Journal of Cognitive Enhancement
https://doi.org/10.1007/s41465-019-00155-2

SUPPORT OF THE NULL HYPOTHESIS

No Effect of Transcranial Direct-Current Stimulation to Dorsolateral Prefrontal Cortex on Naturalistic Prospective Memory in Healthy Young and Older Adults

Nathan S. Rose[1] · Hannah Thomson[2] · Matthias Kliegel[3]

Received: 19 June 2019 / Accepted: 2 October 2019

Abstract

Transcranial direct current stimulation (tDCS), a form of non-invasive brain stimulation, has been shown to enhance working memory and multitasking abilities. Because of the substantial overlap in both cognitive processes (maintenance, monitoring) and neural substrates (dorsolateral prefrontal cortex, DLPFC) that support both working memory and *prospective memory* – the ability to remember to perform intended actions at appropriate moments in the future (taking medications, turning off appliances) – we tested whether tDCS would also enhance young and older adults' prospective memory. If tDCS enhances DLPFC activation, then it should benefit prospective memory performance, particularly for tasks that rely on controlled monitoring processes for prospective memory cue detection. Healthy young and older adults played the Virtual Week game while they received either a session of active tDCS to DLPFC and then, after at least 48 h, a session of placebo-controlled, sham stimulation, or vice versa. The Virtual Week game is a reliable measure of naturalistic prospective memory that includes assessments of five different types of prospective memory tasks that vary in cue-type (time vs. event) and task-regularity and, thus, the extent to which task performance should rely on controlled monitoring processes and DLPFC activation. Active tDCS had no effect on prospective memory performance relative to sham tDCS for either age group or any task type. In contrast, there were reliable practice effects across test sessions regardless of whether active tDCS was applied during the first or second session. A single session of tDCS to DLPFC did not enhance young or older adults' prospective memory performance, but practice did.

Keywords Transcranial direct current stimulation · tDCS · Noninvasive brain stimulation · Prospective memory · Aging · Dorsolateral prefrontal cortex · DLPFC

Introduction

The ability to remember to perform intended actions at the appropriate moment in the future (e.g., taking medications, turning off appliances) – termed *prospective memory (PM)* – is a type of memory that is sensitive to normal age-related changes in cognition (Rose, Rendell, McDaniel, 2010), and is critical for older adults' functional independence (Hering, Kliegel, Rendell, Craik, & Rose, 2018). It is important to establish effective ways to enhance PROSPECTIVE MEMORY because errors can have dire consequences and undermine older adults' ability to 'age in place' – that is, to safely remain at home, living independently (Hering, Rendell, Rose, Schnitzspahn, & Kliegel, 2014; Piau et al., 2014).

There is great hope for the utility of transcranial direct current stimulation (tDCS) for enhancing cognition (Bennabi et al., 2014). Benefits to some everyday tasks have been reported in older adults following working memory training with tDCS (Stephens & Berryhill, 2016), as well as to tasks that measure processes relevant for prospective memory such as vigilance (McIntyre et al., 2014) and multi-tasking (Nelson et al., 2016). However, the current study is the first to examine its efficacy for enhancing prospective memory. We examined the potential benefit of tDCS to performing naturalistic

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s41465-019-00155-2) contains supplementary material, which is available to authorized users.

✉ Nathan S. Rose
nrose1@nd.edu

[1] Department of Psychology, University of Notre Dame, 390 Corbett Hall, Notre Dame, IN 46556, USA

[2] ACU Melbourne, Fitzroy, VIC, Australia

[3] Université de Genève, Geneva, Switzerland

prospective memory tasks during a "Virtual Week" (Rendell & Craik, 2000; Rose et al., 2010) in both young and older adults relative to a placebo-controlled (sham) stimulation session.

Importantly, age differences do not appear to be uniform for all forms of prospective memory (McDaniel & Einstein, 2011; Rose et al., 2010). Theories of prospective memory make a critical distinguish between the types of cues (time vs. event) that should trigger retrieval of one's intended actions and the regularity with which tasks are to be performed (or how 'habitual' the tasks are). These features have important implications for the cognitive processes and neural substrates that are involved, which support the successful performance of such tasks (McDaniel & Einstein, 2011). In general, according to the Dynamic Multi-process framework of prospective memory (Scullin, McDaniel, & Shelton, 2013), tasks that require substantial 'monitoring' of the environment for cues that signal that it is the appropriate moment to perform an intention, such as tasks with time-based cues or cues that are not focally processed as part of one's ongoing activities, tend to activate the dorsolateral prefrontal cortex (DLPFC) (Cona, Bisiacchi, Sartori, & Scarpazza, 2016; Gonneaud, Rauchs, Groussard, Landeau, Mézenge, de La Sayette et al., 2014; McDaniel, LaMontagne, Beck, Scullin, & Braver, 2013) and exhibit larger age-related deficits than tasks with features that permit more spontaneous retrieval (McDaniel & Einstein, 2011; Rose et al., 2010).

Therefore, in the current study, a putatively excitatory form of tDCS was administered to target young and older adults' left DLPFC. This target was selected because prior work has established that certain prospective memory tasks that are to be performed during the Virtual Week, especially time-based tasks with less focally-processed cues, are the tasks that are most strongly associated with age and individual differences in working memory capacity (Rose et al., 2010) and are most likely to rely on the left DLPFC (e.g., Cona et al., 2016). Furthermore, tDCS to left DLPFC has been shown to enhance working memory and multi-tasking functioning (Stephens & Berryhill, 2016; Nelson et al., 2016). Therefore, the aims of the study were to probe the involvement of this brain region in both young and older adults' prospective memory performance, and also to test the efficacy of this form of stimulation for potentially enhancing their prospective memory performance.

Method

Participants

An a-priori power analysis was conducted based on the effect size reported by Stephens and Berryhill (2016) using the means and standard deviations of the between-subjects difference in everyday task performance for active (M = 13.036, $SD = 1.72$) vs. sham ($M = 10.207$, $SD = 2.78$) stimulation conditions. This analysis determined that a sample of at least 12 participants per group was required to obtain 90% power to detect an effect of tDCS (for details and R code, see Supplemental Materials). Healthy, English-speaking young adults ($n = 22$, $M_{age} = 24.9$, $SD = 2.5$) and older adults ($n = 16$, $M_{age} = 69.8$, $SD = 5.7$) with normal or corrected-to-normal vision and hearing participated in the study in exchange for AU$25. Participants were screened for the following contraindications: left-handed, history of psychiatric illness or brain injury, seizure, loss of consciousness for longer than 2 minutes, non-prescription medication containing antihistamines or pseudoephedrine, history of drug/alcohol dependence, suffered from severe or frequent headaches/migraines, metal in their head, had previously had an adverse reaction to tDCS or TMS, or skin disorder affecting the face or scalp.

Older adults were screened for the possible presence of neuropsychological impairment using the Telephone Interview of Cognitive Status (TICS, Brandt et al., 1988, cutoff <29, $M = 39.2$, $SD = 4.1$). The older adults had higher education ($M = 17.9$ years, $SD = 3.8$, vs. $M = 15.2$ years, $SD =$ 1.4) and IQ, estimated with the National Adult Reading Test (NART, Nelson 1982, $M = 121.5$, $SD = 3.7$, vs. $M = 110.2$, $SD = 4.3$), than the young adults. All participants reported normal levels of depression and anxiety (measured with the Hospital Anxiety and Depression Scale (HADS, Zigmond & Snaith 1983), $M = 6.6$, $SD = 2.5$, vs. $M = 6.64$, $SD = 4.33$).

Prospective Memory

Prospective memory was assessed using the Virtual Week game. Virtual Week is a computerized board game in which participants move a token around the board by rolling a die. The board is depicted in Fig. 1 and the task details are described in the Figure caption. Each lap of the board represents events associated with one waking day, but takes only approximately 10 minutes to complete. It has been shown to be a reliable measure of multiple types of naturalistic prospective memory tasks (for a review, see Rendell & Henry, 2009). Split-half reliability coefficients range from .87 to .90 (Rose et al., 2010). Performance on Virtual Week predicts an older adult's level of functional independence, as measured by performance on instrumental activities of daily living (Hering et al., 2018). It is sensitive to differences in prospective memory between various populations with neurotrauma or neuropathological conditions and matched controls (for a review, see Phillips, Henry, & Martin, 2008). For example, in a sample with traumatic brain injury, Mioni et al. (2013) found Virtual Week to have good test-retest reliability compared to standard measures of prospective memory including the Rivermead Behavioral Memory Test, the Cambridge Behavioral

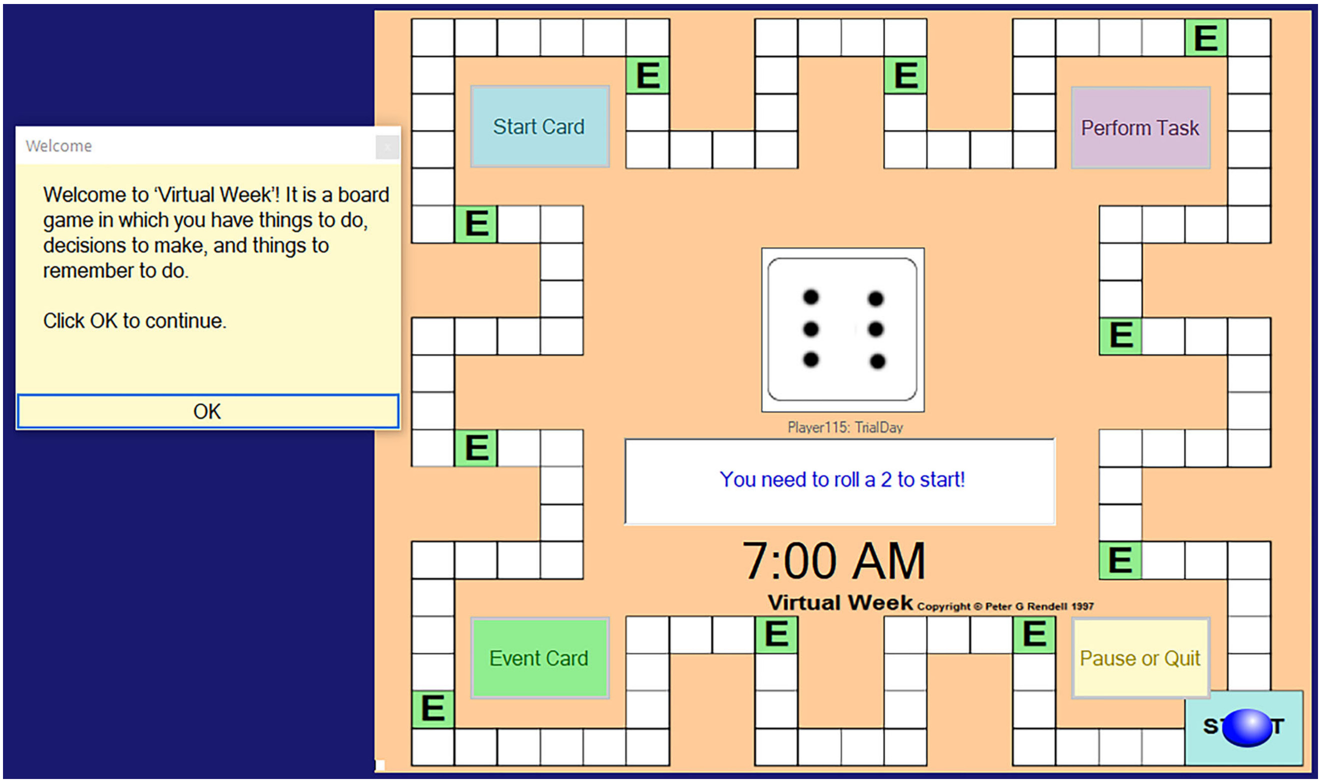

Fig. 1 Opening screen-shot of the Virtual Week computerized board game at the start of the trial day. The game was used to measure prospective memory performance. The participants started the game in the bottom right corner of the board, signified by the blue token. Participants use the computer mouse to click on the die to "roll" it. "Rolling" the die returns a random number of dots between 1 and 6 to indicate the number of squares the participant is to move their token around the board in a clockwise direction. Each "day" started with the first square representing 7 AM and finished after the token passed the last square representing 10 PM; the virtual time of day, indicated in the center of the board, is calibrated to the location of the blue token on the board, with every 2 squares representing 15 minutes. As participants move around the board, they are required to remember to complete prospective memory tasks, while also making choices about daily activities. There are ten prospective memory tasks to be completed each 'day' (four irregular, four regular, and two time-check tasks). The four irregular tasks simulate the kind of occasional duties undertaken in daily life, two of which are time-based (pertaining to the time of the virtual 'day' as displayed on the board), and two of which are event-based (triggered by information shown on an event card, which is picked up after passing a green 'E' square). The four regular tasks simulate the kinds of routine duties undertaken in daily life; again two of these are time-based and two are event-based. The two time-check tasks require participants to monitor real time on a running clock, prominently displayed above the die, and complete tasks when specific time periods pass. The regular- and time-check tasks were identical across the two parallel versions of Virtual Week, however the irregular tasks differed

Prospective Memory Test, the Memory for Intentions Screening Test, and the Royal Prince Alfred Prospective Memory Test, and moderately correlate with such measures. Moreover, performance on Virtual Week predicts young an older adults' performance on a computerized Breakfast Task (specifically the prospective memory component derived from factor analysis of multi-tasking abilities measured with this task; Rose, Luo, Bialystok, Hering, Lau, & Craik, 2015a), and the specificity of young and older adults' planning or 'episodic future thinking' abilities (Terrett, Rose, Henry, Bailey, Altgassen, Phillips ... & Rendell, 2016). For further methodological details about Virtual Week, see Rose et al. (2010) and Rose et al. (2015b). In this study, we used two parallel versions of Virtual Week (four virtual days each) with unique content for participants to play in two testing sessions: one with active- and one with sham-tDCS, counterbalanced across participants, separated by at least 2 days (M = 12.3).

TDCS Protocol

TDCS was administered using a 9 V battery-driven, direct-current stimulator (Trans-Cranial Technologies, www.trans-cranial.com) and a pair of conductive rubber electrodes (7 cm × 5 cm, 35 cm^2) covered in saline-soaked, synthetic sponges and secured using a neoprene headband. In both the active and sham tDCS sessions, the anode targeted the left DLPFC (by centering the length of the electrode over F3 according to the 10–20 International EEG positioning system); the cathode was placed over the contralateral supraorbital ridge (see Fig. 1A). Active tDCS involved 20 minutes at 2.0 mA, preceded by a 60-second ramp-up-period from 0 to 2 mA. Sham tDCS involved the same 60-second ramp-up-period from 0 to 2 mA before it decreased to 0 mA for the remainder of the session. This protocol was selected because it is similar to the protocol that Stephens and Berryhill (2016) used that was found to be most effective for enhancing everyday task performance. This resulted in good blinding of tDCS conditions: during post-experimental debriefing after the second session participants were told that one session involved active (treatment) stimulation while the other involved a placebo-controlled sham form of stimulation. Only ~50% of participants (i.e., chance-level performance) correctly identified whether the first session was the active condition and the second session was the sham condition or vice versa.

Procedure

Participants first completed a tDCS-screening questionnaire via telephone to rule out contraindications; older adults also completed the TICS. Participants provided written informed consent and received safety guidelines about tDCS in accordance with procedures approved by the ACU-Melbourne Research Ethics Board. Participants completed the demographic questionnaire, NART, and HADS. Then they were introduced to the features and procedures of the Virtual Week game and played one practice trial to ensure thorough understanding. Then the tDCS electrodes were prepared. During the 20-minute tDCS period (consisting of either active or sham stimulation), participants played two virtual 'days' of Virtual Week. When tDCS finished, the electrodes were removed and the participant played an additional two virtual 'days'. We restricted the 'online' stimulation duration to 20 minute because this length is within published safety guidelines and is known to be well-tolerated by most healthy young and older adults. We assessed prospective memory performance on two virtual 'days' immediately following tDCS in order to test for a potential difference between the effects of 'online' tDCS on prospective memory performance during the game and 'offline' carryover effects of tDCS on prospective memory performance during the same session following the 20-minutes stimulation period.

Participants returned to the lab for the second testing session after a minimum of two days. On the second session, participants again played the practice trial of Virtual Week to refresh them of the features and procedures of the game. Then either active or sham tDCS was administered (depending on their previous session), while participants completed four new virtual 'days' (two during tDCS, two after).

The experiment employed a crossover, sham-controlled design, in which participants were blind to condition assignment, with full counterbalancing of the prospective memory tasks and virtual day content across participants, both between and within sessions. Such detailed counterbalancing was performed to control for any effects specific to the task content in the experimental design (see Fig. S1). This counterbalancing scheme also allowed us to isolate the potential effects of active vs. sham tDCS while controlling for effects attributable to the order of stimulation, and also to examine potential practice effects within and between the experimental sessions irrespective of tDCS condition.

Analysis

To assess the effects of tDCS condition on prospective memory performance, we first assessed the main effect of tDCS and any potential interaction effects with tDCS phase, age group or prospective memory task type with a 2 (*tDCS condition*: performance on the actual day of testing with active vs. sham tDCS) × 2 (tDCS phase: the two virtual 'days' played during (online) vs. after (offline) the 20 minutes of tDCS) × 2 (*age group*: young vs. old) × 5 (*task type*: Regular-Event, Irregular-Event, Regular-Time, Irregular-Time, Time-Check) mixed, repeated-measures ANOVA. To further test for differences between tDCS condition, phase of tDCS and prospective memory task type, a 2 × 2 × 5, three-way, repeated-measures, factorial ANOVA was conducted for each age group separately. The within-group variables were *tDCS condition* (active vs. sham session), *phase of tDCS* (Phase 1–during tDCS vs. Phase 2–after tDCS), and *prospective memory task type* (Regular-Event, Irregular-Event, Regular-Time, Irregular-Time, Time-Check).

To assess the main effect of practice, the same analysis was conducted, but with the counterbalanced groups for *testing session* (1st actual day vs. 2nd actual day of testing) as a between-group variable added to the model. All tests were two-tailed; an alpha level of $p < .05$ was used; effect sizes were estimated using partial *eta* squared (η^2_p) and Cohen's *d*. Mauchly's test of sphericity was conducted and, in cases where the assumption of sphericity was violated, a Greenhouse-Geisser correction was applied. Post-hoc tests for significant main effects were conducted as pair-wise Bonferroni comparisons, adjusted for multiple comparisons. Bayesian analysis was also conducted to compare performance in the active and sham conditions and to assess evidence in favor of either the Null or Alternative Hypothesis. Given that this study represents the first investigation of the effects of tDCS on prospective memory, default priors were used in the estimation of Bayes Factors for each task type using SPSS 25 (IBM Corp., 2017, Armonk, NY).

Results

The average percentage of prospective memory tasks performed correctly for each task type for the young adults (top panel) and older adults (bottom panel) are shown in Fig. 2A. The main effects of both age group, $F(1,43) = 33.9$, $p < .001$, $\eta^2_p = .44$, and task type $F(3.2136) = 19.66$, $p < .001$, $\eta^2_p = .31$, were highly significant. For young adults there was a

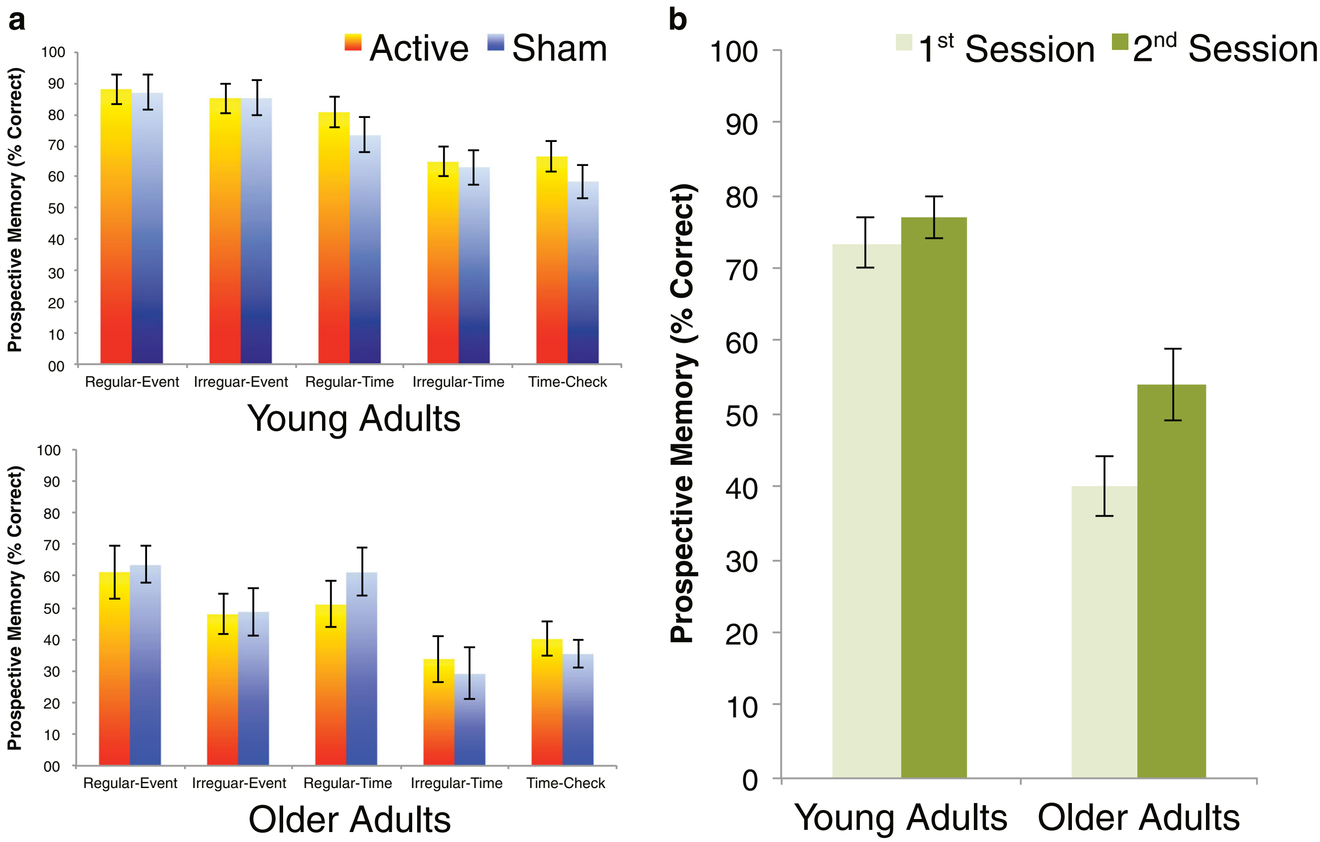

Fig. 2 ***A)*** Neither young nor older adults' prospective memory performance was reliably better during active vs. sham tDCS sessions for any task type; ***B)*** both groups' overall prospective memory performance was significantly better on the 2nd vs. the 1st session, regardless of whether there was active or sham tDCS. Error bars = ±SEM

significant main effect of prospective memory task type, $F(2.91,61.03) = 15.04$, $p < .001$, $\eta^2_p = .41$. Post-hoc analysis revealed that participants performed significantly (all $ps \le .027$) more accurately on regular-event ($M = .88$, $SD = .12$), irregular-event ($M = .85$, $SD = .15$), and regular-time tasks ($M = .77$, $SD = .21$), than on irregular-event ($M = .64$, $SD = .24$) and time-check tasks ($M = .63$, $SD = .22$). All other paired comparisons did not reach significance (all $ps \ge .263$). For older adults, there was a significant main effect of prospective memory task type, $F(2.28,31.87) = 9.43$, $p < .001$, $\eta^2_p = .40$. Post-hoc analysis revealed that participants performed significantly (all $ps \le .03$) more accurately on regular-event ($M = .62$, $SD = .22$), irregular-event ($M = .56$, $SD = .29$), and regular-time tasks ($M = .48$, $SD = .22$), than on irregular-event ($M = .32$, $SD = .23$) and time-check tasks ($M = .38$, $SD = .14$). All other paired comparisons did not reach significance (all $ps \ge .14$). Note that the overall effects of cue-type, task-regularity, and the age differences between healthy young and older adults replicate previous results (e.g., Rose et al., 2010).

No Effects of tDCS There was neither a main effect of tDCS condition, $F(1,43) = 0.18$, $p = .68$, $\eta^2_p = .004$, nor any interaction with any factor (all $ps > .30$). When age groups were analyzed separately, the main effect of tDCS condition was again not significant for either the young adults, $F(1,20) = 2.18$, $p = .154$, $\eta^2_p = .09$, or older adults, $F(1,14) = 0.05$, $p = .83$, $\eta^2_p < .01$. Participants were not reliably more accurate on prospective memory during active tDCS (Young: $M = .77$, $SD = .13$; Old: $M = .47$, $SD = .16$) than sham tDCS (Young: $M = .73$, $SD = .18$; Old: $M = .48$, $SD = .20$). There were also no significant interactions with tDCS condition within either group. The three-way interaction between tDCS condition, tDCS phase, and prospective memory task type was not significant for young adults, $F(4,84) = 1.81$, $p = .135$, $\eta^2_p = .08$, or older adults, $F(4,56) = 1.08$, $p = .38$, $\eta^2_p = .07$. The Bayes Factors provided evidence in favor of the Null hypothesis for both young adults (BFs ranging from 1.60 to 6.13 in favor of the Null) and older adults (BFs ranging from 1.15 to 5.28 in favor of the Null) (see Table 1). These values represent moderate to strong evidence in favor of the Null hypothesis, i.e., that tDCS did not affect prospective memory performance.

SEM = standard error of the mean; BF_{01} = Bayes Factor favoring the null over the alternative hypothesis; t and p from two-tailed tests, uncorrected.

Additionally, for neither young adults nor older adults was there a significant interaction effect of tDCS condition with tDCS phase (during "online" vs. after "offline"), or phase

Table 1 Descriptive and inferential statistics comparing the mean difference in prospective memory performance between active- and sham-tDCS sessions for each task type and age group

Task Type	Active - Sham Difference					Active - Sham Difference				
	Mean	SEM	BF_{01}	*t*	*p*	Mean	SEM	BF_{01}	*t*	*p*
	Young Adults					Older Adults				
Regular Event	0.01	0.05	6.00	0.21	0.84	−0.02	0.08	5.12	−0.27	0.79
Irregular Event	0.00	0.04	6.13	0.00	1.00	−0.01	0.09	5.28	−0.08	0.94
Regular Time	0.07	0.05	2.34	1.44	0.16	−0.10	0.05	1.15	−1.88	0.08
Irregular Time	0.02	0.05	5.73	0.37	0.72	0.05	0.07	4.26	0.68	0.51
Time Check	0.08	0.05	1.60	1.72	0.10	0.05	0.08	4.46	0.60	0.56

with prospective memory task type, all $Fs < 1.0$. Thus, there were no carryover effects that were greater in the active vs. sham testing session that occurred following the 20-minutes period of stimulation. Additional data and analyses regarding performance differences between prospective memory conditions on Virtual Week (irrespective of tDCS) are reported in the supplemental material online.

Effects of Session (I.E., Practice) In contrast to the effects of tDCS, there was a significant main-effect of testing session for both young adults, $F(1,20) = 5.20$, $p = .033$, $\eta^2_p = .20$, $d = 0.20$, and older adults, $F(1,14) = 16.51$, $p = .001$, $\eta^2_p = .54$, $d = 0.80$. Participants were significantly more accurate on the second session than the first session (see Fig. 2B), regardless of whether they had active tDCS on the first session and sham tDCS on the second session, or vice versa. Although the effect size was much larger for the older than the young adult group, the interaction may have been due to the older adult group having more room for improvement and the young adults' performance approaching ceiling level performance. Note that this practice effect replicates the improvements seen previously with repeated performance of tasks with regular cues over a single session of the Virtual Week game for both young and older adults (Rose et al., 2010), as well as for older adults' performance on all task-types over multiple testing sessions in a cognitive training study using the Virtual Week game (Rose et al., 2015b).

Most importantly, the lack of the aforementioned interaction with online vs. offline tDCS phase between the active vs. the sham testing session shows that the practice effect is not confounded with the effects of online vs. offline tDCS. That is, the practice effect between the online portion of the task to the offline portion of the task on the sham session was comparable to the effect on the active session. Moreover, that the task content was counterbalanced across online vs offline portions of the task, and the active and sham testing sessions were counterbalanced across participants also helps rule out any potential confound between the practice effect and the effects of tDCS.

Discussion

The present study examined the potential for anodal tDCS applied to left DLPFC to benefit young and older adults' performance on a variety of naturalistic prospective memory tasks during a 'Virtual Week'. It is important to identify effective ways to enhance prospective memory performance, particularly for older adults who exhibit deficits in performing such tasks, because prospective memory errors can undermine an individual's functional independence. Unfortunately, a single-session of tDCS was ineffective for enhancing prospective memory performance for any task type for either age group. In contrast, there were reliable gains in prospective memory performance across the two sessions irrespective of whether active or sham tDCS was applied.

While there is great hope for tDCS to enhance cognition, and some encouraging preliminary findings reported in the literature (Coffman, Clark, & Parasuraman, 2014), meta-analyses (Horvath et al., 2015; Mancuso et al., 2016), failed replications (Robison et al., 2017), and the "file-drawer" problem (Minarik et al., 2016) call for skepticism. It is important for researchers, laypersons, and companies who are marketing tDCS-related products to consumers to know that tDCS does not cause neuronal firing and only a small percentage of the signal passes the scalp, skull, and pia to potentially modulate cortical excitability in the brain (Bennabi et al., 2014; Underwood, 2016). In order to justify the discomfort, risks, time, and cost associated with undergoing tDCS in an attempt to enhance cognitive performance, at a minimum, tDCS should demonstrate reliable and meaningful advantages over the natural gains that come with practice on a task. The results of the current study show that practice effects were larger than any effect of tDCS on prospective memory performance, especially for older adults. Although the current results may cause some to conclude that the participants did not need tDCS to boost their memory performance (Coffman et al., 2014), they simply needed a bit of practice, the results provide important initial data points to be used in an attempt to map the massive tDCS parameter space that remains to be explored.

More than a single session of tDCS may be required in order to benefit prospective memory performance. Future studies should pair the application of tDCS with prospective memory training programs, which have been shown to result in training gains, as well as far transfer to improvements in performing real world prospective memory tasks and instrumental activities of daily living (Rose et al., 2015b). Another possibility is that alternative tDCS montages could benefit prospective memory performance. High-density montages in particular may provide more focal modulation of DLPFC excitability than the montage used in the present study and, thus, may be more beneficial for prospective memory performance (Bennabi et al., 2014). Future research should also target other brain areas known to be important for distinct prospective memory processes such as right DLPFC, medial PFC, and superior parietal cortex (Cona et al., 2015, 2016, 2017; Gonneaud et al. 2014, 2017; McDaniel et al., 2013, 2015; Peira et al., 2016).

Even though tDCS was ineffective at producing benefits to prospective memory performance in the current study, examining the effects of tDCS can elucidate the causal role of hypothesized neurocognitive processes associated with performing certain types of tasks. Because performing certain types of prospective memory tasks (i.e., irregular tasks with less focal cues) seems to be more strongly associated with age and individual differences in working memory than others (i.e., regular tasks with more focal cues) (Rose et al., 2010) and rely on DLPFC (Cona et al., 2016), it was hypothesized that inducing excitatory stimulation to left DLPFC - a critical node that is known to support working memory functions - would enhance prospective memory performance, especially for irregular tasks with less focal (i.e., time-based) cues, relative to sham stimulation. This hypothesis is a key test of the Dynamic Multiprocess Model of prospective memory and the predicted pattern of age differences that should be observed for tasks that depend on monitoring processes (Scullin et al., 2013); thus, according to this model, such age differences should be mitigated by excitatory stimulation of the left DLPFC. Unfortunately, our study using tDCS did not provide support for this hypothesis.

Thus, a key conclusion from this study is that a single session of anodal tDCS to left DLPFC at 2 mA for 20 minutes was insufficient for modulating healthy young and older adults' performance on naturalistic forms of regularly- or irregularly-occurring event- or time-cued, or time-monitoring, prospective memory tasks, but practice was. Going forward, future research needs to conduct a systematic search to map the parameter space that reliably produces effective stimulation protocols. The current study used a common stimulation protocol that has previously been shown to enhance working memory and multitasking abilities in young and older adults (Stephens & Berryhill, 2016). Thus, there was reason to believe that this protocol would enhance prospective memory, particularly for tasks known to rely on working memory and multitasking abilities and the left DLPFC. The lack of an effect of tDCS may reflect a fundamental difference in the efficacy of tDCS in the domain of prospective memory, as opposed to working memory and multi-tasking, or it may reflect a limitation of this particular stimulation protocol for modulating DLPFC activity and performance on these particular tasks.

Recently, a study that conducted a similar investigation of the effects of tDCS on prospective memory was brought to our attention. Ellis, Veloria, Arnett, Vogel, Pitães, and Brewer (under review) used a similar protocol with anodal tDCS to left DLPFC in an attempt to enhance performance on a well-studied, laboratory-based prospective memory task with focal or less focal cues in samples of healthy young adults (manipulated between subjects). These researchers also found that active tDCS did not benefit prospective memory performance relative to sham stimulation for any of the conditions examined, i.e., tasks with either focal or less focal cues. Collectively the present results and these other recent results cast doubt on the utility of single session anodal tDCS to left DLPFC for enhancing prospective memory in healthy adults.

In sum, this initial investigation did not show benefits of tDCS for enhancing young or older adults' prospective memory performance on a variety of naturalistic prospective memory tasks. However, much research remains to be conducted in order to fully understand how tDCS may be used to causally modulate neurocognitive processes supporting prospective memory and enhance prospective memory functioning in young and older adults. The present study represents an essential first step towards this important goal.

Acknowledgments The study was funded by the Cognition & Emotion Research Centre of ACU-Melbourne. The authors declare no conflict of interest.

Author Contributions HT designed the study with PGR; HT collected the young adult data; NSR collected the older adult data with the help of RV and JS; NSR and HT analyzed the data; NSR and HT wrote the manuscript, with helpful edits from MK.

Compliance with Ethical Standards

Research Disclosure Statements One older adult did not return for the second session and was thus excluded from final analysis. All independent and dependent variables, whether successful or failed, have been reported in the Method section.

References

Bennabi, D., Pedron, S., Haffen, E., Monnin, J., Peterschmitt, Y., & Van Waes, V. (2014). Transcranial direct current stimulation for memory enhancement: From clinical research to animal models. *Frontiers in Systems Neuroscience, 8*.

Brandt, J., Spencer, M., & Folstein, M. (1988). The telephone interview for cognitive status. *Neuropsychology, Neuropsychiatry, and Behavioral Neurology, 1*(2), 111–117.

Coffman, B. A., Clark, V. P., & Parasuraman, R. (2014). Battery powered thought: Enhancement of attention, learning, and memory in healthy adults using transcranial direct current stimulation. *Neuroimage, 85*, 895–908.

Cona, G., Bisiacchi, P. S., Sartori, G., & Scarpazza, C. (2016). Effects of cue focality on the neural mechanisms of prospective memory: A meta-analysis of neuroimaging studies. *Scientific Reports, 6*, 25983.

Cona, G., Marino, G., & Bisiacchi, P. S. (2017). Superior parietal cortex and the attention to delayed intention: An rTMS study. *Neuropsychologia, 95*, 130–135.

Cona, G., Scarpazza, C., Sartori, G., Moscovitch, M., & Bisiacchi, P. S. (2015). Neural bases of prospective memory: A meta-analysis and the "attention to delayed intention"(AtoDI) model. *Neuroscience & Biobehavioral Reviews, 52*, 21–37.

Ellis, D. M., Veloria, G. K. G., Arnett, C. R., Vogel, A. E., Pitães, M., & Brewer, G. A. (under review). No evidence for enhancing prospective memory with anodal Transcranial direct current stimulation across dorsolateral prefrontal cortex. *Journal of Cognitive Enhancement*.

Gonneaud, J., Lecouvey, G., Groussard, M., Gaubert, M., Landeau, B., Mézenge, F., et al. (2017). Functional dedifferentiation and reduced task-related deactivations underlie the age-related decline of prospective memory. *Brain Imaging and Behavior, 11*(6), 1873–1884.

Gonneaud, J., Rauchs, G., Groussard, M., Landeau, B., Mézenge, F., de La Sayette, V., et al. (2014). How do we process event-based and time-based intentions in the brain? An fMRI study of prospective memory in healthy individuals. *Human Brain Mapping, 35*(7), 3066–3082.

Hering, A., Kliegel, M., Rendell, P. G., Craik, F. I. M., & Rose, N. S. (2018). Prospective memory is a key predictor of functional Independence in older adults. *Journal of the International Neuropsychological Society.*

Hering, A., Rendell, P., Rose, N. S., Schnitzspahn, K., & Kliegel, M. (2014). Prospective memory training in older adults and its relevance for successful aging. *Psychological Research, 6*, 892–904. https://doi.org/10.1007/s00426-014-0566-4.

Horvath, J. C., Forte, J. D., & Carter, O. (2015). Quantitative review finds no evidence of cognitive effects in healthy populations from single-session transcranial direct current stimulation (tDCS). *Brain Stimulation, 8*(3), 535–550.

Mancuso, L. E., Ilieva, I. P., Hamilton, R. H., & Farah, M. J. (2016). Does transcranial direct current stimulation improve healthy working memory?: A meta-analytic review. *Journal of Cognitive Neuroscience, 28*(8), 1063–1089.

McDaniel, M. A., & Einstein, G. O. (2011). The neuropsychology of prospective memory in normal aging: A componential approach. *Neuropsychologia, 49*(8), 2147–2155.

McDaniel, M. A., LaMontagne, P., Beck, S. M., Scullin, M. K., & Braver, T. S. (2013). Dissociable neural routes to successful prospective memory. *Psychological Science, 24*(9), 1791–1800.

McDaniel, M. A., Umanath, S., Einstein, G. O., & Waldum, E. R. (2015). Dual pathways to prospective remembering. *Frontiers in Human Neuroscience, 9*, 392.

Minarik, T., Berger, B., Althaus, L., Bader, V., Biebl, B., Brotzeller, F., et al. (2016). The importance of sample size for reproducibility of tDCS effects. *Frontiers in Human Neuroscience, 10*.

Mioni, G., Rendell, P. G., Henry, J. D., Cantagallo, A., & Stablum, F. (2013). An investigation of prospective memory functions in people with traumatic brain injury using virtual week. *Journal of Clinical and Experimental Neuropsychology, 35*(6), 617–630.

Nelson, J., McKinley, R. A., Phillips, C., McIntire, L., Goodyear, C., Kreiner, A., & Monforton, L. (2016). The effects of transcranial direct current stimulation (tDCS) on multitasking throughput capacity. *Frontiers in Human Neuroscience, 10*, 589.

Peira, N., Ziaei, M., & Persson, J. (2016). Age differences in brain systems supporting transient and sustained processes involved in prospective memory and working memory. *NeuroImage, 125*, 745–755.

Phillips, L. H., Henry, J. D., & Martin, M. (2008). Adult aging and prospective memory: The importance of ecological validity.

Piau, A., Campo, E., Rumeau, P., Vellas, B., & Nourhashemi, F. (2014). Aging society and gerontechnology: A solution for an independent living? *The Journal of Nutrition, Health & Aging, 18*(1), 97–112.

Rendell, P. G., & Craik, F. I. (2000). Virtual week and actual week: Age-related differences in prospective memory. *Applied Cognitive Psychology, 14*(7).

Rendell, P. G., & Henry, J. D. (2009). A review of virtual week for prospective memory assessment: Clinical implications. *Brain impairment, 10*(1), 14–22.

Robison, M. K., McGuirk, W. P., & Unsworth, N. (2017). No evidence for enhancements to visual working memory with transcranial direct current stimulation to prefrontal or posterior parietal cortices. *Behavioral Neuroscience, 131*(4), 277–288.

Rose, N. S., Luo, L., Bialystok, E., Hering, A., Lau, K., & Craik, F. I. (2015a). Cognitive processes in the breakfast task: Planning and monitoring. *Canadian Journal of Experimental Psychology/Revue canadienne de psychologie expérimentale, 69*(3), 252.

Rose, N. S., Rendell, P. G., Hering, A., Kliegel, M., Bidelman, G. M., & Craik, F. I. (2015b). Cognitive and neural plasticity in older adults' prospective memory following training with the virtual week computer game. *Frontiers in Human Neuroscience, 9*.

Rose, N. S., Rendell, P. G., McDaniel, M. A., Aberle, I., & Kliegel, M. (2010). Age and individual differences in prospective memory during a" virtual week": The roles of working memory, vigilance, task regularity, and cue focality. *Psychology and Aging, 25*(3), 595.

Scullin, M. K., McDaniel, M. A., & Shelton, J. T. (2013). The dynamic multiprocess framework: Evidence from prospective memory with contextual variability. *Cognitive Psychology, 67*(1–2), 55–71.

Stephens, J. A., & Berryhill, M. E. (2016). Older adults improve on everyday tasks after working memory training and neurostimulation. *Brain Stimulation, 9*(4), 553–559.

Terrett, G., Rose, N. S., Henry, J. D., Bailey, P. E., Altgassen, M., Phillips, L. H., et al. (2016). The relationship between prospective memory and episodic future thinking in younger and older adulthood. *The Quarterly Journal of Experimental Psychology, 69*(2), 310–323.

Underwood, E. (2016). Cadaver study challenges brain stimulation methods. *Science, 352*, 397. https://doi.org/10.1126/science.352.6284.397.

Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica, 67*(6), 361–370.

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