BRAIN STIMULATION CAN IMPAIR LONG-TERM RETENTION OF MEMORY

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Abstract

Using a SAFMEDS task (*Say All Fast a Minute Every Day Shuffled*; designed to build fluency), this study investigates whether anodal transcranial electrical brain stimulation (tES) over the left dorsolateral prefrontal cortex, can modulate both learning ability and subsequent long-term memory retention. Using a within-subject design, participants (N=25) took part in 6 training sessions over consecutive days in which active or sham stimulation was administered randomly (3 of each). A computer based SAFMEDS task was used, containing flags unknown to the participants from countries around the world. Each training session consisted of the repetition of 8 pairs of flag/country names. The aim was to say aloud the name of the countries at least 60 times in one-minute blocks to reach a performance-based threshold. In two testing sessions, one day after the final training session and one week later, participants were tested on all 48 flags they had learnt. The participants were tested on both free recall and recognition. Results showed no difference in learning speed between active and sham stimulation for the training sessions. However, in the sham condition, recognition was significantly greater in the second testing session, compared to the active condition. Marginal significance was found for free recall for the sham condition compared to active, in the second testing session. These results show that for this particular task, anodal-tES was ineffective at improving learning ability and of detriment to performance in subsequent recognition and free recall tests, compared to the sham condition.

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Introduction

Cognitive enhancement, the act of improving performance on a wide range of skills, has received much interest in the past decade, with a wide variety of methods showing improvements for memory (Erickson et al., 2011; Katz et al., 2017), reaction time (Bisson, Contant, Sveistrup, & Lajoie., 2007) and even performance in sport (Xiang, Hou, Liao, Liao, & Hu, 2018). For neuroscientists, observable cognitive enhancement can allow for a greater understanding of the mechanisms in the brain and provide platforms for further research into practical applications, such as in clinical domains. Applied Behavioural Analysis (ABA) is a discipline focussing on learning and behaviour (Baer, Wolf, & Risley, 1987). With its applications easy to administer, it has been effectively used in both clinical and educational settings since the 1960's. Here, using a technique of learning, known as Precision Teaching (PT) and a type of non-invasive brain stimulation, previously shown to improve cognitive functioning (Coffman, Clark, & Parasuraman, 2014); we aim to gain a greater understanding of how learning and memory can be modulated through both behavioural and non-pharmacological interventions. The effectiveness of a particular PT task will be observed in a controlled setting, with and without brain stimulation, to investigate the value of combining the two. Whilst the task used here stems from the discipline of ABA, during this study, a predominantly neuroscientific approach will be taken for both analysis and interpretation.

Precision Teaching

Precision Teaching (PT) is a method of learning and progress monitoring developed by applied behavioural analyst Ogden Lindsley, originally used to help children and adults suffering from psychosis (Lindsley, 1990). Today, PT methods are used predominantly for children with Autism Spectrum Disorder (ASD), with evidence in strong support of its beneficial effects (Kubina, Morrison, & Lee, 2002; Peters-Scheffer, Didden, Korzilius, & Sturmey, 2011). The emphasis of improvement is placed upon the teacher, who is responsible for monitoring the student's performance and subsequently tailoring instructions, in a way that will benefit the student. By focussing on observable behaviour, positive or corrective feedback can be provided, and learning is facilitated through an operant conditioning paradigm, where reinforcement is applied. After PT was found to be successful in a clinical setting, Lindsley realised its potential in education and began introducing it into schools across North America (Lindsley, 1990). Today, PT has developed into a multicomponent instructional system that is used in schools across the globe. When conducting PT, teachers are expected to use a chart known as The Standard Celeration Chart (SCC), developed by Lindsley in the 1960's, (Lindsley, 1990, 1992; Merbitz, Vieitez, Merbitz, & Pennypacker, 2004) to record and observe a child's progression (for a more in depth explanation of the SCC, see; Calkin, 2003, 2005). The most cited example of the effectiveness of PT occurred in Great Falls, Montana (Beck & Clement, 1991). Here, using the SCC and other methods suggested by Lindsley, teachers were able to increase pupils reading skills by 20% and mathematical skills by 40%, compared to a control group (Beck & Clement, 1991). Some of the interventions included in the model involved students practising basic skills with one minute timings, setting high standards (e.g. 70-90 digits per minute or 200 words orally read aloud per minute) and daily charting (Beck & Clement, 1991). The benefits of PT have been shown in many sample populations, from those suffering with learning difficulties (Kubina et al., 2002), to university students (Beverley, Carl Hughes, & Hastings, 2009), young children (Hunter, Beverley, Parkinson, & Hughes, 2016), to older adults (White, 1986).

Behavioural Fluency

PT focuses predominantly on improving behavioural fluency, a concept consisting of a combination of accuracy and speed (Binder, 2003), which can be applied across many domains. By increasing fluency, one can improve performance and efficiency on a task (Binder, 1996). Behavioural analysts will check to see if fluency has been achieved on a particular skill by using the acronym, RESA, developed by Johnson and Layng (1992; adapted from Haughton's "REAPS", 1981). RESA consists of; Retention, to see if the skill can be remembered at a later date; Endurance, to test for stable performance on a skill without fatigue; Stability, to see if the skill can be carried out with distractions; and Application, to see if the skill is transferable to other situations (Fabrizio & Moors, 2017). If all of these aspects have been met, then it can be said that one has achieved true mastery in that specific field.

SAFMEDS

An example of a PT task that aims to build behavioural fluency is a SAFMEDS task, an acronym for *Say All Fast a Minute Every Day Shuffled*. Developed by Lindsley in the late 1970's (Graf & Auman, 2005), a SAFMEDS task could consist of, but is not limited to, a selection of cards with visual prompts on one side and a description or answer on the other. The participant's aim is to work through the cards by vocally recalling as many of the correct answers to the visual prompts as possible. Following this, they are instructed to work through as many of the cards as possible in one minute, putting correct answers in one pile, and incorrect in the other. After counting through the piles and repeating any cards they answered incorrectly, they will eventually be able to answer all correctly (Merbitz et al., 2004). For a comprehensive guide, and the many applications of SAFMEDS, see Graf and Auman (2005) and for recommended thresholds of fluency, Kubina (2002).

The success of the SAFMEDS has been well documented in the literature, in a wide range of settings (Beverley et al., 2009; Hunter et al., 2016). Greene, McTiernan and Holloway (2018) found that when SAFMEDS was used in conjunction with peer tutoring in children, those who used a SAFMEDS task designed to increase mathematical fluency, had a significantly greater ability than that of the control group, post-intervention. The same achievement has been found at higher levels of education. In a university statistics class, Beverley et al., (2015) recruited 55 psychology undergraduate students scoring in the 50th percentile or lower in the first exam of the year. They were then separated in to either a control group or a condition where they were taught to self-administer a SAFMEDS task. Results showed a significant improvement in the group learning with SAFMEDS for each weekly test during the semester, compared to traditional learning methods. The lasting effects of SAFMEDS have also been shown, with knowledge acquired through SAFMEDS still maintained up to 1 month later (Hunter et al., 2016).

A SAFMEDS task has yet to be used as a behavioural measure in a lab-based experiment. Whilst it can be comparable to certain cognitive tasks, one important and key difference is that cognitive tasks generally have a predefined number of trials, thus exposure to stimuli is identical for all participants. For a SAFMEDS task, as learning is understood in ABA to be unique, the task ends when a predefined ability threshold has been met, therefore ability should be equal across all participants. In this instance, this should reduce discrimination of ability and thus allow for clearer behavioural observations following tES.

Transcranial Electrical Stimulation

Whilst PT tasks such as SAFMEDS have been shown to accelerate learning compared to traditional teaching methods, there are other techniques in which cognitive improvements can be found. There is much literature in support of transcranial electrical stimulation (tES) as a method of enhancement across multiple cognitive domains, dependent on task and the site of stimulation (Coffman et al., 2014). Transcranial direct current stimulation (tDCS), a form of tES, delivers a weak electrical current at the site of the electrode placement. By either inducing depolarisation (anodal stimulation) or hyperpolarisation (cathodal stimulation) of neurons (Miniussi, Harris, & Ruzzoli, 2013), it has the potential to alter cortical activity which, in turn, can cause variations in perception, cognition and behaviour (Fertonani & Miniussi, 2017; Nitsche et al., 2008). Whilst there are other forms of tES available, such as tACS, there is far less research into this method, with results inconclusive (Braun, Sokoliuk, & Hanslmayr, 2017; Hanslmayr, Axmacher, & Inman, 2019). Therefore, tDCS was chosen as there is more evidence to suggest it can provide cognitive improvements (see below). Here, the left Dorsolateral Prefrontal Cortex (left-DLPFC) was chosen as the site of stimulation, as this has been shown to be involved in a number of cognitive processes, including decision making performance (Hecht, Walsh, & Lavidor, 2010; Philiastides, Auksztulewicz, Heekeren, & Blankenburg, 2011), working memory performance (WM; Andrews, Hoy, Enticott, Daskalakis, & Fitzgerald, 2011; Fregni et al., 2005), reaction time (Brunoni & Vanderhasselt, 2014; Loftus, Yalcin, Baughman, Vanman, & Hagger, 2015; Zaehle, Sandmann, Thorne, Jäncke, & Herrmann, 2011) and long-term memory performance (LTM; Javadi & Cheng, 2013; Javadi & Walsh, 2012). Hereafter, all references to brain stimulation can be assumed to be concerning the left-DLPFC, unless otherwise stated. The SAFMEDS task follows an information processing sequence of perception, decision making and response, with all aspects of memory and reaction time tested.

tDCS and Working Memory

There is much evidence to suggest that anodal stimulation over the left DLPFC can enhance WM abilities (Andrews et al., 2011; Fregni et al., 2005; for a review, see Brunoni & Vanderhasselt, 2014). This is said to be, in part, due to an increase in oscillatory brain waves in both alpha and theta bands (Zaehle et al., 2011), responsible for improved concentration and memory performances (Klimesch, Doppelmayr, Schimke, & Ripper, 1997; Klimesch, Schimke, & Schwaiger, 1994; Vernon et al., 2003). Using an n-back task, Zaehle and colleagues (2011) found a significant increase in accuracy and decrease in reaction time (RT) for those receiving stimulation, compared to a control group. The same has been shown in a meta-analysis by Brunoni and Vanderhasselt (2014) where, again, both accuracy and RT were improved in almost all studies cited. Furthermore, Nikolin et al., (2015) noted not only a decrease in RT following stimulation, but an increase in the rate of verbal learning. Imaging studies have shown that activity occurs in the DLPFC and hippocampus during WM maintenance, which in turn, is predictive of successful LTM formation (Blumenfeld, 2006; Ranganath, Cohen, & Brozinsky, 2005). However, although these studies have served to highlight the success of tDCS for the improvement of many aspects of memory, there are also many non-findings. In a review, Horvath, Forte and Carter (2015) presented studies investigating multiple elements of cognition, finding no significant standardised mean difference effect sizes for any aspects of memory. This review, however, only focussed on single session tDCS studies.

tDCS and Long-Term Memory

Although not studied as extensively as WM, the effects of brain stimulation over the left-DLPFC have also been shown to improve LTM performances (Gray, Brookshire, Casasanto, & Gallo, 2015; Javadi & Cheng, 2013; Javadi & Walsh, 2012; Manenti, Brambilla, Petesi, Ferrari, & Cotelli, 2013; for a review, see Dedoncker, Brunoni, Baeken, & Vanderhasselt, 2016). Indeed, as little as 1.6 seconds of stimulation prior to stimulus onset has shown to be an effective modulator of verbal declarative memory (Javadi, Cheng, & Walsh, 2012). Using stimulation during a face/name recognition task, Leshikar et al., (2017) found improved recall of face names with only pictures of faces shown, but no improvement in recognition of faces when matched alongside a name. Aside from the self-paced aspect of the above study, it appears to be the most similar to the current study, in that, the participant must match the picture to a word, creating a semantic representation of the two. Other studies have also found improved recall of visual stimuli following anodal tDCS (Balzarotti & Colombo, 2016; Jones, Gözenman, & Berryhill, 2014) however, these increases were only found in certain cases, i.e. stimulation applied at specific time points, or only affecting particular aspects of memory retrieval; highlighting the need for further clarification. As with WM studies, there have been several non-findings for studies of long-term memory (Elmer, Burkard, Renz, Meyer, & Jancke, 2009; Hammer, Mohammadi, Schmicker, Saliger, & Münte, 2011). Furthermore, there is still a debate as to whether stimulation is most effective when administered during encoding (online) or before/after encoding (offline). Medvedeva et al., (2019) found memory improvements only when memorisation was intentional and administered online, with no effects for offline stimulation.

Hypotheses

Here, for the first time, we apply tDCS concurrently with a SAFMEDS task, to ascertain whether learning speed can be further accelerated, and whether the combination of the two positively or negatively affects LTM for items learnt during the task. The SAFMEDS task was computerised and aimed to teach participants flags of the world unknown to them. The analysis and discussion will be entirely from a cognitive perspective, measuring both recognition and free recall ability in the test sessions. With previous literature highlighting the beneficial effects of tDCS over the left DLPFC, for both WM and LTM, it was hypothesised that in the training sessions where brain stimulation was administered, the participant would require less blocks to reach the fluency threshold (in this case, 60 flags recalled per minute). Secondly, it was also hypothesised that as the flags learnt during the active stimulation sessions would have been presented less (assuming learning speed was increased), there would be a detrimental effect on subsequent recognition and free recall tests. Therefore, flags learnt during sham stimulation would be remembered for a greater length of time (see Figure 1 for a visual depiction).

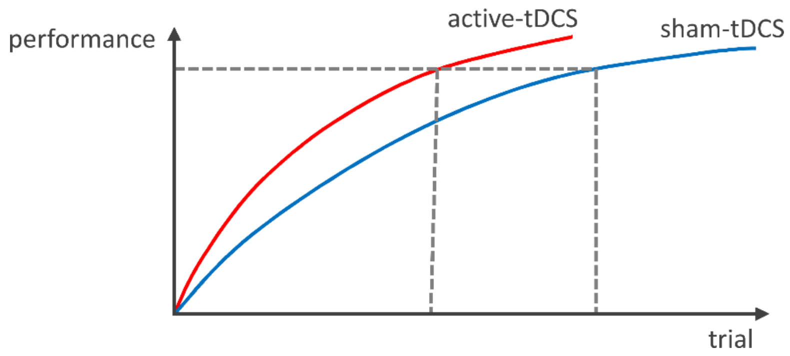

Figure 1. A visual representation of the hypotheses; showing accelerated learning for anodal brain stimulation. Dotted lines indicate hypothetical crucial threshold for long term retention.

Methods

Participants

A total of 25 participants took part in the experiment (21 females, 4 males, age range 18-21, mean [SD] = 19.20[0.84]). Due to both time and resource constraints, the sample size in this study was fixed and therefore a sensitivity power analysis was conducted. With 25 participants at 80% power, the minimum detectable effect size was $f = .29$, a medium effect size according to Cohen's (1988) criteria. All participants spoke fluent English and had normal or corrected to normal vision and hearing and did not report any neurological or learning difficulties. Written informed consent was received from all participants before the study began. The procedure of the study was approved by the local ethics committee in the School of Psychology at the University of Kent.

Study Design

The study adopted a within subject design, with an initial baseline measure completed in the first session to identify how many flags the participant already knew. Participants who knew more than 12 flags (out of 60) were excluded from the study. Following this, over the course of six 30-minute training sessions, participants learnt 48 flags. These six sessions were split over three Active- and three Sham-tDCS, which were pseudo-randomly assigned to each training session with neither stimulation type repeated three times in a row.

Table 1. List of the 60 flags used in the Baseline session, 48 were subsequently chosen at random for the training sessions.

Afghanistan	China	Guatemala	Kyrgyzstan	Nepal	Suriname
Albania	Colombia	Guinea	Laos	Nigeria	Swaziland
Algeria	Comoros	Haiti	Lebanon	Panama	Tanzania
Angola	Croatia	Honduras	Lesotho	Peru	Thailand
Barbados	Cuba	Iceland	Libya	Philippines	Togo
Belize	Egypt	India	Liechtenstein	Qatar	Tunisia
Bhutan	Estonia	Indonesia	Madagascar	Rwanda	Uganda

Botswana	Gabon	Japan	Malta	Seychelles	Vanuatu
Brunei	Georgia	Kazakhstan	Mexico	Somalia	Zambia
Cameroon	Grenada	Kenya	Morocco	Sudan	Zimbabwe

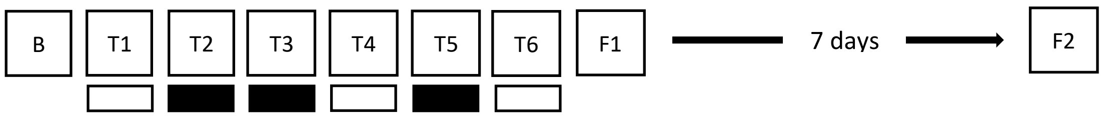

Figure 2. A visual timeline of the study. B indicates the baseline session, T1-6 indicate the six 30-minute training sessions. F1-2 indicates the two 30-minute testing (follow up) sessions, separated by seven days. All sessions (apart from F2) were conducted on consecutive days. Black and White boxes give an example of how the randomization pattern for the stimulation may have looked, Black = Active stimulation; White = Sham stimulation. No stimulation was administered in any other sessions.

SAFMEDS task

Following set up and initiation of the brain stimulation device, training sessions consisted of a computerised variation of a SAFMEDS task, with 8 different flags of uncommon countries presented in each session. The aim was for participants to learn all 8 flags shown in the session and be able to repeat them 60 times in 1 minute (recommended frequency aims for “See/Say task”; Fabrizio & Moors, 2017). Following participant’s response, the experimenter indicated accuracy via a mouse-button click. To assist with pronunciation, for the first minute block, a computerised voice read aloud the name of the country upon mouse click by the researcher, before moving on to the next flag. This continued until there were no longer any errors made and the participant could reach the threshold of 60 flags per minute or a maximum of 17 one-minute blocks. Whilst participants were aware of the aim of the study, they were told not to practise the task outside of the sessions.

tDCS

Using the 10/20 international method for measurement (Homan, Herman, & Purdy, 1987), one anodal 35 x 35 mm saline-soaked surface sponge was placed over the left dorsolateral prefrontal cortex and held in place using a bandage and clips. The reference electrode was placed on the top of the participants left wrist. The stimulation device used was a DC Brain Stimulator Plus (NeuroConn, Ilmenau, Germany). The experiment adopted a single-blind protocol as the stimulation device used did not accommodate for a double-blind protocol. For the active conditions, 1.5mA of anodal stimulation with 10 seconds fade-in and out was delivered for 15 minutes in total, starting 5 minutes prior to the beginning of the task. This was to allow the stimulation to take effect in the Active-tDCS condition. For the sham condition, the procedure was identical, however stimulation was discreetly turned off after 20 seconds. All participants believed they were receiving brain stimulation in some form and were told that varying protocols of stimulation were used, to account for differences in sensation at the site of stimulation.

Testing Sessions

Following the baseline and six training sessions, on the eighth day, participants took part in the first of two follow up sessions. Upon arrival, participants were asked to recall as many of the countries of the flags they had learnt during the six training sessions. This was timed for one minute and their responses were recorded on a voice recorder. Following this, participants took part in a self-paced refresher of all 48 flags, with a computerized voice giving feedback, as in the first block of the training sessions. The refresher was carried out to remove any possible recency effects of the flags. Following the refresher, participants took part in a recognition task consisting of two, 1-minute blocks, to account for both stimulation types (active and sham), without feedback. Correct and incorrect answers were marked by the researcher on paper, on a list generated prior to the study. This concluded the first testing session. The second testing session took part one week later and was identical to the first session.

Statistical Analysis

Data analyses were performed using SPSS (v25; LEAD Technologies, Inc, Charlotte, NC). A paired samples two-tailed t-test was conducted to observe the effectiveness of brain stimulation on learning ability. Two, 2 × 2 repeated measure analysis of variance (rANOVA) were conducted to investigate the main effects of brain stimulation and both testing sessions on recognition and free recall. A post hoc paired samples two-tailed t-test was subsequently run to investigate the differences between Session 1 and 2 for both recognition and free recall. Effect sizes were interpreted based on Cohen's (1988) scales of magnitude. A rANOVA was conducted to investigate whether learning ability increased over training sessions. A post hoc paired samples two-tailed t-test was then run to see if fewer blocks were required to reach the ending criterion from training session 1 to training session 6.

Results

To investigate the effect of anodal brain stimulation on learning ability, a two-tailed paired samples t-test was run to compare the total number of blocks required to reach the threshold (60 flags in 1 minute) during both the Active and Sham stimulation sessions. No significant difference was found between the two, indicating that stimulation had no effect on learning ability; mean[SD], Sham = 8.693[4.282], Active = 9.119[3.889], $t(24) = 0.788$, $p = 0.438$). A 2 × 2 rANOVA was run to determine the main effects of both test sessions and brain stimulation conditions on Recognition. A significant main effect was found for both session number and stimulation condition, with participants recognising more flags in the second session for the sham condition only. Large effect sizes were obtained for both main effect of session ($\eta_p^2 = 0.792$) and stimulation condition ($\eta_p^2 = 0.299$) for recognition. There was no interaction effect (see Table 2). A 2 × 2 rANOVA was run to determine the main effects of both test sessions and brain stimulation conditions on Free Recall. A significant main effect was found for session, but not stimulation condition. Participants recalled more flags in the second session. A large effect size was found ($\eta_p^2 = 0.543$). There was no interaction effect (see Table 2).

Table 2. 2 × 2 rANOVA(s) showing the Main Effects of Session and Stimulation Condition for both Recognition and Free Recall.

	Recognition			Free Recall		
Effect	$F(1,24)$	p	η_p^2	$F(1,24)$	p	η_p^2
Main effect of Session	91.120	.001	0.792	28.470	.001	0.543
Main effect of Stim. Condition	10.254	.004	0.299	1.474	.237	0.058
Interaction of Session & Stim. Condition	1.240	.276	0.049	1.261	.272	0.050

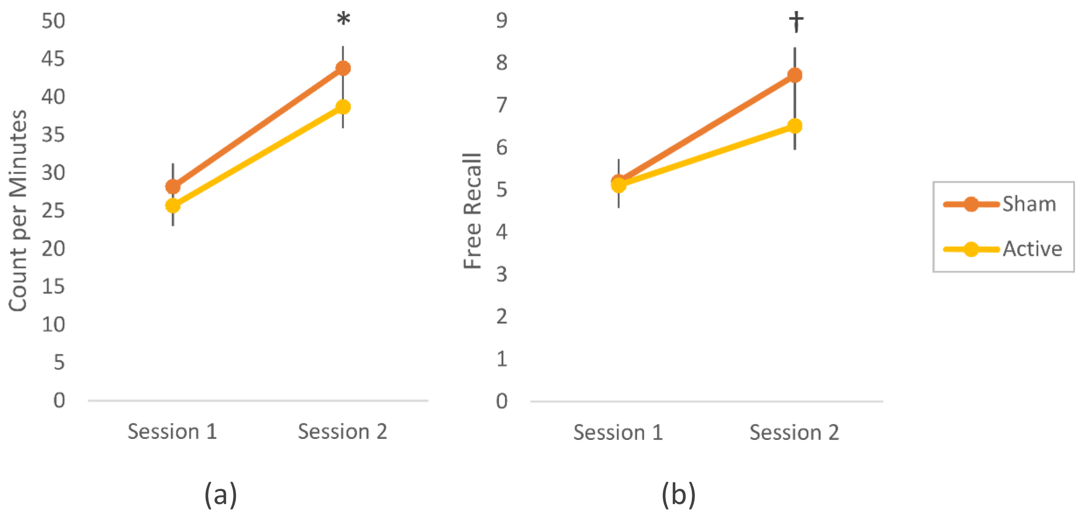

Figure 3. Plotted graph showing results of Recognition and Free Recall tests for both Sessions and Stimulation Conditions. $^{*}p < 0.001$, $^{\dagger}p = 0.078$, Error bars represent S.E.M.

Although there was no significant interaction effect, post-hoc two-tailed t-tests were run to investigate the differences between Session 1 and Session 2 for each type of LTM test; recognition and free recall. Recognition was significantly better in the second session compared to the first. Marginal significance was found for Free Recall between sessions (see Table 3).

Table 3. Paired samples two-tailed t-test showing comparisons between Session 1 and Session 2 for both Recognition and Free Recall.

	Session 1	**Session 2**
Recognition	t(24) = 1.238, *p* = 0.228	t(24) = 4.240, *p* < 0.001
Free Recall	t(24) = 0.118, *p* = 0.907	t(24) = 1.844, *p* = 0.078

To investigate whether learning ability improved as more sessions were completed, a rANOVA was conducted on the number of one-minute training blocks required to reach the threshold. Results suggested a significant difference ($F(5, 120) = 3.565$, p = 0.005, $\eta_p^2 = 0.129$ and therefore a post hoc paired-sample two-tailed t-test was run on the first and last sessions ($t(24) = 3.057$, $p = 0.005$). This suggested that participants increased their learning speed between training sessions 1-6 (see Figure 4).

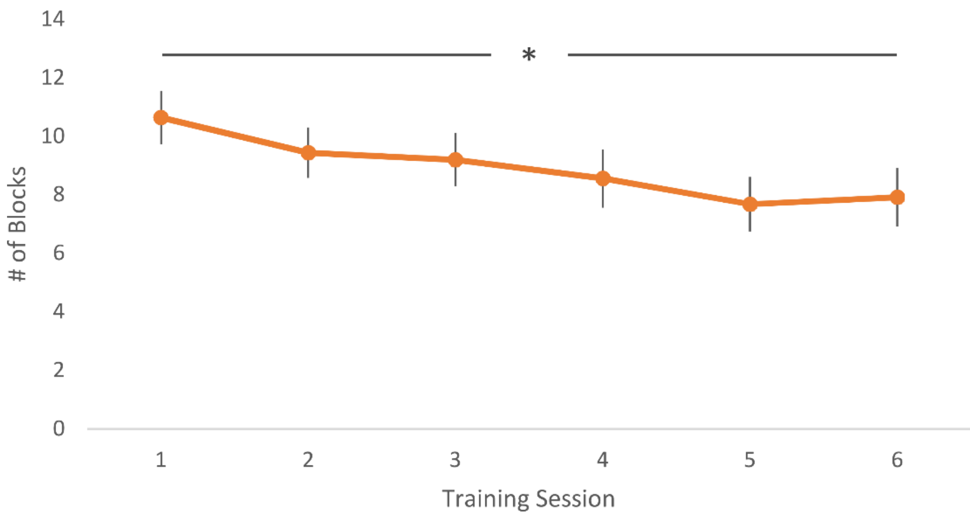

Figure 4. Plot showing the number of blocks required to meet threshold (60 flags) over the six training sessions. $^{*}p = 0.005$, Error bars represent S.E.M.

Discussion

Here, over a period of six training sessions, participants learnt forty-eight flags from around the world whilst receiving either active or sham brain stimulation. They were then tested on these flags both one day and one week later. The results suggest many interesting findings. Firstly, contrary to previous literature, we found no evidence that anodal stimulation over the left DLPFC had an effect on learning ability compared to sham stimulation. Furthermore, anodal stimulation was actually detrimental to subsequent recognition tests, again contradictory to previous research. For free recall tests, results showed a marginally significant difference between stimulation groups, with the sham condition again achieving a higher recall rate (see Table 2, Figure 3). Over the six sessions, participant's task performance increased over sessions (see Figure 4). This may have indicated that participants became familiar with the task, allowing for increases in performance irrespective of stimulation. Another interesting finding is that participants performed significantly better in the second testing session compared to the first, despite it being one week later with no exposure to flags (see Table 3). The following discussion will compartmentalise the results and propose theories of why these may have been obtained.

Context-Dependent Learning

Arguably the most contradictory finding from this study, is that participants recognised and recalled more flags learnt in training sessions following sham stimulation, than active brain stimulation (only significantly in the second testing session). Given that they did not receive brain stimulation during the two testing sessions, perhaps this contradictory result could be attributed to a form of subconscious context/state dependent learning of tDCS: the context in the testing sessions being the same as the sham condition. The following paragraphs will address this finding, referencing only the results from the two testing sessions (see Table 2 and 3 in Results section), thus only LTM, whilst proposing a hypothetical theory of implicit state dependency.

Environmental context dependent learning was first shown in a study by Godden and Baddeley (1975), in which divers were asked to learn and remember certain words either out of the water, or submerged beneath the water. Twenty-four hours later they were asked to recall the words they had learnt whilst either underwater or on dry land. The results showed that those who encoded and recalled words in the same environment achieved higher free recall than those who had their conditions switched.

Context dependency has also been shown using pharmacological interventions, where it is more commonly known as state dependency. There is much evidence to suggest that individuals can recall or recognise objects with greater accuracy when learning is performed in the same "state" as the test phase. For example, it has been shown that when participants were asked to learn words whilst intoxicated by alcohol, they were able to recall significantly more of those words in the retrieval phase when intoxicated, compared to sober (Lowe, 1986; Petersen, 1977; Weingartner, Adefris, Eich, & Murphy, 1976; WEINGARTNER & FAILLACE, 1971). The same has also been shown with caffeine (Kelemen & Creeley, 2003; Sanday et al., 2013) and nicotine (Peters & McGee, 1982; Warburton, Wesnes, Shergold, & James, 1986). Whilst results have been achieved in favour of environmental context dependent learning (Smith & Sinha, 1987), inconsistencies have also been reported, with Smith, Glenberg and Bjork (1978) finding differences in recall ability but not recognition for same context conditions (For a review, see Smith & Vela, 2001), highlighting the complex nature of context/state dependency.

In the current study, the state dependency proposed is far more implicit than both environmental and pharmacological state dependency. Whilst it has been shown that tDCS can evoke neuronal changes in the brain (Nitsche & Paulus, 2000), it is not understood whether an absence of these specific changes in a later test phase, without the presence of stimulation, can interfere with recall and recognition performance. As participants would have almost certainly not perceived any physiological changes, aside from an initial itching sensation at the site of stimulation, it could be suggested that the significantly worse performance observed during recall and recognition may be due to a form of subconscious interference. For transcranial alternating current stimulation (tACS), it has been shown that by encouraging certain oscillatory activity during the encoding phase, more accurate results are found if the same pattern is reinstated during retrieval, compared to a different frequency (Javadi, Glen, Halkiopoulos, Schulz, & Spiers, 2017). Although this is not directly comparable to tDCS, due to varying mechanisms of action (Antal & Herrmann, 2016; Inukai et al., 2016), it highlights that brain stimulation has the ability to produce a form of state dependent learning. However, due to the lack of literature, this claim must be entirely hypothetical until further evidence can confirm its existence. When looking at other studies that have administered anodal tDCS over the left DLPFC during encoding, but not retrieval, LTM performances have shown an increase following stimulation (Javadi et al., 2012; Javadi & Walsh, 2012). This discrepancy in findings may be due in part to varying behavioural tasks used to assess the effectiveness of tDCS in previous literature. In the following section, the SAFMEDS task itself will be discussed.

SAFMEDS Task and tDCS

The SAFMEDS task presented here required the participant to learn eight new flags per session. In every instance during this study, after 30 minutes of training, participants were able to recognise all eight flags by the end of each session, regardless of the stimulation protocol. To complete the task, they had to say aloud these flags at one flag per second (60 in one minute). It is reasonable to suggest that this element of the SAFMEDS task invariably requires some element of working memory and visual processing speed. In subsequent retrieval tests, both free recall and recognition were tested to assess the effectiveness of brain stimulation combined with the SAFMEDS task on LTM retention.

Previous studies investigating the beneficial or inhibitory effects of tES on LTM have often used less cognitively demanding behavioural tasks, such as old/new recognition tasks, where, after initially observing visual stimuli, the participant must indicate if they have seen the word or picture before or not (Javadi & Cheng, 2013; Javadi et al., 2012; Javadi & Walsh, 2012); or paired associate-learning tasks, where they must recall the word originally shown to pair another word (de Lara, Knechtges, Paulus, & Antal, 2017; Garside, Arizpe, Lau, Goh, & Walsh, 2015). With a small number of variables in these tasks, the effects of tDCS on LTM can be easily and reliably observed. The SAFMEDS task used here has a greater degree of variability and complexity. Whilst comparable to a paired associate-learning task, in that a picture is paired with a word, it also requires the participant to instantly retrieve this association under timed pressure. Therefore, this may have been an influence as to why no effect of stimulation was found during training. As far as is known to date, this is the first time a computerised variation of a SAFMEDS task has been used to assess learning speed and LTM under such time constraints and therefore, executive functions it requires can only be speculated.

When understanding how a SAFMEDS task may influence LTM retention, it is important to take into account the number of trials carried out during the task and how this differs from other traditional LTM tasks described above. Whilst old/new or paired associate-learning tasks employ a set number of trials or stimuli to be learnt, the SAFMEDS task is variable and uses a performance threshold. Therefore, to complete the task for that session, the participant is required to attain a certain level of performance, otherwise they must continue until it is reached. This ensures the participant has learnt all of the flags and is able to repeat them sixty times at a fast pace (thus in ABA, achieving fluency) before they leave the session. Whilst this method will undoubtedly have a stronger effect on retention and ultimately consolidation compared to the tasks mentioned above, perhaps the complexity of the task itself is over and above the enhancement capabilities of tDCS.

Brain Stimulation Can Impair Learning and Memory

It is also important to note that, similar to the present study, there are many non-findings of brain stimulation for both working memory, reaction time and long-term memory. For WM, a review by Hill, Fitzgerald and Hoy (2016) found a trend towards improvement for offline (task completed following stimulation) WM accuracy only, with no significant effects found for online (stimulation during task) WM accuracy. They also found just a small improvement of RT, again for offline tasks only. Interestingly, using a WM task completed online, Marshall, Mölle, Siebner and Born

(2005) found RT to increase during a working memory task. As the current study also used an online type task, this may provide some explanation as to why, in this case, fluency thresholds were not met quicker during stimulation sessions.

For LTM, several studies have also shown non-findings following tDCS to the left DLPFC. Both Elmer et al., (2009) and Hammer, Mohammadi, Schmicker, Saliger and Münte (2011) found no effect of anodal stimulation on both short-term learning ability and subsequent retrieval. It should also be noted that, as the majority of studies observing the modulatory effects of stimulation on LTM often adopt varying methodological designs and stimulation protocols, cautious interpretation should be employed. For example, Elmer et al., (2009) administered only 5 minutes of stimulation in total, compared to the 15 minutes used in the current study. Similarly, de Lara et al., (2017) found anodal tDCS over the left DLPFC to have no effect on both encoding and retrieval of verbally presented stimuli. Whilst stimulation was administered for 20 minutes in their experiment, only 1 mA current was given, compared to 1.5 mA used in the current study. Although this again may have been a reason for null effects shown, these varying protocols seem to bare no correlation with subsequent LTM retrieval performances. Even by using 2 mA of high-definition tDCS for 20 minutes, Nikolin et al., (2015) only found an improvement in short term declarative verbal learning and RT, but nothing for subsequent recall and recognition. Furthermore, using 1.5 mA of tDCS for 25 minutes, Leshikar et al., (2017) found a significant improvement in recall ability but not recognition. As the task used here has not been administered concurrently with tDCS before, further research is required to understand the most effective stimulation protocol, if at all.

Moreover, one study has shown anodal tDCS to actually be of detriment to verbal LTM. Using a very similar procedure to the current study, Brunyé, Smith, Horner and Thomas (2018) found anodal tDCS to have no effect on immediate verbal learning. In a subsequent recall test two days later, verbal LTM was actually impaired following anodal stimulation to the left DLPFC. One theory proposed by Miniussi, Harris and Ruzzoli (2013), states that whilst anodal tDCS can faciliatate improvements for well trained or familiar tasks, it is not effective for novel tasks.

This is because when learning a new task, neurons initally fire unsystematically until consolidation of the task has occurred. As anodal tDCS induces membrane depolarisation for neurons around the target area, the stimulation adds to the noise around the site, thus a clear signal cannot emerge. Furthermore, a meta-analysis by Jacobson, Koslowsky and Lavidor (2012) found tDCS to modulate performance for procedural tasks, but rarely cognitive tasks, claiming that cognitive functions are typically supported by richer brain networks, far more complex than motor areas. They also stated that cognitive experiments yield far more heterogenous results, adding controversy to the growing body of literature surrounding tDCS and LTM, but also highlighting the complex nature of LTM mechanisms.

Delayed Improvement

Another interesting finding is that participants recognised a significantly greater number of flags in the second testing session, one week later with no exposure to flags, compared to the first. This was the case for both free recall, before participants had seen any flags, and recognition, where they were shown the flags over two 1-minute blocks. There could be several reasons why such a vast improvement was found after such a long retention interval. Firstly, the SAFMEDS task itself can be compared to a retrieval-based practise task, where instead of traditionally encoding via observation or studying, participants are more frequently tested. Here, during the SAFMEDS task, as participants are required to engage, providing answers and receiving feedback, they are being continually tested. Retrieval based learning has been shown to be considerably more effective than just repeated exposure to stimuli alone (Agarwal, Karpicke, Kang, Roediger, & McDermott, 2008; Karpicke & Grimaldi, 2012; Karpicke, Lehman, & Aue, 2014; Karpicke & Roediger, 2007, 2008; Roediger & Butler, 2011; Roediger & Karpicke, 2006; for a review, see Karpicke & Aue, 2015). One reason for this is said to be due to a reconsolidation effect, where the memory trace is elaborated and alternative pathways are made, thus, creating an overall stronger and more accessible memory (McDaniel & Masson, 1985; Roediger & Butler, 2011; Sara, 2000). This reconsolidation effect would not only be present during the training sessions, but also the first testing session. Therefore, the flag/country name association is likely to have developed into a strong memory trace by the second testing session. It should be noted, however, that the retention interval in the present study is much longer than those in previous studies of LTM (Hsu, Zanto, Anguera, Lin, & Gazzaley, 2015; Javadi & Cheng, 2013; Javadi et al., 2012). Whilst some studies have employed two-day retention intervals (Brunyé et al., 2018; Zaromb & Roediger, 2010) where differences between conditions have been found, they lack an additional test either prior to or following and therefore comparisons cannot be made. One study by Roediger and Karpicke (2006) did however do this. When assessing whether just exposure (studying) or retrieval-based learning was more effective, they employed three tests; 5 minutes, 2 days and 1 week. They found that participants in the retrieval-based learning group had the same score after one week, as the study only group after 2 days. Whilst this does not show an improvement, it does show that different learning methods can aid retention of material for a longer period of time. As there are presently no studies with an identical design and protocols to the current, no direct comparisons can be made.

It is also important not to discount the influence that sleep has for consolidation of new memories. During sleep the brain goes through cycles of rapid eye movement (REM) and slow wave sleep (SWS; Maquet, 2001), the latter of which play an integral part in the formation of LTM. During SWS, the newly acquired memory traces are reactivated and work their way through the hippocampal structure to be distributed into the neocortex, as a stronger, more durable memory formation (Born & Wilhelm, 2012). Offline improvement following sleep has been shown for motor learning (King, Hoedlmoser, Hirschauer, Dolfen, & Albouy, 2017), evident after 24 hours (Javadi, Walsh, & Lewis, 2011; Lugassy, Herszage, Pilo, Brosh, & Censor, 2018; Walker, Brakefield, Morgan, Hobson, & Stickgold, 2002), 36 hours (Walker, Brakefield, Hobson, & Stickgold, 2003) and 1 week later (Meier & Cock, 2014). Offline improvement following sleep has also been demonstrated for declarative memory (Drosopoulos, Wagner, & Born, 2005; Wilhelm, Diekelmann, & Born, 2008), although this has been less extensively studied and with no consistent procedures or tasks. As these studies only adopted short retention intervals (3-12 hours), comparisons with the current study must be done so with caution. Perhaps due to nature of the task, being similar to a retrieval-based task, coupled with a prolonged retention interval, enabled superior consolidation, allowing memory traces to strengthen to such a degree that they were more easily accessible after 1 week. Further research with longer retention intervals is required to make a formal speculation.

Considerations for Future Research

The current study has shown that, a SAFMEDS task, traditionally used in ABA as a method of PT, can be used in a lab based cognitive assessment. As this is the first time it has been used to directly compare learning speed and subsequent retention, with or without tDCS, there are a number of considerations to be outlined. Firstly, SAFMEDS tasks are usually found to be engaging for participants (Greene et al., 2018), ensuring maintained concentration. The task used here contains several variables that may have interfered with the reliability of the study. For example, during data collection, several participants claimed that it was considerably more difficult to learn the flags of the countries that they had not heard of, compared to those they had. Furthermore, others stated that if the flags were similar colours or patterns, or the country names sounded similar, if presented in the same block, errors occurred that may not if there was more differentiation. In future studies, perhaps using stimuli with less variables would provide a cleaner, less discriminative task.

In answer to the question of whether state-dependent learning is possible following tDCS, it would be useful to add an additional condition whereby stimulation is also administered in the test phases. This way, comparisons between the two conditions can be made and a greater understanding of state-dependency following stimulation can be gained.

It would also be interesting to investigate whether the improvement observed in the second testing session was due to a refreshing effect from the first test session. This could be achieved using a mixed design and removing the first test session from one group. Also, it would be of interest to see if a shorter retention interval (comparable to those in previous studies) before the second testing session still yielded improved performance. Furthermore, this study did not allow us to observe whether performance could improve even more so over a longer retention interval. It would be useful to include a follow up test, perhaps two weeks later, to assess whether improvements or at least maintenance are facilitated.

Conclusion

Using a SAFMEDS task, traditionally used in the discipline of ABA, we found no evidence to suggest that anodal tDCS to the left DLPFC can improve learning ability. Furthermore, our study showed this protocol of stimulation to be of detriment to subsequent retrieval of flag/country association. The results obtained pose many further questions, as well as serving to highlight the inconsistent nature of brain stimulation for improving learning and memory. The SAFMEDS task has deeply entrenched roots in ABA, with many applications used for Autism Spectrum Disorder and individuals with learning difficulties. By gaining a greater understanding of how this task works from a neuroscience perspective, its benefits can be seen not only from an educational perspective but could also extend into neuro-rehabilitative domains.

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