Brain Stimulation 13 (2020) 1813–1820

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Transcutaneous auricular vagus nerve stimulation enhances learning of novel letter-sound relationships in adults

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A R T I C L E I N F O

Article history:
Received 18 January 2020
Received in revised form
22 September 2020
Accepted 21 October 2020
Available online 27 October 2020

Keywords:
Plasticity
Reading
Automaticity
Decoding
Intervention
Fluency

A B S T R A C T

Background: Reading is a critical skill in modern society but is significantly more difficult to acquire during adulthood. Many adults are required to learn a new orthography after this window closes for personal or vocational reasons and while many programs and training methods exist for learning to read in adulthood, none result in native-like fluency. Implantable cervical vagus nerve stimulation is capable of driving neural plasticity but is invasive and not practical as a reading intervention.
Objective: The goal of the current study was to evaluate whether non-invasive transcutaneous auricular vagus nerve stimulation (taVNS) is effective at enhancing novel orthography acquisition in young adults.
Methods: We enrolled 37 typically developing participants and randomly assigned them to a computer control, device sham control, earlobe stimulation control, or experimental transcutaneous auricular stimulation (taVNS) group. Participants then learned novel letter-sound correspondences in Hebrew over five training lessons. Performance was assessed using three measures to evaluate various aspects of reading: Letter ID, Automaticity, and Decoding.
Results: The taVNS group significantly outperformed the three control groups on both the Automaticity and Decoding tasks. There was no difference on the Letter ID task.
Conclusions: These results demonstrate, for the first time, that taVNS is capable of improving aspects of reading acquisition in adults. These findings have potential implications for a wide range of cognitive tasks.

Introduction

Reading is a critical skill for modern life, as daily communication relies on print. The development of the brain's reading network is a protracted process, requiring many years of practice, lasting into early adulthood [1–3]. The sensitive period for reading closes around the age of 18–19 [4,5], possibly due to the long trajectory for reading network acquisition and the amount of practice needed to achieve expertise. One marker of expertise is fluency, the ability to read and comprehend a word without decoding individual letters [6,7]. Although adults learning to read in a novel orthography may achieve a level of speed that allows for comprehension, they may never achieve native-like fluency. In spite of this obstacle, there are many situations in which an adult may need to achieve native-like fluency in a new orthography. Some examples include business professionals needing to review documents during international meetings, subsequent generations of immigrant families wanting to read historical scriptures, and military officers needing to communicate with local residents during deployment and times of critical events. Prior research on literacy programs suggests that adults can learn to read when provided adequate training, but the learning time is long and retention performance is poor [4,5]. It is therefore clear that current behavioral programs are insufficient to induce long-term fluency. Thus, the goal of the current study was to

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https://doi.org/10.1016/j.brs.2020.10.012

evaluate a novel method for re-opening the brain's sensitive window for orthography learning.

One established method involves stimulating the vagus nerve to activate the nucleus tractus solitarius (NTS), which has projections to the nucleus basalis (NB) and locus coeruleus (LC). Together, they release key neurotransmitters important for driving brain plasticity and learning and memory: acetylcholine [8] and norepinephrine [9], respectively. In mice, stimulation of NE was found to aid in long term potentiation for an extended period of time [10] and stimulation of the LC aided rats in an auditory perception task [11]. Further, disruption of norepinephrine release in rats blocked plasticity driven by vagus nerve stimulation (VNS) [12,13]. These regions are also tied to learning in humans, as higher LC activation is associated with improved memory on a delayed gratification task [14]. VNS allows for targeted release of norepinephrine and acetylcholine without invasive direct brain stimulation (i.e., deep brain stimulation), providing easier access to this neural plasticity mechanism in patient populations.

Cervical vagus nerve stimulation (cVNS) is FDA approved for the treatment of epilepsy [15,16] and depression [17] and is in clinical trials for stroke [18] and tinnitus [19]. This approach involves surgically implanting a cuff electrode around the vagus nerve, located in the neck, and a pulse generator positioned subcutaneously below the clavicle or axilla. Pairing the timing of cVNS with an external stimulus (e.g., sound or movement) drives long-lasting and meaningful neural plasticity [20–22]. For example, cVNS paired with a specific tone drives sensory plasticity in primary auditory cortex (A1) of a rat, specific to the frequency of the paired tone [21]. This approach led to a novel tinnitus treatment, now in clinical trials [19]. cVNS is also capable of driving plasticity in the motor cortex when paired with specific movements both in the rat model [23–25] and in clinical trials with patients experiencing upper limb motor deficits [18].

In the cognitive domain, cVNS, has increased performance on tasks relying on working memory [26–28]. For example, delivering cVNS after paragraph reading improved recognition of highlighted words [26]. In another study, participants receiving cVNS had decreased error rates during a delayed recall task [27]. cVNS also improved performance on digit-symbol and verbal fluency tasks [28]. Together, results demonstrate that cVNS can increase performance and decrease error rates in cognitive tasks, suggesting it may also aid in other cognitive tasks, such as reading.

In spite of the success with cVNS, such an invasive and expensive procedure is not a practical intervention for cognitive skills like reading. The auricular branch of the vagus nerve (ABVN) projects to the outer ear and can be accessed at either the cymba conchae region of the pinna [29–31] or the posterior surface of the tragus [32]. fMRI studies have demonstrated that transcutaneous auricular vagus nerve stimulation (taVNS) activates similar medullary and deep brain structures as cVNS, without the need for an invasive surgery [29,31]. Growing evidence suggests that taVNS may also provide a comparable neural plasticity effect compared to cVNS. For example, taVNS improved rehabilitation of post-stroke motor function recovery in humans [30] and increased performance on a memory task in older adults [33]. Given the comparable success of taVNS and cVNS on improving motor control after stroke and improving cognitive tasks, we hypothesized that taVNS paired with training would significant improve orthography acquisition in five days.

Methods

Participants

In total, 122 participants were screened for eligibility, with 37 participants meeting these criteria. To be eligible for the study, participants needed to: (a) be a native English speaker, (b) be between the ages of 18 and 35, (c) achieve a standard score of 85 or higher on the KBIT-2 Matrices, (d) achieve standard reading scores of 90 or higher on each of the four measures described below, (e) have no history of neurological disorders, diagnoses, or medications, (f) have no medical implants, and (g) not been previously exposed to Hebrew or a language of similar orthography. We screened 122 individuals, but 4 were excluded for a low IQ score, 44 for low reading scores on one or more measures, 8 for exclusionary medications, 8 for medical implants, procedures, or diagnoses, 2 for previous exposure to a similar orthography, 3 for being outside of the age range, and 14 for issues in scheduling or withdrawing from the study. Two participants were trained but errors were made during administration of outcome assessments. Thus, our final sample included 37 participants. Participant characteristics and assessment scores (mean ± SD) by group are provided in Table 1. The protocol was approved by the Texas Christian University Institutional Review Board, and participants provided written informed consent prior to enrollment.

Participants were assessed using a background survey and a standardized battery to ensure they were fluent readers in their native English. The battery included the matrices subtest of the KBIT-2 [34], as a measure of nonverbal IQ, as well as four reading measures: the Sight Word Efficiency and Phonemic Decoding Efficiency subtests of the TOWRE-2 [35] and the Word ID and Word Attack subtests of the WRMT-3 [36]. In addition to these eligibility measures, we administered additional assessments, including the passage comprehension and oral fluency subtests of the WRMT-3 [36], rapid automatized naming (RAN) of digits and letters (CTOPP-2) [37], and working memory and attention subtests from the WRAML-2 [38]. A second researcher reviewed all scoring, and discrepancies were resolved by a consensus between both researchers. Participants also completed a brief Hebrew Letter ID pre-test to confirm no prior knowledge of to-be-learned letters. All participants scored less than 5% accuracy, with no group differences (Table 1).

taVNS device settings

Prior to placing the auricular neurostimulation device on the left ear (Fig. 1), participants cleaned the skin on and around the ear with an alcohol wipe to remove any excess oils and ensure optimal conductivity. Conductive hydrogels were placed on the earpiece to control current flow and ensure participant comfort. A 1-cm long cylindrical stimulating electrode was placed either at the left cymba conchae or the left earlobe, depending on group assignment. There are well-demonstrated differences in the effect of stimulating the left versus right branches of the vagus [39]. The right branch is connected to the sinoatrial node [40], making this branch more effective at driving cardiac change. To ensure activation of the NTS, which is critical for neural plasticity [20–22], and to avoid cardiac change, we chose to stimulate only the left ear [29,31]. The earlobe was used as a control location as fMRI studies demonstrated stimulation of the earlobe does not activate the NTS [29,31]. The current return electrode (1 cm × 3 cm) was located behind the ear over the mastoid bone. Current was delivered as a square, biphasic pulse, at 5 Hz, and a 200 μs pulse width. These parameters and electrode placement were chosen based on prior work [41,42]. Stimulation intensity was determined for each participant individually, as described below. The device was controlled by custom Python programming to ensure precise timing of the stimulation.

taVNS group assignment and thresholding

Eligible participants were randomized into one of four experimental groups: computer control, device sham control, earlobe

Table 1
Summary of participant demographics and standard scores (M ± SD) from baseline English assessments (N = 37). There were no main effects of group on any measure.

Group	Computer Control $n = 7$	Device Sham Control $n = 7$	Earlobe Stimulation Control $n = 9$	taVNS $n = 14$	F-Value
# Females	4	6	8	9	
Age	22.60 ± 4.88	20.31 ± 1.22	20.05 ± 1.46	21.26 ± 2.81	1.23
KBIT-2 Matrices	106.71 ± 16.00	111.86 ± 12.29	102.44 ± 9.61	107.71 ± 7.84	0.99
TOWRE-2 SWE	109.14 ± 10.96	108.71 ± 12.24	113.13 ± 13.40	106.71 ± 10.91	0.51
TOWRE-2 PDE	109.00 ± 6.95	103.42 ± 5.56	114.25 ± 11.17	107.14 ± 8.35	2.23
WRMT-3 Word ID	111.57 ± 6.58	105.43 ± 8.77	109.78 ± 6.44	108.07 ± 7.25	0.94
WRMT-3 Word Attack	101.43 ± 9.20	100.43 ± 10.31	106.00 ± 10.56	104.57 ± 8.71	0.61
WRMT-3 Passage Comprehension	101.00 ± 9.26	97.29 ± 16.82	95.89 ± 19.97	105.85 ± 9.21	1.12
WRMT-3 Oral Fluency	118.71 ± 13.17	112.57 ± 16.84	118.89 ± 11.05	115.71 ± 7.53	0.50
CTOPP-2 Digits	10.86 ± 2.34	12.29 ± 2.29	11.33 ± 2.00	11.43 ± 1.74	0.61
CTOPP-2 Letters	11.14 ± 1.68	11.71 ± 1.50	10.22 ± 1.48	10.71 ± 3.22	0.58
WRAML-2 Design Memory Core	11.86 ± 2.54	8.86 ± 3.24	10.78 ± 2.44	9.71 ± 2.67	1.73
WRAML-2 Verbal Learning Core	11.14 ± 1.35	11.29 ± 3.82	10.89 ± 2.82	11.43 ± 1.83	0.09
WRAML-2 Finger Windows	11.43 ± 3.41	10.29 ± 3.77	9.56 ± 2.65	9.86 ± 3.16	0.51
WRAML-2 Number Letter	12.14 ± 1.22	11.57 ± 3.82	12.00 ± 2.69	11.43 ± 2.65	0.15
WRAML-2 Design Memory Recognition	9.71 ± 4.54	8.43 ± 3.55	11.33 ± 2.74	10.86 ± 2.48	1.33
WRAML-2 Verbal Learning Recall	10.43 ± 2.76	11.57 ± 3.31	9.78 ± 3.31	11.43 ± 1.95	0.88
Hebrew Pre-Test	0.74 ± 1.97%	0.00 ± 0.00%	0.00 ± 0.00%	0.34 ± 1.27%	0.70

stimulation control, or experimental taVNS. The computer control group ($n = 7$) participants completed the automated training program without any interaction with or knowledge of the stimulator. The remaining participants went through a taVNS thresholding procedure, wore the earpiece, and were told they would receive stimulation during training. To account for placebo effects or beliefs about wearing the earpiece, the device sham control group ($n = 7$) wore the earpiece at the left cymba concha (the same anatomical location as the taVNS group) and was told stimulation would occur, but the device was turned off without the participants' knowledge. All sham participants were told that our thresholding procedure was designed to determine a comfortable stimulation intensity for each individual, and that each person may experience that current differently. At the end of the study, no participants reported being suspicious of their stimulation group.

To determine whether the sensation of stimulation anywhere on the left ear increased performance, the earlobe stimulation control group ($n = 9$) wore the device and received active stimulation to the left earlobe, as earlobe stimulation does not activate the NB or LC [29,31]. Finally, the taVNS group ($n = 14$) wore the earpiece during all training sessions and received stimulation to the left cymba concha.

All participants who wore the device, regardless of the electrode's location, completed a thresholding procedure in which a trained researcher determined a customized amount of current for each participant. Thresholding took place in the location the stimulator would be worn. To determine comfortable current for each participant, we obtained two measurements at minimum threshold and two at the upper level of comfort (Table 2) [31]. The upper level of comfort was defined as the point when stimulation became distracting and uncomfortable but prior to the onset of pain. The average of these four measurements was calculated and used as the current intensity setting during the training sessions. There were no group differences between the device sham control (2.04 ± 1.18 mA), earlobe stimulation control (1.51 ± 0.35 mA), and taVNS groups (1.68 ± 0.87 mA) in thresholding current intensity ($F(2, 27) = 0.81$, $p = 0.46$).

Training program

Eligible participants returned to the lab on five separate days for 30-min training sessions, which were conducted individually in sound-dampened testing rooms in the lab. We chose to train participants over several days to ensure we could measure higher-

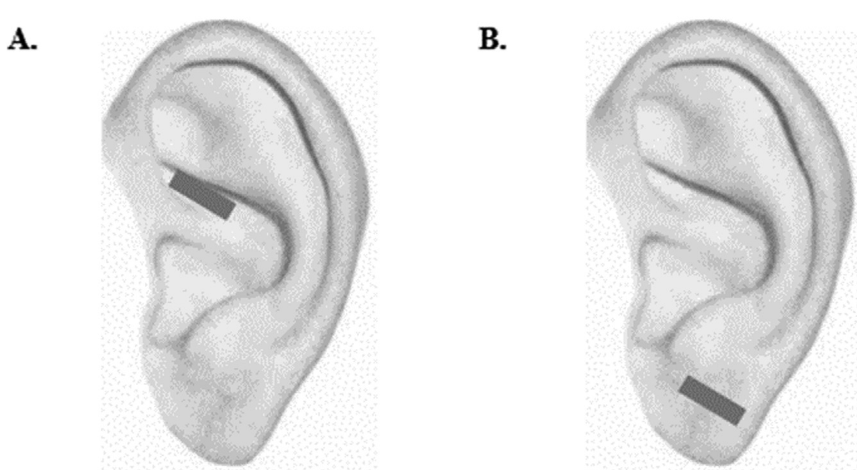

Fig. 1. *Electrode location in groups wearing the device.* The earpiece was placed on participants' left ear at locations shown by the gray bar. For the device sham and taVNS groups, the electrode was placed at the cymba concha region of the left ear (**A**). For the earlobe stimulation control group, the electrode was placed at the earlobe of the left ear (**B**).

Table 2
taVNS thresholding measurements. Thresholding procedure used with all participants in the device sham control, earlobe stimulation control, and experimental taVNS groups. Four measurements were acquired during thresholding for each participant. The average of these four measurements was used in subsequent training sessions and checked for comfort each day.

Value	Dialogue	Intensity (0–10 mA)
1	"Tell me when you feel anything unusual in your ear."	
2	"Tell me when the stimulation feels uncomfortable, but not painful."	
3	"Tell me when you cannot feel any stimulation in your ear."	
4	"Tell me when the stimulation feels uncomfortable, but not painful."	
TTI	Average of Values 1-4	

order reading skills, such as decoding. Lesson length was modeled after commonly used orthography training programs such as DuoLingo. At the beginning of each session, a brief test was conducted to ensure that the participant's customized level of thresholding current was comfortable. Then, the participant completed a self-paced lesson, presented through custom PsychoPy programming [43]. All instructions and feedback were provided by a pre-recorded, female native-English speaker. Participants were instructed to practice reading letters out loud and point along to the letters both during practice as well as during feedback. A trained researcher was always present in the room to ensure participant safety and compliance with instructions. No adverse events occurred during training.

Training lessons were structured in a uniform manner and were designed to mimic best practices for new orthography learning in adults [44]. Each training lesson began with a review of the letters learned on previous days. Next, one or two new letters were introduced and practiced individually (Fig. 2A), followed by practice in series of letters (Fig. 2B). For certain trials, font size and angle were varied to improve generalizability of learned letters. Participants verbally sounded out the sequence of letters and pressed a button when finished. After the participant read the series out loud, the correct responses to the same sequence were presented in the auditory domain while the participant pointed along, ensuring attention to the feedback. Those in the earlobe stimulation control and taVNS groups received stimulation during this multi-sensory auditory and visual feedback to ensure that only correct pairings were reinforced. Stimulation lasted approximately 6–8 s per sequence and occurred during approximately 215 letter-sound pairings per session. Finally, each training session concluded with participants practicing sequences of letters arranged as real or pseudowords, with the instruction to blend the sounds together (Fig. 2C). As in series practice, stimulation was only paired with feedback. After five training lessons, participants had learned two consonants and eight vowels in Hebrew using closely approximated English phonemes (Table 3).

Hebrew assessments

After five lessons, participants were assessed on their knowledge of trained Hebrew graphemes through three assessments: Letter ID, Automaticity, and Decoding. These measures were generated in-house and based on standard English assessments.

During the Letter ID task, participants were presented with sixteen consonant-vowel (CV) combinations, presented individually, and instructed to provide the correct sound, with no time pressure. This measure was based on the Letter ID task from the WRMT-3 [36]. An incorrect answer earned 0 points, a partially correct answer (i.e., getting the consonant or vowel correct, but not both) earned 0.5 points, and a correct answer earned 1 point. Scores were added together and converted to a percentage, where a higher score indicated better performance.

The Automaticity task was based on the RAN subtest of the CTOPP-2 [37]. Participants saw an eight-by-four grid of Hebrew CV combinations. The participant sounded out every CV combination on the entire card as quickly and accurately as possible. A researcher timed the task, rounded the time to the nearest second, and added a 1 s penalty per error made. Thus, better performance was indicated by faster times on this task.

Finally, the Decoding task was based on the Phonemic Decoding Efficiency subtest of the TOWRE-2 [35]. Participants viewed a card of pseudowords written in Hebrew and read through the list as quickly and accurately for 45 s. Performance on this measure was scored as percent correct. Higher performance was indicated by a higher percent correct.

Statistical analysis

A one-way ANOVA was used to evaluate whether there were effects of control condition on performance across the three dependent measures. No group differences were found, so control groups were combined to test our *a priori* hypothesis that taVNS would improve performance on letter-sound learning using one-

Table 3
Hebrew letters and pronunciations learned over the five-day training period. Sixteen letter-sound correspondences were taught over the course of the five training days. Two consonants (h and y) were taught on the first day, and vowels were added each day throughout the training.

Hebrew Letter	ה	י	◌ַ	◌ָ	◌ֶ	◌ֵ	◌ִ	◌ֻ	◌ְ	◌ֹ
Approximate English Translation	h	y	ah	ah	eh	eh	ee	oo	uh	oh

Fig. 2. *Structure of the training program.* **A.** Following review of previously learned graphemes, participants learned 1–2 new letters. For example, the vowel sound "eh," shown here by two dots below the consonant, in the context of previously learned consonants (ה and י). **B.** Participants then practiced all combinations learned to date in a series by reading from right to left. **C.** At the end of each session, participants completed word-like practice. Participants in the earlobe and taVNS groups received stimulation during feedback of series trials and word-like trials (**B**–**C**).

tailed independent-samples *t*-tests. Descriptive statistics for all outcome measures are presented as mean ± SEM.

Additionally, we conducted analyses to evaluate the relationships between English reading measures and performance on Hebrew outcome assessments. Spearman correlations (r_s) were used for the Letter ID task, as participants exhibited a ceiling effect, and Pearson's correlations (r) were used for the Automaticity and Decoding tasks. The Bonferroni correction was used to control for multiple comparisons within each set of correlations comparing English assessments to a single outcome measure (6 comparisons per set).

Results

taVNS improves novel orthography acquisition

Thirty-seven participants completed training and outcome assessments. We first evaluated performance across the control groups to determine whether there was evidence of a placebo effect in any of these conditions. There was no significant main effect of group for the Letter ID task ($F(2, 20) = 0.43$, $p = 0.65$; Fig. 3A), the Automaticity task ($F(2, 19) = 0.52$, $p = 0.60$; Fig. 3B) or the Decoding task ($F(2,19) = 0.83$, $p = 0.45$; Fig. 3C). The control groups were therefore combined for all subsequent analyses (see Supplement for additional analyses).

There was no significant difference in Letter ID performance between the combined control group (96.51 ± 1.20%) and the taVNS group (97.47 ± 1.44%; $t(35) = 0.52$, $p = 0.30$; Fig. 4A). On the Automaticity task, the taVNS group completed the task significantly faster (33.14 ± 2.32 s) than the combined control group (46.27 ± 4.34 s; $t(34) = 2.28$, $p = 0.014$; Fig. 4B). On the Decoding task, the taVNS group had a higher percent correct (66.45 ± 3.68%) than the combined control group (57.49 ± 3.14%; $t(34) = 1.72$, $p = 0.048$; Fig. 4C).

Correlations between English and Hebrew reading measures

Secondary analyses were then conducted to examine the relationship between the six English reading measures (Sight Word Efficiency, Phonemic Decoding Efficiency, Word Identification, Word Attack, Rapid Digit Naming, and Rapid Letter Naming), administered in the initial assessment session and the Hebrew outcome assessments administered after training.

Across all control group participants ($n = 23$), there were nominally significant positive relationships between Rapid Digit Naming with Hebrew Letter ID ($r_s = 0.49$, $p = 0.02$) and Hebrew Automaticity ($r = 0.49$, $p = 0.02$), such that faster digit naming times were related to a higher percent correct on identifying Hebrew letters and on a timed decoding task. None of these comparisons survived correction (Table 4).

To determine whether English measures were predictive of benefits conferred by taVNS, we evaluated the same relationships in the taVNS group alone ($n = 14$). There was a nominally significant relationship such that higher scores on the Phonemic Decoding task in English were related to a higher percent correct on identifying Hebrew letters ($r_s = 0.59$, $p = 0.03$). In these analyses, the English Word Attack measure significantly correlated with all of the Hebrew assessments, such that higher scores on an untimed pseudoword task was related to a nominally higher percent correct on identifying Hebrew letters ($r_s = 0.60$, $p = 0.02$), faster times on a Hebrew Automaticity task ($r = -0.58$, $p = 0.03$), and a higher percent correct on the Hebrew Decoding task ($r = 0.56$, $p = 0.04$). No comparisons survived correction (Table 5).

Discussion

In the current study, we tested the hypothesis that taVNS paired with novel letter-sound correspondence training in Hebrew would improve performance on outcome measures. We observed a significant effect of taVNS paired with training on both Automaticity and Decoding, with no effect on Letter ID. These findings support the hypothesis that taVNS is effective at improving letter-sound learning in young adults.

Relationships between native and novel orthographies

Baseline measures of reading in young children, such as rapid naming and phoneme awareness measures, are predictive of future reading abilities [45]. In the current study, we found various nominally significant correlations between baseline English

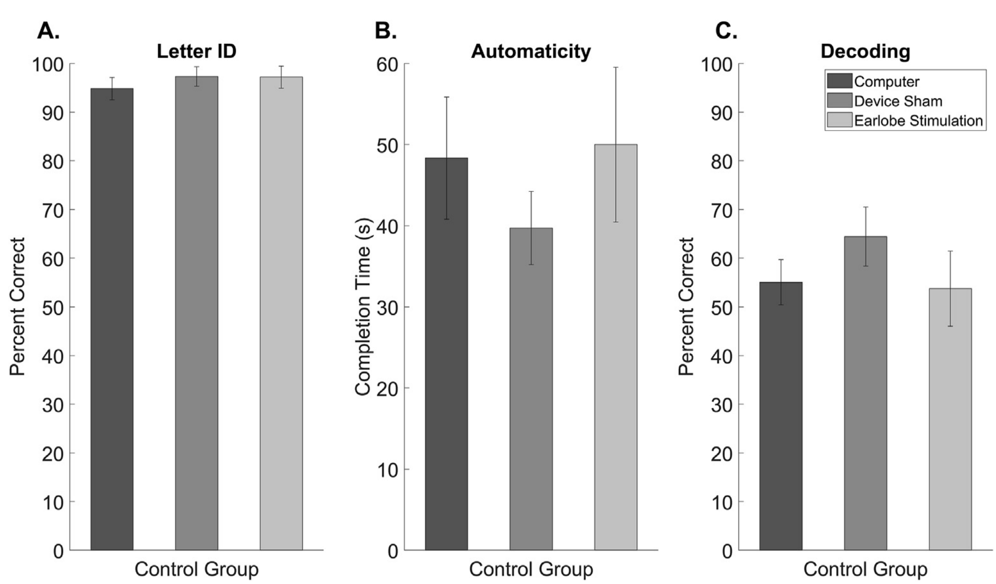

Fig. 3. *Performance on three measures across control groups*. There was no effect of control condition on Letter ID (**A**), Automaticity (**B**), and Decoding (**C**) after five days of training. Error bars represent standard error of the mean.

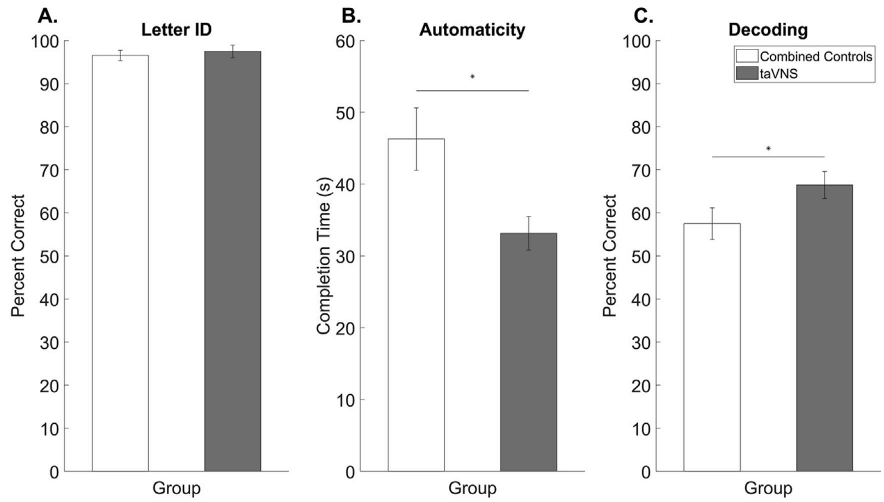

Fig. 4. *Effect of taVNS on three outcome measures.* **A.** There was no effect of taVNS on Letter ID due to a ceiling effect. **B.** taVNS significantly improved speed on the Automaticity task compared to controls. **C.** taVNS significantly improved percent correct on the Decoding task as compared to controls. *$p < 0.05$. Error bars represent standard error of the mean.

assessments and post-training Hebrew assessments. It is important to note that none of these correlations survived correction, so the interpretation of these results should be considered with caution, and future well-powered studies are needed to confirm these findings.

Across the control groups, there were nominally significant positive relationships between rapid digit naming and Letter ID and Decoding in the novel orthography. RAN is a common measure of naming speed and is associated with future reading outcomes in children [45,46]. Thus, it is not surprising that in our sample, individuals with better rapid automatized naming in English performed better on tasks in the novel orthography. It is interesting to note, however, that the relationship was limited to digits, perhaps suggesting that in the short time window of training, novel letters were processed more like symbols than letters. Early in reading acquisition, letter symbols are processed largely by right hemisphere regions as objects, with a leftward lateralization occurring only with practice [3,47]. The brain's reading network is not hard-wired and develops with practice and instruction. The brain may therefore need more practice than provided in our training in order for the VWFA to process a novel orthography as print rather than as symbols. When other symbols, such as houses [48] and faces [49] are used as a system of print, ten training sessions were used to evoke activation in the left VWFA for trained versus untrained stimuli. Future well-powered studies should investigate such training programs over a longer trajectory to determine whether novel orthography symbols are ever processed in the same brain region as native orthographies.

In the subset of participants receiving taVNS, a different pattern of relationships emerged. Interestingly, the relationships between rapid digit naming and the novel orthography measures were no longer significant. Instead, timed decoding was significantly correlated with Hebrew Letter ID, and performance on an untimed pseudoword reading measure (Word Attack) was significantly correlated with every outcome measure. The Word Attack measure in English requires knowledge of the letters, an automatic connection between the letter and the phoneme, and the ability to blend sounds together to decode non-words. It is interesting that the rapid naming measures were not correlated with outcomes in the taVNS group. If RAN scores predict learning of a novel orthography using purely behavioral methods as discussed above, it may suggest that such training approaches encourage the brain to follow the same trajectory as in initial reading acquisition, with novel letters processed as symbols prior to being recognized as print. The lack of relationship between RAN and outcome measures in the taVNS group suggest that taVNS may push the brain to bypass this process and instead take advantage of existing left-hemisphere circuits already well suited for the task at hand. Future work, including neural imaging, is needed to determine whether taVNS accelerates the normal trajectory for orthography acquisition or pushes the brain to use existing circuits more effectively. As discussed above, no correlations survive corrections, so future well-powered studies are needed to see if the findings are replicated.

Applications for non-invasive stimulation

The ability to read fluently in a novel orthography is increasingly important in the modern developed world. Well-known and highly used programs, such as Rosetta Stone and DuoLingo are useful in second language learning and contain an orthography component, but the effects are dubious [50]. The addition of a non-invasive stimulation component may improve orthography learning in typical readers, as our results demonstrate a significant benefit of taVNS on orthography learning in five days.

Table 4
Correlations between six English reading measures and the three Hebrew assessments in control group participants (n = 23).

	Sight Word Efficiency	Phonemic Decoding Efficiency	Word Identification	Word Attack	Rapid Digit Naming	Rapid Letter Naming
Letter ID	0.36	0.31	−0.04	0.15	0.49*	0.07
Automaticity	−0.06	−0.03	−0.26	0.30	−0.41	−0.28
Decoding	0.23	0.17	0.22	−0.17	0.49*	0.28

Note. * signifies $p < 0.05$. No correlations remain significant after adjusting for multiple comparisons.

Table 5
Correlations between six English reading measures and three Hebrew assessments in the taVNS group (n = 14).

	Sight Word Efficiency	Phonemic Decoding Efficiency	Word Identification	Word Attack	Rapid Digit Naming	Rapid Letter Naming
Letter ID	0.16	0.59*	0.48	0.60*	0.17	0.17
Automaticity	−0.24	−0.51	−0.44	−0.59*	0.09	0.05
Decoding	0.21	0.41	0.28	0.56*	0.11	−0.10

Note. * signifies $p < 0.05$. No correlations remain significant after adjusting for multiple comparisons.

In some countries, many individuals never acquire reading as children and are therefore learning to read for the first time as adults. Despite efforts by many international organizations to generate evidence-based literacy programs, most individuals never achieved native-like fluency [4,5,44], and a lack of practice leads to regression into illiteracy [5]. taVNS devices are small and portable and may be useful additives to literacy programs in regions of the world that are difficult to access. In the current study, all participants were well-educated, native readers in English, so it is unknown whether this approach will be effective in novice adults or struggling readers. Future research in these populations is needed to determine whether this approach is effective in illiterate adults.

Limitations

There are three main limitations of the current study. First, while the results were robust, a small sample size recruited from a pool of undergraduate students stunts the ability to generalize findings. Future studies should evaluate this approach in a larger group of individuals, to account for effects of gender, varied backgrounds and occupations, and a range of baseline reading abilities. Second, taVNS is a new technology, so future work is needed to understand parameters and interactions with neurotransmitters like norepinephrine, acetylcholine, and serotonin [12,13]. We chose a stimulation frequency based on previous research in epilepsy, migraine [51], and anti-inflammatory [52] models which demonstrated that lower stimulation frequencies (1–10 Hz) were more effective at activating associated neural structures than higher stimulation frequencies (20–30 Hz). However, VNS may also be effective at other current intensities [41,42] or frequencies, including 25 Hz [30–32], or 30 Hz [26], as well as in subthreshold conditions [53]. Our effect may be muted by the choice of a lower stimulation frequency. Future work should evaluate frequency optimization [41,42] and a comparison of stimulation at and below sensory threshold [53]. Third, we did not investigate whether the addition of taVNS improves retention of learned relationships after training ends. For taVNS to be relevant for the general public, the effects must be long-lasting. Therefore, future studies should include a measure of retention after training.

CRediT authorship contribution statement

Vishal J. Thakkar: Investigation, Formal analysis, Writing - original draft, preparation, Writing - review & editing. **Abby S. Engelhart:** Investigation, Writing - review & editing. **Navid Khodaparast:** Conceptualization, Methodology, Writing - review & editing. **Helen Abadzi:** Methodology, Writing - review & editing. **Tracy M. Centanni:** Conceptualization, Methodology, Software, Data curation, Supervision, Funding acquisition, Writing - review & editing.

Declaration of competing interest

The authors have no conflicts of interest to declare.

Acknowledgments

Aspects of this research were supported by the TCU Science & Engineering Research Center (SERC) [grant numbers 170306, 180535, and 180536 (awarded to Tracy Centanni)]. The authors would like to thank Nexeon MedSystems (https://www.nexeonmedsystems.com/) for the use of their stimulators, provided materials, and technical support. We would also like to thank Caiden Berry, Annie (Danyang) Dang, Jared Fox, Alexis Jefferson, Trinton Kahland, Nick Mattox, Grace Mortenson, Grace Pecoraro, Madeline Pitcock, Zoe Richardson, Rosie Robinson, Carly Stacey, Courtney Weeks, and Katheryn Wisely for their help in data collection and scoring. We would also like to thank Carly Stacey for recording the stimuli and instructions for the training program.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2020.10.012.

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