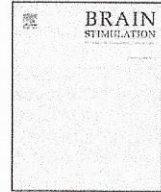


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## Transcranial electrical stimulation improves phoneme processing in developmental dyslexia

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### ARTICLE INFO

#### Article history:

Received 17 April 2018

Received in revised form

18 December 2018

Accepted 11 February 2019

Available online 13 February 2019

#### Keywords:

Developmental dyslexia

Transcranial alternating current stimulation

Transcranial random noise stimulation

Phoneme processing

Auditory temporal resolution

### ABSTRACT

**Background:** About 10% of the western population suffers from a specific disability in the acquisition of reading and writing skills, known as developmental dyslexia (DD). Even though DD starts in childhood it frequently continues throughout lifetime. Impaired processing of acoustic features at the phonematic scale based on dysfunctional auditory temporal resolution is considered as one core deficit underlying DD. Recently, the efficacy of transcranial electrical stimulation (tES) to modulate auditory temporal resolution and phoneme processing in healthy individuals has been demonstrated.

**Objective:** The present work aims to investigate online effects of tES on phoneme processing in individuals with DD.

**Method:** Using an established phoneme-categorization task, we assessed the immediate behavioral and electrophysiological effects of transcranial alternating current stimulation (tACS) and transcranial random noise stimulation (tRNS) over bilateral auditory cortex in children and adolescents with DD (study 1) and adults with DD (study 2) on auditory phoneme processing acuity.

**Results:** Our data revealed that tACS improved phoneme categorization in children and adolescents with DD, an effect that was paralleled by an increase in evoked brain response patterns representing low-level sensory processing. In the adult sample we replicated these findings and additionally showed a more pronounced impact of tRNS on phoneme-categorization acuity.

**Conclusion:** These results provide compelling evidence for the potential of both tACS and tRNS to increase temporal precision of the auditory system in DD and suggest transcranial electrical stimulation as potential intervention in DD to foster the effect of standard phonology-based training.

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### Introduction

Developmental dyslexia (DD) is a neurodevelopmental disorder characterized by a specific difficulty in the acquisition of reading and/or writing skills that is not accounted for by age, intelligence or inadequate schooling. About 10% of the western population suffers from this impairment with profound consequences for school education but also on future professional success [1]. Without an effective intervention the symptoms of DD persist into adulthood

[2,3]. Despite intensive research over the last decades, the exact nature and origin of DD still remains unclear. However, on a neurobiological level, there is convincing evidence on structural alterations in temporal lobe areas predominantly in the left hemisphere [4,5] indexing the involvement of speech and language networks in the etiology of DD [6]. Marked low-level auditory deficits [7,8] resulting in imprecise processing of rapidly changing acoustic features in both speech and non-speech information represent the most evident and frequent symptom in DD [9–11]. This impairment significantly affects processing of information at the phonematic scale, hence, information units that are linguistically meaningful. At a later stage also phoneme-to-grapheme

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correspondence and, finally, reading and writing acquisition are compromised.

The Voice onset time (VOT), a short delay between the release of the closures and the start of voicing which enables to distinguish between voiced (e.g. /d/, /g/, /b/) and unvoiced consonants (e.g. /t/, /k/, /p/) is a well-established linguistic parameter. Precise perception of the VOT requires adequate temporal resolution of the auditory system, which is why individuals with DD typically perform worse than their normally reading and writing peers [12]. Studies demonstrating deficits in pre-attentive processing of auditory temporal information in DD further stresses the sensory basis of this impairment [13–15]. Additionally, reduced abilities to discriminate consonant-vowel stimuli indicate less effectively defined VOT-boundaries. It has been suggested that in DD this is caused by an over-specified perception of acoustic cues in the speech signal: the maturing auditory system of DD individuals does not develop the necessary specialization to perceive the relevant acoustic cues but remains sensitive to irrelevant speech cues such as allophones (i.e. speaker-specific pronunciation of a phoneme which does not lead to a change of meaning) [16]. Accordingly, normalizing the impaired perception of VOT-boundaries in DD is vital to facilitate the acquisition of higher-order language skills essential for successful reading and writing.

On a neurophysiological level, lower gamma oscillations (about 40 Hz) have been suggested as a key mechanism for the processing of acoustic information at the phonematic scale [17–19]. Lower gamma oscillations are also the dominant endogenous activation pattern in the human auditory cortex representing its inherent resonance frequency (RF) [20]. The RF characterizes the sampling rate at which the auditory system parses the incoming acoustic signal and determines the individuals' auditory temporal resolution ability [21,22]. Accordingly, a negative correlation between the individuals' RF and the ability to detect short temporal gaps within acoustic stimuli has been demonstrated recently [23]. A RF of about 40 Hz has been proposed as most functional in the context of phoneme processing since it corresponds with the mean duration of this linguistically meaningful information unit. Both, an increased as well as a decreased RF is thus ineffective and the integration of subsequently incoming linguistic features to a meaningful entity is seriously affected. In fact, increased RFs have been found in adult DD individuals [24,25]. This oversampling of the auditory system might explain the over-specified perception of acoustic cues and the sensitivity to linguistically meaningless variations in the speech signal. The normalization of maladaptive neural oscillations in DD is therefore preferable to restore the auditory temporal resolution acuity and, in consequence, the accurate processing of information units at the phonematic scale.

One approach to modulate neural oscillations is transcranial electrical stimulation (tES). TES is the umbrella term for a number of non-invasive stimulation techniques that apply weak electrical currents to cortical regions. A variation of tES is transcranial alternating current stimulation (tACS). By applying a sinusoidal current at the predefined frequency, tACS causes an alignment of inherent rhythmic activation patterns, i.e. neural oscillations, with the externally applied electrical signal. Accordingly, tACS allows to modulate neural oscillations and the restorative effect of 40 Hz-tACS over the auditory cortex on phoneme categorization has been demonstrated already in a sample with age-related degradation of the auditory temporal resolution [26]. However, these tACS-induced entrainment effects are limited to endogenous oscillations near the applied tACS frequency [27] emphasizing the *a priori* knowledge of the individuals' RF. Since there is only limited data on the RF in DD available – and specifically in children with DD – an intervention that allows to modulate the auditory temporal resolution without knowledge of the RF is desirable. The application of

transcranial random noise stimulation (tRNS) has been suggested to amplify the auditory systems' RF [28] and, in consequence, auditory temporal resolution [29]. The precise mechanism of action tRNS-effects rely on is still under debate. However, since tRNS applies alternating currents of different frequencies, the application does not require the knowledge of the individuals RF. Basing on the beneficial tRNS-effects on the processing of time-critical information in acoustic non-speech stimuli [29], we hypothesized to find a supportive effect of tRNS on the processing of time-critical information in speech stimuli, such as the VOT.

In concrete, the aim of the present work was to investigate the effects of a single dose of tACS and tRNS on auditory temporal resolution, as manifested in the phoneme-categorization acuity in individuals suffering from DD. As the perceptual deficit in DD persists throughout life we considered age-specific effects and assessed a sample of adolescents with DD (study 1) and a sample of adults with DD (study 2). In addition to behavioral performance, we focused on the P50-N1 complex of the auditory event related potential (ERP) since alterations in this brain response pattern characterizes auditory processing deficits in DD [30–32]. We hypothesized that (1) the application of tACS and tRNS improves phoneme categorization in DD and (2) behavioral changes are mirrored by alterations in the P50-N1 complex.

## Material and methods

### Stimulus material and task

The stimulus material consisted of a VOT-continuum ranging from the consonant-vowel (CV) syllable /da/ to the syllable /ta/. The continuum comprised of 11 stimuli from VOT 20 ms to VOT 40 ms in 2 ms steps. Stimuli were presented in three consecutive runs, each separated by a short break. In each run, all stimuli were presented eight times in randomized order. Participants were instructed to decide whether the presented stimulus represented /da/ or /ta/ and to give response via button press. This procedure took about 3.5 min per run. The VOT-categorization task was performed alternately with another auditory task, which is not within the scope of the manuscript and which took about 3.5 min per run. The sequence of the two tasks was balanced between participants.

### Electrical stimulation

TES was applied by means of a battery-driven stimulator (NeuroConn, Ilmenau, Germany) using two rubber electrodes placed in 0.9% saline-soaked sponges. The 5 × 7 cm electrodes were placed horizontally over T7 and T8. Impedance was kept below 15 kOhm. In the tACS condition, tACS at 40 Hz was applied with the intensity adjusted below the participants' threshold for phosphenes or skin sensations (study 1:  $M = 0.95$  mA,  $SD = 0.11$ ; study 2:  $M = 1.33$  mA,  $SD = 0.422$ ). In the tRNS condition, a high frequency random noise (100–640 Hz) was applied with an intensity of 1 mA (study 1) and 1.5 mA (study 2) to ensure a successful blinding procedure [33]. In both verum protocols (tACS, tRNS), the current was turned on after participants completed the baseline VOT-categorization run and was delivered for 20 min with a fade in/fade out sequence of 10 s. In the sham condition, 40 Hz-tACS was applied for 30 s with a fade in/out sequence of 10 s.

### EEG data recording und analysis

In study 1, EEG data was recorded using 3 Ag/AgCl-electrodes (sampling rate 1000 Hz) at Fz, Cz, and Pz by means of a BrainAmp DC-amplifier (BrainVision Recorder 1.20; Brain Products, Munich, Germany). The reference electrode was placed at the tip of the nose,



the ground at AFz. Vertical and horizontal eye movements were monitored from electrodes lateral and below the right eye. Impedances were kept below 10 kOhm. Offline, the data were down sampled to 512 Hz and band pass filtered (1–30 Hz) using the BrainVision Analyzer software (Version 2.1.0.327, Brainproducts, Munich, Germany). Band rejection filters at 40 Hz and 80 Hz ensured that no tACS-artifacts contaminated the EEG signal. Trials containing eye movements or other muscular artifacts with amplitudes greater than 100  $\mu$ V were automatically rejected. The preprocessed data were segmented in 1000 ms epochs including a 200 ms pre-stimulus sequence and were baseline corrected against the –100 to 0 ms period.

The segmented data were average for three VOT-categories of interest: for VOT-stimuli representing the voiced category (/da/: VOT 20, 22, 24), the unvoiced category (/ta/: VOT 36, 38, 40), and the category boundary (VOT 26, 28, 30). This averaging procedure was performed for the three stimulation conditions (tACS, tRNS, sham) separately. A mean number of 36 trials per condition and participant was used for the statistical analysis. Based on the grand means we determined the P50 as the first positive deflection (20–120 ms), the N1 as the first negative deflection (60–160 ms), and the P2 as the second positive deflection (150–250 ms) after stimulus onset. Since ERPs were most pronounced at Cz, we used the peak amplitudes measured at this electrode for the statistical analysis.

In study 2, EEG data were recorded using the same electrode placement as in study 1 by means of the BioSemi ActiveTwo system (BioSemi, Amsterdam NL). The data were recorded at a sampling rate of 512 Hz and the impedances were kept below 25 kOhm. Data preprocessing, segmentation and peak detection procedure were identical to study 1. This approach resulted in a mean number of 45 trials per condition and subject used for the statistical analysis.

### Experimental procedure

In three consecutive sessions, each separated by at least one week, the participants received tACS, tRNS or sham stimulation while performing the phoneme-categorization task (Fig. 1). The order of the tES application was counterbalanced. To familiarize

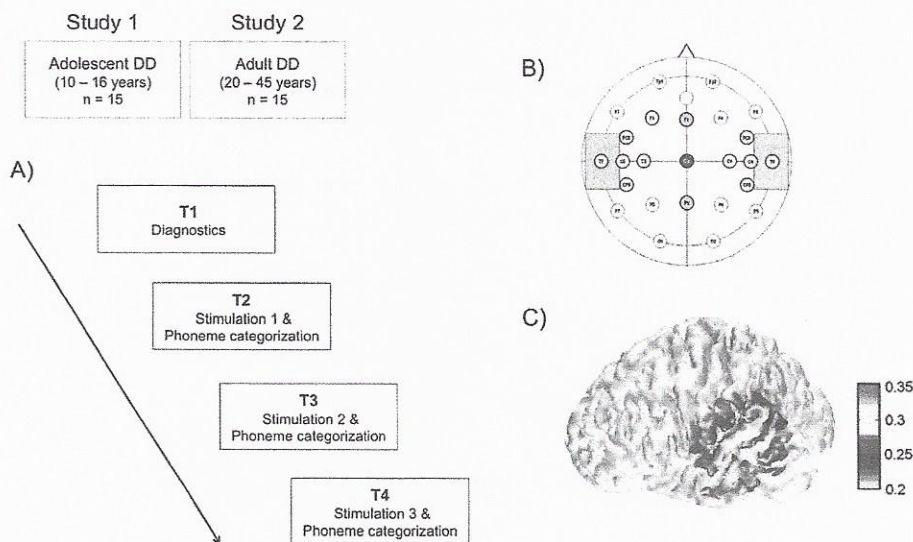
participants with the relevant stimulus dimension they were presented with examples of VOT-stimuli and performed a short training block. Each experimental session consisted of an initial baseline run and two succeeding runs with concurrent tES. During the experiment, participants were seated in a comfortable chair in a dimly lit and acoustically shielded room. Stimulus material was presented via headphones (Sennheiser HD 65 TV) at 65 dB SPL and using the Presentation software, Version 18.1 (www.neurobs.com).

After debriefing, participants were asked to indicate in which sequence tACS, tRNS, and sham was applied. None of the participants was able to correctly indicate the individual sequence, nor the session in which the sham stimulation was applied. Participants in study 2 were additionally asked after each session to complete a short questionnaire about their physical state during and after the stimulation. Analysis of these questionnaires revealed no difference between the three stimulation conditions.

### Statistical analysis

Performance in the VOT-categorization task was evaluated by fitting each participant's behavioral data using a binary logistic regression analysis and then extracting the beta coefficient representing the participants acuity to categorize the presented VOT-stimuli [12,26,34]. This procedure was carried out for each run and for each stimulation condition separately. Since four participants in study 1 showed insufficient model fit in at least one condition, data from these participants were excluded from further analysis.

To analyze the tES-effect on the participants' phoneme-categorization ability we assessed stimulation-induced alterations by calculating the percentage change of the beta coefficient from the baseline run to the stimulation runs. The resulting scores were analyzed in a repeated measures ANOVA with the within-subject factor *stimulation* (tACS, tRNS, sham). To investigate tES-effects on EEG activity during the phoneme-categorization task, the P50-N1 peak-to-peak amplitude and the N1-P2 peak-to-peak amplitude were calculated. For each VOT-category (voiced, voiceless, category boundary) the amplitudes were analyzed in separate repeated measures ANOVAs with the within-subject factor *stimulation* (tACS,



**Fig. 1.** Experimental design. A) At time point T1 all participants underwent a test battery to control for DD. At time points T2–T4, individuals with DD received in a pseudo-randomized sequence transcranial alternating current stimulation (tACS), transcranial random noise stimulation (tRNS), and sham stimulation while they performed an auditory phoneme-categorization task. B) Bilateral auditory cortex regions (T7/T8) were stimulated by means of tACS, tRNS, and sham. Simultaneously, EEG was recorded at the three midline electrodes Fz, Cz, and Pz. C) Computation of the current density in cortical structures for the chosen electrode setup.



tRNS, sham). To ensure that effects of the applied stimulation were not affected by stimulation order the between-subject factor *sequence* was included. We found neither a main effect of the factor *sequence*, nor an interaction *stimulation*  $\times$  *sequence* in any ANOVA and this holds true for the analysis in study 1 and study 2. Greenhouse Geisser-correction was applied in case of violated assumption of sphericity. Subsequently, planned comparisons by means of dependent samples t-tests were run.

## Study 1

### Participants

19 native German-speaking adolescents in the age range 10–16 years participated in this study. All individuals had received a diagnosis in DD previously, which was confirmed by a customized test battery (see Table 1). Participants performed a standardized writing (Hamburger Schreib-Probe HSP) [35] and a reading test (Zürcher Lesetest ZLT II, subtests for reading of wordlists, pseudo words, and texts) [36]. Furthermore, phonemic skills (Phonematischer Gedächtnistest PHOG) [37] and intelligence (CFT 20-R) [38] were assessed. Dyslexia was defined as a deficit in reading or writing ability as assessed with the HSP and the ZLT II (at least 1.5 SD below the PR expected from individual IQ). Hearing performance was controlled by means of a pure tone audiometry using MAICO MA25 (<http://www.maico-diagnostic.com/>) at test frequencies 500 Hz, 1000 Hz, 2000 Hz 3000 Hz, 4000 Hz and 6000 Hz. All participants had a threshold below 25 dB SPL indicating a normal hearing acuity according to the World Health Organization (WHO) criterion for normal hearing. Parents were interviewed with a German translation of the Revised Schedule for Affective Disorders and Schizophrenia for School-Age Children: Present and Lifetime Version [39,40] to exclude participants who fulfilled the criteria for any psychiatric or neurological disorder. Prior to the experiment all participants and their legal representative gave their written informed consent. The procedure was approved by the ethics committee of the Otto von Guericke University Magdeburg and is in accordance with the declaration of Helsinki.

## Results

### Behavioral results

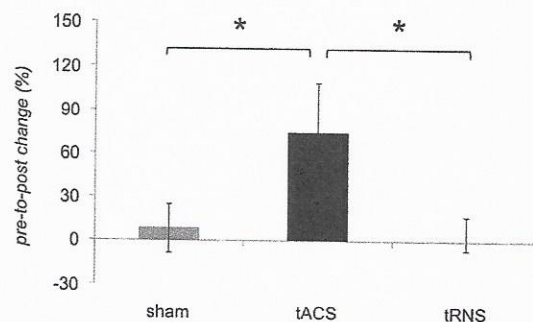
Analysis of the pre-to-post changes revealed a main effect *stimulation* ( $F(2,13) = 6.543$ ,  $p = .014$ ,  $\eta^2 = 0.353$ ) demonstrating that the participants' acuity in categorizing the VOT-stimuli was modulated by the applied electrical stimulation (Fig. 2). TACS led to

**Table 1**

Participant information of the sample of children and adolescent with DD showing mean age, IQ, reading and writing performance, and phonological awareness (standard deviations in parentheses).

Measures	Mean (SD)
Age (years)	13.3 (1.94)
IQ	102.75 (11.37)
Reading <sup>a</sup>	
• Word reading	29.79 (11.02)
• Pseudo-word reading	41.81 (8.45)
Writing <sup>a</sup>	35.69 (8.43)
Phonological Awareness <sup>a</sup>	
• Vowels/syllables	44.23 (13.75)
• Words/sentences	49.54 (23.51)
• Total score	45.33 (8.38)

<sup>a</sup> Measures represent T-values. Note: a T-score of 50 represents the norm mean, while T-scores of 30 and 70 represent scores 2 standard deviations below and above norm mean, respectively.



**Fig. 2.** Behavioral results of the children and adolescent with DD. Mean percent change in phoneme-categorization (steepness of the logistic regression) from baseline run to stimulation runs. Asterisks indicate statistically significant differences between the conditions ( $p < .05$ ). Error bars represent the standard errors (SE).

a stronger increase compared to sham ( $T(15) = 2.116$ ,  $p = .053$ ) and tRNS ( $T(15) = 2.561$ ,  $p = .023$ ). No difference was found between tRNS and sham ( $T(15) = 1.164$ ,  $p = .872$ ). A one sampled *t*-test demonstrated that the tACS-related increase was significantly different from zero ( $T(15) = 2.385$ ,  $p = .032$ ).

### Electrophysiological results

Analysis of the P50-N1 complex measured while participants were presented with stimuli at the category boundary (cf. Fig. 3) revealed a main effect *stimulation* ( $F(2,13) = 3.584$ ,  $p = .041$ ,  $\eta^2 = 0.204$ ) while no *stimulation* effect was found for stimuli representing the voiced (/da/) category ( $F(2, 13) = 0.052$ ,  $p = .949$ ,  $\eta^2 = 0.004$ ) and the unvoiced (/ta/) category ( $F(2,13) = 1.718$ ,  $p = .201$ ,  $\eta^2 = 0.125$ ).

Dependent samples *t*-tests showed that the P50-N1 amplitudes in the tACS condition were significantly increased compared to sham ( $T(15) = 2.726$ ,  $p = .016$ ). No statistically significant difference was found between tRNS and sham ( $T(15) = 1.287$ ,  $p = .219$ ) and between tACS and tRNS ( $T(15) = -1.371$ ,  $p = 0.192$ ).

Finally, there was no statistically significant *stimulation* effect on the N1-P2 peak amplitudes for any of the three VOT categories.

## Study 2

### Participants

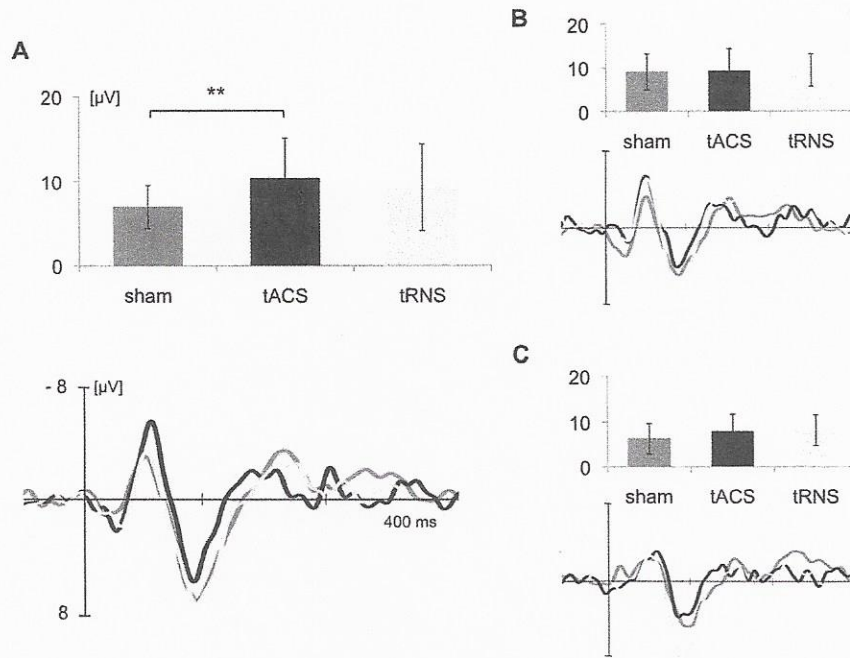
15 native Swiss German speaking adults in the age range 20–45 years participated in this study. All of them had a prior diagnosis of DD, that was confirmed by a customized test battery (see Table 2) identical to that performed in study 1 except that the tests assessing reading and writing performance were replaced by an adequate version (Salzburger Lese- und Rechtschreibtest SLRT-II) [41]. None of them reported any present psychiatric or neurological diseases. Before the experiment all participants gave their written informed consent. The procedure was approved by the Swiss Ethics Committees on research involving humans and was in accordance with the declaration of Helsinki.

## Results

### Behavioral results

Analysis of the pre-to-post changes revealed a main effect *stimulation* ( $F(2,13) = 4.612$ ,  $p = .035$ ,  $\eta^2 = 0.244$ ) demonstrating that the participants' acuity in phoneme categorization was modulated by the applied electrical stimulation (Fig. 4). Compared to sham,





**Fig. 3.** EEG data measured in the sample of children and adolescents with DD during processing of A) VOT-stimuli at the category boundary, B) VOT-stimuli representing the voiced (/da/) category, and C) VOT-stimuli representing the unvoiced (/ta/) category. For each category, bar graphs represent the mean amplitudes of the P50-N1 complex and event related potentials (ERP) measured at the Cz electrodes are illustrated. Magenta represents data measured in the sham condition, black in the tACS condition, and cyan in the tRNS condition. Asterisks indicate statistically significant differences ( $p < .05$ ). Error bars represent the standard errors (SE). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

**Table 2**

Participant information of the adults DD sample showing mean age, IQ, reading and writing performance, and phonological awareness (standard deviations in parentheses).

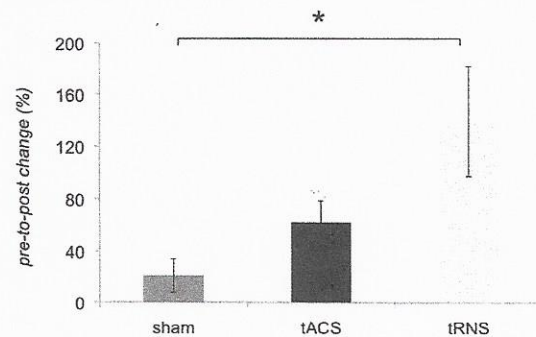
Measures	Mean (SD)
Age (years)	27.77 (7.64)
IQ	109.87 (8.94)
Reading <sup>a</sup>	
• Word reading	34.38 (9.28)
• Pseudo-word reading	33.94 (9.55)
Writing <sup>a</sup>	58.03 (0.98)
Phonological Awareness <sup>a</sup>	
• Vowels/syllables	50.33 (15.10)
• Words/sentences	38.47 (12.42)
• Total score	53.07 (21.11)

<sup>a</sup> Measures represent T-values. Note: a T-score of 50 represents the norm mean, while T-scores of 30 and 70 represent scores 2 standard deviations below and above norm mean, respectively.

task acuity tended to increase in the tACS condition ( $T(15) = 1.917$ ,  $p = .076$ ) and was significantly enhanced in the tRNS condition ( $T(15) = 2.566$ ,  $p = .022$ ). No statistically significant difference was evident between the effect of tRNS and tACS ( $T(15) = -1.682$ ,  $p = .115$ ).

#### Electrophysiological results

Analysis on the P50-N1 complex revealed a main effect *stimulation* ( $F(2,15) = 8.165$ ,  $p = .002$ ,  $\eta^2 = 0.405$ ) for VOT-stimuli at the category boundary. (Fig. 5B). Here, the P50-N1 complex in the tACS condition was significantly increased compared to sham ( $T(15) = 2.769$ ,  $p = .015$ ) and tRNS ( $T(15) = -3.456$ ,  $p = .004$ ). No statistically significant difference was found between tRNS and sham ( $T(2, 15) = -1.109$ ,  $p = .286$ ).



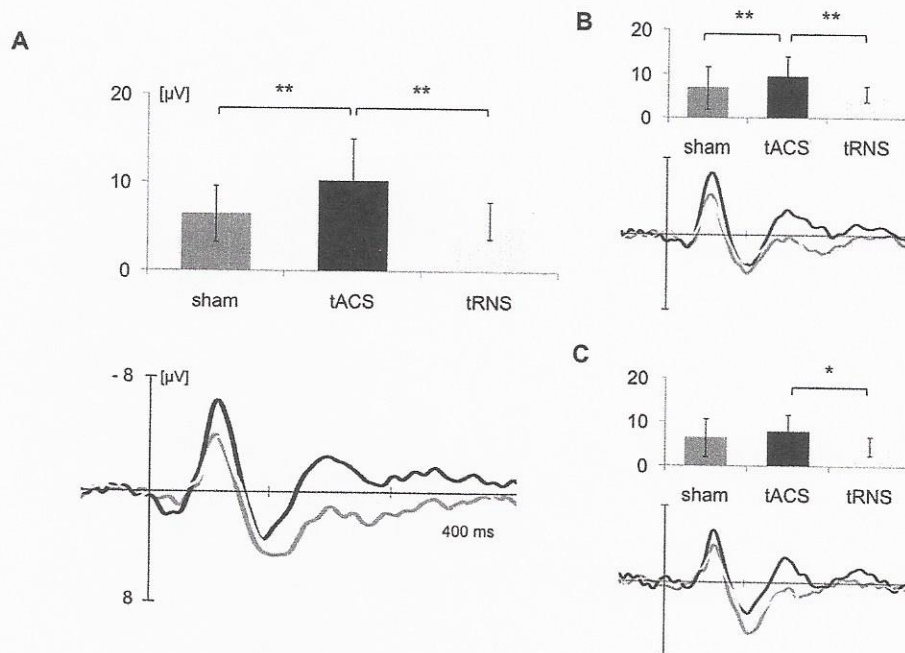
**Fig. 4.** Behavioral results of the adult DD sample. Mean percent change in phoneme categorization (steepness of the logistic regression) from baseline run to stimulation runs. Asterisks indicate statistically significant differences between the conditions ( $p < .05$ ). Error bars represent the standard errors (SE).

We found a main effect *stimulation* for the P50-N1 complex evoked by VOT-stimuli representing the voiced (/da/) category ( $F(2,15) = 4.655$ ,  $p = .020$ ,  $\eta^2 = 0.279$ ) (cf. Fig. 5A). Here, tACS significantly increased P50-N1 amplitudes compared to tRNS ( $T(15) = -3.681$ ,  $p = .002$ ). However, compared to sham, the effect was only marginally significant ( $T(15) = 1.909$ ,  $p = .077$ ). There was no significant difference between tRNS and sham ( $T(15) = -1.008$ ,  $p = .331$ ).

Finally, analysis of the P50-N1 complex evoked by stimuli representing the unvoiced (/ta/) category revealed a trend towards a *stimulation* effect ( $F(2,15) = 3.096$ ,  $p = .064$ ,  $\eta^2 = 0.205$ ). Again, tACS led to a stronger increase of the P50-N1 complex in comparison to tRNS ( $T(15) = -2.789$ ,  $p = .014$ ). No statistically significant difference was found between tACS and sham ( $T(15) = 0.956$ ;  $p = .355$ ) and between tRNS and sham ( $T(15) = -1.680$ ,  $p = .115$ ).

With regard to the N1-P2 complex, no statistically significant stimulation effect for any of the VOT categories was found.





**Fig. 5.** EEG data measured in the adult DD sample during the processing of A) VOT-stimuli at the category boundary, B) VOT-stimuli representing the voiced (/da/)-category, and C) VOT-stimuli representing the unvoiced (/ta/) category. For each category, bar graphs represent the mean amplitudes of the P50-N1-complex and event related potentials (ERP) measured at the Cz electrodes are illustrated. Magenta represents data measured in the sham condition, black in the tACS condition, and cyan in the tRNS condition. Asterisks indicate statistically significant differences between the conditions ( $p < .05$ ). Error bars represent the standard errors (SE). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

## Discussion

In two studies, we investigated the direct consequences of a single dose of tES on phoneme processing acuity in DD. In study 1, we showed that 40 Hz-tACS improved phoneme-categorization acuity in adolescents with DD and this enhancement was paralleled by increased amplitudes of the P50-N1-complex. In study 2, we found a marginally significant tACS-effect at the behavioral level while tRNS significantly improved phoneme categorization in adults with DD. This behavioral modulation was accompanied by increased amplitudes of the P50-N1-complex when 40 Hz-tACS was applied. Accordingly, study 2 replicated the results of study 1 and provided compelling evidence that a single application of 40 Hz-tACS improved phoneme-categorization acuity in DD.

Our results demonstrate that auditory cortex regions in DD are susceptible to the external modulation via tES. Stimulating the auditory system improved the participants' phoneme-categorization ability as reflected by higher preciseness and lower variability in categorical perception of phonemes as well as enhanced P50-N1 responses in the 40 Hz-tACS condition when DD individuals processed VOT-stimuli at the category boundary. This indicates that the tES intervention effected a more efficient temporal resolution of the auditory system. Our results are in line with previous research demonstrating the refining effect of 40 Hz-tACS on phoneme processing in participants with reduced auditory temporal resolution [26] and that gamma-tACS modulates perception of temporal acoustic information [23]. Here, for the first time, we demonstrate that tACS improves auditory temporal resolution in a clinical sample, irrespective of the maturation of the auditory systems. Of note, a single dose of 40 Hz-tACS for 20 min was already sufficient to induce the observed behavioral and electrophysiological effects. Our findings are of particular clinical relevance since DD is the most frequent learning disorder with a prevalence of about 10% (WHO, 2008). Impaired reading and

writing skills not only affect school grades and success in later professional life. The number of adolescents reporting emotional disorders (e.g. low self-esteem, anxiety disorder, depression) is significantly increased in those with DD compared to students with normal reading and writing skills [42–44]. Without a successful intervention the symptoms of DD, in particular limited reading and writing skills, persist in adulthood [2,3]. Despite intensive research over the last decades neurobiological models that account for the DD symptoms remain elusive and there is still no consensus on the effectiveness of common interventions (for a meta analysis on interventions in German speaking DD patients see: [3]). The results of our studies indicate that tES can refine the perception of rapidly changing acoustic features, a process essential to extract linguistically meaningful information in the speech signal and which is typically impaired in DD individuals. Accordingly, tES can be considered as a promising technique to normalize impaired auditory temporal resolution in DD.

Reduced phoneme-categorization acuity in DD has been suggested to rely on an oversensitivity of the auditory system and an allophonic rather than phonemic perception of speech units. This oversensitivity is caused by a dysfunctional sampling of the acoustic stream due to a pathologically increased RF [24]. Thus, in that we applied 40 Hz-tACS to the auditory cortex of DD individuals, the RF might have been shifted towards a more efficient sampling rate that allowed to establish distinct and linguistically meaningful phoneme categories. Interestingly, we found that 40 Hz-tACS increased the adolescents' P50-N1-response also to VOT-stimuli representing the voiced category. Since there is no longitudinal data of VOT-categorization skills in DD individuals available, we can only speculate that the two age-samples might have used different strategies to solve the phoneme categorization task and refer to future studies which will shed more light on developmental aspects of speech processing in individuals suffering from DD.



In contrast to the adolescent sample, we found that also tRNS significantly increased phoneme categorization in adult DD individuals but this effect was not reflected by the EEG-data. Since the precise neurophysiological mechanisms of tRNS are yet not fully understood, our interpretation of the findings can only be of speculative nature. One potential explanation for this age-specific finding is that the two groups might have used different approaches in phoneme-categorization. This task can be solved by either comparing each presented VOT-stimulus with an inherent acoustic template of the voiced (/da/) and unvoiced (/ta/) category or by the continuous articulatory rehearsal of the initially presented /da/ and /ta/ stimuli. While the former process relies on the adequate sampling of the acoustic stimuli, a function dedicated to the RF located in the primary auditory cortex, the latter approach of the continuous rehearsal requires additional activation of the phonological loop located in the dorsal stream of the auditory system [45,46]. The electrophysiological P50-N1-component is most sensitive to (sensory) processes taking place in the primary auditory cortex while it reflects activation in the secondary auditory cortex only in part. Activation of the phonological loop is therefore not evident in the P50-N1. Thus, adult DD individuals might have used a more top-down driven approach to compensate the imprecise sensory processing. In that tRNS increased the excitability of cortical structures assigned to the phonological loop, behavioral performance increased but this alteration was not reflected in the P50-N1. Alternatively, also differences in the tRNS intensity between the two groups might have contributed to the observed age-specific effects. While adult participants received tRNS at 1.5 mA, we limited the intensity in the adolescent group to 1 mA to ensure safety and comfort for this vulnerable sample. To date, however, no systematic investigation on the relationship between tRNS-intensity and (auditory) perception has been performed, neither in an adult, nor in an adolescent sample.

Finally, we did not find tES-effects on the N1-P2 component and this holds true for both age groups and both tES conditions. There is only sparse knowledge on the (sensory and/or cognitive) processes represented by the P2-component but the most common interpretation is that the P2 reflects perceptual learning of the auditory system [47,48]. The lack of tES-evoked effects on the N1-P2 in our study provides further support on the notion that our intervention refined basic sensory processes necessary for the perception of acoustic information at the phonemic scale rather than a higher-level cortical representation of the phoneme-categories.

Despite the encouraging results of the present work, also limiting factors have to be taken into account. In the present study, we included individuals that fulfilled the general diagnostic criteria for DD including potential subtypes [49]. However, both samples assessed in the present study showed only minimal symptom variability (cf. Table 1 and Table 2) and, accordingly, no subtype-analysis on the efficacy of tES could be performed. Furthermore, we decided to forego an additional electrode montage over a control region. Accordingly, our data do not allow for definitive conclusions on the spatial specificity of our intervention.

## Conclusion

The results of the present work demonstrate that a single dose of tES over the bilateral auditory cortex can refine phoneme-categorization acuity in adolescent and adult individuals with DD. This approach characterizes the initial step to facilitate the acquisition of higher order language skills essential for successful reading and writing. Our findings encourage further research on transfer effects of auditory tES on higher order linguistic skills, on the impact of a repetitive tES-application, as well as on long-term effects of this intervention.

## Acknowledgment

### Author contributions

KSR conceived, designed, and performed the experiments. KSR, TZ, and KK analyzed the data and wrote the article. TZ, MM, KK, and HJH contributed materials/analysis tools. The diagnostic procedure was supervised by KK in the adolescent group and by KSR in the adult group.

### Funding

This work was supported by the Swiss National Science Foundation (grant number P2ZHP1\_158941), the Bäsch Stiftung zur Förderung der Angewandten Psychologie, and the Deutsche Forschungsgemeinschaft (ZA 626/2-1), SFB 779/TP2.

### Declaration of interest

None.

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