The Impact of Transcranial Direct-Current Stimulation on Executive Functioning in Healthy Older Adults

Paul T. Evans

November 2013

as partial fulfillment of the requirements for the Degree of Bachelor of Psychology with Honours in the School of Psychology and Speech Pathology at Curtin University, Western Australia.

Declaration Page

I declare that this honours dissertation is my own work and has not been submitted in any form for another degree or diploma at any university or other institute of tertiary education. Information derived from the published or unpublished work of others has been acknowledged in the text and a list of references is given.

Signature:

Date: 08/11/2013

Acknowledgements

First and foremost I would like to thank my supervisor Dr Andrea Loftus for all her assistance and support this year. Thank you to Dr Robert Kane for the statistical advice. Thank you to Dr Frank Baughman for providing the Stroop measure used in this study. Thank you to my lab mates Hayley, Oz and Emily for their friendship and advice. Thank you to my family for all their support. Finally, thank you to all the participants of this study.

Table of Contents

List of Tables

List of Supplementary Materials

Abstract

Previous studies have found that transcranial direct-current stimulation (tDCS) to the dorsolateral prefrontal cortex (DLPFC) can modulate performance on executive functioning (EF) tasks of working memory and set-shifting. Our aim was to determine whether anodal tDCS to the left DLPFC at 2mA for 20 minutes could impact EF in healthy older adults (over the age of 60). Three measures of EF thought to relate to the control processes identified by Miyake et al. (2000) were chosen, specifically the CANTAB™ measures of spatial working memory and intra-extra dimensional set shift, and a computerised version of the colour-word Stroop task. Thirty healthy older adults completed the three measures of EF before and after tDCS. Fifteen of the participants received anodal tDCS to the left DLPFC for 20 minutes, while the other fifteen received sham. We found that anodal tDCS improved working memory through a significant reduction in spatial working memory within and between-errors. Our results support previous findings that anodal tDCS can modulate spatial working memory, providing further support for future application of this technique as a therapeutic tool.

Transcranial direct-current stimulation (tDCS) is a safe, non-invasive brain stimulation technique that can be used to modulate cortical excitability in specific, localized regions of the brain. This is achieved through the delivery of low voltage electrical current through electrodes fitted to the scalp. Stimulation can take the form of anodal (excitatory) stimulation, which depolarises neurons, increasing the probability of firing; cathodal (inhibitory) stimulation, which hyperpolarises neurons, decreasing the probability of firing; and sham (no stimulation) (Been et al., 2007). Research has examined the effects of tDCS on a wide range of cognitive processes in humans, including motor control, language ability, attention, problem solving and mathematical ability (Jacobson, Koslowsky & Lavidor, 2012; Fregni & Pascual-Leone, 2007; Utz, Dimova, Oppenlander & Kerkhoff, 2010). Furthermore, tDCS demonstrates great therapeutic potential for various mood and pain disorders (Been et al. 2007; Fregni & Pascual-Leone, 2007). Studies employing tDCS typically vary in terms of duration, size of electrodes u, and voltage delivered. This variation in testing parameters and a lack of clinical trials examining the long-term effects of stimulation have made it difficult to determine the efficacy of tDCS as a therapeutic tool. One area of particular focus in recent research has been the impact of tDCS on frontal lobe or ‘executive functions’ (Fregni et al., 2005; Leite, Carvalho, Fregni & Goncalves; Gladwin, den Uyl, Fregni & Wiers).

’Executive functioning’ is a multidimensional construct that encompasses a variety of cognitive processes located in the frontal lobe. Executive functions (EF’s) control, organize, manage and integrate other cognitive processes, acting as a cortical ‘control centre’ (Thurston-Snoha & Lewine, 2007). Recent studies have demonstrated that tDCS can modulate performance on general executive functioning tasks, including the Tower of London and Wisconsin Card Sorting Test (WCST) (Dockery, Hueckel-Weng, Birbaumer & Plewnia, 2009; Thurston-Snoha & Lewine, 2007). However, these tasks are known to recruit a number of executive processes, including working memory, set-shifting, planning and inhibition (Miyake, Friedman, Emerson, Witzki & Howerter, 2000). Consequently, it is difficult to delineate which executive processes are impacted by tDCS. Miyake et al. (2000) suggest that underlying EF’s are several control processes, which update and monitor information in working memory (“Updating”), allow for mental set-shifting (“Shifting”) and inhibit pre-potent responses (“Inhibition”). Support for this theory has been provided by recent studies employing factor

analytic and structural equation modelling methods to a wide range of EF measures (Fisk & Sharp, 2004; Hull, Martin, Beier, Lane & Hamilton, 2008; Lehto, Juujarvi, Kooistra & Pulkinnen, 2003).

Evidence from neuroimaging research suggests that the left and right dorsolateral prefrontal cortex (DLPFC) play an important, but not exclusive role in EF (Carpenter, Just & Reichle, 2000). During the course of normal healthy aging, changes to the DLPFC occur in the form of neuronal loss, neurotransmitter depletion, lesions and structural changes (Uylings & Brabander, 2002). Corresponding age-related declines have been observed in healthy older adults (over the age of 60) on EF measures of working memory, set-shifting and inhibition (Fisk & Sharp, 2004).

'Working memory' is the ability to transiently hold a set of items in the mind for manipulation (Baddelley & Hitch, 1974). Of all executive processes, working memory is perhaps the most sensitive to age-related neurological changes. Working memory capacity increases during adolescence before declining steadily from the age of twenty onwards (Salthouse, 1994). Healthy older adults typically demonstrate significant declines in working memory (Salthouse & Babcock, 2003). This trend holds independent of how working memory is measured, with verbal, spatial and numerical measures yielding consistent results (Kane et al., 2004). Several studies have examined the impact of tDCS on working memory. Fregni et al. (2005) found that anodal tDCS at 1 mA intensity for 10 minutes produced significant a reduction in the number of errors committed on a verbal working memory task (compared to sham stimulation) in a sample of healthy young adults. Boggio et al. (2006) administered anodal tDCS at intensities of 1 mA and 2mA to Parkinson's patients. They found that only the 2mA stimulation produced significant improvements in working memory as indexed by response accuracy on a three-back working memory task. These results suggest that magnitude of stimulation may be an important factor in determining the extent of working memory improvement. A recent study by Berryhill and Jones (2012) assessed working memory in older adults using verbal and visuo-spatial tasks. Participants received tDCS at 1.5 mA for 10 minutes to the left or right DLPFC (or sham stimulation). Following a median split of results according to participant's education level they reported that anodal tDCS improved results on both working memory measures, but only for participants with high education. This finding

suggests that individual differences play an important role in determining responsiveness to tDCS.

'Set-shifting' is the ability to display flexibility in problem solving in the face of varying schedules of reinforcement (Ridderinkhof, Span & van der Molen, 2002). An inability to display this flexibility can result in perseverative behaviour, occurring when a person persists with a response which it is clearly ineffective for the situation (Ridderinkhof et al., 2002). Numerous studies have reported that healthy older adults demonstrate significant deterioration in set-shifting and cognitive flexibility (Ashendorf & McCaffrey, 2008; Ridderinkhof et al., 2002). Leite, Carvalho, Fregni and Goncalves (2011) found that healthy young participants given anodal tDCS at 1 mA to the DLPFC for 15 minutes demonstrated significant improvements on a set-shifting task (compared to a sham control group). Notably, they found that the number of shifting errors did not change following tDCS. Instead, performance improved through an increase in reaction time when shifting between competing sets. This mechanism for improvement raises the question of whether tDCS directly impacts on set-shifting ability, or can simply modulate performance through related processes. For example, working memory and cognitive inhibition are both known to impact 'speed of shifting' and reaction time (Salthouse, 1992, 2003; West & Alain, 2000).

The ability to coordinate attention and resolve conflict between responses is known as 'cognitive inhibition'. This function is highly related to attentional processes as it allows a person to selectively process information in their environment by prioritizing relevant aspects and ignoring other irrelevant aspects (Carrasco, 2011). A number of studies have examined inhibitory and attentional processes in older adults. Treitz, Heyder and Daum (2007) found that the ability to control attention declines considerably after the age of 60. Coubard et al. (2010) found that older adults are worse (than their younger counterparts) at suppressing attention for distractors and switching attention for unpredictable events. West and Alain (2000) reported that age-related declines are observed in performance on the Stroop task, a measure sensitive to inhibitory processes. Gladwin, den Uyl, Fregni & Wiers (2012) examined whether tDCS could improve selective attention. Participants were given a Sternberg working memory task with distractors while receiving anodal tDCS at 1mA for 10 minutes. tDCS significantly improved working memory recall, but only when the incorrect choice had been a distractor

stimulus. This suggests that the tDCS-related improvements observed in working memory may be mediated by improvements in selective attention. In light of this, it is plausible that inhibition may also be impacted by tDCS.

Research Aims

There is a clear need for a study examining the effects of tDCS on EFs in healthy older adults, given that previous research has focused primarily on working memory processes. This study will examine whether specific EFs are differentially modulated by tDCS, providing potential insights into the structure of EFs and directions for future research including application to clinical populations. The present study therefore examined whether the application of anodal tDCS to the left DLPFC led to significant changes in spatial working memory, set-shifting and inhibition in a sample of healthy older adults.

Method

Research Design

An experimental research design was used to assess the impact of tDCS on three components of EF in healthy older adults. The two independent variables in this study were tDCS (anodal or sham) and time (pre and post tDCS). There were three dependent variables, including the CANTAB^{TM} measures of spatial working memory (SWM) and intra-extra dimensional set shift (IDED), and a computerised version of the Stroop colour-word task. These three tasks were selected as they are thought to map onto the executive control processes suggested by Miyake et al. (2000). SWM relates to "Updating," IDED relates to "Shifting," and the Stroop task relates to "Inhibition."

Participants

An a priori statistical power analysis was conducted using the software program G-Power. The resulting analysis indicated that 24 participants would be required in order to detect a moderate to large interaction effect (f = .3) with power (1 - β) set at 0.80 and α = .05, two-tailed.

30 healthy older adults (16 women, 14 men, M_{age} = 74.7, SD = 72.68, age range: 60-90 years) were recruited using flyers distributed to local retirement villages and advertisements placed in local newspapers. Participants were compensated with a $40 shopping voucher for participation in the study. Participants were randomly allocated to either the anodal or sham

tDCS condition using a coin toss, and age and gender-matched to reduce between-groups error associated with variation in cognitive ability. Prior to testing, all participants were required to meet the tDCS exclusion criteria and complete the Mini-Mental State Exam (MMSE) to ensure that no global cognitive impairment was present (all scores >24). The study was approved by the Curtin University Human Research Ethics Committee (HR 32/2013). All participants provided written informed consent.

Apparatus

The 1300 Soterix Medical^{TM} low intensity constant-current transcranial direct-current stimulator with saline soaked 5cm x 7cm sponge electrode pads was used to administer tDCS. One touch-screen tablet computer was used to administer the EF measures and Stroop colour-word task.

Measures

Mini-Mental State Exam. To screen for cognitive impairments the Mini Mental State Exam (MMSE) was used. The MMSE is a 30 point questionnaire test that assesses arithmetic, memory and orientation. Scores of 24 were required to be eligible for study inclusion. The MMSE takes approximately 10 minutes to complete.

Spatial Working Memory. The spatial working memory (SWM) task was used to assess the ability to retain spatial information and manipulate in working memory (Cambridge Cognition, 1996). During the task, a number of small ($3cm^2$) boxes are displayed at different positions on the screen. Participants are instructed to touch these boxes in order to reveal a hidden token, which they then have to deposit into an empty column on the right hand of the screen. Participants are instructed to select only one box at a time and that only one token is hidden at a time. Participants are also instructed not to search for tokens in boxes that they have previously found a token, as a token will never appear in the same box twice. The number of tokens present for each trial will be the same as the number of boxes that appear on the screen, which means that each box will contain a token at some point in the trial. The task increases in difficulty as the number of boxes on the screen increases. Participants initially complete three practice trials comprising three boxes. Following this, participants complete four test trials each with 4, 6 and 8 boxes. The task takes approximately 15 minutes to complete.

Spatial working memory ability was assessed according to the number of within and between-errors committed during the test trials. Within-errors occur when a participant returns to an already searched box that was found to contain no token. Between-errors occur when a participant returns to a box from which they have already found a token. The test-retest reliability for the SWM task is good with a Pearson's correlation of $r = .68$ (Lowe & Rabbit, 1998).

Intra-Dimensional Extra-Dimensional Set-Shift. The Intra-Dimensional Extra-Dimensional Set-Shift (IDED) task is used to assess set-shifting ability (Cambridge Cognition, 1996). This test assesses the ability to make simple discriminations, attend to specific attributes of compound stimuli and shift mental set from one dimension to another. Participants are first instructed to select the correct stimulus among a group of stimuli by touching the stimulus on the screen. The correct stimulus is identified based on trial and error and computer generated feedback (correct or incorrect). The task requires participants to identify the underlying rule to determine which of the stimuli is correct. No explicit rules are stated at the beginning of the task and participants are instructed to make their first choice based on a guess. After the first trial, participants are informed that there is a rule that they can learn in order to identify the correct stimuli. They are also informed that the rule could change and they may be required to discover and learn a new rule. In stage 3 of the task distractor stimuli in the form of white lines appear overlying the pre-existing stimuli. Participants are then forced to figure out whether the underlying or overlying stimuli determine which group of stimuli are correct.

Set-shifting ability was measured using extra-dimensional shift errors and total errors. Extra-dimensional shift errors is a measure of errors committed during test trial stage eight (8) when the overlying stimuli is the correct pattern – representing a shift between sets of stimuli. A lower number of errors reflect better set-shifting ability as it shows that participants were able to change their mental set more efficiently and with less effort. As instructed in the CANTAB manual (Cambridge Cognition, 1996), an adjusted score was calculated for participants who failed to reach Stage 8 of the task. The adjusted score was calculated by giving the participant a score of 25 errors. The value of 25 is used as subjects must complete 50 trials before they fail a stage, and 25 of these could be correct by chance alone. Total errors comprise the total number of errors committed during all nine (9) stages of the task. The test-

retest reliability for the IDED is good with a Pearson's correlation of $r = .70$ (Lowe & Rabbit, 1998). The task takes approximately 10 minutes to complete.

Stroop Colour-Word Task. The Stroop colour-word task is a commonly used measure of cognitive inhibition (Stroop, 1935). A computerised, online version of the stroop colour-word task was used in this study (Baughman, 2013). Prior to the task, participants are instructed that they will be presented with two words on the screen. They are asked to decide as quickly and accurately as possible whether the colour of the letters in the word at the top of the screen matches the meaning of the word at the bottom of the screen. Participants select 'correct' if the words match by clicking the left mouse button or 'incorrect' if the words do not match by clicking the right mouse button. Participants have five (5) seconds to respond before the task times out and they are given an incorrect response. Participants are required to click on a fixation cross at the centre of the screen to commence each trial. The task includes seven (7) practice trials followed by 64 test trials with the real or nonsense word at the top of the screen printed in one of four colours (yellow, green, red, or blue), and the word at the bottom the screen printed in grey. The task includes neutral trials in which random sets of letters were presented at the top of the screen (eg., NSLG), and incongruent trials in which a real word was presented that differed both semantically and in colour (eg., YELLOW in blue colour). Therefore, trials were counterbalanced for the experimental design of 4 colours (yellow, green, red and blue) × 2 conditions (neutral or incongruent) × 2 responses (yes or no) which each set of trials carried out four times for a total of 64 trials. The task takes approximately 10 minutes to complete.

To measure inhibition, the mean reaction time difference between correct responses to incongruent trials and correct responses to neutral trials was calculated resulting in an 'interference' score. The total number of errors for combined neutral and incongruent trials was also examined. No reliability information currently exists for this task. However, this is not considered an issue due to the similarity of this task to a range of well validated measures and the well-established strength of the Stroop interference effect (Macleod, 1991).

Procedure

Testing took place at the Curtin Neuroscience Research Laboratory. Each participant completed the three EF measures twice – once before (pre) tDCS and once after (post) tDCS.

The order of task administration was counterbalanced across conditions to reduce the influence of ordering and practice effects.

Two saline-soaked 5cm x 7cm electrode pads were positioned in accordance with the 10-20 system and secured in position using a head strap. For all participants the anodal electrode was positioned at F3 and the reference electrode was positioned at FP1. Participants in the experimental group received anodal tDCS at 2mA for 20 minutes, while participants in the control group received sham stimulation for 20 minutes. During tDCS participants were made as comfortable as possible and invited to watch a video or converse with the researchers.

A testing session generally lasted two hours; however there was no time limit and participants were encouraged to take breaks as necessary.

Results

Two participants did not complete the SWM measure so their data were missing from analysis of SWM between and within errors. A number of outliers were present for each of the measures; however none were influential so no action was taken. Examination of Shapiro-Wilk statistics indicated that the assumption of normality was violated for a number of measures. However examination of histograms, skewness and kurtosis scores indicated that only SWM within-errors and Stroop interference had significant violations. Consequently, square root transformations were conducted on these measures resulting in data that was normally distributed. All measures met the homogeneity of variances assumption for ANOVA. Statistical analysis was conducted with IBM SPSS for Windows (Version 21).

The data were analysed using a repeated measures analysis of variance (ANOVA) for each measure of executive functioning with time (pre, post) as the within-subjects factor and tDCS condition (anodal, sham) as the between-subjects factor. To examine interaction effects between the within and between-subjects factors for the EF measures, pairwise comparisons were conducted.

Table 1

Summary of Means, Standard Deviations and Participant Numbers for each Measure of Executive Functioning Pre and Post-test

	Pre-test		Post-test		*N*
Measure	*M*	*SD*	*M*	*SD*	
SWM Between-Errors	50.54	21.56	41.46	19.69	28
SWM Within-Errors	4	4.54	2.46	3.02	28
IDED Total-Errors	27.10	10	20.40	11.22	30
IDED EDS-Errors	16.5	11.48	7.83	9.21	30
Stroop Interference	1759.53	475.37	343.12	228.47	30
Stroop Total-Errors	7.40	6.70	4.57	4.24	30

For SWM between-errors there was a significant effect of time, F (1, 26) = 9.47, p = .005, η^{p2}= .267. As can be seen in Table 1, between-errors decreased significantly pre to post-test. There was no main effect of group, F (1, 26) = .01, p = .922, η^{p2}= .00. There was a significant group × time interaction, F (2, 54) = 4.36, p = .047, η^{p2}= .14. Pairwise comparisons were conducted to examine this interaction. Pre and post-test differences for each tDCS condition (anodal, sham) were compared. For the anodal group the difference in pre and post-test errors was significant, t(12) = 3.16, p = .008, d = .69. For the sham group the difference was non-significant, t(14) = .817, p = .428, d =.17. Anodal tDCS significantly reduced SWM between-errors pre-test (M = 54.38. SD = 24.77) to post-test (M = 38.38, SD = 21.34). In comparison, sham tDCS did not significantly reduce SWM between-errors from pre-test (M = 47.20, SD = 18.58) to post-test (M = 44.13, SD = 18.47).

For SWM within-errors there was no effect for time, F (1, 26) = 2.50, p = .126, η^{p2}= .09 and no main effect for group, F (1, 26) = .12, p = .735, η^{p2}= .70. There was a significant group × time interaction, F (2, 54) = 4.691, p = .040, η^{p2}= .15. To analyse this interaction, pairwise comparisons were conducted to compare pre and post-test differences for each tDCS condition (anodal, sham). For the anodal group the difference in pre and post-test errors was significant t(12) = 2.42, p = .032, d = .61. For the sham group the difference was non-significant, t(14) = -.452, p = .658, d = -.15. Anodal tDCS significantly reduced SWM within-

errors from pre-test (*M* = 1.89, *SD* = 1.52) to post-test (*M* = 1.07, *SD* = 1.16). In comparison, sham tDCS did not significantly reduce SWM within-errors pre-test (*M* = 1.29, *SD* = .97) to post-test (*M* = 1.42, *SD* = .75).

For IDED total errors there was a significant effect for time, *F* (1, 28) = 9.97, *p* = .004, η^{p2}= .26. As can be seen in Table 1, IDED total errors decreased significantly pre to post-test. There was no main effect for group, *F* (1, 28) = .001, *p* = .976, η^{p2}= .00, with no significant group × time interaction, *F* (2, 56) = 1.11, *p* = .301, η^{p2}= .04.

For IDED extra-dimensional shift errors there was a significant effect for time, *F* (1, 28) = 20.75, *p* = <.001, η^{p2}= .43. As can be seen in Table 1, extra-dimensional shift errors decreased significantly pre to post-test. There was no main effect for group, *F* (1, 28) = .47, *p* = .500, η^{p2}= .02, with no significant group × time interaction, *F* (2, 56) = 1.18, *p* = .287, η^{p2}= .04.

For Stroop interference there was a significant effect for time, *F* (1, 28) = 811.57, *p* <.001, η^{p2}=.97. As can be seen in Table 1, interference decreased significantly pre to post-test. There was no main effect for group, *F* (1, 28) = .83, *p* = .369, η^{p2}= .03, with no significant group × time interaction, *F* (2, 56) = 1.45, *p* = .239, η^{p2}=.05.

For Stroop total errors there was a significant effect for time, *F* (1, 28) = 7.59, *p* = .010, η^{p2}= .213. As can be seen in Table 1, errors decreased significantly pre to post-test. There was no main effect for group, *F* (1, 28) = .03, *p* = .869, η^{p2}= .00, with no significant group × time interaction, *F* (2, 56) = .38, *p* = .543, η^{p2}= .01.

Discussion

The finding that anodal tDCS produced a significant reduction in spatial working memory between and within-errors compared to sham is consistent with the results of Berryhill and Jones (2012) and Fregni et al. (2005) who also noted improvements via this mechanism. Berryhill and Jones (2012) found that tDCS improved working memory only for highly educated older adults; however the current study employed random sampling and did not control for education or other individual differences factors so we were unable to examine any response patterns to tDCS. It is possible that the small significant effects found for both between and within-errors were attenuated to some extent by variability within this sample. While participants were age and gender matched across conditions, the wide age range (60-90

years) is likely to have increased between-group variability. In addition, it is possible that the MMSE failed to effectively screen for all cognitive impairments, given recent evidence that it lacks the sensitivity to detect mild deterioration or selective impairments (Cacho et al., 2010).

The finding that tDCS did not impact significantly upon set-shifting errors is consistent with Leite, Carvalho, Fregni and Goncalves (2011) who found that performance improved through an increase in reaction time when shifting between sets of stimuli. We argue that set-shifting errors is a purer measure of mental set-shifting than reaction time, and the absence of an effect provides evidence that tDCS does not modulate this process. Our reasoning is that in real-world settings set-shifting errors reflect perseveration with an ineffective mental strategy, whereas reaction time or 'speed of shifting' does not involve a shifting of mental set. The rationale behind including a measure of set-shifting in this study was evidence from Thurston-Snoha and Lewine (2007) that tDCS modulates performance on the WCST, a task variously used to measure set-shifting, cognitive inhibition and working memory (Miyake et al., 2000). Consequently, the current findings suggest that observed improvements on the WCST result from modulation of working memory and not set-shifting.

The finding that tDCS did not significantly impact cognitive inhibition may be a result of the involvement of multiple brain areas in this process. According to Blasi et al. (2006) cognitive inhibition recruits the DLPFC, ventrolateral prefrontal cortex (VLPFC) and the parietal cortex. However, given that these regions form a network, we may have expected 'downstream' effects from the tDCS, where stimulation also impacts these regions. Alternatively, it is possible that the Stroop measure used in this study lacked the sensitivity to detect any changes to cognitive inhibition following tDCS. The large time effects observed for Stroop interference and total errors suggest that it took the participants time to adjust to the measure. This may be due to a lack of familiarity with computers amongst the older adults or difficulty remembering the rules of the measure. Future studies could employ simpler measures of cognitive inhibition like the Go/ No-go or Eriksson Flanker task (Botvinick, Braver, Barch, Carter & Cohen).

Limitations

A limitation of this study is one common to studies across the field of cognitive psychology: measure impurity. Specifically, all of the measures used in this study are known to

recruit attentional and inhibitory processes (Miyake et al., 2000). Because of this overlap, it is difficult to determine which processes are modulated by tDCS. It is possible that a single underlying process or mechanism may be responsible for the observed improvements. One likely candidate is speed of information processing which has previously been linked with reaction time, working memory, fluid intelligence and attentional processes (Salthouse, 1992, 2003). On a related note, Marshall, Molle, Siebner and Born (2005) note that task difficulty may determine the extent of performance improvement following tDCS. For example, a more difficult task may require more cognitive resources and consequently participants will show greater improvements following tDCS. According to this theory, a high functioning participant may reach a 'ceiling' in performance pre-test on an easier task and improve relatively little post-test following tDCS.

The tDCS montage used in this study was well tolerated with no side effects reported from participants. The applied voltage of 2mA is the highest that has been proven safe in previous research (Been et al., 2007). In addition, the 20-minute stimulation time and 5 x 7cm electrode pads were selected based on the findings of Fregni et al. (2005) and Boggio et al. (2006) who found that these parameters allowed focal targeting of the DLPFC. These studies found that variation in parameters resulted in cognitive enhancing effects varying in strength and duration. Consequently, the applied parameters are likely to have had an impact on the size of observed effects in this study. In addition, we cannot discount the possibility that the effects of tDCS dissipated over the duration of post-test task administration. However, in theory, the counterbalanced ordering of measures should have minimised any differences between treatment groups.

Future Research and Implications

An important goal for future research will be to develop tDCS paradigms that provide long-term benefits. Recent research has suggested that repeated sessions of tDCS can provide long-term improvements for clinical patients with major depression (Ferrucci et al., 2008) and aphasia following stroke (Hamilton, Chrysikou & Coslett, 2011). However, there remains little consensus between researchers regarding the most appropriate tDCS parameters for the treatment of specific conditions. A recent review paper by Kraus, Marquez-Ruiz and Kadosh (2013) offers a potential mechanism for the cognitive enhancement effects of tDCS. They

suggest that an ideal balance exists between the inhibitory neurotransmitter GABA and the excitatory neurotransmitter Glutamate. tDCS can alter this balance through anodal (excitatory) stimulation which increases Glutamate levels and cathodal (inhibitory) stimulation which increases GABA levels. In the context of this study, this theory may explain the small effects found for working memory and the absence of effects for set-shifting and inhibition. It is likely that participants had varying excitation/inhibition balances before the study, with anodal tDCS potentially reducing task performance for those high in excitation. A major implication is that individual differences need to be an important consideration in future studies. Greater understanding of these differences will allow for the development of tDCS paradigms tailored to the individual in terms of polarity (anodal or cathodal), intensity, duration and treatment frequency.

A potential future application for tDCS is in the rehabilitation of patients with left neglect. This disorder involves a deficit of awareness or 'neglect' of the left hand side of visual space, typically arising from damage to the right temporal-parietal or superior temporal cortices (Karnath & Rorden, 2012). According to Striemer, Ferber and Danckert (2013) severe spatial working memory deficits constitute a core component of neglect. Given that tDCS is affordable, portable and easy to use, it presents an ideal health practitioner or self-administered therapeutic tool for neglect.

Conclusion

This study set out to determine how tDCS impacts EF as defined according to the theoretical framework of Miyake et al. (2000). It was hoped that basing our operational definition on this theory would enable the effects of tDCS on EF to be differentiated, making clear which processes are impacted. The findings of this study do not support the hypothesis that tDCS can modulate distinct EFs in healthy older adults. Instead, this study adds to a growing body of research suggesting that tDCS can reliably produce improvements in spatial working memory.

References

Ashendorf, L., & McCaffrey, R.J. (2008). Exploring age-related decline on the Wisconsin Card Sorting Test. *The Clinical Neurologist, 22,* 262-272.doi: 10.1080/13854040701218436

Baddeley, A.D., & Hitch, G. (1974). *Working Memory.* In G.H. Bower (Ed.) *The psychology of learning and motivation*: *Advances in research and theory* (Vol. 8, pp. 47-89). New York: Academic Press.

Baughman, F. (2013). Stroop colour-word task [Software]. Unpublished instrument. Retrieved from http:// http://www.javares.net/projects/neurocurtin/

Berryhill, M.E., & Jones, K.T. (2012). tDCS selectively improves working memory in older adults with more education. *Neuroscience Letters, 521*(2), 148-151. doi: 10.1016/j.neulet.2012.05.074

Blasi, G., Goldberg, T.E., Weickert, T., Das, S., Kohn, P., Zoltick, B., …Mattay, V.S. (2006). Brain regions underlying response inhibition and interference monitoring and suppression. *European Journal of Neuroscience, 23,* 1658-1664. doi: 10.1111/j.1460-9568.2006.04680.x

Boggio, P.S., Ferrucci, R., Rigonatti, S.P., Covre, P., Nitsche, M., Pascual-Leone, A., & Fregni, F. (2006). Effects of transcranial direct current stimulation on working memory in patients with Parkinson's disease. *Journal of the Neurological Sciences, 1,* 31-38. doi: 10.1016/j.jns.2006.05.062

Botvinick, M.M., Braver, T.S., Barch, D.M., Carter, C.S., & Cohen, J.D. (2001). Conflict monitoring and cognitive control. *Psychological Review, 108,* 624-652. doi: 10.1037/0033-295X.108.3.624

Cacho, J., Benito-Leon, J., Carcia-Garcia, R., Fernandez Calvo, B., Vicente-Villardon, J.L., & Mitchell, A.J. (2010). Does the combination of the MMSE and Clock Drawing Test (Mini- Clock) improve the detection of mild Alzheimer's Disease and Mild Cognitive Impairment? *Journal of Alzheimer's Disease, 22,* 889, 896. doi: 10.3233/JAD2010101182

Cambridge Cognition. (1996). Cambridge Automated Neuropsychological Test Battery (CANTAB). Cambridge, England: Cambridge Cognition Limited.

Carpenter, P.A., Just, M.A., & Reichle, E.D. (2000). Working memory and executive function: Evidence from neuroimaging. *Current Opinion in Neurobiology, 10*, 195-199.

Carrasco, M. (2011). Visual attention: The past 25 years. *Vision Research, 51*, 1484-1525. doi: 10.1016/j.visres.2011.04.012

Dockery, C.A., Hueckel-Weng, R., Birbaumer, N., & Plewnia, C. (2009). Enhancement of planning ability by transcranial direct-current stimulation. *The Journal of Neuroscience, 29*, 7271-7277. doi: 10.1523/JNEUROSCI.0065-09

Edden, R.A.,Crocetti, D., Zhu, H., Gilbert, D.L., & Mostofsky, S. H. (2012).Reduced GABA concentration in attention-deficit/ hyperactivity disorder. *Archives of General Psychiatry, 69*, 750–753. doi:10. 1001/archgenpsychiatry.2011.2280

Ferrucci, R., Bortolomasi, M., Vergari, M., Tadini, L., Salvoro, B., Giacopuzzi, M.,… & Priori, A. (2009). Transcranial direct-current stimulation in severe, drug resistant depression. *Journal of Affective Disorders, 118*, 215-219.

Fisk, J.E., & Sharp, C.A. (2004). Age-related impairment in executive functioning: Updating, inhibition, shifting and access. *Journal of Clinical and Experimental Neuropsychology, 26*, 874-890. doi: 10.1080/13803390490510680

Fregni, F., Boggio, P.S., Bermpohl, F., Antal, A., Feredoes, E., Marcolin, M.A., Rigonatti, S.P., Silva, M.T.A., Paulus, W., Pascual-Leone, A. (2005). Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Experimental Brain Research, 166*, 23-30. doi: 10.1007/s00221-005-2334-6

Fregni, F., & Pascual-Leone, A. (2007). Technology insight: Non-invasive brain stimulation in neurology-perspectives on the therapeutic potential of rTMS and tDCS. *Nature Reviews Neurology, 3*, 383-393. doi: 10.1038/ncpneuro0530

Gladwin, T.E., den Uyl, T.E., Fregni, F.F., & Wiers, R.W. (2012). Enhancement of selective attention by tDCS: Interaction with interference in a Sternberg task. *Neuroscience Letters, 512*, 33-37. doi: 10.1016/j.neulet.2012.01.056

Hamilton, R.H., Chrysikou, E.G., & Coslett, B. (2011). Mechanisms of aphasia recovery after stroke and the role of noninvasive brain stimulation. *Brain and Language*, 118, 40-40.

Hull, R., Martin, R.C., Beier, M, E., Lane, D., & Hamilton, A.C. (2008). Executive function in older adults: A structural equation modeling approach. *Neuropsychology, 22*(4), 508-522.doi: 10.1037/0894-4105.22.4.508

Jacobson, L., Koslowsky, M., & Lavidor, M. (2012). tDCS polarity effects in motor and cognitive domains: A meta-analytic review. *Experimental Brain Research, 1*, 1-10.

Kane, M.J., Hambrick, D.Z., Tuholski, S.W., Wilhelm, O., Payne, T.W., & Engle, R.W. (2004). The generality of working memory capacity: A latent-variable approach to verbal and visuospatial memory span and reasoning. *Journal of Experimental Psychology, 133*(2). doi: 10.1037/0096-3445.133.2.189

Karnath, H.O., & Rorden, C. (2012). The anatomy of spatial neglect. *Neuropsychologia, 50,* 1010-1017. doi: 10.1016/j.neuropsychologia.2011.06.027

Kraus, B., Marquez-Ruiz, & Kadosh, R.C. (2013). The effect of transcranial direct-current stimulation: A role for cortical excitation/inhibition balance? *Frontiers in Human Neuroscience, 7,* 1-4. doi: 10.3389/fnhum.2013.00602

Lehto, J.E., Juujarvi, P., Kooistra, L., & Pulkinnen. (2003). Dimensions of executive functioning: Evidence from children. *The British Journal of Developmental Psychology, 21,* 59-80. doi: 10.1348/026151003321164627

Leite, J., Carvalho, S., Fregni, F., & Goncalves, O.F. (2011). Task-specific effects of tDCS-induced cortical excitability changes on cognitive and motor sequence set shifting performance. *Plos One, 6*. doi: 10.1371/journal.pone.0024140

Lowe, C., & Rabbit, P. (1998). Test/retest reliability of the CANTAB and ISPOCD neuropsychological batteries: theoretical and practical issues. *Neuropsychologica, 36*(9), 915-923

Macleod, C.M. (1991). Half a century of research on the Stroop effect: An integrative review. *Psychological Bulletin, 109,* 163-203.

Marshall, L., Molle, M., Siebner, H.R., & Born, J. (2005). Bifrontal transcranial direct-current stimulation slows reaction time in a working memory task. *BMC Neuroscience, 6,* 1-7. doi:10.1186/1471-2202-6-23

Meiron, O., & Lavidor, M. (2012). Unilateral prefrontal direct current stimulation effects are modulated by working memory load and gender. *Brain Stimulation, 5,* 100-110.

Miyake, A., Friedman, N.P., Emerson, M.J., Witzki, A.H., & Howerter, A. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive Psychology, 41,* 49-100. doi: 10.1006/cogp.1999.0734

Ridderinkhof, K.R., Span, M.M., & van der Molen, M.W. (2002). Perserverative behavior and adaptive control in older adults: Performance monitoring, rule induction and set shifting. *Brain and Cognition, 49,* 382-401. doi: 10.1006/brcg.2001.1506

Rubenstein,J.L.,& Merzenich,M.M. (2003). Model of autism: increased ratio of excitation/inhibition in key neural systems. *Genes, Brain, Behaviour, 2*, 255–267.

Salthouse, T.A. (1992). Influence of processing speed on adult differences in working memory. *Acta Psychologica, 79,* 155-170.

Salthouse, T.A. (1994). The aging of working memory. *Neuropsychology, 8,* 535-543.

Salthouse, T.A. (2003). Executive functioning as a potential mediator of age-related cognitive decline in normal adults. *Journal of Experimental Psychology, 132,* 566-594. doi: 10.1037/0096-3445.132.4.566

Striemer, C.L., Ferber, S., & Danckert, J. (2013). Spatial working memory deficits represent a core challenge for rehabilitating neglect. *Frontiers in Human Neuroscience, 7,* 1-11. doi: 10.3389/fnhum.2013.00334

Stroop, J.R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology, 18,* 643-662. doi: 10.1037/h0054651

Thurston-Snoha, B.J., & Lewine, R.R. (2007). Intact Wisconsin Card Sorting test performance: implications for the role of executive functions in schizophrenia. *British Journal of Clinical Psychology, 46,* 361-369. doi: 10.1348/014466507X173772

Nitsche, M.A., Boggio, P.S., Fregni, F., & Pascual-Leone, A. (2009). Treatment of depressionwith transcranial direct current stimulation (tDCS): A review. *Experimental Neurology, 219,* 14-19. doi:10.1016/j.expneurol.2009.03.038

Treitz, F.H., Heyder, K., & Daum, I. (2007). Differential course of executive control changes during normal aging. *Neuropsychology, Development and Cognition. Section B, Aging, Neuropsychology and Cognition, 14,* 370-393. doi: 10.1080/13825580600678442

West, R., & Alain, T. (2000). Age-related decline in inhibitory control contributes to the Stroop effect observed in older adults. *Psychophysiology, 37,* 179-189

Extended Literature Review

The Impact of Transcranial Direct-Current Stimulation on Executive Functioning in Healthy Older Adults

Paul T. Evans

Curtin University

School of Psychology and Speech Pathology

Executive Functions

The term ’executive functions’ encompasses a variety of processes that control, organize, manage and integrate other cognitive processes, acting as a ‘control centre’ in the human brain. Executive functions (EF) are typically measured using measures of planning, working memory, attention, mental flexibility, problem solving, mental flexibility and task switching. A number of different theoretical models have been developed to account for the role of executive functions in regulating, controlling and managing other cognitive processes.

Norman and Shallice (1980) proposed the supervisory attentional system (SAS), a conceptual model of executive function. According to this model, individuals possess well established schemas that allow them to respond automatically to routine, predictable situations. However, when faced with novel situations, an individual engages the SAS which inhibits situationally-inappropriate schemas, instead activating more appropriate schemas or allowing for the application of general problem solving strategies.

Baddeley and Hitch (1974) proposed a multicomponent model of working memory comprised of two separate domain specific slave sub-systems: the *phonological loop*, responsible for holding and manipulating sound or phonological information and the *visuospatial sketchpad*, responsible for holding and manipulating spatial and visual information. Coordinating these two slave systems is the *central executive*, a supervisory system responsible for binding information from these two sources together into coherent episodes, allowing for shifting between tasks for the control and regulation of cognitive processes. This model was later updated with the addition of a fourth component the *episodic buffer*, a third slave system which integrates phonological and visual/spatial information into chronologically ordered units of meaning that can later be recalled using long-term memory (Baddeley, 2000).

Barkley (2001) approached the study of executive functions from an evolutionary neuropsychological perspective. According to his self-regulatory model, EFs are a biological adaptation that has evolved as a form of self-regulation in response to interpersonal social competition within the human species. Through the development of covert mental representations, human beings are able to shift the control of behaviour from public to private responses, allowing inhibition of behavioural responses and judgments regarding the

hypothetical social future.

Miller and Cohen (2001) suggest that the role of the prefrontal cortex is to actively maintain patterns of activity that represent goals and the means to achieve them. This is achieved by sending biasing signals throughout the rest of the brain, guiding the flow of neural activity along pathways specific to certain features or representations. For example, a person looking for a red coat in a crowd of people will selectively narrow their selective visual attention with the help of their frontal cortex, which increases gain signals for the neurons that respond to the colour red, increasing their chances of spotting the coat.

Miyake, Friedman, Emerson, Witzki and Howerter (2000) postulated that underlying EF's are several control processes whose functions serve to update and monitor information in the environment ("Updating"), inhibit pre-potent responses ("Inhibition") and allow for mental set-shifting ("Shifting"). The authors produced this theory by administering a set of EF tasks to a large group of participants then using latent variable analysis to statistically extract the underlying factors. They found these several control processes were moderately correlated with each other but clearly distinct, indicating that these processes provide the unity and diversity in EF while each contributing differentially to performance on EF tasks. This latent variable approach provides a unified theory of EF by proposing lower level functions that can be clearly operationally defined. In addition, there is good reason to believe that these control processes underlie some of the more widely used EF measures, including the Wisconsin Card Sorting Test (WCST) and Tower of Hanoi (also known as the Tower of London). Further evidence for the fractionation of executive functions into these separate control processes has been provided by recent studies employing factor analytic and structural equation modeling methods to a wide range of EF measures (Fisk & Sharp, 2004; Hull, Martin, Beier, Lane & Hamilton, 2008; Lehto, Juujarvi, Kooistra & Pulkinnen, 2003). The nature of these control processes means that in order to effectively measure the construct of EF it may be apposite to select measures that evidentially map onto them.

This literature review will examine the effects of age on executive functioning, both generally and as it is observed on several domain-specific cognitive processes postulated by Miyake et al. (2000). In addition, recent evidence for the effects of anodal transcranial direct-current stimulation (tDCS) on these processes will also be examined.

Age-Related Declines in EF

Research indicates that healthy older adults (over the age of 60) perform poorly on a broad range of EF measures compared to younger adults. The nature and extent of these age-related declines vary according to the aspect of EF measured (Fisk & Sharp, 2004). These declines are likely due to neuronal loss, lesions, neurotransmitter depletion and other structural changes to associated areas of the prefrontal cortex. The left and right dorsolateral prefrontal cortices (DLPFC) are integral to EF, with evidence that damage to this area can lead directly to dysexecutive syndrome (Uylings & de Brabander, 2002). Along with the effects of normal aging, executive dysfunction can also be produced by a range of aging-related neurological disorders, including Parkinson's disease, frontal lobe dementia, Alzheimer's and the AIDS-dementia complex (Elliott, 2003). Psychiatric disorders including depression, schizophrenia and bipolar disorder can also impair executive performance (Lockwood, Alexopoulos & van Gorp, 2002). Research suggests that EF may mediate age-related cognitive decline in older adults (Salthouse, Atkinson & Berish, 2003) and can act as a predictor for impairment in instrumental activities of daily living (IADLs) (Cahn-Weiner, Malloy, Boyle, Marran & Salloway, 2000). One recent study found that older adults with impairments in executive functioning are at increased risk for automobile accidents (Daigneault, Joly & Frigon, 2002). In addition, executive functions have been shown to be important for social and emotional decision making which are important for maintaining and fostering strong relationships, which in turn have been shown to be integral for healthy aging (MacPherson, Phillips & Della Sala, 2002). These studies suggests that the maintenance of EF in older adults could assist reduce rates of functional decline and allow older adults to care for themselves and maintain their independence for longer. Age-related declines have also been observed in the domain specific executive processes of working memory, cognitive inhibition and set-shifting.

Working Memory

'Working memory' is defined as the ability to transiently hold multiple pieces of information the mind for manipulation (Baddelley & Hitch, 1974). Of all executive processes, working memory is perhaps the most sensitive to lifestyle factors and aging-related neurological changes, with capacity increasing during adolescence before declining steadily from the age of twenty onwards (Salthouse, 1994). Kane et al. (2004) suggest that this trend is

independent of how working memory is measured, with verbal, spatial and numerical measures yielding the same results. Broad individual differences exist in working memory capacity and working memory performance has been correlated with a range of cognitive processes, including fluid intelligence, speed of information processing and IQ. Declines in working memory ability with aging predict impairment in the ability for older adults to complete instrumental activities of daily living (IADLS's) (Bell-McGinty, Podell, Franzen, Baird & Williams, 2002), including the ability to remember to take medications (Insel, Morrow, Brewer & Figueredo, 2006), prepare meals, use appliances, keep appointments and perform a host of other household tasks (Aretouli & Brandt, 2010). The ability to perform these tasks independently is crucial for older adults live independently at home rather than in aged care facilities.

Set-shifting

'Set-shifting' is defined as the ability to display flexibility in problem solving in the face of varying schedules of reinforcement (Ridderinkhof, Span & van der Molen, 2002). This skill is of great importance in our busy modern world as it provides the flexibility to deal with rapidly changing circumstances. Set-shifting is the ability to shift from behavioural schemas that have worked previously to new schemas, often while reconfiguring and redefining tasks to make them more manageable (Norman & Shallice, 1980). An inability to display this flexibility can result in perseverative behavior, occurring when a person persists with an inappropriate response when it is clearly ineffective for the situation (Ridderinkhof et al., 2002). Early neuropsychological studies revealed that older adults with lesions to the dorsolateral frontal lobe have pronounced deficits in set-shifting (Milner, 1963). Studies of set-shifting typically differentiate between intra-dimensional shift, which occurs when a person shifts within dimensions of a set of stimuli (for example: from red to black on a card task) and extra-dimensional set-shift, when a person shifts to different dimensions of a set of stimuli (for example from colour to number on a card task). The Wisconsin Card Sorting Test (WCST; Grant & Berg, 1948) measures set-shifting and is highly sensitive to frontal lobe dysfunction and successful completion also relies upon a range of other intact executive processes, including attention and working memory. A number of studies reveal significant deterioration in set-shifting and cognitive flexibility in healthy older adults (Ashendorf & McCaffrey, 2008;

Ridderinkhof et al., 2002). The results of these studies indicate that the observed age-related decline in performance on the WCST is caused specifically by impairments in general set-shifting ability rather than other associated cognitive abilities.

Cognitive Inhibition

'Cognitive inhibition' allows a person to selectively process information in their environment by prioritizing certain aspects of a visual scene and ignoring other irrelevant aspects (Carrasco, 2011). The ability to coordinate attention is known as cognitive inhibition. Neuroimaging studies reveal that this process activates the anterior cingulate and lateral prefrontal cortex (Botvinick, Braver, Barch, Carter, & Cohen, 2001).

Treitz, Heyder and Daum (2007) found that the ability to divide attention and inhibit prepotent response declines considerably after the age of 60. Coubard et al. (2010) administered a battery of attentional control measures to younger adults (20-30 years), older adults (62-89 years) and Alzheimer's patients. They found that older adults were poorer at suppressing attention for distractors and preparing and switching attention for unpredictable events. Milham et al. (2002) used fMRI to compare the neural activity of older and younger participants during the completion of the color-word Stroop task. Among the older participants they found evidence of decreased responsiveness in the dorsolateral and prefrontal cortices, both structures relating to attentional control.

Transcranial direct-current stimulation

Transcranial direct-current stimulation (tDCS) is a type of safe, non-invasive brain stimulation technique that can be used to modulate the cortical excitability of neurons in specific, localized regions of the brain. This is achieved through the emission of small amounts of electrical current through electrodes fitted to the external scalp. Stimulation can take the form of anodal (excitatory) and cathodal (inhibitory) stimulation, as well as sham (no stimulation) (Been et al., 2007). Recent tDCS research has examined the effects of this technique on a wide range of functions in humans, including motor control, language ability, attention, problem solving and mathematical ability. (Jacobson, Koslowsky & Lavidor, 2012; Fregni & Pascual-Leone, 2007). In addition, tDCS has also shown great promise as a treatment for various mood and pain disorders (Been et al. 2007; Fregni & Pascual-Leone, 2007; Nitsche, Boggio, Fregni & Pascual-Leone, 2009).

Studies employing tDCS typically vary in the duration of stimulation, size of electrodes used and voltage used. This variation in testing parameters and a lack of clinical trials examining the long-term effects of stimulation have made it thus far difficult to determine the true efficacy of tDCS as a potential mainstream treatment for general health conditions. Recent studies have demonstrated that the application of tDCS to the DLPFC can modulate performance on general executive functioning measure including the Tower of London and WCST (Dockery, Hueckel-Weng, Birmbaumer & Plewnia, 2009; Thurston-Snoha & Lewine, 2007). These results suggest that tDCS may also be effective at modulating performance on more specific executive functions including working memory, attention and set-shifting.

The impact of tDCS on Working Memory

A number of recent studies have examined the effect of anodal tDCS to the left DLPFC on the working memory performance of healthy young adults. Fregni et al (2005) found that the application of anodal tDCS at 1 mA intensity for 10 minutes produced significant improvements on a verbal working memory task (compared to sham stimulation) in a sample of healthy young adults. Ohn et al. (2007) found that after 20 minutes of 1 mA stimulation resulted in significantly fewer errors on a verbal working memory task, with further improvements after 30 minutes. These results provide evidence that the duration of tDCS stimulation is important in determining the magnitude of working memory improvement. Teo, Hoy, Daskalakis and Fitzgerald (2011) investigated the effects of tDCS stimulation of 1mA, 2mA and sham stimulation on intra-stimulation performance on an n-back working memory task, and post-stimulation performance on the Sternberg WM task. They found no significant improvements in participant accuracy across conditions; though a significant interaction was found between current strength and reaction time. The authors suggest that the low level of difficulty of the working memory task may have limited the potential to detect any performance benefits from the tDCS stimulation.

Several studies have examined the effect of anodal tDCS to the left DLPFC on working memory in healthy older adults (over the age of 65). Boggio et al. (2006) found that tDCS stimulation of 2mA administered to Parkinson's patients produced significant improvements in working memory as indexed by response accuracy on a three-back working memory task. Seo et al. (2011) administered anodal tDCS at 2mA for 30 minutes to a sample of healthy older

adults. Before and after application of tDCS the participants were tested on a verbal working memory task and a visuospatial working memory task. They found that accuracy on the verbal working memory task improved significantly following stimulation, while accuracy on the visuospatial working memory task was unchanged. A possible explanation for this result is that visuospatial working memory is localized more in the right DLPFC for some individuals and therefore would have impacted less by tDCS (Owen et al., 1999). In addition, Meiron and Lavidor (2012) found that the effects of tDCS on the 'online' performance on a verbal working memory task were gender-dependent, with males benefiting more from stimulation of the left DLPFC and females from stimulation to the right DLPFC.

A recent study by Berryhill and Jones (2012) also employed verbal and visuospatial tasks to test working memory in older adults. In this study participants received either tDCS to the left DLPFC, the right DLPFC or sham stimulation. tDCS was applied at 1.5 mA for 10 minutes in all conditions. The authors performed a median split on the results according to participant education level, finding that anodal tDCS improved results on both working memory measures, but only for participants with high education. A number of reasons have been suggested to account for this difference. It is possible that participants in the high education group may employ a different cognitive strategy than the low education group. This might result in greater reliance on the PFC during working memory tasks and therefore greater improvement from stimulation to this area. Alternatively, more highly educated older adults may experience greater declines in working memory through aging-related neurological changes and regain more previously lost resources. Whatever the mechanism underlying this finding, the paucity of research examining individual differences in responsiveness to tDCS highlights the need for further, more focused investigation.

The impact of tDCS on Set-shifting

Few studies have directly examined the effects of tDCS on set-shifting ability. Leite, Carvalho, Fregni and Goncalves (2011) found that healthy young participants given anodal tDCS at 1 mA to the DLPFC for 15 minutes produced significant improvements on a cognitive set-shifting task (compared to a sham stimulation control group). Notably, they found that the number of shifting errors did not change following tDCS, instead performance improved through an increase in reaction time when shifting between competing sets. These results raise

the question of whether tDCS directly impact on set-shifting ability, or can simply modulate performance through related processes like working memory or inhibition.

The impact of tDCS on Cognitive Inhibition

No studies have examined the effect of tDCS on cognitive inhibition in healthy older adults. However, a study by Kang, Baek, Kim and Paik (2009) found that tDCS at 2mA for 20 minutes applied to the left DLPFC of stroke patients produced significant improvements on a measure of attentional control when compared to sham. Gladwin, den Uyl, Fregni & Wiers (2012) tested whether tDCS could improve selective attention. Participants were given a Sternberg task with distractors while receiving anodal tDCS of 1mA for 10 minutes. The results indicated that tDCS improved working memory recall significantly, but only when the incorrect choice had been a distractor stimulus. The authors suggest that this result indicates that the improvements observed in working memory following tDCS may be mediated by improvements in selective attention.

According to Miyake et al. (2000), attentional control is highly related to cognitive inhibition: the ability to control and inhibit pre-potent responses. Several studies have found that the application of anodal tDCS to the DLPFC can modulate inhibitory control, as demonstrated through reductions in impulsivity **(**Beeli, Casutt, Baumgartner & Jäncke, 2008; Beeli, Koeneke, Gasser & Jancke, 2008). The results of these studies suggest that the application of tDCS to the DLPFC may also modulate the inhibitory processes that underlie attentional control. Additionally, as the ability to control and direct attention is functionally highly related to other executive processes like working memory and set-shifting, there is good reason to believe that tDCS stimulation will also produce measurable improvements in this function.

Rationale

The present research will examine whether anodal tDCS at 2mA for 20 minutes applied to the left DLPFC of healthy older adults (over the age of 60) will result in significant improvements in executive functioning. The construct of executive functioning will be measured using the computerized CANTAB measures of spatial working memory (SWM), intra-extra dimensional set shift (IED), and the stroop colour-word task. The rationale behind choosing these particular tests is that they are thought to map onto the executive control

processes suggested by Miyake et al. (2000). Spatial working memory relates to the control process “Updating,” intra-extra dimensional set-shift relates to “Shifting” and Stroop relates to “Inhibition,”

Results from this study will also inform about the efficacy of tDCS as a method for improving the executive functioning of healthy older adults. Should tDCS prove effective at improving and maintaining these functions, it may have application as a health practitioner or self-administered technique utile to the general aged population. Research has shown that the maintenance of executive functions is important for retaining the ability to live independently and complete IADLS’s (Bell-McGinty, 2002).

References

Albert, D.J. (1966). The effect of spreading depression on the consolidation of learning. *Neuropsychologia, 4*, 40-64.

Aretouli, E., & Brandt, J. (2010). Everyday functioning in mild cognitive impairment and its relationship with executive cognition. *International Journal of Geriatric Psychology, 25*, 224-233. doi: 10.1002/gps.2325

Ashendorf, L., & McCaffrey, R.J. (2008). Exploring age-related decline on the Wisconsin Card Sorting Test. *The Clinical Neurologist, 22*, 262-272.doi: 10.1080/13854040701218436

Austin, M.A., Mitchell, P., Goodwin, G.M. (2001). Cognitive deficits in depression: possible implications for functional neuropathology. *The British Journal of Psychiatry, 178*, 200-206. doi: 10.1192/bjp.178.3.200

Baddeley, A.D., & Hitch, G. (1974). *Working Memory.* In G.H. Bower (Ed.) *The psychology of learning and motivation*: *Advances in research and theory* (Vol. 8, pp. 47-89). New York: Academic Press.

Barkley, R.A. (2001). The executive functions and self-regulation: An evolutionary neuropsychological perspective. *Neuropsychological Review, 11*, 1-26.

Beeli, G., Casutt, G., Baumgartner, T., & Jäncke, L. (2008). Modulating presence and impulsiveness by external stimulation of the brain. *Behavioral and Brain Functions, 4*, 33-39. doi:10.1186/1744-9081-4-33

Beeli, G., Koeneke, S., Gasser, K., & Jäncke, L. (2008). Brain stimulation modulates driving behavior. *Behavioral and Brain Functions, 4*, 34-43. doi: 10.1186/1744-9081-4-34

Bell-McGinty, S., Podell, K., Franzen, M., & Williams, M.J. (2002). Standard measures of executive function in predicting instrumental activities of daily living in older adults. *International Journal of Geriatric Psychology, 17*, 828-834. doi: 10.1002/gps.646

Berryhill, M.E., & Jones, K.T. (2012). tDCS selectively improves working memory in older adults with more education. *Neuroscience Letters, 521*, 148-151. doi: 10.1016/j.neulet.2012.05.074

Boggio, P.S., Ferrucci, R., Rigonatti, S.P., Covre, P., Nitsche, M., Pascual-Leone, A., & Fregni, F. (2006). Effects of transcranial direct current stimulation on working

memory in patients with Parkinson's disease. *Journal of the Neurological Sciences, 1*, 31-38. doi: 10.1016/j.jns.2006.05.062

Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. S., & Cohen, J. D. (2001). Conflict monitoring and cognitive control. *Psychological Review, 108*, 624-652. doi: 10.1037/0033-295X.108.3.624

Cahn-Weiner, D.A., Malloy, P.F., Boyle, P.A., Marran, M., & Salloway, S. (2000). Prediction of functional status from neuropsychological tests in community dwelling elderly individuals. *The Clinical Neuropsychologist, 14*, 187-195. doi: 10.1076/1385-4046(200005)14:2;1-Z;FT187

Carrasco, M. (2011). Visual attention: The past 25 years. *Vision Research, 51*, 1484-1525. doi: 10.1016/j.visres.2011.04.012

Coubard, O.A., Ferrufino, L., Boura, M, Gripon, A., Renaud, M., & Bherer, L. (2011). Attentional control in normal aging and Alzheimer's disease. *Neuropsychology, 25*, 353-367. doi: 10.1037/a0022058

Daigneault, G., Joly, P., & Frigon, J.Y. (2002). Executive functions in the evaluation of accident risk of older drivers. *Journal of Clinical and Experimental Neuropsychology, 24*, 221-238. doi: 10.1076/jcen.24.2.221.993

Elliott, R. (2002). Executive functions and their disorders: Imaging in clinical neuroscience. *British Medical Bulletin, 65*, 49-59.doi: 10.1093/bmb/65.1.49

Fisk, J.E., & Sharp, C.A. (2004). Age-related impairment in executive functioning: Updating, inhibition, shifting and access. *Journal of Clinical and Experimental Neuropsychology, 26*, 874-890. doi: 10.1080/13803390490510680

Fregni, F., & Pascual-Leone, A. (2007). Technology insight: Non-invasive brain stimulation in neurology-perspectives on the therapeutic potential of rTMS and tDCS. *Nature Reviews Neurology, 3*, 383-393. doi: 10.1038/ncpneuro0530

Fregni, F., Boggio, P.S., Bermpohl, F., Antal, A., Feredoes, E., Marcolin, M.A., Rigonatti, S.P., Silva, M.T.A., Paulus, W., Pascual-Leone, A. (2005). Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Experimental Brain Research, 166*, 23-30. doi: 10.1007/s00221-005-2334-6

Gladwin, T.E., den Uyl, T.E., Fregni, F.F., & Wiers, R.W. (2012). Enhancement of selective attention by tDCS: Interaction with interference in a Sternberg task. *Neuroscience Letters, 512,* 33-37. doi: 10.1016/j.neulet.2012.01.056

Grant, A. D., & Berg, E. A. (1948). A behavioral analysis of reinforcement and ease of shifting to new responses in a Weigl-type card sorting task. *Journal of Experimental Psychology, 38,* 404–411.

Hull, R., Martin, R.C., Beier, M, E., Lane, D., & Hamilton, A.C. (2008). Executive function in older adults: A structural equation modeling approach. *Neuropsychology, 22,* 508-522.doi: 10.1037/0894-4105.22.4.508

Insel, K., Morrow, D., Brewer, B., & Figuerdo, A. (2006). Executive function, working memory and medication adherence among older adults. *Journal of Gerontology: Psychological Sciences, 61,* 102-107. doi: 10.1093/geronb/61.2.P102

Iyer, M.B., Mattu, U., Grafman, J., Lomarev, M., Sato, S., & Wassermann, E.M. (2005). Safety and cognitive effect of frontal DC brain polarization in healthy individuals. *Neurology, 64,* 872-875. doi: 10.1212/01.WNL.0000152986.07469.E

Jacobson, L., Koslowsky, M., & Lavidor, M. (2012). tDCS polarity effects in motor and cognitive domains: A meta-analytic review. *Experimental Brain Research, 1,* 1-10. doi: 10.1007/s00221-011-2891-9

Kane, M.J., Hambrick, D.Z., Tuholski, S.W., Wilhelm, O., Payne, T.W., & Engle, R.W. (2004). The generality of working memory capacity: A latent-variable approach to verbal and visuospatial memory span and reasoning. *Journal of Experimental Psychology, 133.* doi: 10.1037/0096-3445.133.2.189

Kang, E.K., Baek, M.J., Kim, S.Y., & Paik, N.J. (2009). Non-invasive cortical stimulation improves post-stroke attention decline. *Restorative Neurology and Neuroscience, 27,* 647-652. doi: 10.3233/RNN-2009-0514

Lehto, J.E., Juujarvi, P., Kooistra, L., & Pulkinnen. (2003). Dimensions of executive functioning: Evidence from children. *The British Journal of Developmental Psychology, 21,* 59-80. doi: 10.1348/026151003321164627

Leite, J., Carvalho, S., Fregni, F., & Goncalves, O.F. (2011). Task-specific effects of tDCS-induced cortical excitability changes on cognitive and motor sequence set shifting

performance. *Plos One, 6*. doi: 10.1371/journal.pone.0024140

Lockwood, K.A., Alexopoulos, G.S., & van Gorp, W.G. (2002). Executive functioning in geriatric depression. *American Journal of Psychiatry, 159*, 1119-1126. doi: 10.1176/appi.ajp.1fsddf59.7.1119

Loo, C.K., Alonzo, A., Martin, D., Mitchell, P.B., Galvez, V., & Sachdev, P. (2012). Transcranial direct current stimulation for depression: 3-week, randomized, shame-controlled trial. *British Journal of Psychiatry, 200*, 52-59. doi: 10.1192/bjp.bp.111.097634

MacPherson, S.E., Phillips, L.H., & Della Sala, S. (2002). Age, executive functioning and social decision making: A dorsolateral prefrontal theory of cognitive aging. *Psychology and Aging, 17*, 589-608.

Meiron, O., & Lavidor, M. (2012). Unilateral prefrontal direct current stimulation effects are modulated by working memory load and gender. *Brain Stimulation, 5*, 100-110.

Milham, M.P., Erickson, K.I., Banich, M.T., Kramer, A.F., Webb, A., Wszalek, T., Cohen, N.J. (2002). Attentional control in the aging brain: Insights from an fMRI study of the stroop task. *Brain and Cognition, 49*, 277-296. doi: 10.1006/brcg.2001.1501

Miller, E.K., & Cohen, J.D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*, 167-202.

Plewnia, C., Zwissler, B., Langst, I., Maurer, B., Giel, K., & Kruger, R. (2012). Effects of transcranial direct current stimulation (tDCS) on executive functions: Influence of COMT Val/Met polymorphism. *Cortex, 48*, 1-7. doi: 0.1016/j.cortex.2012.11.00

Ridderinkhof, K.R., Span, M.M., & van der Molen, M.W. (2002). Perserverative behavior and adaptive control in older adults: Performance monitoring, rule induction and set shifting. *Brain and Cognition, 49*, 382-401. doi: 10.1006/brcg.2001.1506

Rothwell, J.C. (2012). Clinical applications of noninvasive electrical stimulation: Problems and potential. *Clinical EEG and Neuroscience, 43*, 209-214. doi: 10.1177/1550059412444973

Salthouse, T.A. (1994). The aging of working memory. *Neuropsychology, 8*, 535-543. doi: 10.1037/0894-4105.8.4.535

Salthouse, T.A. (2003). Executive functioning as a potential mediator of age-related cognitive

decline in normal adults. *Journal of Experimental Psychology, 132,* 566-594. doi: 10.1037/0096-3445.132.4.566

Seo, M.H., Park, S.H., Seo, J.H., Kim, Y.H., & Ko, M.H. (2011). Improvement of the working memory by transcranial direct current stimulation in healthy older adults. *Journal of the Korean Academy of Rehabilitation Medicine, 35,* 201-206.

Teo, F., Hoy, K.E., Daskalakis, Z.J., & Fitzgerald, P.B. (2011). Investigating the role of current strength in tDCS modulation on working memory performance in healthy controls. *Frontiers in Psychiatry, 2,* 1-10. doi: 10.3389/fpsyt.2011.00045

Thurston-Snoha, B.J., & Lewine, R.R. (2007). Intact Wisconsin Card Sorting test performance: implications for the role of executive functions in schizophrenia. *British Journal of Clinical Psychology, 46,* 361-369. doi: 10.1348/014466507X173772

Treitz, F.H., Heyder, K., & Daum, I. (2007). Differential course of executive control changes during normal aging. *Neuropsychology, development and cognition. Section B, Aging, neuropsychology and cognition, 14,* 370-393. doi: 10.1080/13825580600678442

Utz, K.S., Dimova, V., Oppenlander, K., & Kerkhoff, G. (2010). Electrified minds: Transcranial direct current stimulation (tDCS) and Galvanic Vestibular Stimulation as methods of non-invasive brain stimulation in neuropsychology-A review of current data and future implications, *Neuropsychologia*, *48*, 2789-2810. doi: 10.1016/j.neuropsychologia.2010.06.002

Milner, B. (1963). Effects of different brain lesions on card sorting. *Archives of Neurology, 9,* 90–100.

Miyake, A., Friedman, N.P., Emerson, M.J., Witzki, A.H., & Howerter, A. (2000). The unity and diversity of executive functions and their contributions to complex “frontal lobe” tasks: A latent variable analysis. *Cognitive Psychology, 41,* 49-100. doi: 10.1006/cogp.1999.0734

Ohn, S.H., Park, C., Yoo, W.K., Ko, M.H., Choi, K.P., Kim, G.M., Lee, Y.T., & Kim, Y.H. (2007). Time-dependent effect of transcranial direct current stimulation on the enhancement of working memory. *Neuroreport, 19,* 43-47. doi: 10.1097/WNR.0b013e3282f2adfd

Owen, A.M., Herrod, N.J., Menon, D.K., Clark, J.C., Downey, S.P.M.J., Carpenter, T.A., Minhas, P.S., Turkheimer, F.E., Williams, E.J., Robbins, T.W., Sahakian, B.J., Petrides, M., & Pickard, J.D. (1999). Redefining the functional organization of working memory processes within human lateral prefrontal cortex. *European Journal of Neuroscience, 11*, 567-574. doi: 10.1046/j.1460-9568.1999.00449.x

Supplementary Materials

The Impact of Transcranial Direct-Current Stimulation on Executive Functioning in Healthy Older Adults

Paul T. Evans

Curtin University

School of Psychology and Speech Pathology

Assumption Testing

Missing Data and Outliers

Case numbers 28 and 18 failed to complete the SWM measure, so consequently were missing from the analysis of SWM between-errors and within-errors.

Case number 16 was an outlier for SWM between-errors post-test; case numbers 6, 15, 27 and 19 were outliers for SWM within-errors post-test; case numbers 4, 9 and 23 were outliers for IDED EDS-errors post-test; case number 5 was an outlier for Stroop total-errors pre-test; case number 3 was an outlier for Stroop interference post-test. None of these outlier scores were greater than the standardised score of >3.29 standard deviations from the mean identified by Tabachnick and Fidell (2012) as being influential, so were consequently included in the analysis.

Normality and Homogeneity of Variances

Shapiro-Wilk statistics indicated that the assumption of normality was violated for the measures of SWM within-errors pre and post-test, IDED EDS-errors pre and post-test, Stroop total-errors pre and post-test and Stroop Interference post-test. Examination of histograms indicated that the data was normally distributed for all measures except for SWM within-errors post-test and Stroop Interference post-test, which had skewness and/or kurtosis scores in excess of 2. Consequently square-root transformations were conducted on these measures in accordance with the advice of Tabachnick and Fidell (2012). This procedure resulted in data that met the normality assumptions for ANOVA analysis.

Homogeneity of variances was examined by calculating the F_{max} statistic for each measure pre and post-test. All scores were less than 10, indicating that homogeneity of variances can be assumed (Allen & Bennett, 2012)

Initial Assumption Testing Output for all Measures

Descriptives				
			Statistic	Std. Error
SWMPRE_BETWEEN	Mean		50.54	4.075
	95% Confidence Interval for Mean	Lower Bound	42.17	
		Upper Bound	58.90	
	5% Trimmed Mean		49.92	
	Median		49.50	
	Variance		464.999	
	Std. Deviation		21.564	
	Minimum		11	
	Maximum		110	
	Range		99	
	Interquartile Range		29	
	Skewness		.388	.441
	Kurtosis		.773	.858
SWMPOST_BETWEEN	Mean		41.46	3.722
	95% Confidence Interval for Mean	Lower Bound	33.83	
		Upper Bound	49.10	
	5% Trimmed Mean		41.87	
	Median		39.50	
	Variance		387.813	
	Std. Deviation		19.693	
	Minimum		4	
	Maximum		72	
	Range		68	
	Interquartile Range		32	
	Skewness		-.285	.441
	Kurtosis		-.738	.858
SWMPRE_WITHIN	Mean		4.0000	.85758
	95% Confidence Interval for Mean	Lower Bound	2.2404	
		Upper Bound	5.7596	
	5% Trimmed Mean		3.5556	
	Median		3.0000	
	Variance		20.593	

	Std. Deviation		4.53791	
	Minimum		.00	
	Maximum		16.00	
	Range		16.00	
	Interquartile Range		7.00	
	Skewness		1.388	.441
	Kurtosis		1.645	.858
SWMPOST_WITHIN	Mean		2.4643	.57155
	95% Confidence Interval for Mean	Lower Bound	1.2916	
		Upper Bound	3.6370	
	5% Trimmed Mean		2.1032	
	Median		2.0000	
	Variance		9.147	
	Std. Deviation		3.02437	
	Minimum		.00	
	Maximum		12.00	
	Range		12.00	
	Interquartile Range		2.50	
	Skewness		1.967	.441
	Kurtosis		3.618	.858
IDEDPRE	Mean		27.54	1.926
	95% Confidence Interval for Mean	Lower Bound	23.58	
		Upper Bound	31.49	
	5% Trimmed Mean		27.56	
	Median		28.50	
	Variance		103.888	
	Std. Deviation		10.193	
	Minimum		8	
	Maximum		49	
	Range		41	
	Interquartile Range		17	
	Skewness		-.304	.441
	Kurtosis		-.444	.858
IDEDPOST	Mean		20.71	2.176
	95% Confidence Interval for Mean	Lower Bound	16.25	
		Upper Bound	25.18	
	5% Trimmed Mean		20.07	

	Median		20.50	
	Variance		132.582	
	Std. Deviation		11.514	
	Minimum		6	
	Maximum		51	
	Range		45	
	Interquartile Range		19	
	Skewness		.706	.441
	Kurtosis		.026	.858
IDEDPRE_EDSERRORS	Mean		16.5000	2.12226
	95% Confidence Interval for Mean	Lower Bound	12.1455	
		Upper Bound	20.8545	
	5% Trimmed Mean		16.2540	
	Median		15.5000	
	Variance		126.111	
	Std. Deviation		11.22992	
	Minimum		3.00	
	Maximum		35.00	
	Range		32.00	
	Interquartile Range		21.50	
	Skewness		.178	.441
	Kurtosis		-1.657	.858
IDEDPOST_EDSERRORS	Mean		7.7500	1.75604
	95% Confidence Interval for Mean	Lower Bound	4.1469	
		Upper Bound	11.3531	
	5% Trimmed Mean		7.0556	
	Median		3.0000	
	Variance		86.343	
	Std. Deviation		9.29207	
	Minimum		.00	
	Maximum		28.00	
	Range		28.00	
	Interquartile Range		10.25	
	Skewness		1.325	.441
	Kurtosis		.412	.858
STROOPERRORSPRE	Mean		7.18	1.244
	95% Confidence Interval for	Lower Bound	4.63	

	Mean	Upper Bound	9.73	
	5% Trimmed Mean		6.59	
	Median		6.00	
	Variance		43.337	
	Std. Deviation		6.583	
	Minimum		0	
	Maximum		27	
	Range		27	
	Interquartile Range		8	
	Skewness		1.452	.441
	Kurtosis		1.995	.858
STROOPERRORSPOST	Mean		4.21	.655
	95% Confidence Interval for	Lower Bound	2.87	
	Mean	Upper Bound	5.56	
	5% Trimmed Mean		4.03	
	Median		3.50	
	Variance		12.026	
	Std. Deviation		3.468	
	Minimum		0	
	Maximum		12	
	Range		12	
	Interquartile Range		4	
	Skewness		.902	.441
	Kurtosis		-.081	.858
STROOPPRE_INTERFERENCE	Mean		1755.8027	91.65687
	95% Confidence Interval for	Lower Bound	1567.7384	
	Mean	Upper Bound	1943.8671	
	5% Trimmed Mean		1736.4794	
	Median		1800.7040	
	Variance		235227.481	
	Std. Deviation		485.00256	
	Minimum		1042.44	
	Maximum		2913.35	
	Range		1870.91	
	Interquartile Range		686.34	
	Skewness		.410	.441
	Kurtosis		-.146	.858

STROOPPOST_INTERFERENCE	Mean		334.4507	42.32335
	95% Confidence Interval for Mean	Lower Bound	247.6103	
		Upper Bound	421.2910	
	5% Trimmed Mean		318.7326	
	Median		305.0585	
	Variance		50155.457	
	Std. Deviation		223.95414	
	Minimum		-20.22	
	Maximum		1038.30	
	Range		1058.51	
	Interquartile Range		278.99	
	Skewness		1.252	.441
	Kurtosis		2.432	.858

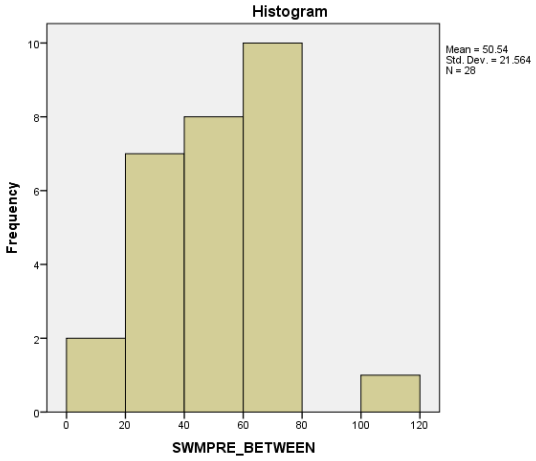
Tests of Normality

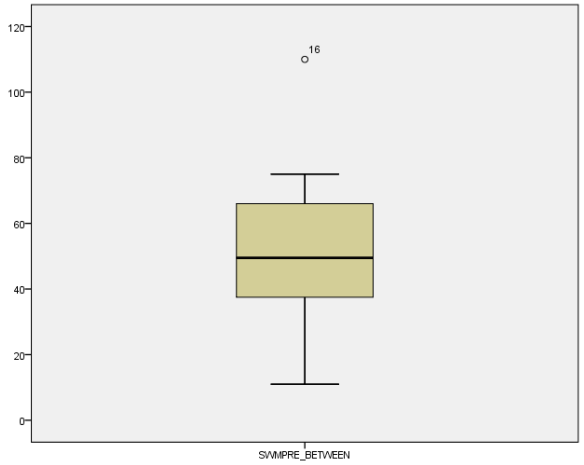
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
SWMPRE_BETWEEN	.093	28	.200*	.966	28	.478
SWMPOST_BETWEEN	.099	28	.200*	.959	28	.336
SWMPRE_WITHIN	.189	28	.012	.822	28	.000
SWMPOST_WITHIN	.311	28	.000	.736	28	.000
IDEDPRE	.133	28	.200*	.950	28	.195
IDEDPOST	.149	28	.115	.933	28	.073
IDEDPRE_EDSERRORS	.194	28	.008	.872	28	.003
IDEDPOST_EDSERRORS	.267	28	.000	.759	28	.000
STROOPERRORSPRE	.189	28	.011	.859	28	.001
STROOPERRORSPOST	.203	28	.004	.897	28	.010
STROOPPRE_INTERFERENCE	.102	28	.200*	.962	28	.398
STROOPPOST_INTERFERENCE	.140	28	.169	.921	28	.037

*. This is a lower bound of the true significance.

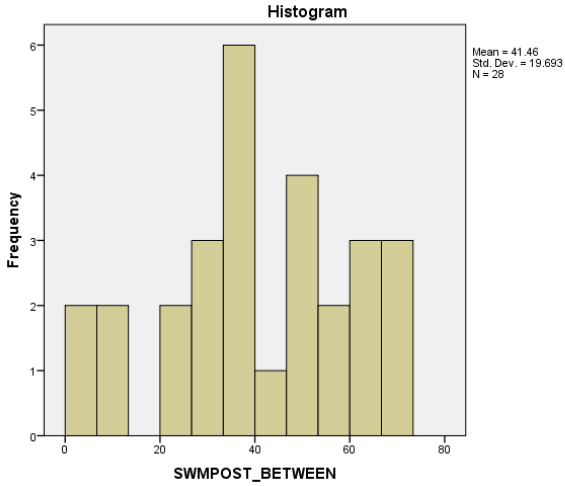
a. Lilliefors Significance Correction

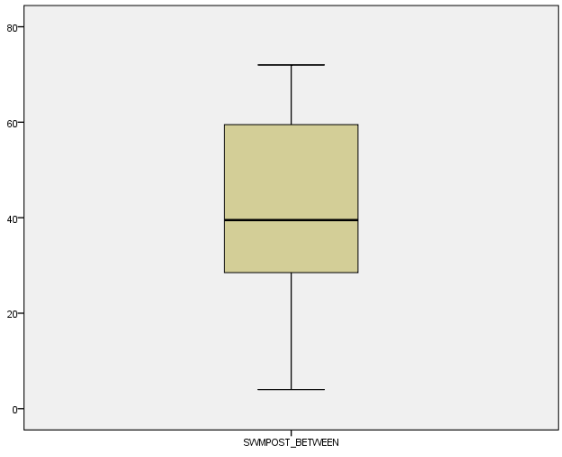
SWMPRE_BETWEEN



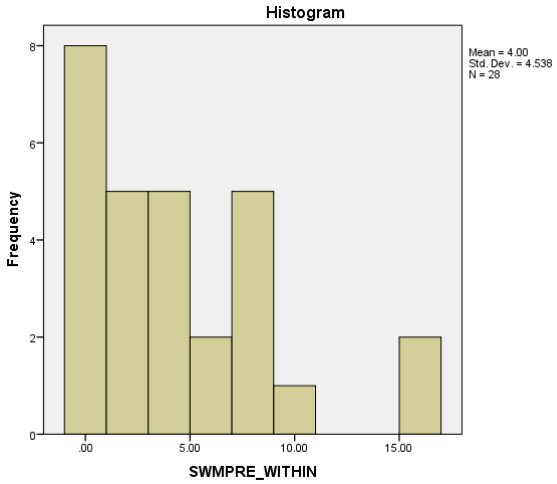


SWMPOST_BETWEEN

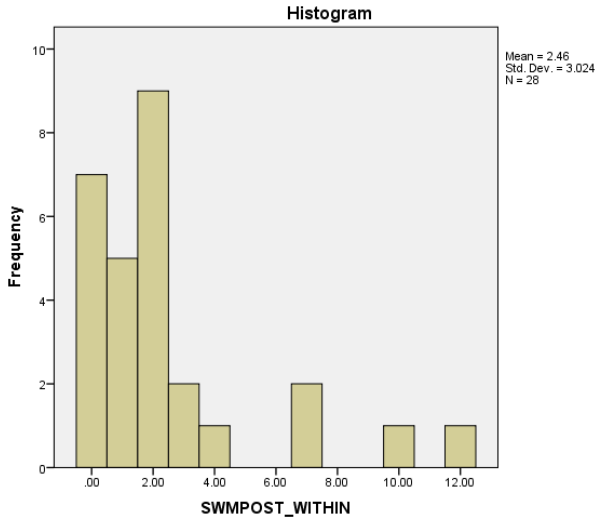




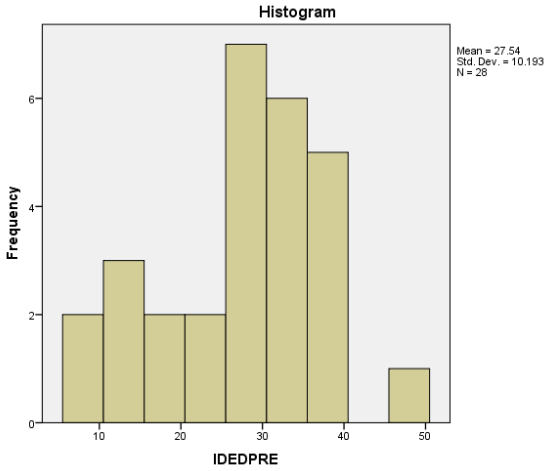
SWMPRE_WITHIN

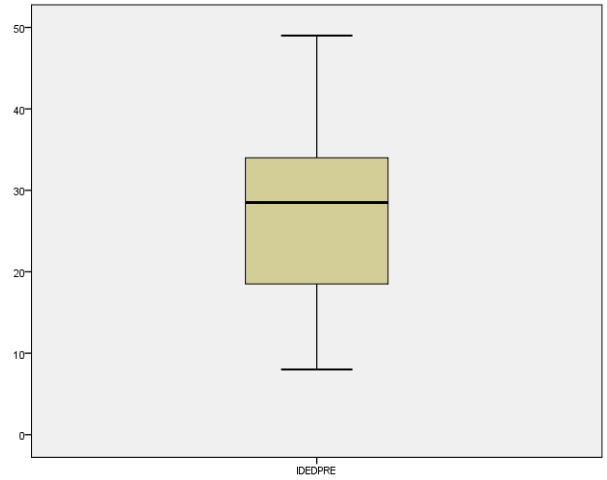


SWMPOST_WITHIN

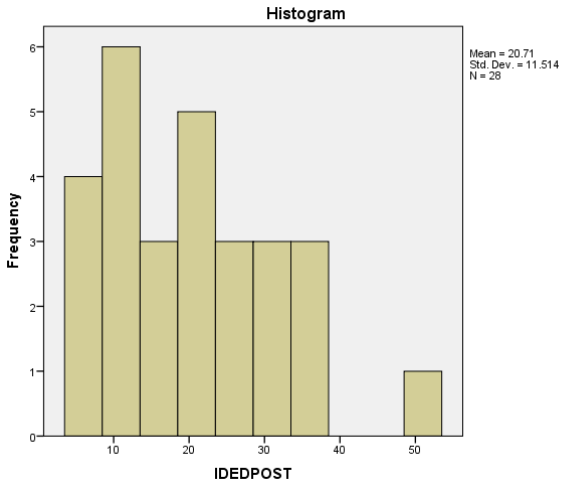


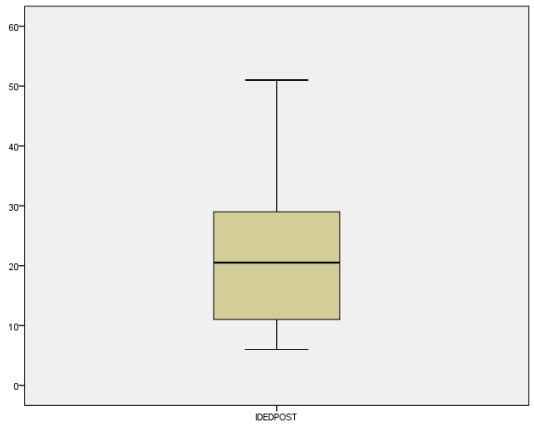
IDEDPRE



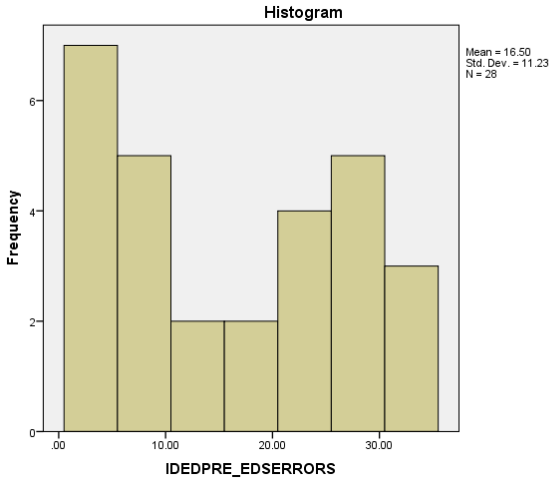


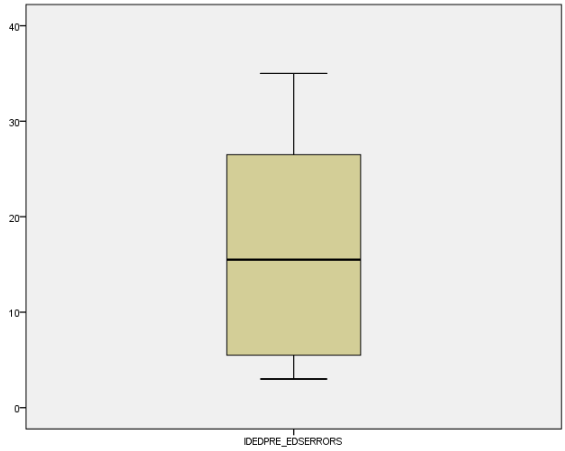
IDEDPOST



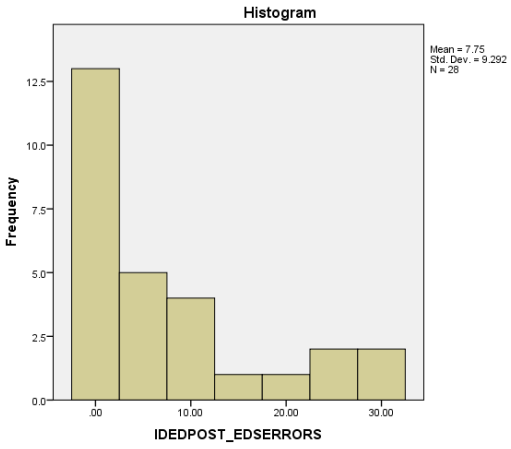


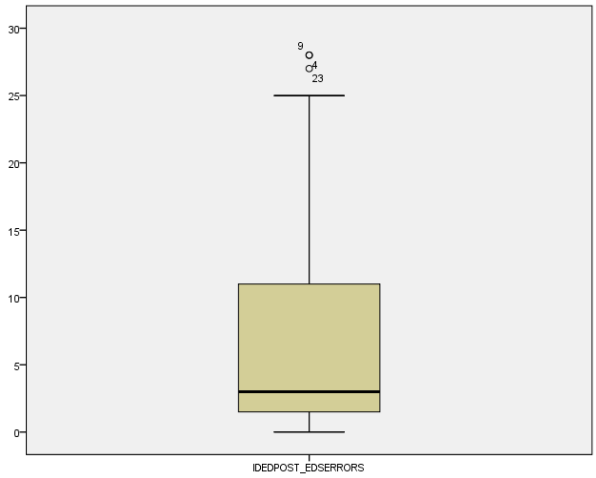
IDEDPRE_EDSERRORS



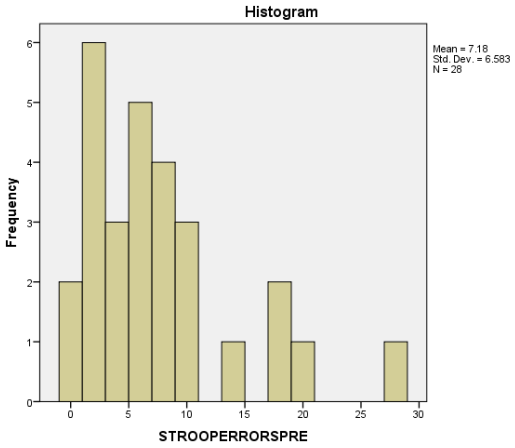


IDEDPOST_EDSERRORS

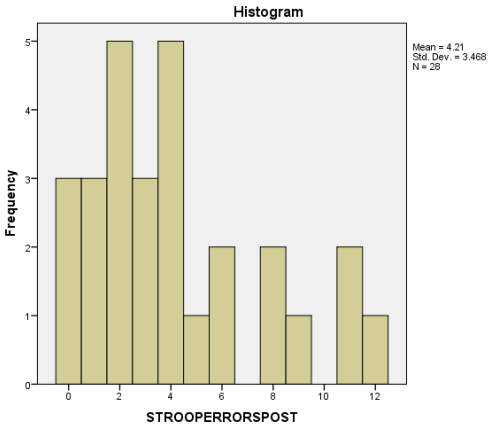


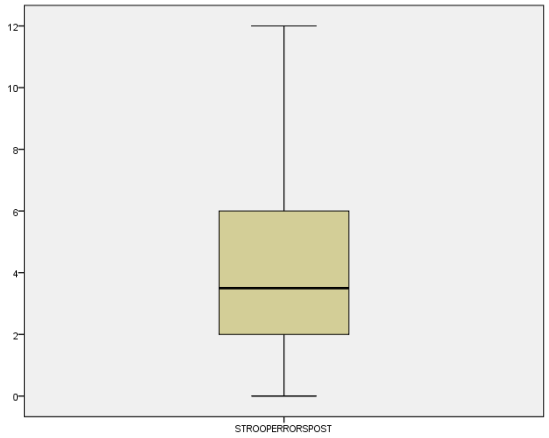


STROOPERRORSPRE

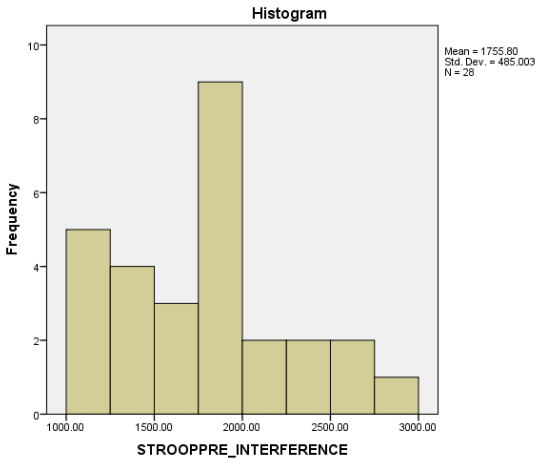


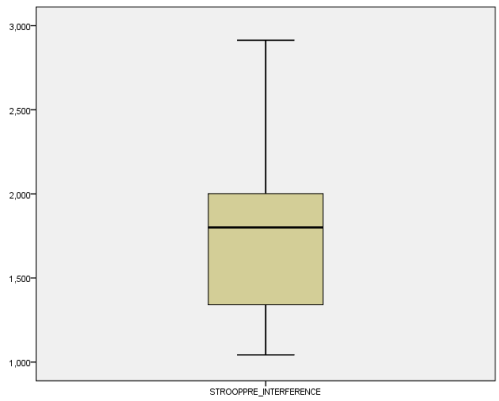
STROOPERRORSPOST



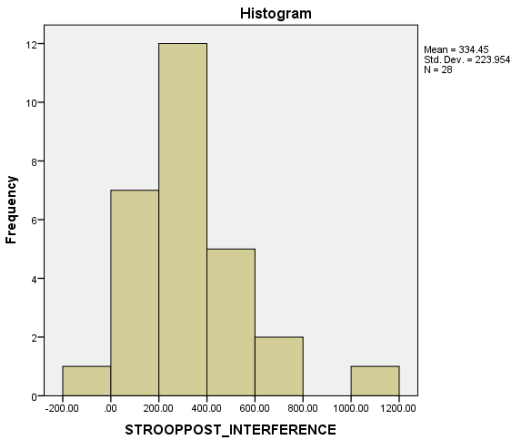


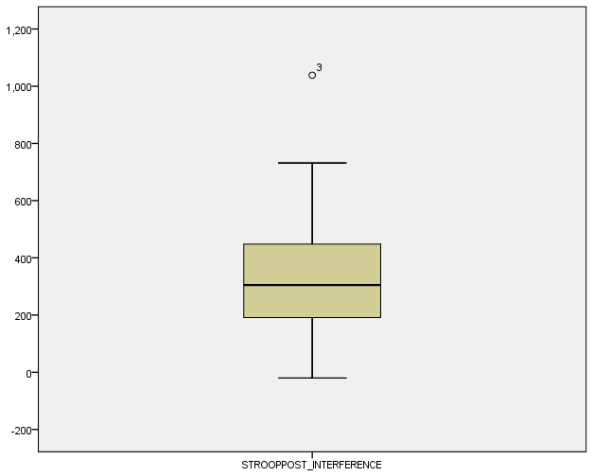
STROOPPRE_INTERFERENCE





STROOPPOST_INTERFERENCE





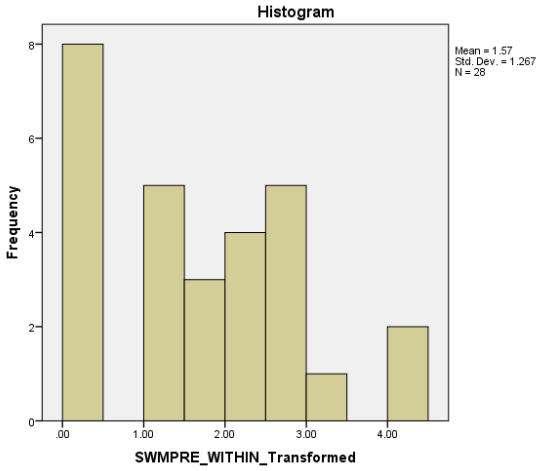
Assumption Testing Output for SWM Within-Errors and Stroop Interference Following Square-Root Transformation

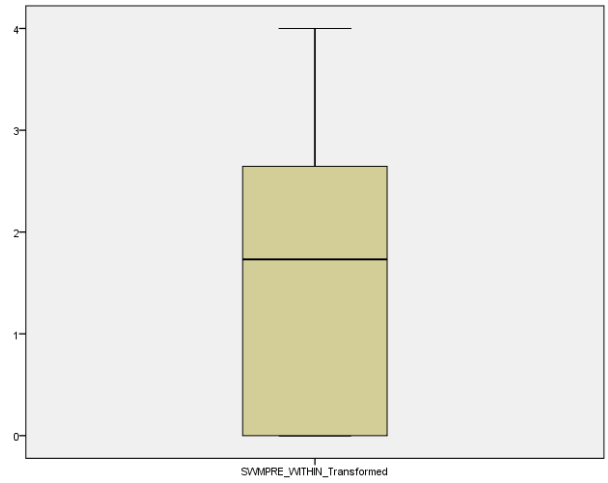
Descriptives

			Statistic	Std. Error
SWMPRE_WITHIN_Transformed	Mean		1.5657	.23950
	95% Confidence Interval for Mean	Lower Bound	1.0743	
		Upper Bound	2.0571	
	5% Trimmed Mean		1.5174	
	Median		1.7321	
	Variance		1.606	
	Std. Deviation		1.26729	
	Minimum		.00	
	Maximum		4.00	
	Range		4.00	
	Interquartile Range		2.65	
	Skewness		.197	.441
	Kurtosis		-.945	.858
SWMPOST_WITHIN_Transformed	Mean		1.2539	.18176
	95% Confidence Interval for Mean	Lower Bound	.8810	
		Upper Bound	1.6269	
	5% Trimmed Mean		1.2056	
	Median		1.4142	
	Variance		.925	
	Std. Deviation		.96177	
	Minimum		.00	
	Maximum		3.46	
	Range		3.46	
	Interquartile Range		1.40	
	Skewness		.445	.441
	Kurtosis		.008	.858
STROOPPRE_INTERFERENCE_Transformed	Mean		41.5158	1.09280
	95% Confidence Interval for Mean	Lower Bound	39.2735	
		Upper Bound	43.7580	
	5% Trimmed Mean		41.3873	
	Median		42.4347	

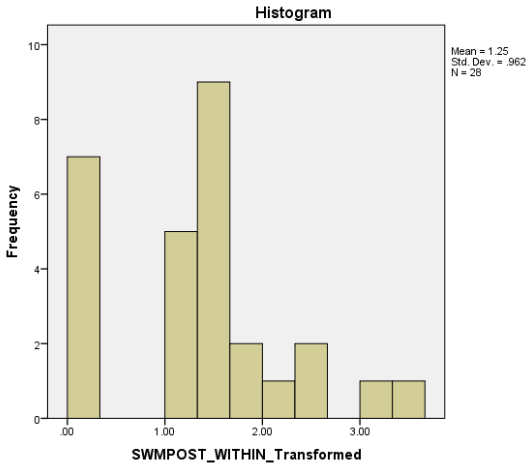
	Variance		33.438	
	Std. Deviation		5.78255	
	Minimum		32.29	
	Maximum		53.98	
	Range		21.69	
	Interquartile Range		8.45	
	Skewness		.108	.441
	Kurtosis		-.494	.858
STROOPPOST_INTERFERENCE_Transformed	Mean		17.3510	1.13590
	95% Confidence Interval for Mean	Lower Bound	15.0204	
		Upper Bound	19.6817	
	5% Trimmed Mean		17.2750	
	Median		17.4658	
	Variance		36.128	
	Std. Deviation		6.01062	
	Minimum		4.50	
	Maximum		32.22	
	Range		27.72	
	Interquartile Range		7.87	
	Skewness		.200	.441
	Kurtosis		.561	.858

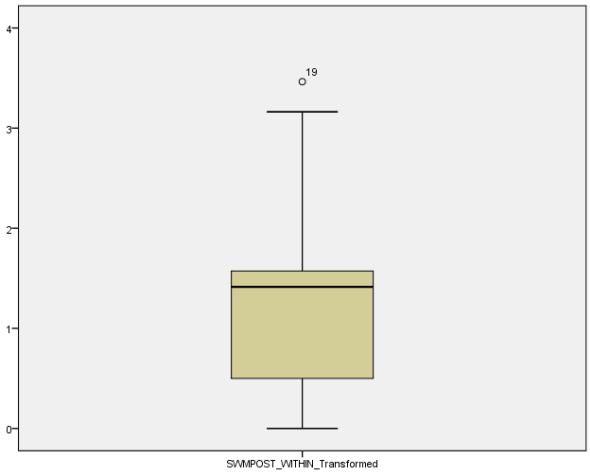
SWMPRE_WITHIN_Transformed



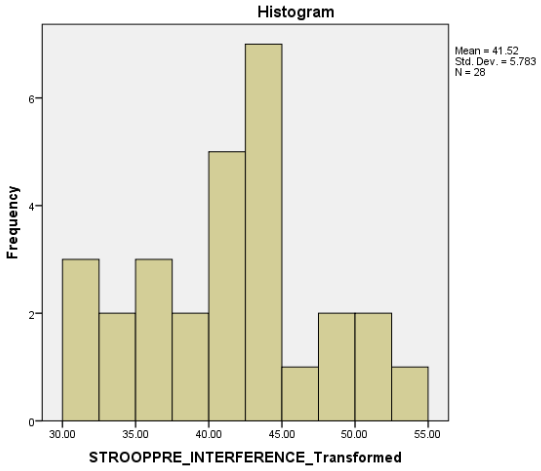


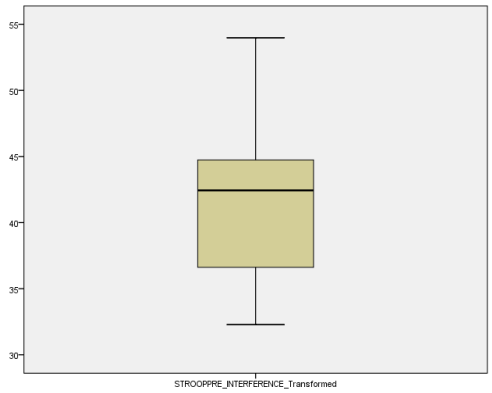
SWMPOST_WITHIN_Transformed



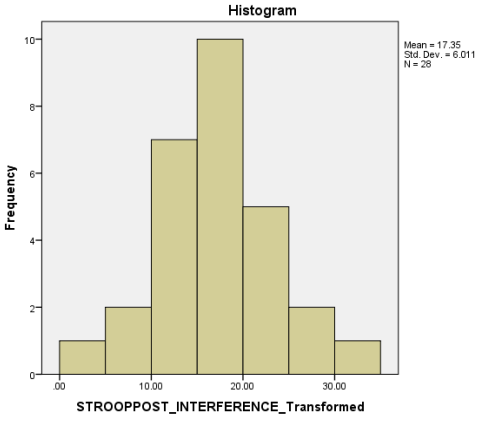


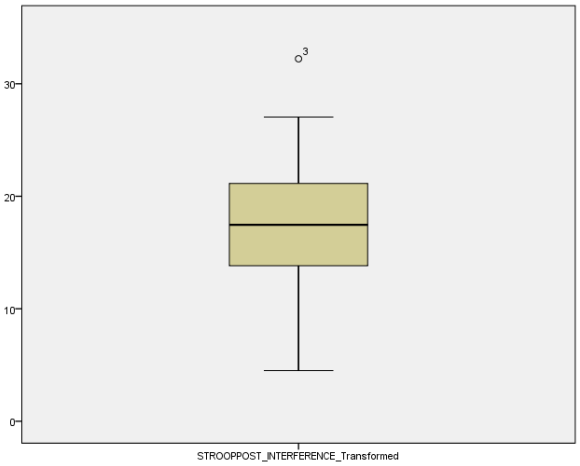
STROOPPRE_INTERFERENCE_Transformed





STROOPPOST_INTERFERENCE_Transformed





Anova Output for SWM Within and Between-Errors

Descriptive Statistics

	Groupingvar	Mean	Std. Deviation	N
SWMPRE_BETWEEN	Control	47.20	18.583	15
	Experimental	54.38	24.767	13
	Total	50.54	21.564	28
SWMPOST_BETWEEN	Control	44.13	18.473	15
	Experimental	38.38	21.337	13
	Total	41.46	19.693	28
SWMPRE_WITHIN_Transformed	Control	1.2880	.96785	15
	Experimental	1.8860	1.52091	13
	Total	1.5657	1.26729	28
SWMPOST_WITHIN_Transformed	Control	1.4161	.75222	15
	Experimental	1.0668	1.16203	13
	Total	1.2539	.96177	28

Tests of Within-Subjects Contrasts

Source	Measure	Time	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Time	SWM_Between	Linear	1265.890	1	1265.890	9.473	.005	.267
	SWM_Within_Transformed	Linear	1.663	1	1.663	2.498	.126	.088
Time * Groupingvar	SWM_Between	Linear	582.462	1	582.462	4.359	.047	.144
	SWM_Within_Transformed	Linear	3.124	1	3.124	4.691	.040	.153
Error(Time)	SWM_Between	Linear	3474.467	26	133.633			
	SWM_Within_Transformed	Linear	17.315	26	.666			

Tests of Between-Subjects Effects

Transformed Variable: Average

Source	Measure	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	SWM_Between	118022.894	1	118022.894	161.830	.000	.862
	SWM_Within_Transformed	111.433	1	111.433	60.761	.000	.700
Groupingvar	SWM_Between	7.179	1	7.179	.010	.922	.000
	SWM_Within_Transformed	.215	1	.215	.118	.735	.004
Error	SWM_Between	18961.821	26	729.301			
	SWM_Within_Transformed	47.683	26	1.834			

Pairwise Comparisons for SWM Within and Between Errors

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	SWMWITHINANODALpre	1.8860	13	1.52091	.42182
	SWMWITHINANODALPOST	1.0668	13	1.16203	.32229
Pair 2	SWMWITHINSHAMPRE	1.2880	15	.96785	.24990
	SWMWITHINSHAMPOST	1.4161	15	.75222	.19422
Pair 3	SWMBETWEENANODALpre	54.3846	13	24.76738	6.86924
	SWMBETWEENANODALPOST	38.3846	13	21.33674	5.91775
Pair 4	SWMBETWEENSHAMpre	47.2000	15	18.58263	4.79802
	SWMBETWEENSHAMPOST	44.1333	15	18.47340	4.76981

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	SWMWITHINANODALpre - SWMWITHINANODALPOST	.81917	1.21848	.33794	.08285	1.55549	2.424	12	.032
Pair 2	SWMWITHINSHAMPRE - SWMWITHINSHAMPOST	-.12802	1.09588	.28296	-.73490	.47886	-.452	14	.658
Pair 3	SWMBETWEENANODALpre - SWMBETWEENANODALPOST	16.00000	18.23001	5.05610	4.98371	27.01629	3.164	12	.008
Pair 4	SWMBETWEENSHAMpre - SWMBETWEENSHAMPOST	3.06667	14.54288	3.75495	-4.98691	11.12024	.817	14	.428

Anova Output for IDED Total Errors, IDED EDS Errors, Stroop Total Errors and Stroop Interference

Descriptive Statistics

	Groupingvar	Mean	Std. Deviation	N
IDEDPRE	Control	25.93	8.980	15
	Experimental	28.27	11.126	15
	Total	27.10	10.005	30
IDEDPOST	Control	21.47	10.378	15
	Experimental	19.33	12.280	15
	Total	20.40	11.224	30
IDEDPRE_EDSERRORS	Control	16.6000	11.27450	15
	Experimental	16.4000	12.08777	15
	Total	16.5000	11.48537	30
IDEDPOST_EDSERRORS	Control	10.0000	10.46081	15
	Experimental	5.6667	7.50873	15
	Total	7.8333	9.21424	30
STROOPERRORSPRE	Control	7.87	6.479	15
	Experimental	6.93	7.116	15
	Total	7.40	6.704	30
STROOPERRORSPOST	Control	4.40	3.661	15
	Experimental	4.73	4.877	15
	Total	4.57	4.240	30
STROOPPRE_INTERFERENCE_Transformed	Control	42.9829	5.73622	15
	Experimental	40.1670	5.42134	15
	Total	41.5749	5.66782	30
STROOPPOST_INTERFERENCE_Transformed	Control	17.9672	6.81694	15
	Experimental	17.1767	5.44828	15
	Total	17.5720	6.07666	30

Mini-Mental State Exam

Participant ID_____ **Date**_____

Orientation		**Response**	**Score**
1. What is today's date?	Date (day/month/year). 1 point for each correct OR		/3 OR
(if participant does not answer question1 correctly e.g., only responds 21st ask 1a,b) 1a What is the year? 1b What is the month?	1 point each for year, month, date (e.g., 21st)		/3
2. What day is today?	e.g., Monday		/1
3. Can you tell me what season it is? Allow 2 weeks flexibility	Summer= 1st Dec-28th Feb; Autumn= 1st March-31st May; Winter= 1st June-30th Aug; Spring= 1st Sep-30th Nov		/1
		Total	**/5**
4. Can you tell me the name of the ***Institution*** we are in? Can you name the ***Department*** we are in? If participant responds ParkC, you can prompt "can you tell me the institution?" e.g., ECU to get the full points.	**2 points= Curtin Neurolab** **1 point= Curtin** If conducting at nursing home take name of nursing home. If conducting at home, take name of street and house number.		/2
5. What City/Suburb are we in?	Bentley		/1
6. What State are we in?	Western Australia		/1
7. What Country are we in?	Australia		/1
		Total	**/5**

Immediate Recall		**Response**	**Score**
"I'm going to say some words. Listen carefully and when I have said all the words, please repeat them to me. So I say the words and then you say them". BALL (pause) FLAG (pause) TREE 1 point for each correct response	"Ball" "Flag" "Tree" Number of trials_____ This first repetition determines the participants score (0-3) but keep saying them until the participant can repeat all 3. Up to 6 trials- but use judgement.		**/1** **/1** **/1** **Total /3**

Attention/Calculation	**Response**		**Response**	
"I've got some mental arithmetic for you. Starting with 100 take away 7, then take away 7 from that number, and keep taking away by 7 until I tell you to stop." *continue for 5 subtractions.* AND Word **Backwards. No need** to get them to spell it forward "Spell the word "WORLD" as in the world that we live in" backwards, *This may be accompanied by a physical prompt as to what the word is.* When scoring, count an error as the number of moves the word is out of order. E.g., DRLOW is only 1 move from being correct, so only 1 error 4 points. (Score both of these tests)	**93** **86** **79** **72** **65**	If asked, you may prompt with the previous answer they gave. However, note the prompt and do not score the response as correct even if calculation is correct.	**D** **L** **R** **O** **W**	
Total		**/5**		**/5**

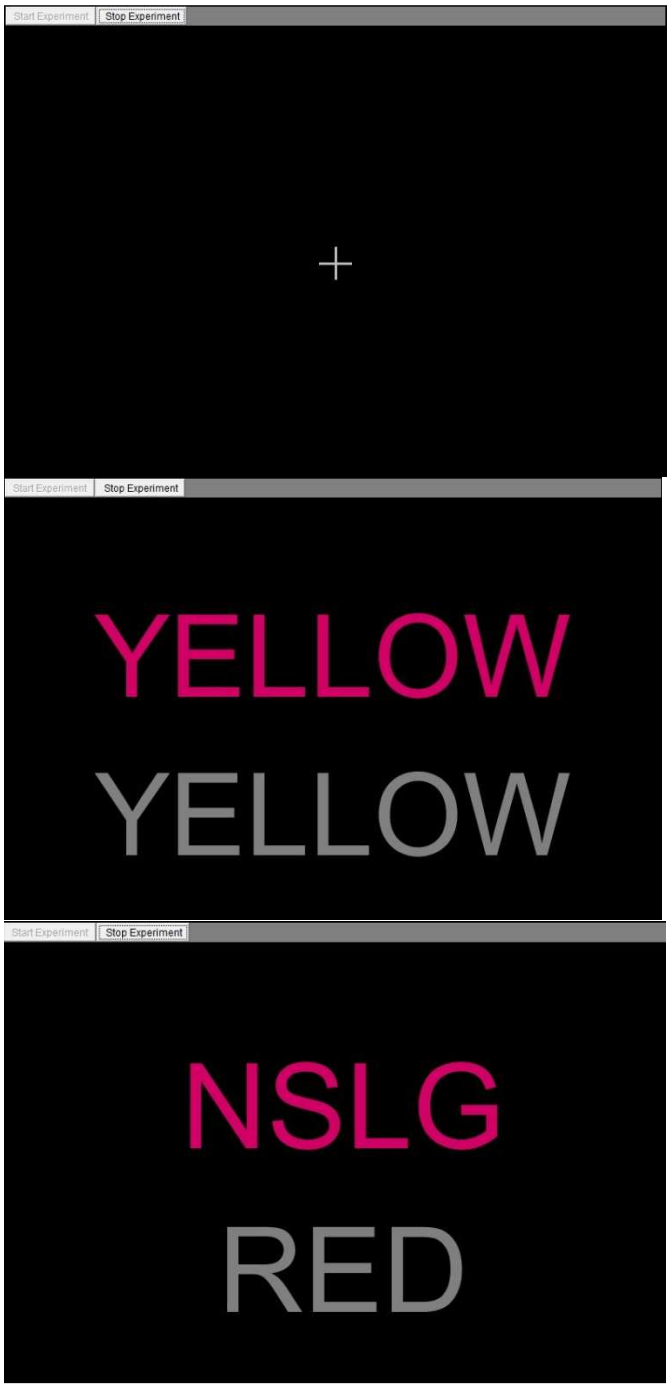
Recall		**Response**	**Score**
I asked you to repeat some words earlier. Can you tell me what they were? *You may tell the participant that you did not ask them to remember the words at the time.*	"BALL" "FLAG" "TREE"		**/1** **/1** **/1** **Total /3**

		Response	**Score**
NAMING "What is this called?" *Show wrist watch* "And this?" *show a pencil*	Watch Pencil *(do not let the participant touch the objects)*		 **/1** **/1**
REPETITION "I'm going to say a sentence to you. It's an unusual one. Please listen carefully and then repeat after me. So I say the sentence and then you say it" (pause) **"NO IFS, ANDS, OR BUTS"**	"*No ifs, and or buts" is not acceptable*		**/1**
3-STAGE COMMAND **Hold blank paper close to yourself with both hands. Give instructions then present the paper with <u>both hands</u> to the person's midline** "I want you to listen carefully and then do what I say". "Take this piece of paper in your right hand *(pause)* fold it in half *(pause)* and place it on your knee".	Takes paper in right hand Folds it in half Puts paper on knee		**/1** **/1** **/1**

WRITING Give the participant a blank piece of paper. Say to participant: **“**Now I would like you to write a sentence *(pause).* “Write anything you like as long as it make sense.” You may also say “It doesn’t have to be long”. If you are unsure what the sentence says, ask the participant to read it aloud.	The sentence has to be written spontaneously. It must contain a subject and a verb and be sensible. Correct grammar and pronunciation are not necessary. (Go away!= pass; Happy Birthday=Fail).		**/1**

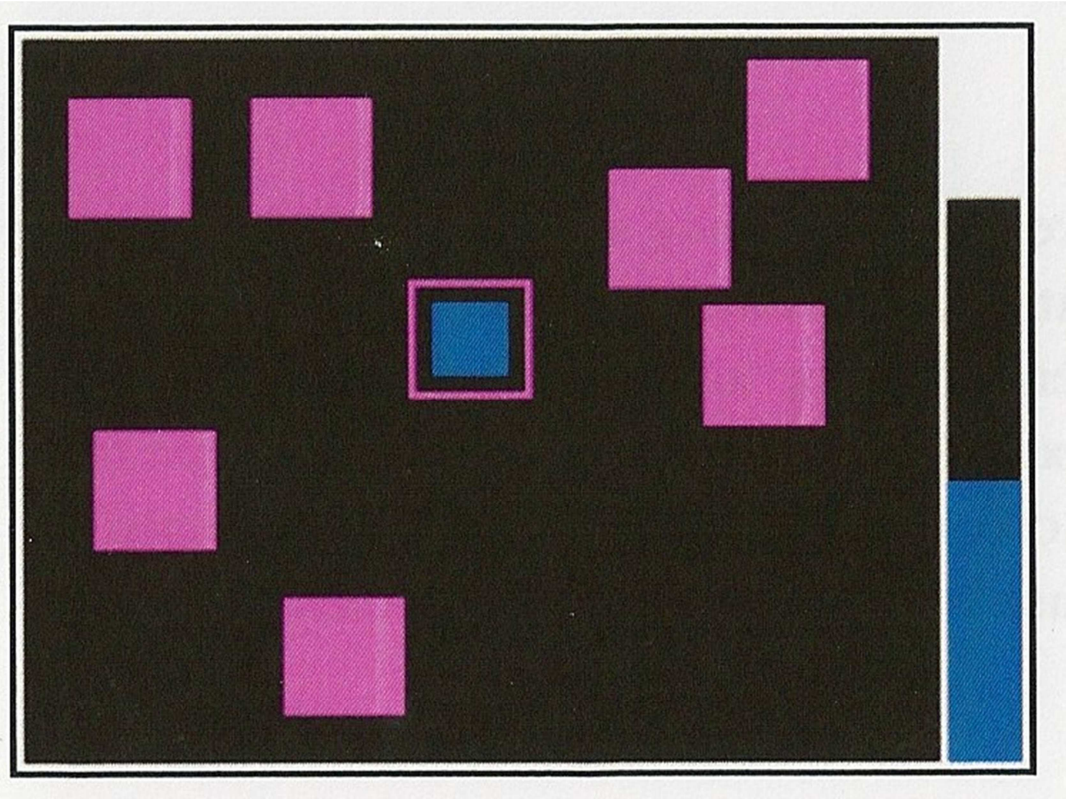
COPYING Show participant the pentagons. “Now I would like you to copy this picture exactly as it is. It doesn’t have to be a work of art, just get all the corners in”.	All 10 angles must be present and 2 must intersect to form a four sided figure to score 1 point. Tremor and rotation are ignored.		**/1**
READING COMMAND “I’m going to show you a sentence and I want you to read and do what it says.” Show participant the piece of paper with the sentence “CLOSE YOUR EYES”. If there is uncertainty, ask the participant to read it out loud. If they read it but don’t do it, prompt the person and score as zero. Prompt: “Please do as it says”.	Score correct only if the participant actually closes their eyes. You may prompt to establish whether the participant has forgotten the command.		**/1** **Total** **/9**
TOTAL SCORE SERIAL 7S	**TOTAL SCORE WORLD BACKWARDS**		
TOTAL SCORE (maximum score is 30)			

Colour-Word Stroop Task



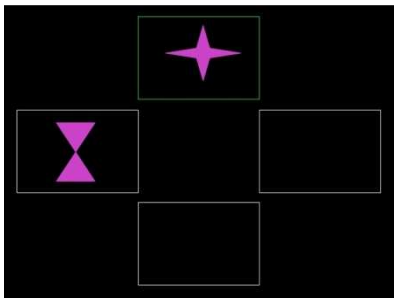
Note: Stroop conditions. The image in the centre is an incongruent trial because the meaning of the word at the top of the screen interferes with the colour. The image at the bottom is a neutral trial because the set of random letters does not interfere with the colour.

Spatial Working Memory Task

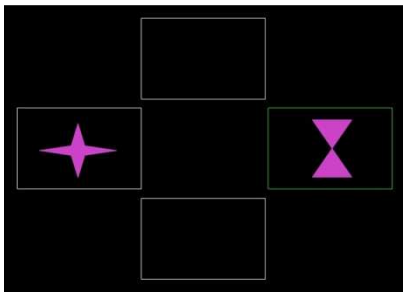


Note: An example screen of an eight-box problem for the Spatial Working Memory Task. Participants had to touch a box to reveal a hidden token and with their finger drag the token and drop it in the column on the right. Participants had to remember not to return to this box again as a token will never appear in the same box twice.

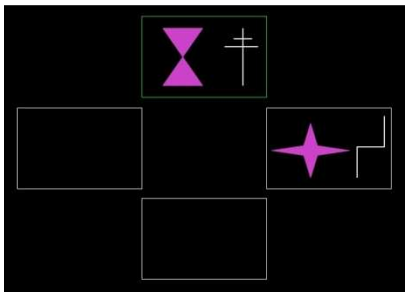
Intra-Dimensional Extra-Dimensional Set-Shift Task



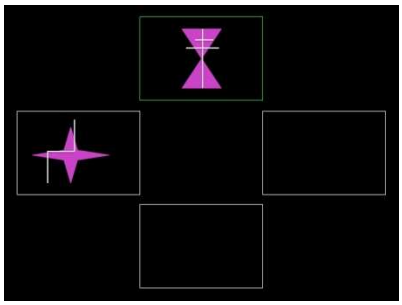
1. Simple Discrimination



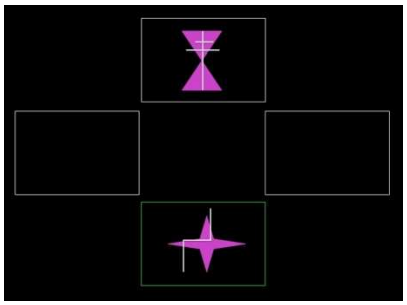
2. Simple Reversal



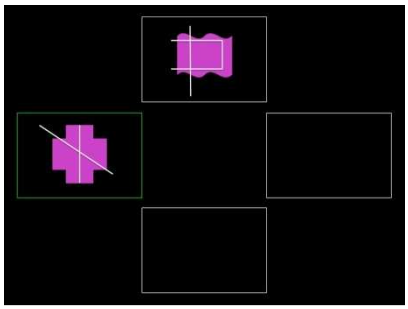
3. Compound Discrimination I



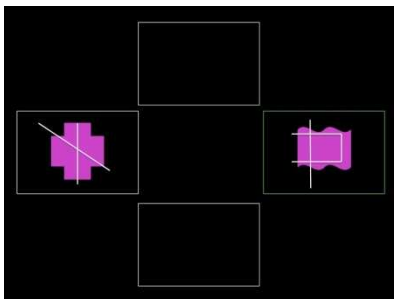
4. Compound Discrimination II



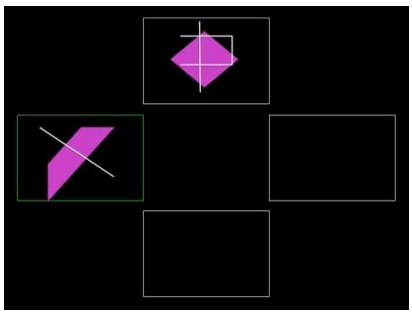
5. Compound Reversal



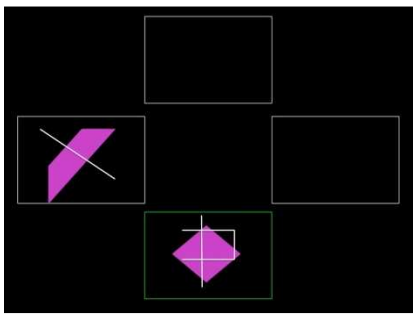
6. Intradimensional Shift



7. Intradimensional Shift Reversal



8. Extradimensional Shift



9. Extradimensional Shift Reversal

Stages 1 to Stage 9 of the IDED set shifting task.

Curtin University of Technology

The Impact of Transcranial Direct Current Stimulation (tDCS) on Executive Functioning:
tDCS Exclusion Criteria

You cannot participate in this research project if you have had any of the following procedures or if any of the following conditions apply to you:

- Any neurological disorder or brain surgery
- Any history of epilepsy
- Currently taking psychoactive medication
- Any active skin disease (such as eczema) on the scalp
- Any unstable medical condition (for example, un-controlled diabetes)
- Any history of migraine
- Any history of episodes of faintness (one isolated incident is not an episode)
- Any history of asthma
- Any metal implants or devices in your body (e.g. surgical clip, coronary stent)

Note: metal dental fillings or metal dental braces will not exclude you from participating.

- Currently using a hearing aid

Please indicate whether any of the above exclusion criteria apply to you
YES [ ]
NO [ ]

Participant Information Sheet

PROJECT TITLE

The Impact of Non-Invasive Brain Stimulation on the Planning Abilities of Healthy Older Adults.

INVITATION

You are being asked to take part in a research study being conducted by Paul Evans, a Psychology honours student at the Curtin Neuroscience Laboratory. This study is uses transcranial direct current stimulation (tDCS) – a mild, form of electrical brain stimulation. This study will test whether this stimulation can improve brain functions related to problem solving, attention and memory. This project is being supervised by Dr Andrea Loftus and has been approved by the Curtin Research Ethics Committee (Approval Number HR 32/2013).

WHAT WILL HAPPEN

You will be asked to attend the Curtin Neuroscience Laboratory at a time convenient to you. Upon arrival at the lab you will be asked to complete an informed consent form. At the commencement of the testing session you will be asked to complete three (3) computerised tasks using a touch-screen computer. You do not have to be familiar with computers to complete these tasks. You will then receive tDCS via two electrodes on your scalp, during this you may feel a mild tingling sensation on your scalp. tDCS will take approximately 20 minutes to administer, during which you are welcome to have a tea or coffee, read a magazine or converse with the researchers. Following completion of the tDCS you will be asked to again complete the computerised tasks.

TIME COMMITMENT

The testing session will take an hour to complete. You are welcome to take regular breaks.

PARTICIPANTS' RIGHTS

You may decide to stop being a part of the research study at any time without explanation. You have the right to ask that any data you have supplied to that point be withdrawn/destroyed as appropriate and without penalty. You will still be paid for your contribution. You have the right to omit or refuse to answer or respond to any question that is asked of you. You have the right to have your questions about the procedures answered. If you have any questions as a result of reading this information sheet, you should ask the researcher before the study begins.

BENEFITS AND RISKS

tDCS poses a small risk to participants who have a history of epilepsy, migraines and fainting. Questions relating to these conditions will be asked during the screening process, but if you have any concerns please inform the researchers.
It is common to experience a sensation of tingling or warmth when receiving tDCS, this is harmless and in many cases the feeling diminishes during stimulation.

COST, REIMBURSEMENT AND COMPENSATION

Your participation in this study is voluntary. You will receive a $20 Coles-Myer gift card for participation in the study as a means of thanks.

CONFIDENTIALITY/ANONYMITY

Your participation in this study is completely confidential and data we collect will be de-identified and not linked to you in any way. Data collected will be stored on a computer for five years in accordance with NHMRC guidelines.

FOR FURTHER INFORMATION

Dr Andrea Loftus is supervising this study and will be happy to answer any questions or concerns you may have. She can be reached by phone on 9266 2308 or by email at andrea.loftus@curtin.edu.au

If you want to find out about the results of this study, please let the researchers know and they will update you about the study results at its conclusion via phone or email.

This study has been approved by the Curtin University Human Research Ethics Committee (Approval Number HR 32/2013). The Committee is comprised of members of the public, academics, lawyers, doctors and pastoral carers. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or by emailing

Participant Consent Form

PROJECT TITLE

The impact of non-invasive brain stimulation on the planning abilities of Healthy Older Adults.

PROJECT SUMMARY

This study is using transcranial direct current stimulation (tDCS) – a mild, completely safe form of electrical brain stimulation to test whether applying this stimulation to the frontal region of the brain can improve brain functions related to problem solving, attention and memory.
This project is being supervised by Dr Andrea Loftus and has been approved by the Curtin Research Ethics Committee (Approval Number HR 32/2013)

By signing below, you are agreeing that: (1) you have read and understood the Participant Information Sheet, (2) questions about your participation in this study have been answered satisfactorily, (3) you are aware of the potential risks (if any), and (4) you are taking part in this research study voluntarily (without coercion).

_____

Participant's Initials

_____ _____

Participant's signature* Date

_____ _____

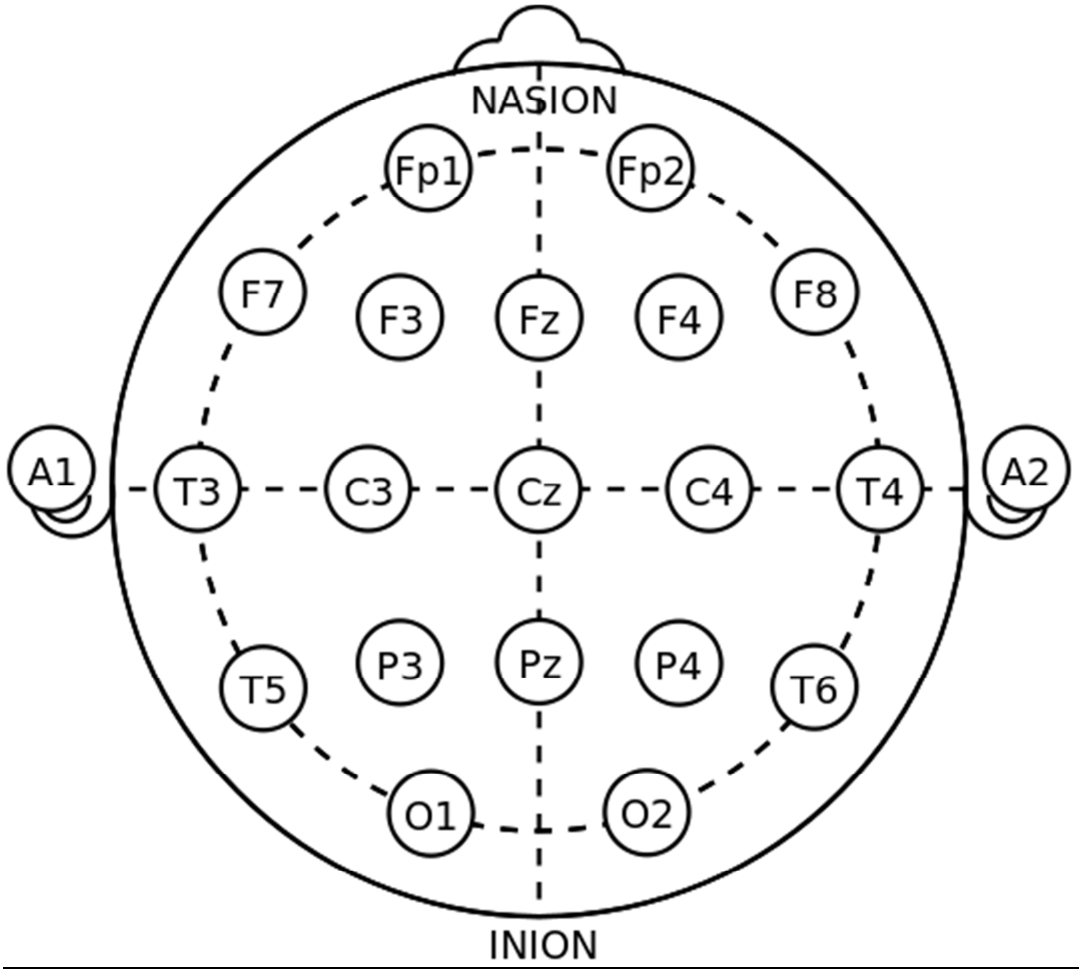
Name of person obtaining consent (Printed) Signature of person obtaining consent

I am aware that participation in this study involves completion of some standardised tests [specify as relevant] which are routinely used as preliminary screens for clinical conditions/impairments of which I might not be aware. I understand that these assessments are not sufficient for diagnostic purposes, nor will they be used in this manner in this study. I also understand that the researchers cannot inform participants of individual test scores, but in the event that I produce scores of potential clinical concern, researchers should (check one and provide relevant contact information):

_____Contact me at:_____

_____ Do nothing. I absolve the researchers of any obligation to contact me about this.

International 10-20 System for Placement of Scalp Electrodes



Ethics Letter

Curtin University

Memorandum

To	Dr Andrea Loftus, Psychology and Speech Pathology
From	Professor Stephan Millett, Chair, Human Research Ethics Committee
Subject	Protocol Approval **HR 32/2013**
Date	6 March 2013
Copy	

Office of Research and Development
Human Research Ethics Committee

TELEPHONE 9266 2784
FACSIMILE 9266 3793
EMAIL hrec@curtin.edu.au

Thank you for providing the additional information for the project titled "*The Impact of transcranial direct current stimulation on executive functioning*". The information you have provided has satisfactorily addressed the queries raised by the Committee. Your application is now **approved**.

- You have ethics clearance to undertake the research as stated in your proposal.
- The approval number for your project is **HR 32/2013.** *Please quote this number in any future correspondence*.
- Approval of this project is for a period of four years **01-03-2013** to **01-03-2017**.
- Your approval has the following conditions:
  i) Annual progress reports on the project must be submitted to the Ethics Office.
  ii) Registration as a clinical trial.
  Chapter 3.3 of the National Statement on Ethical Conduct in Human Research states:
  A clinical trial is a form of human research designed to find out the effects of an intervention.
- **It is your responsibility, as the researcher, to meet the conditions outlined above and to retain the necessary records demonstrating that these have been completed.**

Applicants should note the following:

It is the policy of the HREC to conduct random audits on a percentage of approved projects. These audits may be conducted at any time after the project starts. In cases where the HREC considers that there may be a risk of adverse events, or where participants may be especially vulnerable, the HREC may request the chief investigator to provide an outcomes report, including information on follow-up of participants.

The attached **FORM B** should be completed and returned to the Secretary, HREC, C/- Office of Research & Development:
When the project has finished, or

- If at any time changes/amendments occur, or
- If a serious or unexpected adverse event occurs.

Yours sincerely

Professor Stephan Millett
Chair Human Research Ethics Committee

Statistical Advice from Dr Robert Kane

Paul Evans 14293823

Research Question:

The present research will examine whether the application of anodal tDCS at 2mA for 20 minutes to the left DLPFC of healthy older adults (over the age of 65) will result in significant improvements in executive functioning (EF). The construct of EF will be measured using several domain-specific measures, specifically the CANTAB measures of spatial working memory (SWM) and intra-extra dimensional set shift (IDED), and a computerised version of the stroop colour-word task.

The rationale behind choosing these particular tests is that they are thought to map onto the executive control processes suggested by Miyake et al. (2000). Spatial working memory relates to "Updating," intra-extra dimensional set-shift relates to "Shifting," and the colour-word stroop task relates to "Inhibition."

Hypotheses:

It is hypothesised that tDCS will produce significant improvements on the three measures of executive functioning, both when comparing pre and post test scores in the stimulation group and when comparing scores between the sham and stimulation group.

Sample size required based on Power Analysis:

An a priori statistical power analysis was conducted using the software program G-Power. The resulting analysis indicated that 30 participants would be required in order to detect a small effect ($d = .3$) with power ($1 - \beta$) set at 0.80 and $\alpha = .05$, two-tailed.

Sampling strategy:

Thirty healthy older adults (over the age of 65 with no history of illness that could impact cognitive performance) will be randomly allocated into either an experimental or control group, each containing 15 participants.

Participants will be sourced from the West Australian Participant Pool, based at the University of Western Australia. In order to guarantee enough participants, advertisements for volunteers will also be placed in local newspapers.

Measures (include number of factors and alpha reliability where applicable)

Spatial Working Memory

The spatial working memory task is used to assess working memory through the ability to retain spatial information and manipulate in working memory (Cambridge Cognition, 1996). Spatial working memory ability will be assessed according to the number of errors committed during the test trials.

The test-retest reliability for the SWM task is adequate with a Pearson's correlation of r = .68 (Lowe & Rabbit, 1998).

Intra-Dimensional Extra-Dimensional Set-Shift

The Intra-Dimensional Extra-Dimensional Set-Shift task (IDED) will be used to assess set-shifting ability (Cambridge Cognition, 1996). This test assesses the ability to make simple discriminations, attend to specific attributes of compound stimuli and shift mental set from one dimension to another. Set-shifting ability will be assessed according to the number of errors committed during test trial stage eight (8). The test-retest reliability for the IDED is adequate with a Pearson's correlation of r = .70 (Lowe & Rabbit, 1998)

Stroop Colour-Word Task

The Stroop colour-word task is a commonly used measure of cognitive inhibition (Stroop, 1935). An online version of the Stroop colour-word task will be used in this study. No reliability information currently exists for this task (typical and not considered to be a problem).

Planned Analyses

For each measure of EF (SWM, IDED and Stroop) a 2x2 factorial repeated measures ANOVA will be performed to assess whether there is a statistically significant main effect when comparing the mean scores on the within subjects factor of tDCS

condition (anodal and sham stimulation) and when comparing the mean scores on the between subjects factor of time (average pre and post-stimulation participant test scores).

Prior to running the tests, the assumptions of normality and homogeneity of variances will be tested using Shapiro Wilk and F_{max} tests respectively. As sample sizes are equal and ANOVA is robust against small violations on these tests, no critical violations of these assumptions are anticipated.

If an interaction effects exist between the within and between subjects factors on any of the EF measures, post-hoc analyses in the form of a Bonferroni pairwise comparisons will be conducted to examine any significant simple effects.

Further post-hoc analysis may be conducted to examine the zero-order correlations between the participant scores (combined pre and post) on each of the three measures of EF. This procedure may provide insights about the structure of these functions through examination of the degree to which they overlap or are separable.

Specific Questions for Statistical Consultant.

Is a 2x2 factorial repeated measures ANOVA the most suitable analysis for this study?
Is it worthwhile examining the correlations between scores on the measures to gain insights into the structure of EF – obviously the resulting zero-order correlation will be a result of the relationship between the measures and the reliability of the measures etc.

TO BE COMPLETED BY STATISTICAL ADVISOR

☐ **No changes required**

☐ **The following changes are required:**

✓**The following comments should be taken on board**

Research design

You describe the following 2 x 2 mixed design.

	Pre-test	Post-test

Anodal (n = 12)		
Sham (n = 12)		

Participants will be randomly allocated to the two levels of the between-subjects factor, and then tested before stimulation (anodal or sham) and after stimulation on three executive functioning tasks, namely, spatial working memory, set shift, and Stroop. Are you looking at both RT and accuracy on the Stroop task?

Hypotheses

H1: For spatial working memory, there will be a significant pre-post improvement for the anodal group but little change for the sham group.

H2: For set shift, there will be a significant pre-post improvement for the anodal group but little change for the sham group.

H3: For the Stroop task, there will be a significant pre-post improvement for the anodal group but little change for the sham group.

Hypothesis testing

Each hypothesis predicts a Group x Time interaction and can therefore be tested with a 2 x 2 mixed ANOVA. Significant interactions should be investigated by testing the simple main effect of time within each of the two groups. The ANOVAs are hypothesis-driven and can therefore be evaluated at the conventional per-test alpha-level of .05 – no Bonferroni correction required.

Additional analyses

You could evaluate the test-retest reliability of each DV by correlating pre and post scores for the sham group. With only 12 participants, however, the reliability coefficient won't be that stable. Also, you could examine the intercorrelations among the pre-test measures (N = 24). If the measures are being driven by a common executive functioning construct, then you might expect the correlations to be relatively strong.

Sample size (alpha = .05, power = .8)

Your hypotheses predict a significant 2 x 2 interaction. You'll therefore need a sufficient number of participants to detect this interaction. According to G*Power, you'll require 24 participants (12 in each group) to detect a 'moderate to large' (f = .3) interaction effect.

References

Allen, P., & Bennett, K. (2010). *Pasw Statistics by SPSS: A Practical Guide: Version 18* (1st ed.). South Melbourne, Australia: Cengage Learning.

Tabachnick, B.G., & Fidell, L.S. (2012). *Using Multivariate Statistics* (6th ed.). Boston: Allyn and Bacon.