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# The use of noninvasive brain stimulation techniques to improve reading difficulties in dyslexia: A systematic review

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## Abstract

Noninvasive brain stimulation (NIBS) allows to actively and noninvasively modulate brain function. Aside from inhibiting specific processes, NIBS may also enhance cognitive functions, which might be used for the prevention and intervention of learning disabilities such as dyslexia. However, despite the growing interest in modulating learning abilities, a comprehensive, up-to-date review synthesizing NIBS studies with dyslexics is missing. Here, we fill this gap and elucidate the potential of NIBS as treatment option in dyslexia. The findings of the 15 included studies suggest that repeated sessions of reading training combined with different NIBS protocols may induce long-lasting improvements of reading performance in child and adult dyslexics, opening promising avenues for future research. In particular, the "classical" reading areas seem to be most successfully modulated through NIBS, and facilitatory protocols can improve various reading-related subprocesses. Moreover, we emphasize the need to further explore the potential to modulate auditory cortex function as a preintervention and intervention approach for affected children, for example, to avoid the development of auditory and phonological difficulties at the core of dyslexia. Finally, we outline how future studies may increase our understanding of the neurobiological basis of NIBS-induced improvements in dyslexia.

**KEYWORDS**
developmental dyslexia, language, noninvasive brain stimulation, phonology, reading, transcranial direct current stimulation

## 1 | INTRODUCTION

In the past years, our understanding of human brain function has undergone dramatic changes. Neuroimaging and noninvasive brain stimulation (NIBS) techniques have substantially enriched our knowledge of the neurobiological bases of cognition and process-specific network interactions. Functional neuroimaging (fMRI) is a powerful technique that provides correlational information about structure–function relationships with a high spatial resolution (for reviews of fMRI on language processing, see Price, 2010, 2012). Neuroimaging is complemented by NIBS techniques that allow to determine the causal relevance of brain areas for certain processes or functions (Parkin, Ekhtiari, & Walsh, 2015; Vosskuhl, Strüber, & Herrmann, 2018). NIBS protocols have become increasingly popular across numerous disciplines, including electrophysiological applications, cognitive neuroscience, and neurological and psychiatric research (e.g., see Fertonani & Miniussi, 2017; Sandrini, Umiltà, & Rusconi, 2011; Terranova et al., 2019). Consequently, functional neuroimaging and NIBS have significantly advanced the current knowledge about neural networks for cognition in the human brain, including language organization and reorganization (Hartwigsen, 2016, 2018; Saur & Hartwigsen, 2012). More recently, the combination of NIBS and neuroimaging is increasingly being used to map plastic after-effects or direct consequences of NIBS at the neural network level (Bergmann & Hartwigsen, 2020; Siebner, Hartwigsen, Kassuba, & Rothwell, 2009). Moreover, NIBS is used as a neuromodulatory intervention tool to alleviate various cognitive deficits and weaknesses (for a meta-analysis, see Begemann, Brand, Curčić-Blake, Aleman, & Sommer, 2020), such as in aphasic patients (Norise, Sacchetti, & Hamilton, 2017), or individuals with learning disabilities (e.g., Cancer & Antonietti, 2018).

Developmental dyslexia (henceforth dyslexia) is a hereditary learning disorder characterized by severe impairments in reading and writing despite normal intelligence (the official diagnosis is "specific learning disability with impairments in reading and written expression"; DSM V, American Psychiatric Association, 2013). These impairments present as a delay and increased difficulties during the acquisition of reading and writing, as well as long-term impairments that may persist into adulthood. NIBS has been extensively used to inform the study of language (Devlin & Watkins, 2007; Hartwigsen, 2015), and recently the focus has also shifted to investigating how NIBS studies inform the neurobiology of reading (see review of Turker & Hartwigsen, 2021). Although NIBS protocols provide unique tools to investigate the underlying reading network and gain further insight into the contribution of core reading areas to reading-related processes in dyslexics, only a handful of studies have addressed these issues to date. Compared with the plethora of neuroimaging studies with dyslexics, NIBS studies that aim to improve reading performance in individuals with reading impairments are scarce.

The aim of the present systematic review is to provide a state-of-the-art synthesis of NIBS studies with dyslexics to increase the current insight into the neurobiology of impaired reading. Furthermore, we aim to elucidate the potential of NIBS for treatment purposes, and hence evaluate specific reading interventions used in these studies and discuss their success and applicability. Finally, we pinpoint challenges and avenues for future research.

## 2 | BACKGROUND

### 2.1 | Reading and dyslexia

Although it feels natural for us to read and write, we should not forget that reading and writing are cultural achievements (Landis, Umolu, & Mancha, 2010). Both are nowadays required to participate in everyday social life, work, as well as interpersonal communication and interaction. Modern societies rely heavily on communication via written language, making literacy one of the central keys to education, employment, and a fulfilling social life. Given the importance of these skills, it is striking that a significant proportion of children fail to successfully master literacy acquisition despite adequate instruction. These children have what is commonly termed dyslexia (see Shaywitz & Shaywitz, 2005). Dyslexia is one the most frequently encountered learning disabilities affecting around 5–10% of school-aged children worldwide (see summary in Turker, 2018; and a new approach for estimations used in Wagner et al., 2020). Dyslexics face severe difficulties during literacy acquisition despite adequate educational opportunities and normal cognitive functioning and intelligence (Bishop & Snowling, 2004). The most widely accepted theory explaining the underlying deficits in dyslexia argues in favor of a phonological coding deficit (Ramus, White, & Frith, 2006), suggesting that many dyslexics suffer from problems with decoding and identifying phonological properties of speech input and accessing phonological representations in the brain (Shaywitz & Shaywitz, 2005). In other words, most dyslexics have an underlying sensory dysfunction in the form of an auditory and/or phonological deficit (e.g., see summaries Goswami, 2011, 2015). For children with a risk of developing dyslexia, it is essential to observe and assess pre-literacy skills, start targeted prevention, and offer intervention as early as possible. Since red flags during early literacy skill acquisition can be measured at preschool age already, it is vital to identify and screen preschool children early, that is, to implement an early risk identification in pediatric practice (Sanfilippo et al., 2020). There is also evidence that dyslexia leads to emotional and behavioral difficulties, mental health issues (e.g., anxiety, conduct disorder), and unemployment later in life (Aro et al., 2019; Carroll, Maughan, Goodman, & Meltzer, 2005), further emphasizing the need for support.

Although reading and writing are central to life and their neural underpinnings have received widespread interest in the past years, much more research is needed to understand the neuroanatomical and neurofunctional underpinnings of reading impairments. In the past decades, much research has explored the trajectory of brain activation patterns during literacy acquisition in typically developing and disabled readers (e.g., see reviews and meta-analyses by Martin, Kronbichler, & Richlan, 2016, Pugh et al., 2001, Richlan, Kronbichler, & Wimmer, 2009, and Shaywitz et al., 2002). These studies revealed that reading primarily relies on three highly intertwined, and mostly universal, reading circuits: (a) the left inferior frontal cortex, which is associated with the storage of sound information and sequencing information in general; (b) the left dorsal temporo-parietal cortex (TPC), which is thought to act as decoding center for grapheme–phoneme conversion; (c) the left ventral occipito-temporal cortex (vOTC; containing the visual word form area), which is most likely specialized for the orthographic coding of written language (Pugh et al., 2001; Kearns, Hancock, Hoeft, Pugh, & Frost, 2019; for details on vOTC function, see Dehaene & Cohen, 2011, or Price & Devlin, 2003). Note that a very recent NIBS review in healthy volunteers by Turker and Hartwigsen (2021) emphasizes the importance of other language areas outside the classical reading regions, such as the left posterior parietal cortex, or the anterior temporal lobe, which are causally relevant for subprocesses related to reading.

With respect to impaired reading, neuroimaging studies show that child and adult dyslexics exhibit significantly less activation in the above-mentioned core reading regions during reading-related tasks (e.g., phoneme elision, lexical decision, and overt reading). Functional activation differences have been confirmed in at-risk children (Vandermosten, Hoeft, & Norton, 2016), reading-impaired children (see summary in Turker, 2018), and adults (Richlan, Kronbichler, & Wimmer, 2011), with slight differences between the different age groups. In previous studies, at-risk children displayed underactivation primarily in the left TPC and marginally in the vOTC, as well as the cerebellum. Reading-impaired children, on the other hand, showed significantly less activation also in left inferior frontal areas. In a meta-analysis, Richlan et al. (2011) found that underactivation in the left TPC was only present in adult dyslexics, while underactivation spread to bilateral regions of the inferior parietal lobe (IPL; i.e., the TPC) in children with dyslexia. In meta-analyses focusing on adults, Maisog, Einbinder, Flowers, Turkeltaub, and Eden (2008) and Richlan et al. (2009) found that impaired reading processing was characterized by underactivation in the left IPL and the temporo-parietal junction (TPJ) (both are vital parts of the TPC). In another meta-analysis, Linkersdörfer, Lonnemann, Lindberg, Hasselhorn, and Fiebach (2012) focused on the overlap between structural and functional activation differences, and found a large overlap between reduced gray matter and relative underactivation in the left fusiform gyrus (vOTC) and the IPL as well.

Two regions that are not typically addressed in studies with dyslexics but are clearly of central importance are the primary and secondary auditory cortices. As many dyslexics suffer from auditory and/or phonological deficits, a core contribution of auditory-related skills is undeniable (see Giraud & Ramus, 2013, for a genetic and neurophysiological explanation). While theories of dyslexia highlight the importance of temporal processing as an underlying core deficit in dyslexics (e.g., Goswami, 2011; Lizarazu et al., 2015), also differences in auditory cortex myelination and morphology have been found in dyslexic children and adults (Kuhl et al., 2020; Serrallach et al., 2016; Skeide et al., 2018). These findings emphasize the importance of the auditory cortex for reading processing and hence also dyslexia (Goswami, 2014).

Interestingly, so far, only neural, but no behavioral measures have reliably predicted reading gains in dyslexics. Hoeft et al. (2011) found that improvements in reading performance over 2.5 years in children with dyslexia could be predicted by several neural measures, namely (a) whole brain activation during reading (>90% accuracy), (b) right prefrontal activation during reading, and (c) white matter tracts in the right hemisphere (right arcuate fasciculus and superior longitudinal fasciculus) (72% accuracy). However, no behavioral measure performed above chance in their analyses. Still, diverse behavioral therapies are currently being applied and tested with the hope to improve reading performance in affected and at-risk children (e.g., see single study results in Nukari et al., 2019; or meta-analytic evidence provided by Galuschka et al., 2020). In contrast to the progress made in behavioral interventions, however, only few studies so far have investigated whether a modulation at the neural level is equally or even more successful. Hence, there is a great demand to test the potential of neurostimulation techniques in the reading network in children or adolescents struggling with reading and writing (e.g., see discussion in van den Noort, Struys, & Bosch, 2015), but limited research has been performed so far.

## 2.2 | NIBS techniques and Reading impairments

In research, NIBS is usually used for three purposes, namely (a) to probe the functional relevance of specific brain regions for particular cognitive tasks, (b) to examine functional network interactions and compensatory reorganization after NIBS-induced perturbation, and (c) to modify behavior and skills, mostly with the aim of improving certain cognitive and motor functions and assist training or therapeutic interventions (Hartwigsen, 2016; Pascual-Leone, Walsh, & Rothwell, 2000). The most precise and most widely applied NIBS method in adults is transcranial magnetic stimulation (TMS). TMS is a noninvasive tool for the electro-magneto-electric stimulation of the human cortex. The basic mechanisms of this technique have been covered in many previous reviews (e.g., see Bestmann, 2008; Siebner & Rothwell, 2003). In short, by producing a brief electric high-current pulse through a magnetic coil, TMS generates a high-intensity magnetic field that causes electrical currents in the underlying brain tissue and thus elicits action potentials in neuronal axons (Hallett, 2007). The elicitation of these action potentials leads to the release of neurotransmitters at terminal synapses, and hence modulates brain activity (Priori, Hallett, & Rothwell, 2009; Ridding & Rothwell, 2007).

Most studies with children and adolescents use transcranial direct current stimulation (tDCS), a NIBS method that delivers weak electrical currents (intensity: usually 1–2 mA) through two electrodes placed on the scalp for a duration of up to 30 minutes (Nitsche & Paulus, 2011). Rather than inducing action potentials, tDCS is thought to modulate the resting membrane potential of cortical neurons, which either increases or decreases the likelihood of spontaneous or task-evoked firing (Priori et al., 2009). Such modulation may alter neuronal activity and behavior, leading to improvements or deteriorations in task performance. Whereas anodal tDCS (the anode placed over a region of interest) is commonly thought to increase brain activation, cathodal tDCS (the cathode placed over a region of interest) is expected to decrease brain activation in the targeted area. These changes in brain activation are thought to in turn map onto the respective behavioral consequences (Krause, Márquez-Ruiz, & Cohen Kadosh, 2013). The focality of tDCS is not fully understood, but biophysical modeling studies indicate that a large area under the electrode is polarized, although approximately half of the applied current is shunted through the scalp (Miranda, Lomarev, & Hallett, 2006) and another significant amount through the cerebrospinal fluid (Nathan, Sinha, Gordon, Lesser, & Thakor, 1993). It is generally assumed that the strongest tDCS effect should occur in the stimulated area under the electrode (Nitsche et al., 2003), but functional effects also engage distant neural networks (Nitsche et al., 2005). Given the overall low focality of tDCS, direct structure–function relationships are hard to establish, especially with respect to the induced behavioral changes (Seibt, Brunoni, Huang, & Bikson, 2015).

Aside from TMS and tDCS, more recent NIBS approaches include the application of alternating currents at fixed frequencies [transcranial alternating current stimulation (tACS)] or random frequencies [transcranial random noise stimulation (tRNS); see Vosskuhl et al., 2018 for a review]. Both techniques can be used to entrain or modulate specific neuronal oscillations in the brain. The plastic aftereffects of such protocols may also have therapeutic potential but very few studies have been conducted to date.

Due to the very promising results of NIBS in clinical populations, such as patients with depression (Martin et al., 2003), obsessive–compulsive disorder (Guo, Li, & Wang, 2017; Schulz, Gerloff, & Hummel, 2013), and aphasia (Saur & Hartwigsen, 2012), NIBS could be a promising intervention for learning disabilities as well (e.g., van den Noort et al., 2015). With respect to reading impairments, it is particularly interesting to explore network interactions within reading areas, and map potential increases and decreases of activity in specific brain areas after stimulation (see Figure 1). Nevertheless, only few studies have used neurostimulation to modulate the reading network in children or adolescents struggling with reading and writing to date. A review by van den Noort et al. (2015) suggests that rTMS might be a valuable tool for investigating questions related to reading research, but only one study to date (Costanzo, Menghini, Caltagirone, Oliveri, & Vicari, 2013) has used TMS in dyslexics. More recently, Cancer and Antonietti (2018) summarized the findings of several tDCS studies exploring reading processing in children and adults with reading impairments or weak reading skills. Overall, they reported improvements in reading subprocesses after NIBS to reading-related regions, but also suggested that future research is needed to confirm these preliminary findings. Recently, Wilcox, Galilee, Stamp, Makarenko, and MacMaster (2020) reviewed the potential of reading interventions for dyslexics on a general level, and further discussed several NIBS studies combined with reading interventions that were partly also dealt in earlier work (again, see Cancer & Antonietti, 2018).

While these reviews brought forward interesting ideas and highlighted the potential of using NIBS to elucidate reading-related processes and potentially improve reading abilities in individuals with dyslexia, their conclusions are limited by the overall small number of studies included. Moreover, none of the previous reading studies considered the effects of NIBS on network interactions and adaptive short-term plasticity. Adaptive short-term plasticity refers to the ability of the brain to flexibly adapt to perturbations by upregulating other areas of the same network or other networks (Hartwigsen, 2018). Since reading is associated with a network of distributed brain areas, we believe that dyslexia should be considered a network disorder and taking a modulatory perspective beyond the contribution of single areas may be helpful to increase treatment efficiency of neurostimulation approaches. In the present review, we aim to provide the first comprehensive synthesis based on NIBS studies with dyslexics, and discuss how and when different NIBS techniques could help alleviate difficulties encountered by dyslexics.

## 3 | METHODS

The search methods for the present review follow the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines (Moher et al., 2009, 2015; see Figure 2). Eligibility criteria regarding study characteristics were as follows:

1. The study applied a NIBS protocol (either single session or multiple sessions) with either a between or within-subject design, where a cortical brain region was targeted with NIBS (either facilitatory or inhibitory stimulation).
2. The study applied a reading (e.g., word, pseudoword, or text reading), or reading-related task (e.g., auditory processing) with the aim of modulating performance on the respective task with NIBS.
3. Subjects had a diagnosis of dyslexia according to country-specific regulations and criteria.

Studies in all languages that were available through the literature search were included. However, only studies in English were found. Likewise, all publications regardless of publication date were included if they met the eligibility criteria. To avoid a publication bias, also studies

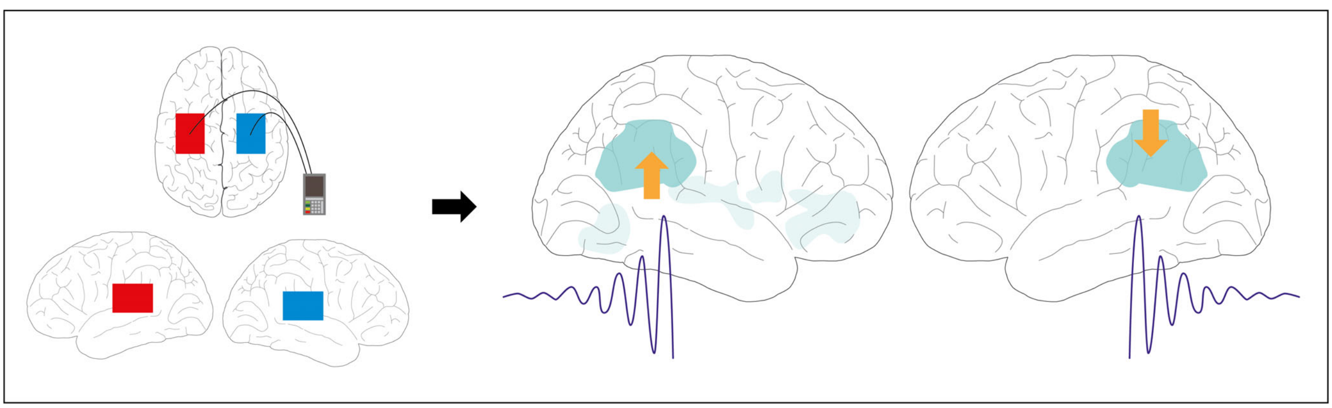

**FIGURE 1** Setup and schematic model of potential up- and down-regulation of reading areas following bilateral TPC stimulation (facilitation of left TPC and inhibition of right TPC) as applied in several studies in the present review

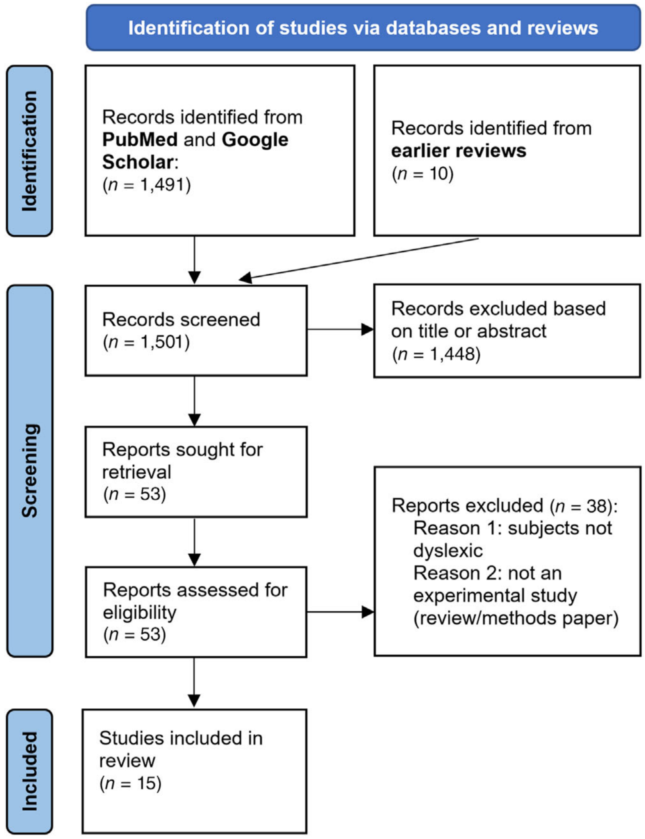


**FIGURE 2** PRISMA flowchart displaying the process of literature search and screening (see Moher et al., 2009, 2015). Cut-off date for the publication of studies was March 2021

that have not been published yet were included after individual quality assessment.

First, studies were collected from previous reviews (Cancer & Antonietti, 2018; van den Noort et al., 2015; Wilcox et al., 2020). Then, two literature databases, namely PubMed and Google Scholar were used as information sources. Searches included the key words "dyslexia" in combination with "transcranial magnetic stimulation," "transcranial direct current stimulation," and "non-invasive brain stimulation." The three searches yielded a total of 36 results in PubMed (11, 18, and 7, respectively, for the searches), and a total of 5,305 studies in Google Scholar (3,800, 1,050, and 455 results, respectively; only the first 500 for the first two search combination were screened due to the little relevance from 500 onward). Overall, 1,51 studies were screened for matching the inclusion criteria (by checking title and abstract), most of which had to be excluded based on the title or abstract ($n = 1{,}438$). Fifty-three were more thoroughly assessed as they met all initial inclusion criteria. All studies were screened, and their quality was assessed by two independent researchers. We also included two pre-prints and a thesis consisting of three separate studies, two of which met the inclusion criteria for the present review. Both authors independently assessed these unpublished works and decided that they were of sufficient quality to be included in the present review. However, the results will be interpreted with caution. Specific study details are provided in Table 1. Overall, 15 experimental studies met the eligibility criteria and are presented in the present review.

## 4 | RESULTS

Since only a subset of dyslexics has been found to respond to reading interventions (for evidence, see Al Otaiba et al., 2009, or McMaster, Fuchs, Fuchs, & Compton, 2005), the combination of reading interventions with NIBS could lead to a much higher success rate of reading interventions. All combined NIBS and reading intervention studies except for one used transcranial electrical stimulation (tDCS or tACS) and the majority targeted the left TPC [including the posterior middle and superior temporal gyri (pMTG/pSTG)] repeatedly before different reading tasks (word reading, pseudoword reading, and text reading in most cases; for a summary of all studies, see Table 1). These studies followed the assumption that the TPC is usually underactivated in individuals with dyslexia, and anodal stimulation might increase the responsiveness of this region to reading training. While it is too early to judge the efficacy of NIBS as a treatment for reading disorders and provide strong conclusions with respect to the most promising target site, the initial results are encouraging (see summary of results in Figure 3). A combination of repeated behavioral interventions and NIBS seems the best way to change underlying mechanisms, single-session NIBS interventions might also be helpful in determining brain regions with causal relevance for reading-related processes. Therefore, we will present the findings of repeated and single session interventions separately. In the following sections, we provide an in-depth presentation of these results. We will first focus on multiple session tDCS reading intervention studies, then discuss NIBS studies with single stimulation sessions, and finally consider tACS studies targeting the auditory cortex. Since several simulation sites around the TPC overlapped, in particular when targeted with tDCS, Figure 3 displays the overall findings in three separate figures, one presenting the findings of adults, one of children, and one of auditory cortex stimulation.

### 4.1 | Combining NIBS with behavioral interventions as a key to treatment success in dyslexia

Repeated sessions of behavioral reading training combined with anodal tDCS of the left TPC revealed long-lasting after-effects of facilitatory stimulation on reading performance, such as better pseudoword reading and artificial orthographic learning in dyslexia. Please note that all studies that applied multiple session interventions in children were performed by the same research group, and subjects overlapped in some of these studies (which has also been mentioned in the respective publications).

Costanzo et al. (2016a) used the identified optimal protocol of a previous single session study (left anodal/right cathodal tDCS of the left TPC; see Section 4.2) and applied it in a multiple session intervention during a cognitive and phonic reading training, which basically

**TABLE 1** NIBS studies with dyslexics [Corrections added after online publication, 15 November, 2021: In table 1, corrections has been added to 'Site' and 'Summary of results' column.]

| Study | Subjects | Method | Site | Task | Design | Summary of results |
|---|---|---|---|---|---|---|
| Costanzo et al., 2013 *Neuropsychologia* | 10 adults (Italian)[a] | Offline rTMS 5 Hz | L IPL<br>R IPL<br>L STG<br>R STG | Word reading, pseudoword reading, text reading | Single session without reading training | *rTMS at 5 Hz of left STG* → increased word reading speed and text reading accuracy<br>*rTMS at 5 Hz left/ right IPL* → improved pseudoword reading accuracy |
| Costanzo et al. (2016b) *NeuroReport* | 19 children/ teenagers (Italian)[a] | Online tDCS (bihemispheric)<br>1 mA for 20 min | L/R TPJ | Word, pseudoword and text reading, lexical decisions, and phoneme blending | Single session without reading training | *Left anodal/right cathodal tDCS of TPJ* → improvements in text reading |
| Costanzo et al. (2016a) *Restorative Neurology and Neuroscience* | 18 children/ teenagers (Italian)[a] | Online atDCS<br>1 mA for 20 min<br>18 sessions spread over 6 weeks | L/R TPJ | Word, pseudoword, and text reading | Multiple sessions with reading training | *Left anodal/right cathodal tDCS of TPJ + training for 6 weeks* → reduced low frequency word reading errors and decreased pseudoword reading times |
| Costanzo et al. (2019) *Neuropsychologia* | 26 children/ teenagers (Italian)[a] | Online atDCS<br>1 mA for 20 min<br>18 sessions spread over 6 weeks | L/R TPJ | Word, pseudoword, and text reading | Multiple sessions with reading training | *Left anodal/right cathodal tDCS of TPJ + training for 6 weeks* → long-lasting benefits, specifically for pseudoword reading and low-frequency word reading |
| Cummine et al. (2020) *Neurobiology of Language* | 32 adults/ (English) | Online atDCS<br>1.5 mA for 15 min<br>Phoneme segmentation training before tDCS | L SMG | Word, pseudoword and pseudo-homophone reading, ran | Single session after reading training | No effect of atDCS |
| Heth and Lavidor (2015) *Neuropsychologia* | 19 adults (Hebrew)[a] | Online atDCS<br>1.5 mA for 20 min<br>5 sessions spread over 2 weeks | L V5/MT | Text reading, rapid automatized naming | Multiple sessions without reading training | *Multiple sessions of atDCS of left V5/MT* → improved reading speed and fluency |
| Lazzaro et al. (2020) *Scientific Studies of Reading* | 26 children/ teenagers[a] (Italian) | Online atDCS<br>1 mA for 20 min<br>18 sessions spread over 6 weeks | L/R TPJ | Word and pseudoword reading | Multiple sessions with reading training | *Left andoal/right cathodal tDCS of TPJ + training for 6 weeks* → changes in responsiveness of training to improve word reading fluency |
| Lazzaro et al. (2021) *Brain Sciences* | 10 children/ teenagers (Italian) | Online a/ctDCS<br>1 mA for 20 min | L/R TPJ | Word, pseudoword and text reading, lexical decisions, phoneme blending, working memory, RAN | Single session without reading training | *Left anodal/right cathodal tDCS of TPJ* → improved text reading accuracy, word recognition, speed, motion perception, and modified attentional focusing |

**TABLE 1** (Continued)

| Study | Subjects | Method | Site | Task | Design | Summary of results |
|---|---|---|---|---|---|---|
| Marchesotti et al. (2020) *PLoS Biology* | 15 adults/ (French) | 30 and 60 Hz tACS average peak-to-peak stimulation intensity of 1.1/1.2 mA for 20 min + EEG | L auditory cortex | Phonemic awareness, pseudoword reading, and text reading | Single session without reading training | *tACS at 30 Hz of left auditory cortex →* improved phonemic awareness and reading accuracy in dyslexics compared with SHAM and 60 Hz stimulation but no long-lasting effect *EEG results →* stimulation of left auditory cortex decreased 30 Hz activity in auditory cortex and surrounding STG |
| McMillan (2017) (PhD thesis; Study 1) | 20 adults (English) | Online atDCS 1.5 mA for 20 min + EEG | L TPC | Word reading pseudoword reading | Single session without reading training | *atDCS of left TPC →* significant increase in pseudoword reading performance (accuracy and times) in dyslexics and controls with a bigger effect in dyslexics |
| McMillan (2017) (PhD thesis; Study 2) | 16 adults (English) | Online atDCS 1.5 mA for 20 min + EEG | L TPC | Artificial orthographic learning | Single session without reading training | *atDCS of left TPC →* higher sensitivity to consistency and better frequency manipulations in dyslexics only |
| Rahimi et al. (2019) *Experimental Brian Research* | 17 children (Indian) | Online atDCS/ctDCS 1 mA for 20 min | L STG | Auditory-evoked potentials, gap in noise test | Single session without reading training | *atDCS of left STG →* decrease in threshold values and higher accuracy during gap in noise test |
| Rios et al. (2018) *Child Neurology Open* | 12 children/ teenagers (Portuguese) | Online atDCS 2 mA for 30 min 5 sessions spread over 5 days | L MTG/ pMTG | Letter reading, syllable reading, pseudoword reading, text reading | Multiple session without reading training | *atDCS of left MTG/pMTG →* increases in pseudoword and text-reading speed |
| Rodrigues De Almeida and Hansen (2019) *Preprint/ unpublished results* | 6 adults (Portuguese) | Online tDCS (bihemispheric) 2 mA for 20 min + fMRI | L IFG | Word reading, lexical decision, and speech perception | Single session without reading training | *atDCS of left IFG →* larger facilitation for the speech perception than the production task and larger compensation for speech perception under cathodal tDCS |
| Rufener, Krauel, Meyer, Heinze, and Zaehle (2019) *Brain Stimulation* | 15 adolescents 15 adults (German) | Offline gamma-tACS at 40 Hz for 20 min Offline tRNS (100–640 Hz) at 1 mA for 20 min + EEG | L/R auditory cortex | Voice onset discrimination | Single session without reading training | *Bilateral 40 Hz-tACS of left auditory cortex* → increased phoneme-categorization in children/ adolescents |

(Continues)

**TABLE 1** (Continued)

| Study | Subjects | Method | Site | Task | Design | Summary of results |
|---|---|---|---|---|---|---|
| | | | | | | *Bilateral tRNS →* increased phoneme categorization in adults *EEG result →* Stimulation altered the P50-N1-complex involved in auditory processing |

Abbreviations: a/ctDCS, anodal/cathodal transcranial direct current stimulation; IFG, inferior frontal gyrus; IPL, inferior parietal lobe; (p)MTG, posterior middle temporal gyrus; SMG, supramarginal gyrus; STG, superior temporal gyrus; tACS, transcranial alternating current stimulation; TPC, temporo-parietal cortex; TPJ, temporo-parietal junction; V5/MT, middle visual field.
[a]Between-subject design (i.e., only half of the participants received active stimulation, the other placebo stimulation).

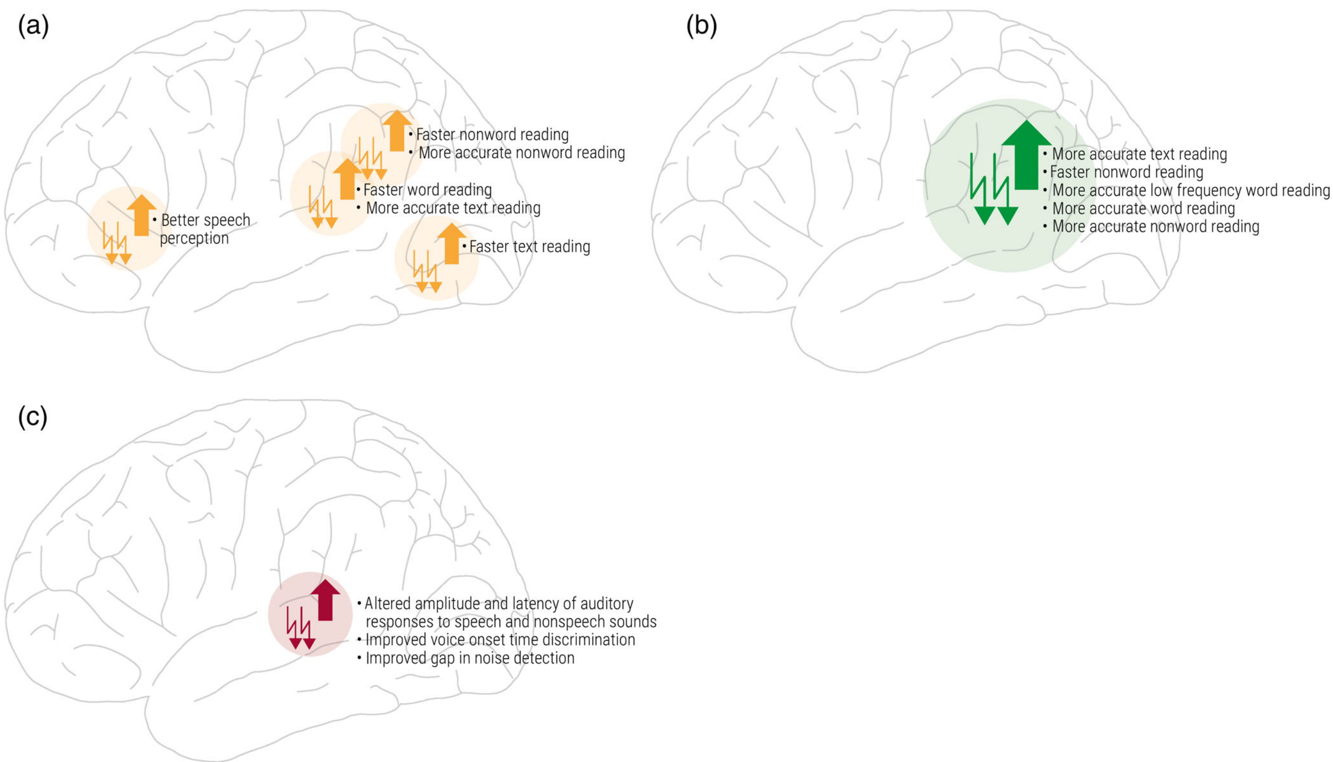


**FIGURE 3** Significant results of NIBS studies targeting reading-related regions in adults, children, and teenagers with dyslexia. The two panels on top display the specific target sites, as well as the results of the NIBS studies with dyslexic adults (a) (Costanzo et al., 2013; Heth & Lavidor, 2015; two studies by McMillan, 2017; Rodrigues De Almeida & Hansen, 2019); and dyslexic children (b) (twice Costanzo et al., 2016a, 2016b; Costanzo et al., 2019; Lazzaro et al., 2020, 2021; Rios et al., 2018). The panel below (c) displays the results of studies targeting the auditory cortex in dyslexia (Marchesotti et al., 2020; Rahimi et al., 2019; Rufener et al., 2019)

included the learning of letter-sound rules. In this intervention, 18 intervention sessions with NIBS and the aforementioned training were spread over 6 weeks. The authors found significant improvements in low frequency word reading accuracy and pseudoword reading speed. Interestingly, these effects persisted for 1 month after the end of the intervention. Based on these results, it was concluded that tDCS mainly improved phonological processing and letter-sound mapping through facilitation of the left TPC, and simultaneous inhibition of the right TPC.

A second multiple session intervention study by the same group (Costanzo et al., 2019; 18 sessions spread over 6 weeks) replicated the earlier findings of a significant improvement in low frequency word and pseudoword reading in a larger group of adolescents with dyslexia. Using the same tDCS protocol (facilitation of the left TPC, inhibition of the right TPC), this study provided first evidence for a long-term efficacy of tDCS in combination with training in a follow-up test 6 months after the end of the intervention. While these results speak in favor of a contribution of the bilateral TPC to challenging reading conditions (i.e., low frequency word and pseudoword reading), the authors suggested that the combination of excitatory (anodal) and inhibitory (cathodal) stimulation may have helped rebalancing abnormal cortical activation in dyslexics. It thus seems plausible that the employed bilateral montage changed the weight of the overall contribution of both TPC regions to reading and thus led to improvements in low frequency word and pseudoword reading. However, this explanation remains speculatory and should be explored in future studies with combined tDCS and neuroimaging.

Recently, Lazzaro et al. (2020) (same research group of Costanzo et al.) found that anodal tDCS of the left TPC/TPJ (i.e., no bilateral montage) may change the responsiveness of children to reading training to improve word reading fluency. In other words, stimulating the TPC with anodal tDCS did not lead to significant group level results, but it had a positive effect on the administered behavioral training, so that the individual responsiveness to the behavioral intervention could be altered. Despite the absence of significant improvements on the group level, the authors argued that the stimulation influenced the individual responsiveness to training, which might indicate that tDCS could be more efficient and successful in children with more severe forms of dyslexia. This, however, remains speculatory. These results further suggest that NIBS should always be combined with behavioral training as it most likely modulates the learning and training experience, not the underactivation in affected areas per se.

The only tDCS study with literacy-impaired adults was performed by Heth and Lavidor (2015) and included an intervention that comprised five stimulation sessions with anodal tDCS over the left middle temporal visual area (left V5/MT) spread over 2 weeks. The authors tested text reading speed and accuracy before, immediately after and a week after the end of the intervention. They found that text reading speed was significantly improved in the stimulation group as compared with the sham (i.e., placebo) group, but only in the follow-up session 1 week after the intervention. These results might indicate that the plastic after-effects of the intervention needed time to evolve and might not be measurable directly after the end of an intervention. Moreover, the findings suggest that not only a modulation of the TPC, but also of visual areas (in proximity to the vOTC) may be capable of improving reading performance, at least in adults.

### 4.2 | NIBS studies without interventions: Short-term effects in dyslexic children and adults

Studies with a single session of NIBS have been performed with both children and adults, and all except for one study used tDCS. These studies targeted the left TPC, the left IFG, the left pMTG, and the left SMG. First, all studies in which the TPC were targeted will be presented. Thereafter, we discuss the single study results for the other regions.

To date, only one study by Costanzo et al. (2013) has used TMS as a potential treatment option in dyslexia. In that study, the left and right IPL, as well as the left STG were targeted in single sessions in dyslexic adults. Effects were assessed for word, pseudoword and text reading after 5 Hz rTMS. The authors found faster word reading speed and higher text reading accuracy after rTMS over the left STG. In contrast, rTMS over the left and right IPL selectively improved pseudoword reading accuracy without affecting word or text reading. Two (preliminary) conclusions can be drawn from this study. First, the results suggest that even single session interventions may significantly improve reading in dyslexic adults. In other words, even a temporary modulation can successfully modulate reading skills, even if most likely only for a short period of time. Secondly, this study supports the notion of a differential role of the STG and the IPL for reading. Since both regions are part of the TPC, which is usually treated as one single region with a single main function during reading, future studies need to further disentangle the differential roles of these regions within the larger TPC area.

In a later tDCS study, Costanzo et al. (2016b) explored the optimal polarity of stimulation in a single-session within-subject intervention. In this study, tDCS was applied before the assessment on several tasks, including lexical decisions, text reading, word, and pseudoword reading, as well as auditory phoneme blending and working memory (n-back task). Three different stimulation protocols were tested, namely left anodal/right cathodal, right anodal/left cathodal and sham stimulation of the left TPC. The results showed a significant improvement in text reading accuracy for a bilateral montage with left anodal/right cathodal tDCS (i.e., facilitating the left and inhibiting the right TPC), as well as an increase in errors after left cathodal/right anodal TPC stimulation. This study served as basis for the earlier presented multiple session interventions.

Most recently, Lazzaro et al. further investigated a tDCS-induced modulation of reading performance, while at the same time assessing other reading-relevant processes, such as motion perception and visuo-spatial working memory (Lazzaro et al., 2021). Left anodal/right cathodal tDCS of the left TPC (as in previous studies) improved text reading accuracy, word recognition and motion perception. However, word or pseudoword reading were not significantly modulated as in earlier studies by the same group. At the same time, stimulation modified attentional focusing, and improvements in text reading performance were explained by a modification of visuo-spatial working memory following left TPC stimulation. These results indicate that tDCS-induced improvements may not fully be explained by the modulation of core reading processes but may (also) reflect improvements in domain-general support functions such as working memory and attention. More research is needed to confirm this preliminary finding, but it highlights the complex interaction between regions and the functions they contribute to.

Three more studies targeted the left TPC. Two were conducted by McMillan (2017) who reported improved pseudoword reading performance (higher accuracy and faster reading times) in both controls and dyslexics after anodal tDCS over the left TPC. However, the effect was stronger in the dyslexics. Moreover, tDCS diminished an early increase in the P1 amplitude over left posterior electrodes in dyslexics, which the author interpreted as reflecting a cost of attention. In a second study, the same author investigated differences in artificial orthographic learning (combining artificial characters with associated phonemes) following anodal tDCS over the left TPC. Interestingly, dyslexics showed an increased sensitivity to the consistency of vowel sounds and an improved ability to retain frequency benefits 1 week post training, while the control group did not show any effects. Yet, there were no significant differences between sham or anodal stimulation in the EEG, leaving the neurophysiological correlates underlying the observed behavioral improvements unclear.

The last study targeting the TPC was performed by Cummine, Boliek, McKibben, Jaswal, and Joanisse (2020). The authors applied anodal tDCS to the left SMG with the aim to improve reading performance (text reading, word reading, pseudoword reading, and rapid automatized naming) in adult dyslexics. Before the stimulation period, participants also received a phoneme segmentation training. Overall, they did not find any significant facilitatory effect of anodal tDCS of the left SMG/TPJ on reading performance. It seems that also the phoneme segmentation training did not lead to any differences in performance. This suggests that either the left SMG is not critically involved in reading in adult dyslexics, or methodological limitations (e.g., choice of training) led to the null results. It is particularly surprising that the phoneme segmentation training did not have any effect on performance, since even adult dyslexics are expected to show improvements in this domain after training.

Despite its key role in semantic and phonological processes, only one study to date has targeted the left IFG in dyslexic adults (Rodrigues De Almeida & Hansen, 2019). In that study, the authors tested how task load of different measures of phonological processing would interact with tDCS. Anodal and cathodal tDCS were applied to the left IFG during word reading, lexical decisions, and speech comprehension (categorical perception). Since the left IFG is a key node for pseudoword processing, the authors expected better pseudoword reading performance after stimulation. As an unexpected finding, anodal tDCS improved performance in speech comprehension but did not affect speech production and word reading at all. A subsequent fMRI session was included to relate behavioral changes to a potential modulation of task-related activity in the reading network, but no significant effects of tDCS on brain activation patterns in the left IFG or STG were found. Consequently, it remains unclear how to interpret these unexpected findings.

The last single session study targeted the left pMTG in dyslexic children. Rios et al. (2018) aimed to verify the contribution of this area to establishing sound–symbol associations in children and teenagers with dyslexia. The authors found increased reading performance for pseudowords and words in text reading after anodal tDCS, while syllable, letter, and single word reading remained unaffected. The authors argued that especially the simpler tasks involving syllables and letters showed a pattern of improvement in younger children but might have been too easy for teenagers. They concluded that it might be worthwhile to differentiate age groups (e.g., children with little reading experience vs. adolescents/teenagers with more experience) in future research. These results also emphasize the impact of inter-individual differences and the need for individualized intervention approaches.

## 4.3 | Modulating the auditory system through transcranial electrical stimulation

From a neurophysiological perspective, acoustic information at the phonematic scale is highly dependent upon lower gamma oscillations (25–45 Hz), which are also the dominant endogenous activation pattern in the auditory cortex (see Morillon, Liégeois-Chauvel, Arnal, Bénar, & Giraud, 2012). It was suggested that impaired auditory sampling and a particular lack of hemispheric specialization for gamma oscillations, as found in adult dyslexics (Lehongre, Ramus, Villiermet, Schwartz, & Giraud, 2011), might affect the perception of acoustic cues and the sensitivity to linguistic stimuli. Modulating the auditory system could hence lead to higher precision and lower variability in categorical phoneme perception, which might in turn impact phonological processing and thus reading. So far, three studies have used tACS, tRNS, and tDCS with the aim of modulating temporal aspects of word processing (see below for a definition) and phoneme perception in dyslexia.

The first study by Rufener et al. (2019) used 40 Hz-tACS and tRNS of the left auditory cortex with the aim of improving phoneme categorization in adolescents and adults with dyslexia. Stimulation was applied in three sessions during a phoneme-categorization task. tACS led to a higher acuity in voice onset time categorization (i.e., perceiving the time between air release and vocal cord vibration) compared with sham and tRNS in adolescents. In other words, auditory perception was successfully modulated through tACS in young teenagers. The authors further used EEG to measure the amplitude of the auditory response (P50-N1) and found that tACS increased the amplitude when compared with sham, meaning that the observed behavioral effect was also observable on the neurophysiological level. In the adult group, however, only tRNS led to a higher acuity (the effect for tACS was not statistically significant). Surprisingly, the opposite pattern was found at the neurophysiological level: only tACS modulated the P50-N1 (measures of sensory gating and stimulus matching) complex compared with sham and tRNS. This may indicate that neurophysiological parameters may be more sensitive in detecting NIBS-induced modulatory effects than behavioral measures (see also Kroczek, Gunter, Rysop, Friederici, & Hartwigsen, 2019). The absence of a significant modulation of the P50-N1 complex by tRNS may be due to the application of random frequencies which might not result in a clear neurophysiological correlate. However, this explanation remains speculatory and needs to be further explored. In sum, tACS successfully modulated auditory responses both in adults and adolescents, but only adolescents also showed improvements in voice onset time categorization following stimulation.

Another study by Marchesotti et al. (2020) targeted the left auditory cortex to improve phonemic awareness and reading accuracy. Before applying tACS, the authors confirmed significantly lower 30 Hz activity in the left but not right auditory cortex in dyslexics as compared to controls. They then applied either 30 Hz, 60 Hz tACS or sham to the left auditory cortices of controls and dyslexics on four separate days. The authors found that offline gamma-tACS at 30 Hz improved reading accuracy (texts and pseudowords) and phonemic awareness, while 60 Hz tACS only improved phonemic awareness. Interestingly, no improvements on the syllable level could be found. The effects were strongest in the 30 Hz group, which led to higher improvements than the sham and 60 Hz simulation. On the neurophysiological level, 30 Hz tACS led to a power increase (higher oscillatory response) in the left auditory cortex and the surrounding STG region. The authors further reported that the facilitation was most pronounced in those with poor reading skills, while a slight disruption was found in the very good readers in the control group. They interpreted this finding in the control group as a negative interference on reading induced by 30 Hz tACS. Overall, tACS at 30 Hz improved pseudoword reading and text reading accuracy by about 15%. However, the results were only observable directly after stimulation and not 1 hour later in the second testing session. This suggests that tACS may only induce a mere temporary modulation of phoneme processing that does not lead to long-lasting changes, which might however be induced by a multiple session intervention.

The third study by Rahimi et al. (2019) investigated the effect of tDCS on the left STG in child and adolescent dyslexics. To test the effect on auditory temporal processing, they used a gap detection task, which requires participants to detect the distances between white noise, and measured long-latency auditory-evoked responses to speech sounds. Twenty minutes of tDCS with a bilateral montage over the STG (to increase cortical excitability in the left STG and decrease it in the right STG) modulated the amplitudes of the P1, N1, and P2 responses to the speech stimuli. More specifically, the latencies of all three responses were reduced compared with baseline and sham, and the amplitude was increased. Behaviorally, stimulation led to higher accuracy and lower threshold values for the gap in noise test. This study further supports the notion that left auditory cortex stimulation alters auditory responses to speech both in term of latency and amplitude, with significant improvements in auditory discrimination tasks. It remains to be shown how these improvements in auditory discrimination might be relevant for reading-related tasks.

While these preliminary results are certainly promising, the potential for long-term changes of behavioral performance after tACS remains to be determined. One may speculate that long-term changes would require repeated sessions of tACS, although single session interventions already provide encouraging results in different learning paradigms (e.g., Antonenko, Faxel, Grittner, Lavidor, & Floël, 2016). Moreover, future work should probe the efficacy of different frequency bands (e.g., also alpha or beta tACS) and investigate the induced neurophysiological changes in the long run. Last, direct consequences for reading processing need to be further investigated.

## 5 | DISCUSSION

### 5.1 | The potential of NIBS to improve (prerequisites of) reading

Since only few studies to date have investigated the potential of NIBS to modulate the reading network in impaired readers, these preliminary findings need to be interpreted with caution. So far, only two regions have been reported in several studies with similar stimulation protocols. These are the left auditory cortex and the left TPC. The vOTC, a core region of the reading network, has not been targeted with NIBS in the study of dyslexia so far. This may be partly explained by difficulties in targeting this area with NIBS, especially with TMS, given its proximity to the shoulder and the neck. Yet, some previous TMS studies in healthy volunteers have successfully targeted this area (see Turker & Hartwigsen, 2021) and stimulation with tDCS or tACS should be feasible. Moreover, only one study targeted the left IFG and did not find effects on the neurophysiological level that could explain the behavioral improvements these authors reported. Also, the study is a preprint and results should be interpreted with caution.

Based on the above discussed results, we conclude that a neuromodulation of the left auditory cortex through gamma-tACS has the potential to improve auditory processing, in particular phoneme processing. Modulatory effects can be reliably observed both at the behavioral and neurophysiological level, with tACS leading to altered responses to auditory stimuli in the form of decreased latencies and higher amplitudes. A major question that arises when looking at the results of the few tACS studies that successfully modulated auditory processing of speech stimuli is whether the NIBS-induced effects will also impact reading performance as has been shown in the tDCS studies. In other words, only one study (Marchesotti et al., 2020) tested whether the changes in auditory processing had a measurable effect on reading performance. More information on the consequences for various reading-related measures are needed to determine the usefulness of auditory cortex stimulation in dyslexia.

Regarding multiple session interventions, studies provide evidence that repeated sessions of tDCS combined with reading interventions can successfully improve reading performance. In these studies, anodal tDCS over the left TPC, and cathodal tDCS over the right TPC, combined with reading training (mostly phonology-based interventions) improved several reading measures, such as pseudoword or low frequency word reading. Even though these results have only been observed on the behavioral level so far, it has been argued that the inhibition of the right TPC and the simultaneous facilitation of the left TPC changed an underlying imbalance that could be at the core of dyslexia. However, it remains yet to be explored how stimulation of these areas alters network-level plasticity and activation/deactivation in the core reading areas during reading processing. When looking at the single studies targeting other regions, it becomes clear that several other areas and stimulation protocols bear the potential to alleviate reading difficulties in dyslexia. A major problem, however, is to determine which reading process can be modulated by which protocol and which area should be targeted, considering the large inter-individual differences on the neural level, which remain underexplored to date.

Finally, it should be noted that the observed heterogeneity between studies might be partly explained by differences in stimulation parameters. The optimal stimulation intensity for TMS, tDCS, and tACS in the study of reading and dyslexia (and other cognitive functions) is unknown and varies in the included studies (e.g., 1–1.5 mA for the included tDCS studies). Electrode size and montages may further influence the observed outcome and optimal stimulation frequencies for tACS studies remain also elusive. As consensus about these parameters is currently lacking in most studies of cognition. Therefore, future studies on reading and dyslexia should systematically explore the optimal stimulation parameters. For example, the use of-high definition tDCS has been proven promising for enhancing treatment outcome in patients with poststroke aphasia (e.g., Richardson, Datta, Dmochowski, Parra, & Fridriksson, 2015), but no study with high-definition tDCS has been performed with dyslexics so far. Such approaches may be promising in the treatment of dyslexia.

With respect to the targeting procedure for the stimulation site, all included tDCS studies used the 10–20 EEG system to guide electrode placement. While TMS studies are usually more precise and rely on the targeting of specific brain coordinates via neuronavigation systems (e.g., see Hartwigsen, 2015 for a review), the lower precision and focality of tDCS may be an advantage for treatment purposes because such effects likely rely on modulatory network effects and the exact target areas may not be known. Combining NIBS with neuroimaging will be vital in future studies to investigate the assumed NIBS-induced modulation on the neurophysiological level, and explore whether functional connectivity between the core reading areas is altered through stimulation as well.

### 5.2 | Task-specific network interactions and the modulation of reading-related brain areas

The fact that tDCS combined with a behavioral intervention (i.e., reading training) is relatively effective in improving reading likely reflects altered synaptic plasticity in the underlying neural network (Cirillo et al., 2017; Kronberg, Bridi, Abel, Bikson, & Parra, 2017). Testing the claim that learning effects are mediated by changes in synaptic plasticity, Kronberg et al. (2017) found that NIBS modulates rather than induces synaptic plasticity in hippocampal slices of the rat brain. In other words, combining NIBS with behavioral learning tasks is likely to link enhanced synaptic plasticity to the specific task, which should result in a "gating effect" on endogenous synaptic plasticity. This suggests that NIBS should always be combined with a specific training in individuals with dyslexia but might not be effective as a treatment without an adequate behavioral intervention. The modulation of endogenous synaptic plasticity may also explain the frequently observed task-specificity of NIBS effects on different interventions or trainings. Especially with respect to nonfocal tDCS, it is it is unlikely that task specificity can be fully explained by spatial selectivity of the induced current flow (see Datta et al., 2009). The observed task specificity in numerous studies of cognition most likely results from a selective stimulation-induced modulation of endogenous synaptic plasticity (Kronberg et al., 2017). Although the exact cellular mechanisms underlying the physiological after-effects of NIBS (e.g., gene activation/regulation, de novo protein expression, and modified network properties) are still unclear, these changes likely modify synaptic excitability and plasticity, which might in turn lead to long-lasting, therapy-relevant changes in the brain (Cirillo et al., 2017).

It is a pity that only few of the included reading intervention studies mapped the effects of stimulation on brain functioning. Consequently, the current NIBS studies do not allow for any strong conclusions on the neurophysiological correlates of the observed behavioral improvements. Nevertheless, the induced behavioral changes are likely reflected in increased or decreased task-related activity in the stimulated area and remote regions. For example, almost all studies by Costanzo et al. placed the anode over the left TPC/IPL and the cathode over the right-hemispheric homolog. The authors suggest that the observed behavioral improvements reflect a facilitation of the left TPC, and a concurrent inhibition of the right TPC. This interpretation would favor an imbalance of the contribution of both hemispheres in dyslexia, with a stronger contribution of the right hemisphere relative to healthy controls. The stronger contribution of the right TPC might result in lower reading performance as compared with nonimpaired readers who process reading primarily in the left hemisphere. The bilateral montage might result in a re-shift of the balance between both hemispheres, with a facilitation of the "underactivated" left hemisphere and concurrent inhibition of the "overactivated" right hemisphere, which would in turn lead to an increase in reading accuracy and speed. In other words, we may speculate that the pathological "underactivation" was enhanced through stimulation, such that the activation pattern resembled more closely those of nonimpaired readers, which might have led to a temporal facilitation of phonological access. However, it seems unlikely that the access to phonological representations can be permanently facilitated through single sessions of NIBS, or that the phonological representations that have been neglected for years or decades are strengthened so quickly that performance improves immediately. Rather, it seems that studies combining a behavioral intervention with NIBS could provide first evidence for a direct modulation of pathogenic mechanisms in dyslexia in so far as new learning is strengthened and synaptic plasticity is changed by the combination of NIBS and reading training. It also remains to be shown if this effect is persisting and normalizes aberrant brain activation or functioning in dyslexics in the long run. Overall, without the inclusion of neuroimaging data, this remains speculative. Also, the small number of participants in the included studies and the use of between-subject designs and different tasks limits the generalization of such effects and the conclusions about potential underlying neural effects.

The studies in which the auditory cortex was targeted, on the other hand, clearly showed a modulation on the neurophysiological level, although it remains to be explored if changes in the amplitude and latency of auditory stimuli (be it speech or not) maps onto reading skills as well. So far, several event-related potentials associated with primary auditory processing showed changes following gamma-tACS to the left auditory cortex, even though these neurophysiological alterations may only last for short periods of time.

In general, a major limitation of behavioral NIBS studies is that the observed behavioral effects might not only reflect local changes in task-related activity but also the modulation of structurally or functionally connected areas and could thus reflect either a network effect or a remote effect in a distant region. In such cases, the assumption of the functional relevance of the targeted area for a given process would not be valid. The combination of NIBS protocols with subsequent or simultaneous neuroimaging may help to address this issue, which is a promising avenue for future studies on reading processing in the healthy and dyslexic brain.

### 5.3 | Conclusions with respect to the neurobiology of reading

Zooming into the findings of the presented NIBS studies (see Figure 3) provides a very uniform picture, particularly in children. Facilitating the left TPC does not only help children and teenagers with dyslexia to read pseudowords faster and with higher accuracy, but also low frequency word and text reading might be improved. Even if neurostimulation primarily affected the decoding process, this would be very unlikely to directly lead to an effect on text reading, especially in teenagers who are expected to use sight word reading despite their reading impairment. Therefore, the role of the left TPC in text (or potentially also sentence) reading deserves further attention to clarify how the so-called "decoding" center may impact text reading.

The present results in dyslexic adults, on the other hand, seem to be largely in accordance with a neurobiological dual-stream model of reading (for a recent account, see Coltheart, 2006; see further neurobiological summaries in Kearns et al., 2019; Turker & Hartwigsen, 2021), with the exception that NIBS-induced facilitation of the left pSTG leads to faster word and more accurate text reading. Even though these findings should be interpreted with caution due to the very limited number of studies, they certainly highlight the organization of reading in distributed large-scale networks, rather than restricted modules.

### 5.4 | Limitations

Unfortunately, replication studies are scarce and most studies that we discuss in the present review are small-scale studies that are underpowered. More studies with more participants are desperately needed to confirm the successful application of NIBS in dyslexic populations. Regarding age, it does not seem to make a difference whether stimulation was applied in children, adolescents or adults since effects were found in all age groups. In other words, a modulation of the reading network may not be limited to interventions in the developing reading network in children, but also bears the potential to alter reading performance in adult dyslexics. Nevertheless, very few longitudinal studies were reported and the results were rather mixed, leaving the long-term outcome of stimulation unclear.

## 6 | GENERAL CONCLUSIONS AND FUTURE DIRECTIONS

Overall, tDCS studies combined with reading interventions have been shown to alleviate reading difficulties for specific reading subprocesses and skills in dyslexic adults and children. Apart from the successful tDCS studies, studies using gamma-tACS at different frequencies applied to the left auditory cortex also led to a successful (short-term) alteration of the neurophysiological response of the auditory cortex to speech and nonspeech stimuli. Additionally, these neurophysiological changes were linked to behavioral changes in different tests assessing auditory temporal processing, which has often been reported as deficient in a large proportion of dyslexics (Goswami, 2011).

In future studies, researchers should combine NIBS protocols with neuroimaging to map stimulation-induced changes at a larger network level to increase the current understanding of the neural correlates associated with behavioral modulation. Such studies will provide a more comprehensive picture of how the reading network in impaired readers works and responds to neurostimulation. Since the effects of NIBS protocols are often less focal than expected and the functional relevance of remote effects has been demonstrated in previous work (e.g., Hartwigsen et al., 2017), a network perspective will help to better understand the functional relevance and interaction of different key areas for reading. Moreover, such combinations will also provide insight into potential compensatory changes in response to disruptive NIBS protocols at a larger network level. For example, previous work in the language domain has demonstrated that inhibition of core language regions with TMS results in compensatory upregulation of other left-hemispheric language areas and homologous right-hemispheric regions and also changes task-related connectivity between these areas (Andoh & Paus, 2011; Hartwigsen et al., 2013, 2017; Jung & Lambon Ralph, 2016). Such changes are referred to as compensatory short-term reorganization (Hartwigsen, 2018) and may provide insight into the potential of the language (or reading) network to adapt to challenges induced by neurostimulation. A better understanding of the flexible interplay within and between specialized networks may further help to inform treatment approaches about promising target regions that show strong functional connectivity with other parts of the reading network. We believe that aside from focusing on the potential of different NIBS protocols to support treatment in reading impaired individuals, NIBS studies in the healthy reading network will help to increase the current understanding of the neural basis of reading.

To sum up, studies to date have targeted different areas with different stimulation protocols (except for those studies performed by the same group with overlapping participants) and none of the combined reading and NIBS intervention studies has included a control group without reading training. Therefore, more studies are needed to identify the optimal length and intensity of behavioral interventions combined with NIBS and the duration of the induced after-effects. Since the overall number of studies is scarce, it is necessary for future studies to identify the relevance of specific regions for reading processes, test larger samples and combine stimulation with different forms of behavioral interventions. From a methodological viewpoint, most studies applied tDCS and are therefore clearly limited in spatial resolution. Using high-definition tDCS or TMS could help to overcome this issue. Even if TMS studies in children are not easy to realize due to safety precautions, it seems equally promising to use well-designed studies in dyslexic adults to enrich our understanding of the reading-impaired brain. Additionally, recent advances in biophysical modeling of the NIBS-induced currents in the brain may help to optimize electrode montages for tDCS interventions and coil positions for TMS application (e.g., Opitz, Fox, Craddock, Colcombe, & Milham, 2016; Weise, Numssen, Thielscher, Hartwigsen, & Knösche, 2020). Finally, the use of rhythmic TMS or tACS may offer the possibility to further target and modulate specific atypical oscillatory patterns (Kraus, 2012) in dyslexia, and link these to reading processes. Doubtlessly, identifying and modulating task-specific oscillatory patterns during different reading processes may further increase the knowledge of the neurobiology of reading and reading disorders.

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Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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