% to 10% in adults.[10-12] This disorder is associated with alterations in neurotransmitters such as norepinephrine, serotonin, and especially dopamine.[13] Functional alterations have been described in the brain regions of affected individuals, such as the prefrontal cortex, caudate nucleus, globus pallidus, corpus callosum, and cerebellar vermis.[13-16]

Pharmacologic treatment with stimulants are the first choice (methylphenidate, dexmethylphenidate, and amphetamines) according to guidelines, and this is based on the pathophysiological mechanisms involved.[17,18] Despite the proven efficacy of these drugs, many individuals continue to have compromised

[1] Department of Neuroscience and Mental Health, Medical School of Bahia, Federal University of Bahia, Salvador, Bahia, Brazil
[2] Professor Edgard Santos University Teaching Hospital, Federal University of Bahia, Salvador, Bahia, Brazil
[3] Department of Pediatrics, Medical School of Bahia, Federal University of Bahia, Salvador, Bahia, Brazil

Corresponding Author:
Igor Dórea Bandeira, MD, Department of Neuroscience and Mental Health, Medical School of Bahia, Federal University of Bahia, Praça XV de Novembro, s/n - Largo do Terreiro de Jesus, Salvador, Bahia 40025, Brazil.
Email: igordbandeira@gmail.com

social and academic performance, and some of them experience significant side effects that prevent the maintenance of treatment.[19]

In the last decade, several noninvasive brain stimulation techniques were tested in neuropsychiatric diseases with favorable results,[20-28] among them the transcranial direct current stimulation (tDCS). In a review on the safety of transcranial direct current stimulation in children and adolescents, Krishnan et al[29] evaluated the published studies and found that transcranial direct current stimulation is safe to be applied in the pediatric population. The same data were obtained in a recent study in children, which showed that the technique was safe and well tolerated, demonstrating mild adverse effects.[30]

The transcranial direct current stimulation uses an electrical current of low amplitude applied by electrodes on the scalp. This technique has several advantages: it is not painful and is inexpensive, safe, easy to use, and with proven efficiency in double-blind studies.[31] Current knowledge on the pathophysiology of ADHD and the neurophysiological effects of transcranial direct current stimulation suggest its effectiveness in controlling some manifestations that induce social or academic impairment.[32-35] The possible benefits of transcranial direct current stimulation on the left dorsolateral prefrontal cortex in children and adolescents with ADHD have not been investigated.

Methods

Participants

This is a noncontrolled auto-matched clinical trial. The population consisted of 9 individuals from Professor Edgard Santos University Teaching Hospital's child neurology unit, of both genders, with suspected ADHD according to the *Diagnostic and Statistical Manual of Mental Disorders* (*Fifth Edition*; DSM-5) criteria. Diagnostic confirmation was performed after neurologic evaluation by 2 pediatric neurologists.

We included only children and adolescents aged 6 to 16 years who were right-handed, literate, attending regular schools, living in the Salvador metropolitan areas, without pharmacologic treatment during the transcranial direct current stimulation period, with no epileptogenic electroencephalograph (EEG) activity, and with the consent of those responsible for participation in the study. If the child or adolescent was on medication, the parents were instructed to suspend the use for 7 days before the first study evaluation. Exclusion criteria were a sensory and intellectual deficit, other neuropsychiatric morbidity, and epileptogenic discharges in the electroencephalogram. In the initial interview, the parents were informed about the objectives and stages of the study.

Intervention

The stimulation was performed with 7×5 cm (35 cm^2) electrodes in saline-soaked sponges and were held in place by elastic bandages (we used the Striat device [Ibramed, Amparo-SP, Brazil] as approved by the Brazilian Health Agency [ANVISA]). The anode was positioned on the left dorsolateral prefrontal cortex (F3 according to the 10-20 system for EEG) and the cathode on the right supraorbital area because previous studies reported that stimulation of left dorsolateral prefrontal cortex can improve parameters in neuropsychological tests and also working memory and attention.[36-38] Five sessions were held on consecutive days in the presence of a skilled physician for possible complications. In the first minute, a current intensity of 1 mA was maintained and at the second minute the current was increased to 2 mA. In the 29th minute, transcranial direct current stimulation was reduced to 1 mA and held for a further minute. The parameters of electrode array size, current strength, and current duration values were previously tested for their safety in children.[30]

Subjects were asked to perform activities to stimulate the activation of the dorsolateral prefrontal cortex during the transcranial direct current stimulation sessions. The employed activity was the game "Super Lynx" consisting of a tray with 264 figures and 264 illustrated cards matching the same figures printed in this tray, in which the individual must match identical pictures and try to find a possible number of associations in the shortest amount of time possible. The game is recommended for any child from age 5 years and has different levels of difficulty that were being raised through the sessions.

Procedures

Children and adolescents who met the inclusion criteria participated in neuropsychological evaluation in which we investigated the intellectual level estimation and the child's performance in attentional processes, working memory, and inhibitory control. The SNAP-IV questionnaire was applied to parents and teachers to investigate the diagnostic criteria for ADHD in DSM-5.

All participants were evaluated by tests performed by experienced neuropsychologists, using the following instruments:

- Intellectual Screening: Wechsler Intelligence Scale for Children (WISC-III; The Psychological Corporation, 2002). Application of the subtests Cubes and Vocabulary to estimate the Intelligence Quotient (IQ).
- Visual Attention Test (TAVIS-3; CNA Psychology and Education, 2007). A Brazilian computerized instrument used to assess children with age ranging from 6 to 17 years. The child is asked to press and hold the button of a joystick as soon as it sees the stimulus target that appears on a screen. The test has 2 versions: for age 7 to 11 years (target stimulus = clock lasting 6 minutes) and another for age 12 to 17 years (stimulus-target = red dot lasting 10 minutes). Each task has the following scores: reaction time, errors per share, errors by omission, and number of hits. Errors per share are the records of the filing of an answer when it should not be given, which can be understood as difficulty of inhibiting a response, whereas the error by omission is considered the lack of response to a target stimulus. The average reaction time is defined by the time in milliseconds (ms) that the child takes to push the button, from the time that the stimulus appears on the screen until the issue of the child's response in control. Task 1 (selective attention) involves selecting a target stimulus among the other distractors stimuli. The participant must press a button when the target stimulus appears. Task 2 (alternating attention) consists of alternating between 2 types of answers requested. The participant must identify identical geometric shapes or forms of the same color depending on the requested command. These 2 conditions are being alternated along the task. Task 3 (sustained attention): assessing sustained attention (concentration) through a continuous performance test.
- Digit Span subtest of the WISC-III: it constitutes an attention and working memory measure. It is applied in the forward and

Table 1. Clinical and Epidemiological Characteristics of Children and Adolescents With ADHD.

	Gender	Age	Estimated IQ	SNAP-IV Attention deficit (0-27)	SNAP-IV Hyperactivity and impulsivity (0-27)	SNAP-IV ODD (0-24)	SNAP-IV Total (0-78)
1	M	10	80	19	24	21	64
2	M	14	88	21	25	10	47
3	M	11	100	21	16	4	41
4	M	12	82	19	18	8	45
5	M	13	112	25	10	9	44
6	F	11	97	14	18	8	40
7	M	7	94	22	24	25	71
8	M	15	88	22	16	13	51
9	M	7	94	21	18	17	56

Abbreviations: ADHD, attention-deficit and hyperactivity disorder; ODD, oppositional defiant disorder.

backward orders of the digits: for testing auditory attention in the forward order and to test auditory working memory in backward order. In this subtest, the examiner reads aloud a sequence of numbers. For each item in the forward order, the child repeats the numbers in the same order in which they were spoken. In backward order, the child repeats the numbers in reverse order.

- Corsi cubes are used to evaluate visual working memory. The evaluated subject must repeat sequences of touches in different cubes, representing working memory. In the forward order, visual attention is tested and in backward order the visuospatial sketch of visual memory is tested.
- Inhibitory control (IC): battery subtest of the Neuropsychological Development Assessment (NEPSY-II, on Brazilian regulation phase). Assesses the ability to inhibit the desire to engage in a pleasant task and/or stop an automatic behavior that is part of the executive functions. This time-measured subtest is performed so that the examinee looks at a series of shapes or arrows, black and white, and must name the shape or direction or an alternative response, depending on the color or shape of the arrow. Uncorrected errors occur when the examinee provides an incorrect answer or jumps one way or arrow and does not correct the incorrect or skipped answer. Any form or arrow unanswered due to time limitation should be considered a mistake not corrected. Self-corrected errors occur when the examinee provides an incorrect answer or jumps one way or arrow but corrects the incorrect answer. Total errors are the sum of uncorrected errors and self-corrected errors for each condition (naming: select information; inhibition: the ability to inhibit an automatic response; switching: the ability to switch attention).

The tests Cubes and Vocabulary of the WISC-III and SNAP-IV were performed only on the first day of evaluation of patients. The TAVIS-3, Digit Span subtest of the WISC-III, Corsi cubes, and inhibitory control subtest of NEPSY-II were performed at baseline before the first and after the last transcranial direct current stimulation sessions.

At the end of each transcranial direct current stimulation day, the subject was asked about any adverse effects occurred during the procedure or in the period after the intervention, as proposed by Brunoni et al.[39] All adverse events reported by parents were recorded and classified in the following categories: mild, moderate, or severe. At the end of the fifth and final day of transcranial direct current stimulation, the Patient Global Impression of Improvement was applied, in which parents measured the evolution of the child at the end of treatment in 7 levels: 1 (very much better), 2 (much better), 3 (slightly better), 4 (no change), 5 (slightly worse), 6 (much worse), or 7 (very much worse).

All parents of the patients included in this study were in accordance with the methodology used and signed an informed consent form. The statistical analysis was performed by using the Wilcoxon test to evaluate the difference between the scores before and after transcranial direct current stimulation using the SPSS statistical package, version 21.0, for Windows.

Results

The study included 9 subjects of both genders living in Salvador, Bahia, Brazil, with suspected ADHD according to DSM-5 criteria, and whose diagnoses were confirmed after pediatric neurology evaluation. Table 1 shows the clinical and epidemiologic characteristics of the study population. Eight subjects were male. The average age was 11.11 years ($\pm$2.8). In 3 patients (33.33%) comorbidity with oppositional defiant disorder was observed. The average IQ was estimated to be 92.77 $\pm$ 9.79. Regarding the SNAP-IV, the score related to hyperactivity, and impulsivity criteria ranged from 10 to 25 with an average of 18.77 $\pm$ 4.84. The score relating to inattention characteristics was 14 to 25 with an average of 20.44 $\pm$ 3. For indicative expressions of oppositional defiant disorder, the variation was 4 to 25 with a mean of 12.77 $\pm$ 6.88. Five participants in the study have used methylphenidate in the past.

Tables 2 and 3 show average results obtained in TAVIS-3 before and after transcranial direct current stimulation. Table 2, task 1 (selective attention) of TAVIS-3 shows a statistically significant difference between the scores for errors by omission before and after transcranial direct current stimulation. In tasks 2 and 3, there was no difference in average before and after transcranial direct current stimulation. There were significant differences in the average value of the cluster between the 3 tasks with regard to the number of errors by omission (raw score), showing a reduction (Table 3). There was no difference in the parameters obtained in the Digit Span subtest and Corsi cubes (Tables 4 and 5). Table 6 shows statistically significant differences in some steps of "inhibition." After transcranial direct current stimulation, there was a reduction in the performing time (P = .016) and in the total errors in the change

Table 2. Visual Attention Test (TAVIS-3): Average per Task.

	Pre-tDCS	Post-tDCS	P (<.05)
Errors by omission (raw score)			
Task 1	9 ± 8.71	7.22 ± 7.77	.031
Task 2	4.55 ± 2.69	2.66 ± 1.41	.141
Task 3	0.33 ± 1	0.33 ± 0.7	1
Errors per share (raw score)			
Task 1	11 ± 22.96	3 ± 2.91	.156
Task 2	6.88 ± 4.42	3.66 ± 3.39	.7
Task 3	15.88 ± 34.9	2.33 ± 2.44	.313
Hits (raw score)			
Task 1	11.77 ± 6.7	12.55 ± 5.12	.406
Task 2	16.66 ± 3.5	18.55 ± 2.69	.078
Task 3	49.77 ± 12.81	49.77 ± 13.03	1
Average reaction time (raw score)			
Task 1	0.52 ± 0.24	0.54 ± 0.16	.82
Task 2	0.71 ± 0.15	0.69 ± 0.17	1
Task 3	0.69 ± 0.24	0.73 ± 0.23	.2

Abbreviation: tDCS, transcranial direct current stimulation.

Table 3. Visual Attention Test (TAVIS-3): Mean Values of the Agglomerates.

	Pre-tDCS	Post-tDCS	P (<.05)
Errors by omission	4.62 ± 3.58	3.4 ± 2.9	.023
Errors per share	11.25 ± 20.19	3 ± 1.73	.063
Hits (raw score)	26.07 ± 2.8	26.96 ± 3.76	.063
Average reaction time (raw score)	0.64 ± 0.15	0.65 ± 0.14	.426

Abbreviation: tDCS, transcranial direct current stimulation.

Table 4. Digit Span Subtest of the WISC-III.

	Pre-tDCS	Post-tDCS	P (<.05)
Raw score	10.66 ± 1.65	10 ± 1.65	.266
Weighted score	9 ± 2.17	8.11 ±1.9	.125
Forward order	4.88 ± 0.92	4.22 ± 0.66	.125
Backward order	3.66 ± 1.11	3.33 ± 0.7	.531

Abbreviation: tDCS, transcranial direct current stimulation.

Table 5. Corsi Cube.

	Pre-tDCS	Post-tDCS	P (<.05)
Forward raw score	7.11 ± 1.69	6.33 ± 2.17	.477
Backward raw score	4.44 ± 1.87	4.66 ± 1.65	1
Forward order	5.33 ± 1.22	4.88 ± 1.26	.281
Backward order	4.22 ± 1.39	4 ± 0.7	.813

Abbreviation: tDCS, transcranial direct current stimulation.

step (P = .012). The number of uncorrected errors increased after the procedure (P = .023). It was not possible to categorize groups by age and gender and compare them according to their response to transcranial direct current stimulation because of the small sample size.

Table 6. Inhibitory Control—Battery Subtest Neuropsychological Development Assessment (NEPSY-II).

	Pre-tDCS	Post-tDCS	P (<.05)
Naming			
Uncorrected errors	1.66 ± 2.12	2.55 ± 5.5	.594
Self-corrected errors	1.22 ± 1.56	1 ± 1.22	.75
Total errors	3 ± 2.54	3.55 ± 5.29	.359
Completion time (seconds)	58.88 ± 13.72	52.11 ± 11.43	.016
Inhibition			
Uncorrected errors	7.66 ± 6.74	8.66 ± 10.86	.738
Self-corrected errors	3.55 ± 2.87	1.88 ± 1.9	.141
Total errors	11.22 ± 5.23	10.55 ± 10.1	.617
Completion time (seconds)	85.77 ± 21.11	80.22 ± 18	.172
Switching			
Uncorrected errors	12.66 ± 6.96	8 ± 6.89	.023
Self-corrected errors	4 ± 2.17	4.66 ± 4.27	.848
Total errors	16.66 ± 7.03	12.44 ± 8.66	.012
Completion time (seconds)	105.66 ± 22.14	96.44 ± 26.59	.285
Total score (3 conditions)	30.88 ± 11.72	26.55 ± 20.56	.164

Abbreviation: tDCS, transcranial direct current stimulation.

Regarding the scale Patient Global Impression of Improvement, parents of 4 children found that after transcranial direct current stimulation, they were "slightly better" (score = 3). One child was considered "much better" (score = 2), and one "very much better" (score = 1) after the procedure. One child was considered "much worse" (score = 6) and the profile "no change" (score = 4) was observed just one time.

Considering all the participants in all the days of intervention, there were 99 records of adverse effects, of which 5% was related to headache (mild in 100%), 1% to neck pain (mild in 100%), 18.18% to tingling in the anode positioning site (considered mild in 83.33% and moderate in 16.66% of cases), 31.31% to itching (mild in 61.29% and moderate in 38.7% of cases), 24.24% to burning sensation (mild in 41.66% and moderate in the other), 13.13% local redness (mild in 92.3% and moderate in 7.6% of cases), and 1% to mild sleepiness. Sense of shock accounted for 6% of adverse events (mild in all cases).

Discussion

There is still limited evidence about the impact of transcranial direct current stimulation in ADHD. The data presented suggest that transcranial direct current stimulation can modify some parameters on neuropsychological tests in children and adolescents with this disorder. It is believed that activation of prefrontal neuronal circuits can enlarge dopaminergic neurotransmission and increase attention.[40]

In this study, an improvement was observed in the selective attention and reduction in patterns of attention deficit spectrum identified by TAVIS-3. In the inhibitory control subtest (NEPSY-II) the time to check information and the frequency of errors in alternating attention task decreased. Moreover, it appears that in most subtests, the number of errors and run time was shorter after transcranial direct current stimulation, and we must consider the clinical relevance of these findings. The number of uncorrected errors was reduced after transcranial direct current stimulation, which can be explained by the fact that there was a reduction in the total number of errors.

It should be noted that the inclusion of a female in this clinical trial does not constitute bias considering that she had the same phenotypic profile as the other participants (combined presentation). In addition, previously studies showed no differences in response to transcranial direct current stimulation between genders, except during teenage and adult life because of the influence of hormonal variations in females.[41]

Regarding Patient Global Impression of Improvement, most parents reported a reduced intensity of the symptoms of ADHD after transcranial direct current stimulation. Caution in interpretation of the Patient Global Impression of Improvement scores is recommended. A "slightly better" or "slightly worse" score probably has no significance and is influenced by the open label nature of the study, and this could just represent an expected variance within the group, especially because of the small number of participants. The only individual rated much worse (score = 6) in Patient Global Impression of Improvement had oppositional defiant disorder as comorbidity and the highest total score of the SNAP-IV among the subjects included in the study. It is possible that a cessation of drug therapy used by them for neuropsychological assessment and transcranial direct current stimulation may have influenced the negative results reported by parents.

Adverse effects reported during transcranial direct current stimulation were mostly mild and self-limited, as well as what was recorded in a previous study performed in children with language disorders.[30] However, in addition to the adverse effects reported by Brunoni et al,[39] some patients reported the feeling of "shock" during transcranial direct current stimulation sessions. This effect was added to the inventory of adverse events in the study group. Because of the difficulty of perception of change of skin color (local redness) at the site of electrode placement in African American children, this side effect may have been underestimated, justifying their low frequency in the population studied.

One of the biggest challenges of the study was to ensure the full participation of children and adolescents with ADHD, both in assessment tests and in the proposed activities during the transcranial direct current stimulation to modulate the target area. Therefore, it is believed that perhaps some data could be more representative on comparing pre– and post–transcranial direct current stimulation results, being biased by its own clinical features of the disorder. As it is a self-compared study, the bias is minimized because each child was his own control.

It is noteworthy that as an area of recent interest in neuroscience, the transcranial direct current stimulation parameters are still controversial. One of the issues is related to active stimulation of the individual during attention tasks. According to Ridding and Ziemann,[42] perhaps performing cognitive tasks to stimulate attention during the application of transcranial direct current stimulation is less favorable to the consolidation of neuroplasticity. Furthermore, a study that addressed the role of transcranial direct current stimulation in aphasia showed more exuberant results after transcranial direct current stimulation when performing specific activities for each patient during the session. The argument of the authors was that the language stimulation for the technique could have positively influenced the results observed.[43] Another aspect to be considered is the lack of knowledge about the late impact of transcranial direct current stimulation on the developing brain. Concerns about aberrant plasticity are far from been diminished.[44]

Recently, a randomized, double-blind, sham-controlled trial was performed to determine the impact of transcranial direct current stimulation in adults with ADHD. There was no difference in the go–no go test in the intervention group when compared to the sham group. However, the current employed was 1 mA, stimulation time was 20 minutes, and the procedure included only 1 session.[20]

Test-retest effect did not occur in this study because of the unpredictable nature of the instruments used. As an open study with a small sample, the results should be interpreted with caution. Furthermore, it is not possible to translate the findings into improved functional gains observed in some tests. The short follow-up time does not allow to determine persistent gains. The fact of having found improvement in some evaluation parameters even with limited sample may mean that further studies may produce results with more supportive evidence, which may enable the strengthening of this new therapeutic approach in children and adolescents with ADHD, especially for those who do not fit in the standard pharmacologic treatment.

There are few published articles on the use of transcranial direct current stimulation in the pediatric population, and this study is perhaps the first to test the potential benefits of this technique in children and adolescents with ADHD through the stimulation of the dorsolateral prefrontal cortex. The results, although not consistent, confirm the safety and tolerability of this technique in children and suggest potential benefits of transcranial direct current stimulation in individuals with ADHD. Double-blind, randomized, sham-controlled trials with larger clinical samples should be performed in the future and aim to achieve more solid levels of evidence; in addition, a follow-up should be considered to evaluate the long-term effects of transcranial direct current stimulation in this population.

Conclusion

The transcranial direct current stimulation seems to improve aspects of selective attention, minimizing attention-deficit spectrum characteristics of ADHD in children and adolescents, both in the segmented analysis of the tasks when in the mean values of the agglomerates of TAVIS-3. The transcranial direct current stimulation appears to reduce the time needed for children and adolescents with ADHD to select new information, as evidenced by the improvement in the standards of the naming step of subtest inhibitory control (NEPSY-II), and appears to reduce the total number of errors when alternating attention is used. There were clinical improvements post–transcranial direct current stimulation compared to baseline in ADHD children, according to the perception of parents. Adverse effects were mild, transient, self-limited, and similar to the ones in the adult population.

Acknowledgments

We thank Paulo Mattos for conceding the rights to use the test TAVIS-3 in this clinical trial, Neuromodulation Study Group (NEMO) for all the support, especially Chrissie Ferreira de Carvalho and Fernanda Costa de Queirós, and Sheila Neves for her help in reviewing the article's translation.

Author Contributions

IDB, RSQG, JGJ, TLB, and JRJS collected the data. IDB and RSQG organized and analyzed data and wrote the first draft. SNS, NA and RL recruited the patients. SNS, JRJS and RL evaluated the patients. RL provided support and mentorship. All authors reviewed the manuscript. IDB and RSQG are the equally contributing first authors.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval

This study was approved by research ethics committee/institutional review board of Professor Edgard Santos University Teaching Hospital, Salvador, Bahia, Brazil. The IRB approval number is: 108. All parents were asked to sign an informed consent document.

References

1. Harpin VA. The effect of ADHD on the life of an individual, their family, and community from preschool to adult life. *Arch Dis Child*. 2005;90(suppl 1):i2-i7.
2. Arnold LE, Hodgkins P, Kahle J, Madhoo M, Kewley G. Long-term outcomes of ADHD: academic achievement and performance. *J Atten Disord*. 2015 Jan 12.
3. Mannuzza S, Klein RG. Long-term prognosis in attention-deficit hyperactivity disorder. *Child Adolesc Psychiatr Clin N Am*. 2000; 9:711-726.
4. Barbaresi WJ, Katusic SK, Colligan RC, et al. How common is attention-deficit hyperactivity disorder? Incidence in a population-based birth cohort in Rochester, Minn. *Arch Pediatr Adolesc Med*. 2002;156:217-224.
5. Narad ME, Garner AA, Antonini TN, et al. Negative consequences of poor driving outcomes reported by adolescents with and without ADHD. *J Atten Disord*. 2015 Mar 16.
6. Park J, Kim B. Comorbidity and factors affecting treatment non-persistence in ADHD. *J Atten Disord*. 2015 May 25.
7. Langley K, Fowler T, Ford T, et al. Adolescent clinical outcomes for young people with attention-deficit hyperactivity disorder. *Br J Psychiatry*. 2010;196:235-240.
8. Faraone SV, Biederman J, Mick E. The age-dependent decline of attention-deficit hyperactivity disorder: a meta-analysis of follow-up studies. *Psychol Med*. 2006;36:159-165.
9. Cheung CH, Rijdijk F, McLoughlin G, Faraone SV, Asherson P, Kuntsi J. Childhood predictors of adolescent and young adult outcome in ADHD. *J Psychiatr Res*. 2015;62:92-100.
10. Polanczyk GV, Willcutt EG, Salum GA, Kieling C, Rohde LA. ADHD prevalence estimates across three decades: an updated systematic review and meta-regression analysis. *Int J Epidemiol*. 2014;43:434-442.
11. Kooij JJ, Buitelaar JK, van den Oord EJ, Furer JW, Rijnders CA, Hodiamont PP. Internal and external validity of attention-deficit hyperactivity disorder in a population-based sample of adults. *Psychol Med*. 2005;35:817-827.
12. Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. *Am J Psychiatry*. 2007;164: 942-948.
13. Tripp G, Wickens JR. Neurobiology of ADHD. *Neuropharmacology*. 2009;57:579-589.
14. Kooij SJ, Bejerot S, Blackwell A, et al. European consensus statement on diagnosis and treatment of adult ADHD: the European Network Adult ADHD. *BMC Psychiatry*. 2010;10:67.
15. Bush G, Valera EM, Seidman LJ. Functional neuroimaging of attention-deficit hyperactivity disorder: a review and suggested future directions. *Biol Psychiatry*. 2005;57:1273-1284.
16. Kieling C, Goncalves RR, Tannock R, Castellanos FX. Neurobiology of attention-deficit hyperactivity disorder. *Child Adolesc Psychiatr Clin N Am*. 2008;17:285-307, viii.
17. Asherson P. Clinical assessment and treatment of attention-deficit hyperactivity disorder in adults. *Expert Rev Neurother*. 2005;5: 525-539.
18. Kendall T, Taylor E, Perez A, Taylor C. Diagnosis and management of attention-deficit hyperactivity disorder in children, young people, and adults: summary of NICE guidance. *BMJ*. 2008;337: a1239.
19. Graham J, Banaschewski T, Buitelaar J, et al. European guidelines on managing adverse effects of medication for ADHD. *Eur Child Adolesc Psychiatry*. 2011;20:17-37.
20. Cosmo C, Baptista AF, de Araujo AN, et al. A randomized, double-blind, sham-controlled trial of transcranial direct current stimulation in attention-deficit hyperactivity disorder. *PLoS One*. 2015;10:e0135371.
21. Bunse T, Wobrock T, Strube W, et al. Motor cortical excitability assessed by transcranial magnetic stimulation in psychiatric disorders: a systematic review. *Brain Stimul*. 2013;7:158-169.
22. Lu C, Wei Y, Hu R, Wang Y, Li K, Li X. Transcranial direct current stimulation ameliorates behavioral deficits and reduces oxidative stress in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced mouse model of Parkinson's disease. *Neuromodulation*. 2015;18:442-446.
23. Batista EK, Klauss J, Fregni F, Nitsche MA, Nakamura-Palacios EM. A randomized placebo-controlled trial of targeted prefrontal cortex modulation with bilateral tDCS in patients with crack-cocaine dependence. *Int J Neuropsychopharmacol*. 2015;18.

24. Koops S, van den Brink H, Sommer IE. Transcranial direct current stimulation as a treatment for auditory hallucinations. *Front Psychol*. 2015;6:244.
25. Val-Laillet D, Aarts E, Weber B, et al. Neuroimaging and neuromodulation approaches to study eating behavior and prevent and treat eating disorders and obesity. *Neuroimage Clin*. 2015;8:1-31.
26. Pereira Junior Bde S, Tortella G, Lafer B, et al. The Bipolar Depression Electrical Treatment Trial (BETTER): design, rationale, and objectives of a randomized, sham-controlled trial and data from the pilot study phase. *Neural Plast*. 2015;2015:684025.
27. Saba G, Moukheiber A, Pelissolo A. Transcranial cortical stimulation in the treatment of obsessive-compulsive disorders: efficacy studies. *Curr Psychiatry Rep*. 2015;17:36.
28. Nowak DA, Grefkes C, Ameli M, Fink GR. Interhemispheric competition after stroke: brain stimulation to enhance recovery of function of the affected hand. *Neurorehabil Neural Repair*. 2009;23:641-656.
29. Krishnan C, Santos L, Peterson MD, Ehinger M. Safety of noninvasive brain stimulation in children and adolescents. *Brain Stimul*. 2015;8:76-87.
30. Andrade AC, Magnavita GM, Allegro JV, Neto CE, Lucena Rde C, Fregni F. Feasibility of transcranial direct current stimulation use in children aged 5 to 12 years. *J Child Neurol*. 2014;29: 1360-1365.
31. Nitsche MA, Cohen LG, Wassermann EM, et al. Transcranial direct current stimulation: State of the art 2008. *Brain Stimul*. 2008;1:206-223.
32. Loftus AM, Yalcin O, Baughman FD, Vanman EJ, Hagger MS. The impact of transcranial direct current stimulation on inhibitory control in young adults. *Brain Behav*. 2015;5:e00332.
33. Spieser L, van den Wildenberg W, Hasbroucq T, Ridderinkhof KR, Burle B. Controlling your impulses: electrical stimulation of the human supplementary motor complex prevents impulsive errors. *J Neurosci*. 2015;35:3010-3015.
34. Krause B, Cohen Kadosh R. Can transcranial electrical stimulation improve learning difficulties in atypical brain development? A future possibility for cognitive training. *Dev Cogn Neurosci*. 2013;6:176-194.
35. Demirtas-Tatlidede A, Vahabzadeh-Hagh AM, Pascual-Leone A. Can noninvasive brain stimulation enhance cognition in neuropsychiatric disorders? *Neuropharmacology*. 2013;64:566-578.
36. Kang EK, Baek MJ, Kim S, Paik NJ. Non-invasive cortical stimulation improves post-stroke attention decline. *Restor Neurol Neurosci*. 2009;27:645-650.
37. Oliveira JF, Zanao TA, Valiengo L, et al. Acute working memory improvement after tDCS in antidepressant-free patients with major depressive disorder. *Neurosci Lett*. 2013;537:60-64.
38. Boggio PS, Bermpohl F, Vergara AO, et al. Go-no-go task performance improvement after anodal transcranial DC stimulation of the left dorsolateral prefrontal cortex in major depression. *J Affect Disord*. 2007;101:91-98.
39. Brunoni AR, Amadera J, Berbel B, Volz MS, Rizzerio BG, Fregni F. A systematic review on reporting and assessment of adverse effects associated with transcranial direct current stimulation. *Int J Neuropsychopharmacol*. 2011;14:1133-1145.
40. Bush G. Attention-deficit hyperactivity disorder and attention networks. *Neuropsychopharmacology*. 2010;35:278-300.
41. Krause B, Cohen Kadosh R. Not all brains are created equal: the relevance of individual differences in responsiveness to transcranial electrical stimulation. *Front Syst Neurosci*. 2014;8:25.
42. Ridding MC, Ziemann U. Determinants of the induction of cortical plasticity by non-invasive brain stimulation in healthy subjects. *J Physiol*. 2010;588(pt 13):2291-2304.
43. Baker JM, Rorden C, Fridriksson J. Using transcranial direct-current stimulation to treat stroke patients with aphasia. *Stroke*. 2010;41:1229-1236.
44. Muller-Dahlhaus F, Ziemann U. Metaplasticity in human cortex. *Neuroscientist*. 2015;21:185-202.