



Modulation of temporal resolution and speech long-latency auditory-evoked potentials by transcranial direct current stimulation in children and adolescents with dyslexia

Vida Rahimi¹ · Ghassem Mohamadkhani¹ · Javad Alaghband-Rad² · Fatemeh Ranjbar Kermani² · Hossien Nikfarjad³ · Saman Marofizade⁴

Received: 1 August 2018 / Accepted: 4 January 2019 / Published online: 12 January 2019
© Springer-Verlag GmbH Germany, part of Springer Nature 2019

Abstract

In recent years, transcranial direct current stimulation (tDCS) has been used as a safe and non-invasive method for children and adolescents with dyslexia. Our aim in this study was to investigate the effect of tDCS on variables of temporal resolution and speech long-latency auditory-evoked potentials with two electrode arrays on superior temporal gyrus (STG). A total of 17 children and adolescents with dyslexia (age 9–12 years) were included in our study. All participants underwent the gap in noise (GIN) test and long-latency auditory-evoked potentials recording at baseline without applying tDCS, sham (placebo), and after 20 min of exposure to two different tDCS polarities: anode of tDCS on left STG/cathode on the right shoulder and anode on the left STG/cathode on right STG to enhance left lateralization. Our results showed significant decreases in the threshold value and increases in the percentages of correct responses in the GIN test. We also found reduced latency and increased amplitude of the P1, N1, and P2 waves in two stimulation polarities compared with baseline and sham. Our findings indicate the potential role of tDCS on improving the characteristics of central auditory processing, especially temporal information processing in children and adolescents with dyslexia, and could introduce a new strategy to facilitate the rehabilitation of central auditory processing disorders in future.

Keywords Transcranial direct current stimulation · Dyslexia · Temporal resolution · Auditory-evoked potentials

Introduction

Developmental dyslexia is a neurodevelopmental disorder that affects 5–17% of children. It is defined as a persistent deficit in learning to read and is characterized by performance levels that are lower than expected in terms of the child's age, educational status, and intelligence level

(Turkeltaub et al. 2012; Ferrer et al. 2010; Shaywitz et al. 2003). Some theories have explained the fundamental causes of dyslexia based on the visual, auditory, motor, and attentional systems (Vellutino et al. 2004); however, the theory of phonological deficit (Boets et al. 2007) that proposes underlying impairment of the phonological component of language as the cause for the disorder (Ramus et al. 2003; Liberman et al. 1989; Khan et al. 2011) is considered the most important. Another theory proposes that developmental dyslexia is caused by auditory temporal processing or rapid auditory processing deficits. The role of central processing of auditory information in patients with dyslexia is prominent, and researchers have reported that children with dyslexia face difficulties particularly with processing rapidly changing or transient acoustic events (Farmer and Klein 1995; Boets et al. 2007). In addition, the ability to process rapid successive information is crucial to the development of the phonological system, and poor language skills in patients with dyslexia might arise from general deficits in processing rapid temporal information (Boets et al. 2007; Tallal 2004;

✉ Ghassem Mohamadkhani
mohamadkhani@tums.ac.ir

¹ Department of Audiology, School of Rehabilitation, Tehran University of Medical Sciences, Piche-Shemiran, Enghelab Ave., 1148965141 Tehran, Iran

² Department of Psychiatry, Roozbeh Psychiatric Hospital, Tehran University of Medical Sciences, Tehran, Iran

³ Department of Cognitive Science, ACECR, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁴ Department of Epidemiology and Reproductive Health, Reproductive Epidemiology Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran

Raschle et al. 2014). In the functional view, some children with dyslexia were reported to exhibit rapid auditory processing deficits at the upper brainstem and auditory cortex levels. As a result, the brain of a person with dyslexia is unable to efficiently and reliably process the short, sequential speech and transient stimuli (Cohen-Mimran and Sapir 2007). This functional impairment in patients with dyslexia is accompanied by changes in brain imaging evidence. Imaging studies have clearly shown an altered cortical network in dyslexic subjects that contains left and right superior temporal cortices, left inferior temporal–occipital cortices, and left and right inferior frontal and posterior temporo-parietal cortices (Schlaggar and McCandliss 2007). Studies have shown hypo-function cortical activity in left superior temporal gyrus (STG) and fusiform in children with dyslexia, and reduction in gray matter volume has been found in areas relevant to speech and language processing (Blau et al. 2010; Steinbrink et al. 2008; Lohvansuu et al. 2014).

There exists a relationship between dyslexia and poor performance in central auditory processing tests, particularly in auditory temporal processing tests (Iliadou et al. 2009; King et al. 2003). A number of behavioral and electrophysiological studies have provided evidence for auditory temporal processing deficits and abnormal potentials (amplitude, latency, and morphology) for speech and non-speech sounds in children and adults with dyslexia (Schulte-Körne and Bruder 2010; Regaçone et al. 2014; Frizzo 2015; Richardson et al. 2004; Putter-Katz et al. 2005; Oliveira et al. 2013). In the behavioral domain, children with dyslexia performed poorly in temporal order judgment and gap detection in noise tasks (Farmer and Klein 1995; Iliadou et al. 2009), which are the most commonly used methods to measure auditory temporal resolution, a subgroup of temporal processing (Sanayi et al. 2013).

From an electrophysiological point of view, long-latency auditory-evoked response (LLAEP) is a type of auditory-evoked potential (AEPs) that used to study the underlying brain processes and mechanisms that characterize neurological speech processing, examination of auditory abnormalities and clinical evidence of hearing impairment in children and adults (Hall 2007; Didoné et al. 2014). It seems that it is the proper way for investigation of dysfunction in the central auditory processing pathway and beneficial for monitoring rehabilitation effect. It is evident that the latency and amplitude of AEP are sensitive measures of the complexity of phonological processing in skilled and dyslexic readers (Hall 2007; Putter-Katz et al. 2005; Regaçone et al. 2014). Moiescu-Yiflach and Pratt (2005), Regaçone et al. (2014), and Frizzo (2015) reported increased latency and reduced amplitude of long-latency auditory-evoked response (LLAEP) waves in response to non-speech and speech stimuli (da) in dyslexia that can be related to the reduced amount of electrical activity involved in processing primary and secondary

areas in supratemporal auditory cortex, also indicating a defect in synchronizing central information and in passive processing of auditory sensory information. Also, Event-related potential (ERP) findings revealed altered neurophysiological processes in individuals with dyslexia to speech stimuli and evidence for deficits processing certain general acoustic information such as temporal pattern (Schulte-Körne and Bruder 2010).

There are several ways to rehabilitate central auditory processing (Iliadou et al. 2017). Neurophysiological studies of rehabilitation indicate that some changes in brain function may be a critical mechanism for improving behavior (Krause et al. 2013). Direct induction of brain changes can lead to positive effects in performance. Use of non-invasive transcranial direct current stimulation (tDCS) provides a method beyond traditional cognitive and rehabilitation methods that can be proportional to stimulation polarity and the duration of stimulation, and leads to an increase or decrease in cortical activity (Turkeltaub et al. 2012; Heimrath et al. 2016). Anodal tDCS typically has an excitatory effect on the local cerebral cortex, while cathodal tDCS decreases the cortical excitability. Also tDCS is an effective technique of brain modulation that uses weak direct current to change neuronal spontaneous firing and change in the concentration of neurotransmitters especially glutamate and GABA (Nitsche et al. 2003, 2008). The effects of tDCS can last from a few minutes to several hours after the stimulation (Krause and Cohen Kadosh 2013; Stagg and Nitsche 2011; Zaehle et al. 2011). In humans, neuromodulatory effects of transcranial direct current stimulation (tDCS) have been observed for cognitive functions, sensory-specific lower order processing stages, and motor functions (Zaehle et al. 2011). In the auditory domain, although studies have reported tDCS-induced alterations of auditory cortex (AC) reactivity, evidence regarding related changes is still sparse (Heimrath et al. 2016). Most studies provide evidence of behavioral changes associated with tDCS, whereas only few studies explain the direct electrophysiological consequences of effective tDCS modulations of the human AC. However, several studies have been conducted on the effects of tDCS on the temporal resolution feature of central auditory processing in healthy subjects (Ladeira et al. 2011; Heimrath et al. 2014). Ladeira et al. (2011) stated their results encourage further studies exploring tDCS in central auditory processing disorders. Some researchers also believe that future studies need to focus on the associations between deficient auditory processing and hypofunctioning of the auditory-related areas (Gaab et al. 2007; Chobert et al. 2012; Raschle et al. 2014). Heimrath et al. (2014) believed an enhancement of left AC reactivity will result in an improvement of such perceptual processes. Thus, their findings also might have clinical implications by fostering potential approaches for a treatment of speech-related pathologies such as dyslexia.

Also, Zaehle et al. (2011) for first time investigated cortical reactivity of the human AC after anodal and cathodal tDCS by LLAEP recording. They showed tDCS-induced modulations of auditory-evoked brain activity as a function of stimulation site and condition.

About the effect of tDCS on dyslexia, tDCS has been used as a safe and non-invasive method for children and adolescents in reading domain (Costanzo et al. 2013, 2016a, b), but it seems that no study has been conducted to investigate the effect of tDCS on some features of central auditory processing such as temporal resolution and AEPs in this group. Considering the importance of central auditory processing in the development of reading disorders (Nittrouer 1999), we decided to study the effects of tDCS on auditory temporal resolution and speech LLAEP using two electrode arrays in children and adolescents with dyslexia by enhancing cortical activity through the anodal tDCS on the left STG to observe modulations in the auditory temporal resolution and LLAEP.

Methods

This study with quasi-experimental design was conducted after approval by the Ethics Committee in research of Tehran University of Medical Sciences (number: 96543) in accordance with the World Medical Association's Declaration of Helsinki. After explaining the research process and its risk, informed consent was taken from the child's parents, and they were free to leave the investigation at any moment.

Participants

Seventeen children and adolescents with dyslexia with age range 9–12 years and mean \pm SD age 10.35 ± 1.36 (nine males, mean \pm SD age: 10.87 ± 1.30 and eight females, mean \pm SD age: 9.88 ± 1.35) participated in the study. A definitive diagnosis of dyslexia was given by the child and adolescent psychiatrist, using the DSM-5 criteria (American Psychiatric Association 2013) and speech therapist's opinion with specific speech language pathology procedures include clinical history, systematic clinical evaluation according to Persian word and nonword lists (a set of 40 high-frequency words, 40 low-frequency words, 40 nonword) with reading tests of NAMA (Kormi Noori et al. 2008; Moradi et al. 2016) in Roozbeh Hospital. The mean \pm SD of some reading measure factors in participants is shown in Table 1.

All participants were monolingual (native Persian speakers) with normal vision and right-handed (according to the Edinburgh Handedness Inventory). None of the children had a personal history of neurological disease especially epilepsy and neurological accompanying disorders. Air and bone-conduction pure tone audiometry thresholds at 250–8000 kHz frequencies were normal (threshold better

Table 1 The means \pm SD of reading errors and total times in reading tests of NAMA in participants

Reading measure factors	Mean \pm SD
High-frequency word errors	2.64 \pm 1.27
High-frequency word times ^a	131.41 \pm 11.20
Low-frequency word errors	5.23 \pm 1.71
Low-frequency word times ^a	154.29 \pm 17.88
Nonword reading errors	6.05 \pm 1.67
Nonword reading times ^a	157.52 \pm 20.66
Text-reading errors	7.52 \pm 1.41
Text-reading times ^a	204 \pm 29.27

^aTotal time (second)

than 20 dBHL) (Regaçone et al. 2014). Also, none of the participants had any other significant cognitive activity, such as painting or music. Due to normal IQ criteria in this research, the intellectual performance assessment was conducted by a psychologist, using the application Wechsler Intelligence Scale for Children/revised (WISC-IV; Wechsler 2010). Nonverbal IQ rang in participants was within limits 90–132 (mean \pm SD 107.29 ± 14.28).

Experimental design

All participants were exposed to four statuses at intervals of 1 week to avoid interference (Deike et al. 2016). These conditions include the stimulatory state with an active anode electrode on the left STG and a cathode electrode on the right STG with a bilateral bipolar-balanced type of electrode montage for increase cortical excitability in left STG and inhibition in right STG, active anode electrode on left STG and cathode electrode on right shoulder with unilateral monopole type of electrode montage only for increase cortical excitability in left STG, sham or placebo in which there is no effective stimulation and baseline status without applying tDCS. The order of four statuses was randomized. Also participants were blind relative to the type of situation.

tDCS stimulation was applied using Electrical Brain Stimulator (Neurostim, MGT Co, Japan) and two rubber conductive electrodes covered with 9% saline-soaking synthetic sponges. To increase focal precision, we used a small 5 cm \times 5 cm active electrode in two intervention polarities. Also we used a non-cephalic cathode electrode (right shoulder) to eliminate potential confounding effects of the reference electrode (Nasseri et al. 2015).

Electrodes were placed over STG areas according to 10–20 system for EEG electrode placement by measuring the size of each participant's skull (anodal T7 and cathodal T8 in one polarity and anodal T7 and cathodal electrode on shoulder in other polarity). This area included planum temporal and auditory cortices (Mattai et al. 2011; Lewald

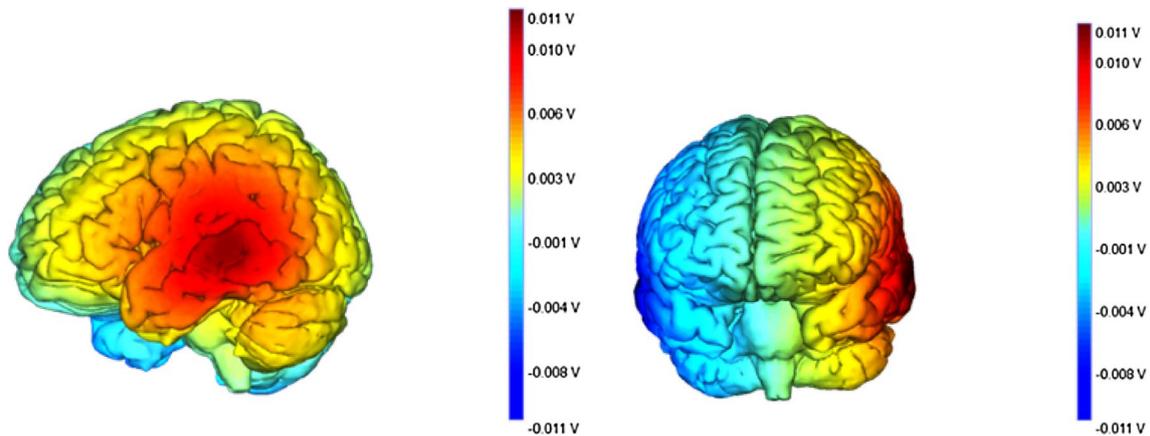


Fig. 1 **a** Modeling of stimulation induced by anodal tDCS on left STG. **b** Increased excitability in left STG and inhibit in right STG with enhancing left lateralization of the STG

2016) (Fig. 1). At the beginning of stimulation, the current was increased during the first 30 s (ramp up). Next, 1-mA constant direct current was delivered for 20 min and the current was decreased to 0 mA during the last 30 s. In the sham status, the current flow was applied only for 30 s to create an initial sensation of stimulation. This was enough time to create a sense of stimulation in the person (Costanzo et al. 2016a, b).

In this way, none of the participants were able to determine whether or not they received real or sham (Zaehle et al. 2011). Evaluations (GIN test and LLAEP) were conducted at baseline (B), immediately after the removal of the tDCS electrodes at sham (placebo; S) (after 20 min of applying the tDCS electrode without effective stimulation) and after 20 min of exposure to 1-mA current from two different tDCS polarities; anode electrode on left STG/cathode electrode on right shoulder (L) and anode electrode on the left STG/cathode electrode on right STG (LR) with 1-week interval between each status.

Behavioral assessment

Gap in noise test

A gap detection task (GDT) is the most common method used to measure auditory temporal resolution (Heimrath et al. 2014). Stimuli were presented via a CD player that was connected to the audiometer AC-40 in right ear with TDH-39 headphone. Stimuli of GIN are a set of bursts of white noise with a 6-s duration up to three gaps in every segment. Gap durations were 2–3–4–5–6–8–10–12–15–20 ms and the silence epoch between every set was 6 s. In this test, the patient is asked to listen to a noise while identifying the number of distances (silence) in the white noise

in most comfortable level (MCL). An approximate gap in noise threshold (GIN_{Th}) and percentage of the correct responses (GIN_P) are two criteria for this test. The gap in noise threshold is referred to the shortest silence gap noticed by the subject at least four out of six times and percentage of the correct responses is calculated from formula 1 in GIN test (Sanayi et al. 2013).

The number of correct intervals detected – false positives / total number of presentations.

Electrophysiological recording

LLAEP with speech stimuli was performed in baseline (B) and sham (placebo) (S) after 20 min of applying the tDCS electrode without effective stimulation, and after completing the stimulation of the tDCS in two stimulation polarities in dyslexic participants using with the EBNeuro Sirius electroencephalography (EEG) system (EBNeuro/Florence, Italy) (bandpass 0.01–30 Hz). While recording LLAEP, to prevent muscle artifacts, the child was asked to sit on the comfort chair and look at the cartoon images of the monitor's screen. To reduce time wasting, children's skin was cleansed with ten-twenty cleansing gel to improve impedance in all conditions. The average duration of LLAEP recording without preparation time was 10 min. The electrode impedance and inter-electrode impedance were < 5 k Ω and < 2 k Ω , respectively. The test was carried out in an acoustic room with no electrical interference.

The response was recorded with Ag–AgCl active electrodes on at midline electrode sites (Fz, Cz, and Pz), reference electrode placed at the right and left mastoid (A1 and A2), and the ground electrode on the forehead (Fpz) according to the 10/20 International system (Jasper 1958).

Eye movements were monitored with a bipolar electrode montage (supraorbital to lateral canthus). Also a strict artifact-rejection criterion of 45 mV was used for the cortical recordings. The speech stimuli/da/with 170-ms duration was transferred with ER-3A insert earphones (polarity, rarefaction; intensity, 80 dBHL; sweep, 200; rate, 1.1; gain, 50,000, sampling rate 512).

Data analysis

Digital filters were applied off-line (low pass filter of 30 Hz, high pass filter of 0.1 Hz). The LLAEP is a sequence of peaks with positive and negative polarity in 80- and 350-ms intervals after stimuli (Frizzo 2015). So post-stimulus time was considered 533 ms with pre-stimulus time 100 ms. The positive–negative biphasic waveform cortical-evoked potential elicited by the/da/stimulus displayed P1, N1, and P2 (P1') waves. The peak analysis was performed at channel Fz. The absolute latencies and amplitudes of these variables in four statuses were identified and analyzed. LLAEP amplitudes were quantified by measuring the baseline-to-peak and latency was defined as time interval between the onset of the stimulus and the appearance of a change in the waveform of auditory-evoked potential (Zaehle et al. 2011).

Statistical analysis

Data analysis was done with SPSS for Windows, version 16.0 (SPSS Inc., Chicago, IL, USA). In this study, continuous variables were presented as mean ± standard deviation (SD). The normality of data was checked using the Kolmogorov–Smirnov test. A repeated measure ANOVA, followed by the Bonferroni test, was used to compare between statuses (Pairwise Comparisons). Mauchly’s sphericity test was used to evaluate the sphericity assumption. If this assumption was violated, the Greenhouse–Geisser correction was used. All statistical tests were two sided and a $P < 0.05$ was considered statistically significant and partial eta squares (η_p^2) have been reported as effect size.

Results

Gap in noise test results

As seen in Table 2, repeated measures ANOVA showed significant effects of stimulation (in both polarities of stimulation) in gap in noise threshold and percentage of correct responses in the GIN test, respectively [$F_{(1.68,26.94)} = 55.51, P < 0.001, \eta_p^2 = 0.776$], [$F_{(1.41,22.7)} = 40.02, P < 0.001, \eta_p^2 = 0.714$]. So that, the lower GIN thresholds (a significant improvement in the GIN threshold) are seen in anode electrode of tDCS on left STG/cathode electrode on right shoulder and anode electrode on the left STG/cathode electrode on right STG compared with baseline and sham statuses ($P < 0.001$ in both them). Post hoc analysis showed no significant difference in GINTh between two stimulation polarities ($P = 0.24$) in GINP, Percentage of correct responses in anode electrode of tDCS on left STG/cathode electrode on right shoulder was more than baseline, sham, anode electrode on the left STG/cathode electrode on right STG statuses (all $P < 0.001$). Also this percentage significantly improved in anode electrode on the left STG/cathode electrode on right STG mode than baseline and sham ($P < 0.001$ in both them). Indeed, percentage of correct responses in GIN test in anode electrode on left STG/cathode electrode on right shoulder polarity was slightly more than the other stimulus polarity ($P = 0.02$). It is important to note that no difference was found between the baseline and the sham state in GINTh and GIN P variables, respectively ($P = 1$), ($P = 0.1$).

Electrophysiological results

All 17 subjects showed P1, N1, and P2 in response to speech stimuli. Table 3 shows the mean of P1, N1, and P2 amplitude, and P1, N1, and P2 absolute latency.

Repeated measures ANOVA revealed a significant main effect of the stimulation factor on P1, N1, and P2 amplitude [$F_{(1.14,18)} = 245.9, P < 0.001, \eta_p^2 = 0.93$], [$F_{(1.3,20.0)} = 90.8,$

Table 2 The means ± SD of gap threshold and percentage of the correct responses in gap in noise test and comparison between research statuses

	Status				<i>F</i>	<i>P</i>	Effect size (η_p^2)	Pairwise comparisons ^a
	Baseline (B)	Sham (S)	Left anode (L)	Left anode/ right cathode (LR)				
GINTh	7.35 ± 1.45	7.23 ± 1.30	5.58 ± 1.06	5.82 ± 1.01	$F_{(1.68,26.94)} = 55.51$	<0.001	0.776	S = B > L = LR
GINP	58.41 ± 0.81	59.29 ± 0.82	64.94 ± 1.02	64.34 ± 0.97	$F_{(1.41, 22.7)} = 40.02$	<0.001	0.714	B = S < LR < L

B baseline, S sham, L anode electrode on left superior temporal gyrus/cathode electrode on right shoulder, LR anode electrode on left superior temporal gyrus/cathode electrode on right superior temporal gyrus, GINTh gap in noise threshold, GINP percentage of the correct responses

^aBonferroni test was used

Table 3 The means \pm SD of amplitude and latency variables and comparison between research statuses

	Status				<i>F</i>	<i>P</i>	Effect size (η_p^2)	Pairwise comparisons ^a
	Baseline (B)	Sham (S)	Left anode (L)	Left anode/ right cathode (LR)				
P1A	0.73 \pm 0.28	0.75 \pm 0.29	1.14 \pm 0.35	1.13 \pm 0.35	$F_{(1.14, 18)} = 245.9$	< 0.001	0.939	L = LR > S = B
N1A	-2.70 \pm 0.51	-2.75 \pm 0.48	-3.35 \pm 0.43	-3.30 \pm 0.44	$F_{(1.3, 20.0)} = 90.8$	< 0.001	0.850	B = S > L = LR
P2A	0.83 \pm 0.24	0.83 \pm 0.25	1.26 \pm 0.33	1.24 \pm 0.33	$F_{(1.1, 17.4)} = 226.7$	< 0.001	0.934	L > LR > B = S
P1L	60.24 \pm 4.53	59.77 \pm 4.54	52.33 \pm 3.67	52.45 \pm 4.72	$F_{(1.2, 19.34)} = 98.61$	< 0.001	0.86	B = S > LR = L
N1L	133.95 \pm 11.7	133.06 \pm 12.3	124.77 \pm 11.24	125.15 \pm 10.84	$F_{(1.8, 29.02)} = 178.57$	< 0.001	0.91	B = S > L = LR
P2L	194.0 \pm 10.5	193.64 \pm 10.4	181.70 \pm 10.2	182.17 \pm 10.43	$F_{(1.10, 17.70)} = 371.93$	< 0.001	0.959	B = S > L < LR

B baseline, *S* sham, *L* anode electrode on left superior temporal gyrus/cathode electrode on right shoulder, *LR* anode electrode on left superior temporal gyrus/cathode electrode on right superior temporal gyrus, *P1A* P1 amplitude, *N1A* N1 amplitude, *P2A* P2 amplitude, *P1L* P1 latency, *N1L* N1 latency, *P2L* P2 latency

^aBonferroni test was used

$P < 0.001$ $\eta_p^2 = 0.85$], [$F_{(1.1, 17.4)} = 226.7$, $P < 0.001$, $\eta_p^2 = 0.93$]. Amplitude increased after anode electrode of tDCS on left STG/cathode electrode on right shoulder and anode electrode on the left STG/cathode electrode on right STG compared with baseline and sham statuses in P1, N1 and P2 waves (All $P < 0.001$). Pairwise comparisons showed no significant difference between baseline and sham in P1 ($P = 0.17$), N1 ($P = 0.23$) and P2 amplitude ($P = 1$). There were no significant differences between the two stimulation polarities in P1 ($P = 0.49$) and N1 ($P = 0.37$). But this difference was significant between the two transcranial direct current stimulation polarities in P2 ($P = 0.008$).

Table 3 shows the effect of stimulation on the absolute latency P1, N1 and P2 in stimulation polarities [$F_{(1.2, 19.34)} = 98.61$, $P < 0.001$, $\eta_p^2 = 0.86$], [$F_{(1.8, 29.02)} = 178.57$, $P < 0.001$, $\eta_p^2 = 0.91$], and [$F_{(1.10, 17.70)} = 371.93$, $P < 0.001$, $\eta_p^2 = 0.95$]. As seen, latency N1, P1, and P2 reduced after two stimulation polarities compared with baseline and sham statuses (All $P < 0.001$). Similarly to the amplitude, no significant difference was found between the two stimulus polarities in the absolute latency of P1 ($P = 1$), N1 ($P = 0.37$) and except P2 ($P = 0.003$).

Also post hoc pairwise test revealed no significant difference between baseline and sham statuses in P1 ($P = 0.062$), N1 ($P = 0.20$) and P2 latency ($P = 0.093$).

Discussion

In the present study, we investigated the effect of tDCS on temporal resolution and auditory-evoked potentials in children and adolescents with dyslexia. The GIN test was applied to this study for behavioral assessment. Because GIN is reportedly a valid test for assessing temporal resolution,

particularly in patients with central auditory processing disorders (Musiek et al. 2005); further, GIN can index primary cortical processing (Ladeira et al. 2011).

The assumption that polarity-related changes of cortical excitability are simply reflected in behavioral effects is rather vague (Jacobson et al. 2012; Miniussi and Ruzzoli 2013). Accordingly, the acquisition of direct electrophysiological data by recording the EEG or ERP during and after the application of tDCS may help to assess the underlying physiological basis and therewith to improve the efficiency of auditory tDCS pattern as well as to identify the actual brain–behavior relationship (Sale et al. 2015).

So, we used LLAEP test (as ERP) as one of the promising measures used in research in central auditory processing that reflects cortical activity, ranging from simple to the most complex auditory skills after tDCS in dyslexic children (Regaçone et al. 2014). These waves are generated in the supratemporal auditory cortex, the primary site of the auditory pathway (Regaçone et al. 2014; Frizzo 2015).

We found significant decreases in the threshold values and increases in the percentages of correct responses in the GIN test for behavioral assessment as well as reduced latency and increased amplitude of the P1, N1, and P2 waves in the electrophysiological test after anodal stimulation on left STG/cathodal stimulation on right STG and anodal stimulation on left STG/cathodal stimulation on right shoulder compared with baseline and sham statuses. These findings confirm the hypothesis that tDCS can induce the modulation of auditory temporal resolution and speech LLAEP in children and adolescents with dyslexia.

These results indicate that increased activity of the left superior temporal region by the dual action of left anodal and right cathodal tDCS is helpful to induce improvement in some aspect of central auditory processing in children and adolescents with dyslexia. Also increased activity in the left

STG alone induced modulation of temporal resolution and LLAEP. Our assumption was that temporal acoustic information processing is done mainly in the left hemisphere, and tDCS can induce normalization of their abnormal (hypoactivity) cortical activity in left STG of children with dyslexia and increasing activity in this area can improve feature of central hearing processing in this study.

Many previous studies have reported central auditory system anomalies in children with dyslexia. Neville et al. (1993) reported abnormal auditory ERP responses associated with STG processing in a subgroup of children with reading and language impairment who displayed poor performance in the auditory temporal discrimination tasks. Studies have also indicated impairments in evoked auditory responses, including delayed middle and late auditory responses, as indicators of deficits in speech comprehension in people with learning disabilities (Leppanen and Lyytinen 1997; Frizzo 2015). The exogenous or sensory waves P1–N1–P2–N2 in LLAEP response depend on the perceived acoustic and temporal characteristics of the central auditory system. In children with learning disorders, especially dyslexia, delayed latencies of N1 and P2 components may be associated with failures related to onset of auditory processing, but specifically to deficits in synchronizing auditory cortical information (Regaçone et al. 2014; Frizzo 2015; Cunningham et al. 2001). Several studies mentioned that temporal processing deficit in dyslexia and believed latency differences in LLAEP in dyslexic subjects compared with normal cases may be related to a common deficit in timing and rapid auditory information accompanied with deficient phonological processing (Nittrouer 1999; Boets et al. 2007; Regaçone et al. 2014; Ladeira et al. 2011). Also decrease in N1 amplitude may be related to the reduced amount of electrical activity involved in processing primary and secondary areas, in supratemporal auditory cortex (Regaçone et al. 2014). Some studies have proved left auditory cortex (AC) is responsible for processing timing cue and rapid temporal acoustic information that have roles in LLAEP wave (Heimrath et al. 2014, 2016; Ladeira et al. 2011). In the other hand, studies have shown that at a cellular level, tDCS modulates the level of neuronal excitability by altering cell membrane potential and modifies the spike firing probability, so that anodal stimulation with an effect on cellular depolarization increases the number of neuronal firing rate. It also improves neuronal synchronization (Nitsche et al. 2008; Krause et al. 2013). So we suppose that anodal tDCS with its effect on increased neuronal synchronization, neuronal firing rate and amount of electrical activity involved in processing primary and secondary areas in AC especially STG can improve temporal resolution (improvement in the GIN threshold was achieved by discovering the least time variation, thereby increasing the percentage of accurate answers). Also due to the role of the factors mentioned above in amplitude and

latency changes (Hall 2007), anodal tDCS can reduce the latency and increase the amplitude P1, N1, and P2 waves in dyslexic children. In our study, the N2 wave was instable during recording, impeding its statistical analysis. In addition, the origin of the N2 wave is deeper and is related to the activities of the limbic and reticular system in the region of thalamus (Perrault and Picton 1984; Hall 2007), which are less likely to be affected by our method in terms of excitation depth and current intensity.

The results of our study were in agreement with the study of Zaehle et al. (2011) which showed an increased auditory P1 amplitude using anodal stimulation on left temporal cortex in normal cases. The results of our study on temporal resolution improvement were in line with the results of the study by Ladeira et al. (2011) that anodal tDCS on T7 and T8 areas with the reference electrodes over the right deltoid muscle improved 22.5% subjects' performance in random gap detection test compared to baseline in normal adults. Also our results like the study of Heimrath et al. (2014) showed the predominance of the left auditory cortex for processing of temporal information using anodal tDCS. However, the opposite results in reducing the processing of rapid temporal information with anodal stimulation can be due to neurophysiological differences between normal and dyslexic cases. Also this difference might be related to an inverted U-shaped dose–response relationship between AC reactivity and auditory perception. Since the influence of tDCS on auditory activity state is possibly a multifactorial phenomenon, increasing the level of arousal over the optimal point can lead to a decrease in GIN responses (Heimrath et al. 2014). In line with the results obtained in our study, Heimrath et al. (2014, 2016) believed enhancing the left AC reactivity will result in the neuromodulatory effect of tDCS on auditory rapid temporal processes involved in stop-consonant discrimination, and thus provide a possible method for the treatment of dyslexia and recovery in temporal processing from the view of the theory of auditory temporal processing deficit.

About electrode montage in dyslexic cases, Dyslexic brains are often characterized by reduced asymmetry, particularly at the posterior superior temporal gyrus, i.e., symmetrical planatemporale in the posterior Sylvian fissure, which might affect the brain activation originating from these areas involved in speech and language processing (Lohvansuu et al. 2014). Several studies in reading aspect in dyslexic group believed successful reading and speech comprehension is mediated by a growth activation in the typically hypoactive left-hemisphere regions (“normalization”) and inhibit the right-hemisphere regions (“compensation”) by bilateral bipolar-balanced type of electrode montage (Turkeltaub et al. 2012; Krause and Cohen Kadosh 2013; Costanzo et al. 2016a, b; Hoeft et al. 2011); this view was used by Costanzo et al. (2016a, b, 2018) to improve

reading skills in children, and adolescent with dyslexia with short- and long-lasting effects. In these studies, anodal and cathodal electrodes of tDCS were placed on parieto-temporal cortex in left and right hemispheres. In 2013, the same author showed the improvement of word reading speed and text reading accuracy with high-frequency repetitive transcranial magnetic stimulation (hf-rTMS) on left STG in dyslexic adults (Costanzo et al. 2013). In our study, we used two types of electrode montage; unilateral monopole and bilateral bipolar-balanced. In the first mode, only the left hemisphere was excited, while in the bilateral bipolar-balanced state, the left hemisphere was excited and the right hemisphere was inhibited. Nevertheless, the improvement of temporal resolution and auditory-evoked potentials with CV stimuli was obtained in both modes of intervention.

In each electrode arrangement, homeostatic control of cortical excitability is crucial for allowing efficient information transfer in the brain. So it is important to maintain the balance of stimulation and inhibition (*E/I* balance) in. In some central nervous system disorders, this balance has been lost, so we can artificially create this balance brain (Krause et al. 2013). In dyslexia, the excitation by anodal stimulation can occur only in left AC due to hypo-function in this area to establish balance between the two hemispheres; (Heimrath et al. 2016; Krause et al. 2013). On the other hand, other researchers believed with the excitation in one hemisphere, the other hemisphere should be inhibited due to compensation effect in the other brain hemisphere in reading (Turkeltaub et al. 2012; Costanzo et al. 2016a, b; Lohvansuu et al. 2014; Lewald 2016). In our study, we examined both approaches. Because of the superiority of the left hemisphere in the variables under study, the results of the two electrode arrangements did not statistically significantly differ for most variables. Therefore, the creation of left lateralization by inhibition of the right cortex did not lead to considerable differences in our results. Furthermore, the central compensation in the right hemisphere did not seem to occur because our study participants were children and adolescents without a history of rehabilitation. Given that our study group comprised children and adolescents, further studies are warranted to enable the use of unilateral monopole arrangement in the absence of the superiority of bilateral bipolar-balanced state owing to less manipulation in the brain regions.

In conclusion, our results indicate significant decreases in the threshold value and increases in the percentages of correct responses in the GIN test. We also found reduced latency and increased amplitude of the P1, N1, and P2 waves in two stimulation polarities compared with a baseline and sham in children and adolescents with dyslexia in form of offline. This improvement was created by increasing the left lateralization of auditory cortex activity by tDCS with bilateral bipolar-balanced montage and also by increasing left

auditory region activity with unilateral monopole type of electrode montage. Our findings indicate the potential effects of tDCS on improving the characteristics of central auditory processing, especially temporal information processing in children and adolescents with dyslexia, and could introduce new strategy to facilitate the rehabilitation of central auditory processing disorders in future.

Finally, there are some limitations to this study. Our study seems to be the first to examine the effect of tDCS on central auditory processing in a dyslexic population as a group of people with central auditory processing disorders. Therefore, further investigation is needed to explore the basic mechanisms of the effects of tDCS on the characteristics of central auditory processing in this population. Moreover, the measures of EEG and ERP are given by low spatial resolution on the scalp, limiting our interpretation of the stimulation effects at a particular point. Therefore, future studies should use high spatial resolution tools. We suggest future studies to examine the effects of the tDCS on other waves, such as mismatch negativity (MMN). Further studies should be undertaken with more intervention sessions and in combination with the rehabilitation training program. Also the long-term tDCS effects should be measured.

Acknowledgements This research has been supported by Tehran University of Medical Sciences & Health Services grant No 97-02-32-47110. We thank the Rozbeh Hospital and Miss Zohreh Mousavi for their cooperation in the implementation of this research.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

References

- American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders, 5th edn. American Psychiatric Association, Arlington
- Blau V, Reithler J, van Atteveldt N, Seitz J, Gerretsen P, Goebel R et al (2010) Deviant processing of letters and speech sounds as proximate cause of reading failure: a functional magnetic resonance imaging study of dyslexic children. *Brain* 133:868–879
- Boets B, Wouters J, van Wieringen A, Ghesquière P (2007) Auditory processing, speech perception and phonological ability in pre-school children at high-risk for dyslexia: a longitudinal study of the auditory temporal processing theory. *Neuropsychologia* 45(8):1608–1620. <https://doi.org/10.1016/j.neuropsychologia.2007.01.009>
- Chobert J, Francois C, Habib M, Besson M (2012) Deficit in the preattentive processing of syllabic duration and VOT in children with dyslexia. *Neuropsychologia* 50:2044–2055
- Cohen-Mimran R, Sapir S (2007) Auditory temporal processing deficits in children with reading disabilities. *Dyslexia* 13(3):175–192
- Costanzo F, Menghini D, Caltagirone C, Oliveri M, Vicari S (2013) How to improve reading skills in dyslexics: the effect of high

- frequency rTMS. *Neuropsychologia* 51(14):2953–2959. <https://doi.org/10.1016/j.neuropsychologia.2013.10.018>
- Costanzo F, Varuzza C, Rossi S, Sdoia S, Varvara P, Oliveri M (2016a) Evidence for reading improvement following tDCS treatment in children and adolescents with Dyslexia. *Restor Neurol Neurosci* 34(2):215–226. <https://doi.org/10.3233/RNN-150561>
- Costanzo F, Varuzza C, Rossi S, Sdoia S, Varvara P (2016b) Reading changes in children and adolescents with dyslexia after transcranial direct current stimulation. *Neuroreport* 27(5):295–300. <https://doi.org/10.1097/WNR.0000000000000536>
- Costanzo F, Rossi S, Varuzza C, Varvara P, Vicari S, Menghini D (2018) Long-lasting improvement following tDCS treatment combined with a training for reading in children and adolescents with dyslexia. *Neuropsychologia*. <https://doi.org/10.1016/j.neuropsychologia.2018.03.016>
- Cunningham J, Nicol T, Zecker SG, Bradlow A, Kraus N (2001) Neurobiologic responses to speech in noise in children with learning problems: deficits and strategies for improvement. *Clin Neurophysiol* 112(5):758–767
- Deike S, Deliano M, Brechmann A (2016) Probing neural mechanisms underlying auditory stream segregation in humans by transcranial direct current stimulation (TDCS). *Neuropsychologia* 91:262–267. <https://doi.org/10.1016/j.neuropsychologia>
- Didoné DD, Garcia MV, da Silveira AF (2014) Long latency auditory evoked potential in term and premature infants. *Int Arch Otorhinolaryngol* 18(1):16–20. <https://doi.org/10.1055/s-0033-1358658>
- Farmer ME, Klein RM (1995) The evidence for a temporal processing deficit linked to dyslexia: a review. *Bull Rev* 2(4):460–493. <https://doi.org/10.3758/BF03210983>
- Ferrer E, Shaywitz BA, Holahan JM, Marchione K, Shaywitz SE (2010) Uncoupling of reading and IQ overtime: empirical evidence for a definition of dyslexia. *Psychol Sci* 21:93–101. <https://doi.org/10.1177/0956797609354084>
- Frizzo AC (2015) Auditory evoked potential: a proposal for further evaluation in children with learning disabilities. *Front Psychol* 6:788. <https://doi.org/10.3389/fpsyg.2015.00788>
- Gaab N, Gabrieli JD, Deutsch GK, Tallal P, Temple E (2007) Neural correlates of rapid auditory processing are disrupted in children with developmental dyslexia and ameliorated with training: an fMRI study. *Restor Neurol Neurosci* 25:295–310
- Hall JW (2007) *New handbook of auditory evoked responses*. Allyn and Bacon, Boston
- Heimrath K, Kuehne M, Heinze HJ (2014) Transcranial direct current stimulation (TDCS) traces the predominance of the left auditory cortex for processing of rapidly changing acoustic information. *Neuroscience* 261:68–73
- Heimrath K, Fiene M, Rufener KS, Zaehle T (2016) Modulating human auditory processing by transcranial electrical stimulation. *Cell Neurosci* 10:1–18. <https://doi.org/10.3389/fncel.2016.00053>
- Hoelt F, McCandliss BD, Black JM, Gantman A, Zakerani N, Hulme C et al (2011) Neural systems predicting long-term outcome in dyslexia. *Proc Natl Acad Sci USA* 108(1):361–366. <https://doi.org/10.1073/pnas.1008950108>
- Iliadou V, Bamiou DE, Kaprinis S, Kandyli D, Kaprinis G (2009) Auditory processing disorders in children suspected of learning disabilities a need for screening? *Int J Pediatr Otorhinolaryngol* 73(7):1029–1034
- Iliadou VV, Ptok M, Grech H, Pedersen ER, Brechmann A, Deggouj N (2017) A European perspective on auditory processing disorder-current knowledge and future research focus. *Front Neurol* 8:622. <https://doi.org/10.3389/fneur.2017.00622>
- Jacobson L, Koslowsky M, Lavidor M (2012) tDCS polarity effects in motor and cognitive domains: a meta-analytical review. *Exp Brain Res* 216:1–10. <https://doi.org/10.1007/s00221-011-2891-9>
- Jasper HH (1958) The ten-twenty electrode system of the international federation. *Electroencephalogr Clin Neurophysiol* 10:371–375
- Khan A, Hämäläinen JA, Leppänen PH, Lyytinen H (2011) Auditory event-related potentials show altered hemispheric responses in dyslexia. *Neurosci Lett* 498(2):127–132. <https://doi.org/10.1016/j.neulet.2011.04.074>
- King WM, Lombardino LJ, Grandell CC, Leonard CM (2003) Comorbid auditory processing disorder in developmental dyslexia. *Ear Hear* 24(5):448–456
- Kormi Noori R, Moradi A, Akbari Zardkhaneh ZH (2008) Nama reading and dyslexia test. Jahad University Teacher Education Branch, Tehran
- Krause B, Cohen Kadosh R (2013) Can transcranial electrical stimulation improve learning difficulties in atypical brain development? A future possibility for cognitive training. *Dev Cogn Neurosci* 6:176–194. <https://doi.org/10.1016/j.dcn.2013.04.001>
- Krause B, Márquez-Ruiz J, Cohen Kadosh R (2013) The effect of transcranial direct current stimulation: a role for cortical excitation/inhibition balance? *Front Hum Neurosci* 7:602. <https://doi.org/10.3389/fnhum.2013.00602>
- Ladeira A, Fregni F, Campanhã C, Valasek CA, De Ridder D, Brunoni AR, Boggio PS (2011) Polarity-dependent transcranial direct current stimulation effects on central auditory processing. *PLoS One* 6(9):253–253. <https://doi.org/10.1371/journal.pone.0025399>
- Leppänen PH, Lyytinen H (1997) Auditory event-related potentials in the study of developmental language-related disorders. *Audiol Neurootol* 2(5):308–340
- Lewald J (2016) Modulation of human auditory spatial scene analysis by transcranial direct current stimulation. *Neuropsychologia* 84:282–293. <https://doi.org/10.1016/j.neuropsychologia.2016.01.030>
- Liberman IY, Shankweiler D, Liberman AM (1989) *The alphabetic principle and learning to read*. International Academy for Research in Learning Disabilities Monograph Series, Bethesda
- Lohvansuu K, Hämäläinen JA, Tanskanen A, Ervast L, Heikkinen E, Lyytinen H (2014) Enhancement of brain event related potentials to speech sounds is associated with compensated reading skills in dyslexic children with familial risk for dyslexia. *Int J Psychophysiol* 94(3):298–310. <https://doi.org/10.1016/j.ijpsycho.2014.10.002>
- Mattai A, Miller R, Weisinger B, Greenstein D, Bakalar J, Tossell J et al (2011) Tolerability of transcranial direct current stimulation in childhood-onset schizophrenia. *Brain Stimul* 4(4):275–280. <https://doi.org/10.1016/j.brs.2011.01.001>
- Miniussi C, Ruzzoli M (2013) Transcranial stimulation and cognition. *Handb Clin Neurol* 116:739–750. <https://doi.org/10.1016/B978-0-444-53497-2.00056-5>
- Moiescu-Yiflach T, Pratt H (2005) Auditory event related potentials and source current density estimation in phonologic/auditory dyslexics. *Clin Neurophysiol* 116(11):2632–2647
- Moradi A, Hosaini M, Kormi Nouri R, Hassani J, Parhoon H (2016) Reliability and validity of reading and dyslexia test (NEMA). *Adv Cogn Sci* 18(1):22–34
- Musiek FE, Shinn JB, Jirsa R, Bamiou DE, Baran JA, Zaida E (2005) GIN (gaps-in-noise) test performance in subjects with confirmed central auditory nervous system involvement. *Ear Hear* 26(6):608–618
- Nasseri P, Nitsche MA, Ekhtiari H (2015) A framework for categorizing electrode montages in transcranial direct current stimulation. *Front Hum Neurosci* 9:54. <https://doi.org/10.3389/fnhum.2015.00054>
- Neville HJ, Coffey SA, Holcomb PJ, Tallal P (1993) The neurobiology of sensory and language processing in language-impaired children. *J Cogn Neurosci* 5(2):235–253. <https://doi.org/10.1162/jocn.1993.5.2.235>
- Nitsche MA, Liebetanz D, Antal A, Lang N, Tergau F, Paulus W (2003) Modulation of cortical excitability by weak direct current

- stimulation—technical, safety and functional aspects. *Suppl Clin Neurophysiol* 56:255–276
- Nitsche MA, Cohen LG, Wassermann EM, Priori A, Lang N et al (2008) Transcranial direct current stimulation: state of the art 2008. *Brain Stimul Basic Transl Clin Res Neuromodulation* 1(3):206–223
- Nittrouer S (1999) Do temporal processing deficits cause phonological processing problems? *J Speech Lang Hear Res* 42:925–942
- Oliveira JC, Murphy CF, Schochat E (2013) Auditory processing in children with dyslexia: electrophysiological and behavior evaluation. *Codas* 25(1):39–44
- Perrault N, Picton TW (1984) Event-related potentials recorded from the scalp and nasopharynx. II. N2, P3 and slow wave. *Electroencephalogr Clin Neurophysiol* 59(4):261–278
- Putter-Katz H, Kishon-Rabin L, Sachartov E, Shabtai EL, Sadeh M, Weiz R (2005) Cortical activity of children with dyslexia during natural speech processing: evidence of auditory processing deficiency. *J Basic Clin Physiol Pharmacol* 16(2–3):157–171
- Ramus F, Rosen S, Dakin SC, Day BL, Castellote JM, White S, Frith U (2003) Theories of developmental dyslexia: insights from a multiple case study of dyslexic adults. *Brain* 126(4):841–865
- Raschle NM, Stering PL, Meissner SN, Gaab N (2014) Altered neuronal response during rapid auditory processing and its relation to phonological processing in pre reading children at familial risk for dyslexia. *Cereb Cortex* 24:2489–2501. <https://doi.org/10.1093/cercor/bht104>
- Regaçone SF, Gução ACB, Giacheti CM, Romero AC, Frizzo ACF (2014) Long latency auditory evoked potentials in students with specific learning disorders. *Audiol Commun Res* 1:8–13
- Richardson U, Thomson JM, Scott SK, Goswami U (2004) Auditory processing skills and phonological representation in dyslexic children. *Dyslexia* 10(3):215–233
- Sale MV, Mattingley JB, Zalesky A, Cocchi L (2015) Imaging human brain networks to improve the clinical efficacy of non-invasive brain stimulation. *Neurosci Biobehav Rev* 57:187–198. <https://doi.org/10.1016/j.neubiorev.2015.09.010>
- Sanayi R, Mohamadkhani G, Pourbakht A, Jalilvand L, Jalayi S, Shokri S (2013) Auditory temporal processing abilities in early azari-persian bilinguals. *Iran J Otolaryngol* 25(73):227–232
- Schlaggar BL, McCandliss BD (2007) Development of neural systems of reading. *Annu Rev Neurosci* 30:465–503
- Schulte-Körne G, Bruder J (2010) Clinical neurophysiology of visual and auditory processing in dyslexia: a review. *Clin Neurophysiol* 121(11):1794–1809. <https://doi.org/10.1016/j.clinph.2010.04.028>
- Shaywitz SE, Shaywitz BA, Fulbright RK, Skudlarski P, Mencl WE, Constable RT et al (2003) Neural systems for compensation and persistence: young adult outcome of childhood reading disability. *Biol Psychiatry* 54(1):25–33
- Stagg CJ, Nitsche MA (2011) Physiological basis of transcranial direct current stimulation. *Neuroscientist* 17:37–53. <https://doi.org/10.1177/1073858410386614>
- Steinbrink C, Vogt K, Kastrup A, Müller HP, Juengling FD, Kassubek J et al (2008) The contribution of white and gray matter differences to developmental dyslexia: insights from DTI and VBM at 3.0 T. *Neuropsychologia* 46(13):3170–3178. <https://doi.org/10.1016/j.neuropsychologia.2008>
- Tallal P (2004) Improving language and literacy is a matter of time. *Nat Rev Neurosci* 5(9):721–728
- Turkeltaub PE, Benson J, Hamilton RH, Datta A, Bikson M, Coslett HB (2012) Left lateralizing transcranial direct current stimulation improves reading efficiency. *Brain Stimul* 5(3):201–207. <https://doi.org/10.1016/j.brs.2011.04.002>
- Vellutino FR, Fletcher JM, Snowling MJ, Scanlon DM (2004) Specific reading disability (dyslexia): what have we learned in the past four decades? *J Child Psychol Psychiatry* 45(1):2–40
- Wechsler D (2010) WISC-IV—wechsler intelligence scale for children—IV. NCS Pearson Ltd., London (**Psykologien kustannus, Helsinki**)
- Zaehle T, Beretta M, Jäncke L, Herrmann CS, Sandmann P (2011) Excitability changes induced in the human auditory cortex by transcranial direct current stimulation: direct electrophysiological evidence. *Exp Brain Res* 215(2):135–140. <https://doi.org/10.1007/s00221-011-2879-5>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.