Exploring Compensation Theory: The Impact of Non-Invasive Brain Stimulation on Spatial Working Memory and Fine Motor Control in Older Adults.

Dissertation submitted by
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As partial fulfilment 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

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 Information derived from the published or unpublished work of others has been acknowledged in the text and a list of references is given.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 7/11/2014

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Abstract

As people age they experience declines in both Spatial Working Memory (SWM) and Fine Motor Control (FMC), which impacts significantly upon their functionality. Evidenced based therapies to manage declines in SWM and FMC are limited. The present study examined the efficacy of transcranial Direct Current Stimulation (tDCS) to improve both SWM and FMC in the context of the compensation theory. The compensation theory posits that SWM serves a compensatory purpose for FMC in older adults, by assisting motor performance. The aim of the present study was to determine whether 20 minutes of 2mA anodal tDCS over the left dorsolateral prefrontal cortex (DLPFC) could improve SWM performance and consequently, improve FMC performance. A repeated measures experimental design was used. Twenty nine healthy older adults (60+) participated, fifteen participants received anodal tDCS whilst the other fourteen received sham (control) tDCS. Participants completed one measure of SWM and two measures of FMC before, immediately following, and two weeks post tDCS. The results provide some support for the compensation theory. A relationship was observed between SWM and FMC, indicating that better SWM performance was associated with better FMC performance. Although no significant impact of tDCS was observed, the limitations of the current study are highlighted for consideration in future tDCS research.

As people age they experience declines in both cognition and movement, which impacts significantly on their ability to live independently and maintain functionality (Grigsby, Kaye, Baxter, Shetterly, & Hamman, 1998; Jurado & Rosselli, 2007; Ward, 2006). Evidenced-based therapies for the management of cognitive and motor declines in healthy older adults are limited (Solfrizzi et al., 2008). In light of the impact these declines have upon quality of life, it is important to explore therapies that will assist in improving cognition and motor function in healthy older adults (Solfrizzi et al., 2008).

Executive Function (EF) is a broad term used to describe various complex cognitive processes (Elliott, 2003). EFs enable an individual to adapt to novel and demanding situations, and to engage in goal directed behaviour (Huizinga, Dolan, & van der Molen, 2006). Intact EF comprises the ability to plan ahead, formulate a goal, implement goal directed strategies, and do so efficiently (Gilbert & Burgess, 2008; Jurado & Rosselli, 2007). Intact EFs are vital for functioning as an independent and productive individual, as they enable an individual to adapt to their ever-changing environment and complete daily tasks effectively (Jurado & Rosselli, 2007).

Older adults generally experience a decline in EF over time, which is associated with a decrease in everyday functionality (Grigsby et al., 1998; Jurado & Rosselli, 2007). One specific aspect of EF that is impacted significantly by ageing is Spatial Working Memory (SWM; Kessels, Meulenbroek, Fernández, & Olde Rikkert, 2010). SWM enables a person to hold spatial information, such as the location of an object in the environment for later retrieval (Nyberg, Lövdén, Riklund, Lindenberger, & Bäckman, 2012). Cansino et al. (2013) examined SWM performance across a range of age groups (20-80 years old). Using a visuospatial *n*-back task, they found that SWM deteriorated with increasing age. Compared to verbal working memory, declines in SWM were much more pronounced. The first significant decline in SWM was observed in the 31-40 age group, and SWM performance continued to significantly decrease with increasing age.

Fine Motor Control (FMC) also deteriorates with healthy ageing (Ward, 2006). FMC is the ability to perform small and precise movements with the hand and fingers, and is essential to tasks such as writing and retrieving small items (Ranganathan, Siemionow, Sahgal, & Yue, 2001). Declines in FMC adversely affect the ability to perform everyday tasks such as dressing oneself or completing basic chores (Ranganathan et al., 2001). Loss of FMC impacts significantly upon independent living and quality of life in older adults (Seidler et al., 2010).

Research concerning EF and motor control has revealed a shared pattern of cortical activation in older adults (Heuninckx, Wenderoth, & Swinnen, 2008). Using fMRI imaging, Heuninckx et al. (2008) examined brain activation patterns in young and older participants whilst they performed a motor task. For older adults, areas of the prefrontal cortex were activated when performing the motor task, but no such activation was evident for the younger participants. It is important to note that the prefrontal cortex is associated primarily with higher-order cognitive abilities, such as EF, and is not typically associated with motor control (Elliott, 2003; Huizinga & Smidts, 2010). It has been suggested that the activation of the prefrontal cortex in older adults represents a compensatory mechanism, whereby prefrontal areas are recruited (in addition to the motor cortex) to lessen the impact of age-related decline in motor function (Heuninckx et al., 2008; Seidler et al., 2010)

Two main theories have been proposed to account for the observed prefrontal activation in older adults when performing a motor task (Seidler et al., 2010). The non-selective recruitment theory suggests that prefrontal activation during a motor task reflects an 'inefficiency' in the older brain (Riecker et al., 2006). In accord with this theory, cortical degeneration means that specific cortical areas of the brain become less associated with a particular function, resulting in 'inefficiency' (Seidler et al., 2010). Consequently, the older brain has to recruit additional cortical regions beyond the motor cortex to perform a motor task, whereas a younger brain uses a specific cortical area (motor cortex) to achieve the same purpose (Riecker et al., 2006; Seidler et al., 2010). This inefficiency means that the older brain has to recruit more cortical areas to achieve a motor goal (Seidler et al., 2010).

The compensation theory suggests that the prefrontal activation observed when older adults perform a motor task reflects its compensatory role (Seidler et al., 2010). It has been suggested that this prefrontal activation supports effective motor control by providing additional resources to complete the task at hand (Heuninckx et al., 2008). In support of this, increased prefrontal activation is associated with increased motor performance in older adults (Heuninckx et al., 2008). There is a large body of evidence in support of the compensation theory (Cabeza, Anderson, Locantore, & McIntosh, 2002; Heuninckx et al., 2008; Mattay et al., 2002). Harada, Miyai, Suzuki, and Kubota (2009) investigated compensatory activation in the context of gait control in older adults, using functional near-infrared spectroscopy imaging. The results indicated that as the difficulty of the motor task increased, so did the activation of the prefrontal cortex. Additionally, participants with better gait demonstrated more prefrontal activation than those with comparatively worse

gait. These findings are consistent with the compensation theory, as improved motor function was associated with increased prefrontal activation.

Atrophy in the brain is thought to be responsible for the observed deterioration of cognition and movement with age (Seidler et al., 2010). Prefrontal atrophy is an unavoidable aspect of normal, healthy aging (Seidler et al., 2010). Therapies that support prefrontal functioning may serve to enhance the compensatory role of prefrontal activation in ageing. One potential unexplored therapy is transcranial Direct Current Stimulation (tDCS; Fregni et al., 2005). tDCS is a non-invasive brain-stimulation technique which can increase or decrease neural activation (Utz, Dimova, Oppenländer, & Kerkhoff, 2010). Two electrodes are placed on the scalp and a weak electrical current flows between them (Jacobson, Koslowsky, & Lavidor, 2012). Anodal (positive) tDCS depolarises neurons under the electrode and allows them to fire more spontaneously (Utz et al., 2010). Conversely, cathodal tDCS hyperpolarizes neurons under the cathode electrode and suppresses spontaneous firing.

When placed over the prefrontal cortices, tDCS improves performance for tasks involving EF (Fregni et al., 2005). Fregni et al. (2005) investigated the impact that 10 minutes of 1 mA anodal tDCS over the left dorsolateral prefrontal cortex (DLPFC) had upon performance in an EF task. Fifteen participants took part aged between 19 and 22. Participants were randomly assigned to a control group (sham tDCS) or an anodal tDCS group. Participants had to complete an *n*-back assessment of working memory, a task which requires EF. The task required participants to watch rapidly presented letters, and to recall whether the last letter presented matched the letter presented three times prior. Participants who received anodal stimulation over left DLPFC significantly improved, in terms of their accuracy, in comparison to the control group. The authors attributed the improvement to the depolarisation of the stimulated neurons, making them more likely to fire. The therapeutic potential of tDCS is promising, but further research is required (Nitsche et al., 2005; Rothwell, 2012).

Prefrontal areas are activated when an older adult performs a motor task. The compensation theory postulates that the activation of prefrontal areas provides additional resources to support motor function in older adults. These prefrontal areas underlie EF (Elliott, 2003). tDCS over the left DLPFC, as reported by Fregni et al. (2005), can lead to improved EF. In accord with compensation theory, improved SWM (an aspect of EF) should provide additional compensatory resources for FMC. Therefore improved SWM should be associated with improved FMC.

The aims of the present study are multifold. This study first examines the relationship between SWM and FMC in healthy older adults. A significant relationship between SWM and FMC would support the compensation theory. Second, this study examines the impact of anodal tDCS over left DLPFC on SWM and FMC. It is important to note that the left DLPFC is primarily associated with SWM (Fregni et al., 2005). Any impact of tDCS on FMC following stimulation of left DLPFC may, therefore, be due to enhanced SWM. No study to date has explored the use of tDCS on older adults to improve SWM and FMC in the context of compensation theory.

The following hypotheses are proposed:

1. There will be a significant negative relationship between SWM (errors on CANTAB™ task) and FMC (Purdue and tapping) at baseline (pre), such that increased performance on SWM (decreased errors) will be associated with increased FMC.
2. Anodal tDCS over the left DLPFC cortex will lead to improved SWM and FMC in older adults, compared to a sham stimulation group. It is anticipated that improvement will be observed immediately following tDCS (post1) and two weeks later (post2).

Method

Research Design

An experimental repeated measures design was used. The independent variable was the between groups factor, tDCS condition (anodal, sham). The within groups factor was testing time point (pre, post1, post2). The dependent variables were the two measures of FMC (Purdue and tapping) and the measure of SWM (CANTAB™ task). Participants were randomly assigned to the anodal or sham tDCS condition.

Participants

The study recruited 29 healthy older adults aged 60+ for participation (M = 67.9, SD = 6.1; 15 experimental, 14 control). Participants confirmed that they did not meet exclusion criteria for tDCS prior to providing written informed consent. Participants were recruited via a radio advertisement and a database of older adults who had previously indicated interest in research with Dr Loftus. An a priori analysis using the G*Power program indicated that, for a power of .8, approximately 30 participants were required. The analysis was based upon a Bonferroni corrected (α = .017), medium effect size (f=.28)

estimate in accord with Jacobson et al. (2012). The study was approved by the Human Research Ethics Committee at Curtin University (HR 32/2013).

Apparatus

The CANTAB™ SWM task was administered using a touchscreen computer. To administer tDCS, a Sortix™ Medical low intensity stimulator, with two 5x7cm saline solution soaked electrode pads was used. An iPad and Purdue Pegboard were used to administer FMC tests.

Measures

Spatial working memory task. The SWM task was administered using the Cambridge Neuropsychological Test Automated Battery (CANTAB™). The CABTAB™ SWM task is an established measure used for both clinical and research purposes (Smith, Need, Cirulli, Chiba-Falek, & Attix, 2013). The task requires the participant to locate a blue token hidden amongst a number of coloured boxes (see Figure 1). The participant was informed that only one token was hidden at a time and that a token was never hidden within the same box twice. When a token was located the participant moved the token to a holding area on the right of the screen. One trial was complete when all the tokens were found. The number of boxes increased from trial to trial to make the task more difficult. To successfully complete the task, the participant was required to hold spatial information within their working memory (Smith et al., 2013). If a participant selected a box where a token has been previously found, or revisited an empty box, it was counted as an error. Total errors were used as an indicator of SWM, with lower scores (less errors) indicative of better SWM. The CANTAB™ SWM task has a good test re-test reliability of .68 (Lowe & Rabbitt, 1998) and correlates well with other measures of SWM (Smith et al., 2013).

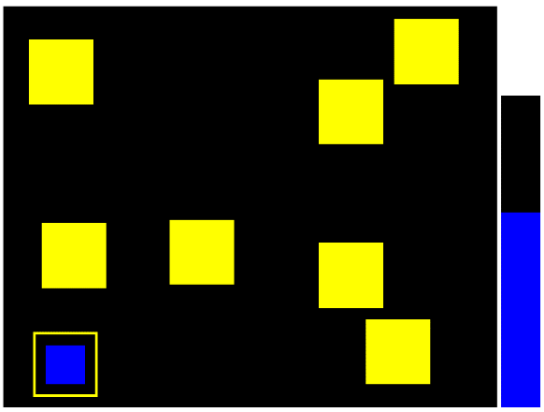

Figure 1. Image of the "Spatial Working Memory" task, adapted from the CANTAB™ (Image taken from http://cambridgeneurosciences.info/images/swm.png).

Purdue pegboard assembly task. The Purdue Pegboard test is a standardised measure of fine motor control (Desrosiers, Herbert, Bravo, & Dutil, 1995). The task required the participant to assemble objects together. The task began by the insertion of a peg into the board with the dominant hand, then placing a washer on the peg, followed by a collar, and finally another washer to complete the assembly. Hands are alternated for each assembly component. The participant assembles as many objects as they can for one minute, working down a vertical line of holes on the board. A count of total parts assembled is taken, with a higher score indicating better FMC performance. The test correlates well with other FMC measures and has good test re-test reliability (.69-.91; Desrosiers et al., 1995; Mathiowetz, Weber, Kashman, & Volland, 1985).

Sequential tapping task. Sequential finger tapping tasks have been used in previous research, and are considered a good indication of FMC (Arunachalam, Weerasinghe, & Mills, 2005; Mostofsky et al., 2006). The Sequential finger tapping test required the participant to tap their fingers in sequence, from index to middle to ring to little finger, repeatedly. The number of taps was recorded using the iPad application 'Digital Finger Tapping Task', which was developed for research purposes (Sybu, 2014). The program counts the number of times a square on the screen is tapped. The iPad was placed on a table along the participant's midline and at a distance comfortable for their arm length. The forearm and wrist rested flat against the iPad to prevent upper arm movement. A higher score indicated better fine motor control. The test was performed using the non-dominant (left) hand only. Computerised finger tapping tests correlate well with traditional tapping tests and have a good test re-test reliability (.91; Christianson & Leathem, 2004; Hubel, Yund, Herron, & Woods, 2013).

Procedure

Participants who indicated interest in the study were contacted via telephone. They were given a brief overview of the study and confirmed a booking for assessment. Assessment took place at the Curtin Neurosciences Laboratory. Participants first completed the exclusion criteria form for tDCS, and were given the opportunity to ask any questions they had regarding the study. If there were no contradictions for the use of tDCS, participants then provided written informed consent. Baseline measures were completed prior to the application of tDCS (pre). The SWM, Purdue pegboard, and sequential finger tapping tasks were administered in that order.

Random assignment was used to allocate participants to either (i) the anodal tDCS of the left DLPFC, or (ii) tDCS sham condition. In accord with the 10-20 international

system the anodal electrode was positioned over F3 and the cathodal electrode over F4 (Milnik, 2009). Anodal tDCS was administered at a current of 2.0mA for a period of 20 minutes. For sham tDCS the montage remained the same but participant received only 30 seconds of ramp up/down stimulation. During tDCS participants talked to the researcher or read a magazine. Immediately following completion of the tDCS phase, participants completed the same measures as baseline (post1). Participants then completed the same measures again two weeks later (post2). The initial tDCS session (pre, post1) took approximately two hours and the follow up session (post2) took approximately 30 minutes. Participants were offered regular breaks during testing.

Results

The data were screened for missing values, which indicated that 3.4% of the whole data were missing. Two participants were unable to complete post2 measures and three participants did not complete the Purdue assembly task at post2. No substitution method was used as it was not considered appropriate and was not required for subsequent analyses. Mean scores and standard deviations for all tasks are presented in Table 1.

Table 1

Summary of Means and Standard Deviations for all Ages at the Three Testing Points.

Assessment	Condition	Time Point		
		Pre (Baseline) M (*SD*)	Post1 M (*SD*)	Post2 M (*SD*)
Spatial Working Memory	Anodal	38.60 (20.0)	37.07 (24.25)	33.15 (19.99)
	Sham	29.31 (14.72)	23.69 (13.93)	26.00 (13.27)
Purdue Assembly	Anodal	23.87 (4.75)	26.33 (5.86)	25.85 (5.41)
	Sham	25.77 (4.66)	27.85 (4.60)	24.10 (6.61)
Sequential Tapping	Anodal	69.4 (15.93)	73.2 (11.93)	73.69 (11.86)
	Sham	71.54 (18.60)	73.15 (21.43)	78.15 (18.96)

Age and gender sorted means and normative data are presented in Table 2. In accord with normative data, three participants were deficit on the Purdue assembly measure.

Table 2

Mean and Standard Deviations of Scores at Baseline Split for Age and Gender with Normative Data.

Assessment	Age group	Present Study M (*SD*)	Published Norms M (*SD*)
Spatial Working Memory	*Males*		
	60-69 (n=12)	30.42 (16.51)	29.5 (23.7)
	70-79 (n=1)	63	38.9 (18.9)
	80-89 (n=3)	41.67 (29.74)	52.3 (24.8)
	Females		
	60-69 (n=11)	29.91 (15.4)	38.2 (17.5)
	70-79 (n=2)	48.5 (10.6)	45.0 (20.4)
Purdue Assembly	*Males*		
	60-69 (n=12)	25.17 (3.33)	28.0 (5.06)
	70-79 (n=1)	20	27.5 (5.06)
	80-89 (n=3)	16.67 (2.31)	21.5 (4.81)
	Females		
	60-69 (n=11)	29.27 (7.14)	31.7 (6.83)
	70-79 (n=2)	23 (1.41)	29.1 (4.85)

Note: Purdue norms are derived from Agnew, Bollawilson, Kawas, and Bleecker (1988) and SWM norms were provided by CANTAB (Cambridge Cognition, 2014). There were no normative data available for the sequential tapping task.

To examine whether there was a significant negative relationship between SWM and FMC at baseline, bivariate correlations were performed. Although the Shapiro-Wilk test indicated a violation of normality for SWM, skewness and kurtosis values demonstrated that SWM met normality assumptions. The bivariate correlations are presented in Table 3. As can be seen, significant negative relationships were observed between SWM and both FMC measures (Purdue assembly and sequential tapping). A significant positive relationship existed between Purdue assembly and sequential tapping.

Table 3.
Bivariate Correlations (Pearson's r) at Baseline Time Point.

	Spatial Working Memory	Purdue Assembly	Sequential Tapping
Spatial Working Memory	1		
Purdue Assembly	-.329*	1	
Sequential Tapping	-.357*	.740**	1

**Correlation is significant at p<.05 level (1-tailed)*
*** Correlation is significant at p<.01 level (1-tailed)*

To examine whether anodal tDCS over the left DLPFC improved SWM and FMC in older adults (compared to sham tDCS), Generalised Linear Mixed Models (GLMM) were used. A GLMM was conducted for each dependent variable separately. GLMM's are robust to violations of assumptions that more traditional tests, such as ANOVA, may be impacted by. GLMM can cope with unequal group sizes and missing data. The assumptions of normality and homogeneity of variance were assessed for SWM and were met. For both Purdue assembly and sequential tapping, however, the assumption of sphericity was violated (Mauchly's test, $p < .05$). To accommodate this, an auto regressive matrix was used in the GLMM for these measures.

For SWM, the GLMM revealed no significant group x time interaction, F (2, 76) = 0.424, p = .66, η^2 = .005. This demonstrates that the anodal and sham tDCS groups did not differ in SWM performance over the pre, post1 and post2 time points. There was no significant effect of group, F (1, 76) = 3.138, p = .08, η^2 = .040, or time F (2, 76) = 1.934, p = .15, η^2 = .025.

For Purdue assembly, the GLMM revealed no significant group x time interaction, F (2, 73) = 1.072, p = .35, η^2 = .014. This demonstrates that the anodal and sham tDCS groups did not differ significantly in Purdue performance across the three time points. There was no significant effect of group, F (1, 73) = 0.240, p = .63, η^2 = .003. A significant effect of time was observed, F (2, 73) = 10.201, $p < .001$, η^2 = .123, which indicates a simple learning (practice) effect.

For sequential tapping, the GLMM revealed no significant group x time interaction, F (2, 76) = 1.436, p = .244, η^2 = .019, demonstrating that the anodal and sham tDCS groups did not differ in sequential tapping over the three time points. No significant group

effect was observed, F (1, 76) = 0.155, p = .695, η^2 =.002. A significant time effect was observed, F (2, 76) = 3.846, p = .026, η^2 = .048, which indicates a simple learning (practice) effect.

Discussion

The present study examined the relationship between SWM and FMC. The results demonstrated that hypothesis one was supported. A significant, moderate, negative relationship was revealed between SWM and both measures of FMC. These findings indicate that better SWM performance (less errors) was associated with better FMC performance. Such results are in line with the compensation theory, that better EF (SWM) performance indicates more compensatory resources available to support FMC in older adults (Seidler et al., 2010). These results, however, should be treated with caution. The present findings demonstrate a relationship between SWM and FMC. No causal inferences can be made, therefore it remains unclear whether better SWM results in better FMC in older adults.

The current results do not support hypothesis two, that anodal tDCS would improve SWM and FMC. Anodal stimulation of the left DLPFC did not significantly impact SWM or FMC. That is, the anodal and sham groups did not significantly differ for these measures across the time points. This conflicts with tDCS literature, as previous research has shown anodal tDCS to improve performance on a range of cognitive and motor tasks (Fregni et al., 2005; Jacobson et al., 2012). A number of reasons are postulated to be behind the inconsistency between the present results and previous studies.

Both measures of FMC demonstrated significant time effects, with moderate to large effect sizes. This is consistent with a learning effect as participants improved on the FMC tasks over time. Noguchi, Demura, Nagasawa, and Uchiyama (2006) examined whether the Purdue pegboard was susceptible to practice effects. The authors concluded that the Purdue pegboard demonstrates learning effects, as participants improved over subsequent trials. If present in the current study, a learning effect would be detrimental as it would make the impact of anodal tDCS harder to observe. If participants are improving in the FMC tasks regardless of their tDCS condition, then any impact due to anodal tDCS may be masked by the improvements observed due to practice alone. Therefore, the measures of FMC used in the present study may have been compromised as a result of learning effects. Nevertheless, it is reassuring that the participants were able to improve on the FMC measures, as motor learning is thought to be impaired in older adults (Onushko, Kim, & Christou, 2014). To reduce the impact practice has upon the Purdue Pegboard,

Noguchi et al. (2006) recommended that multiple trials be run and aggregated for each testing session.

As reported by Fregni et al. (2005), anodal simulation of the left DLPFC was anticipated to improve EF. Due to the limited scope of the current study, one measure of EF was used (SWM). EF is a broad construct comprising many higher order functions such as, planning, goal directed behaviour, working memory, and SWM (Elliott, 2003). EF is multidimensional, using factor analysis Miyake et al. (2000) concluded that although EF can be considered a unitary construct, it is underpinned by separate distinguishable cognitive processes. Using the SWM task may have failed to cover the scope of EF, due to the myriad of behaviours EF encapsulates. Therefore, improvements in EF due to anodal tDCS may have been overlooked, as the current study focused on one aspect of EF. If a broader range of EF measures had been used then improvements in other aspects of EF may have been observed.

A very recent study by Wu et al. (2014), which was unavailable prior to the commencement of the current study, examined the impact of anodal tDCS over the DLPFC on SWM. The findings revealed that anodal tDCS significantly improved performance on a SWM task. However, this was only true when the SWM task was at its most difficult level. The authors concluded that the participants only benefited from tDCS when the greatest demand was placed upon their SWM abilities. Anodal tDCS is postulated to work by priming stimulated neurons to fire more spontaneously (Utz et al., 2010). Although we can only speculate, perhaps this 'priming' is only of assistance when the demand upon the stimulated area is sufficient enough. In the present study no participants were identified as deficit on the SWM task, indicating that the task may have been too easy. Therefore, the SWM task used in the current study may not have been difficult enough to observe any impact of anodal tDCS.

In terms of electrode placement for tDCS, Wu et al. (2014) differed from the current study. Wu et al. (2014) placed the anode electrode over F4 and the cathode electrode on the left cheek. The cathode electrode was placed on the left cheek to avoid 'contaminating' other brain regions. Two other studies which observed significant impacts of tDCS; Berryhill, Wencil, Branch Coslett, and Olson (2010) and Hsu et al. (2011), also placed the cathode electrode on the cheek. Research into tDCS is still relatively new and no consensus exists on electrode placement (Jacobson et al., 2012). However, these aforementioned studies demonstrate merit in placing the cathode electrode on the cheek. Berryhill et al. (2010) stated that placement of the cathode on the cheek ensures that it does

not stimulate any areas of the brain, thus only the impact of anodal stimulation is observed. Therefore, the positioning of electrodes in the current study could account for the non-significant results observed. The placement of the cathode electrode over F4 may have resulted in unwanted stimulation in that area, impacting upon the effectiveness of the anodal tDCS.

Another explanation for the incongruity between the current study and existing literature could be the presence of a publication bias. Publication bias is the tendency for journals to favour and publish significant results (Hopewell, Loudon, Clarke, Oxman, & Dickersin, 2009). A publication bias would mean that the efficacy of tDCS is overestimated in current literature. Hummel et al. (2008) conducted a review of tDCS use in stroke patients and determined that it is likely a publication bias exists. Hummel et al. (2008) concluded that the publication of non-significant findings in tDCS research should be encouraged. Therefore the current findings may not be abnormal, rather previous research has found non-significant results which have not been published.

Future Research

Based upon the aforementioned limitations of the current study, future research should consider altered electrode placement. Additionally, future research should ensure the measures used are appropriate. Multiple measures of EF should be used to properly capture the breadth of the construct. Furthermore, multiple trials of FMC measures should be administered and aggregated at each testing session to reduce the impact of learning effects. Based upon Wu et al. (2014) the difficulty of the measures should also be sufficient enough to observe any improvements tDCS may have. Employing measures with a degree of difficulty will not only avoid a ceiling effect, but also determine whether tDCS is only effective when a high demand is placed upon the participant.

With regard to compensation theory, the current results indicate that a relationship does exist between SWM and FMC. Future research should aim to further delineate this relationship and examine if EF has a causal role in supporting FMC in older adults. The present study failed to improve EF via the use of tDCS. Other means of improving EF should be utilised to examine compensation theory. One possible intervention could be a cognitive training program. Dahlin, Nyberg, Backman, and Neely (2008) revealed that a 5 week cognitive training intervention significantly improved EF in older adults. Moreover, these improvements were maintained at an 18 month follow up. Future studies should examine whether such interventions cannot only improve EF in older adults, but also consequently, improve FMC in accord with the compensation theory.

Summary

Following the compensation theory, the present study hoped that anodal tDCS over the left DLPFC would improve SWM and FMC. Although tDCS was found to have no impact, a relationship was observed between SWM and FMC. While this is not definitive evidence that compensation theory is correct, the present findings still provide some support for the theory. Several limitations were highlighted in the current study. As tDCS is a relatively new research field, it is important that subsequent studies learn from and build upon the limitations of the present study. To do so will enable the refinement of tDCS research to better evaluate the efficacy of anodal tDCS as a potential treatment intervention.

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Extended Literature Review

Exploring Compensation Theory: The Impact of Non-Invasive Brain Stimulation on Spatial Working Memory and Fine Motor Control in Older Adults.

Dissertation submitted by

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Declines in Fine Motor Control across the Lifespan

Hand function is largely reliant upon the ability to perform fine motor skills (Ranganathan, Siemionow, Sahgal, & Yue, 2001). Fine motor control involves the coordination of small and precise movements which enable the grasping and manipulation of objects (Vieluf, Mahmoodi, Godde, Reuter, & Voelcker-Rehage, 2012). Many daily tasks rely upon fine motor control of the hand, such as the ability to tie shoelaces, write a note, or pick up small objects (Ranganathan et al., 2001). Reduced fine motor control of the hand has been linked to a reduced ability to perform daily tasks, which impacts upon the ability of an individual to live independently (Diermayr, McIsaac, & Gordon, 2011).

Research suggests that age negatively impacts upon fine motor control in healthy adults (Jiménez-Jiménez et al., 2011; Ward, 2006). Agnew, Bollawilson, Kawas, and Bleecker (1988) examined the relationship between age and performance on the Purdue Pegboard task in 212 healthy adults between the ages of 40 and 89. The Purdue Pegboard task is a standardised measure of fine motor control which requires the participant to perform various fine motor tasks, using the hand, as quickly as possible (Desrosiers, Herbert, Bravo, & Dutil, 1995). The findings revealed that performance on all aspects of the Purdue Pegboard declined significantly with increasing age. For the Purdue assembly task, which requires the participant to sequentially assemble small component parts, participants aged 40-49 years old assembled significantly more parts (39.8) compared to those aged 80-89 group (21.5). The findings of this study highlight the impact of age on fine motor control. One limitation of the study was the use of a cross-sectional research design, as the observed differences could be attributed to cohort effects.

Caçola, Roberson, and Gabbard (2013) examined the manner in which fine motor control changes with normal healthy ageing. The study involved 99 healthy participants who were allocated to one of three age groups; young (18-32), middle aged (40-63), and older adults (65-93). Participants completed timed sequential finger-tapping tasks which have been identified as an effective means of evaluating fine motor function (Mostofsky et al., 2006).The findings revealed that older participants took significantly longer to complete the task compared to the middle aged and younger participants, indicating that fine motor control performance declined with age. A plethora of studies indicate that fine motor control and aging are inversely related (Agnew et al., 1988; Caçola et al., 2013; Diermayr et al., 2011; Jiménez-Jiménez et al., 2011; Seidler et al., 2010; Ward, 2006)

Declines in fine motor control may adversely impact both an individual's ability to function independently and their quality of life (Incel, Sezgin, As, Cimen, & Sahin, 2009).

Age-related decline in fine motor control is associated with a reduced ability to perform everyday tasks, such as dressing and washing (Diermayr et al., 2011). Consequently, the individual will, with age, become increasingly dependent upon others to perform basic everyday tasks (Diermayr et al., 2011). A number of studies have reported that older people who have reduced fine motor control are more likely to require nursing-home care (Diermayr et al., 2011; Incel et al., 2009; Manandhar, 1995; Williams, Hadler, & Earp, 1982). In light of its impact, is important to develop evidence based approaches to minimise the loss of fine motor control with ageing (Diermayr et al., 2011).

Reasons Underlying Loss of Fine Motor Control with Ageing

A number of mechanisms may underlie age-related loss of fine motor control (Seidler et al., 2010). Changing brain matter in older adults is thought to contribute to age-related deficits (Seidler et al., 2010). A number of studies indicate that older adults demonstrate declines in grey and white matter volume in the brain (Courchesne et al., 2000; Ge et al., 2002; Good et al., 2001; Jernigan et al., 2001). A longitudinal study by Resnick, Pham, Kraut, Zonderman, and Davatzikos (2003) followed a group of healthy older adults and documented any changes in white and grey tissue volume over the course of four years. The results revealed significant declines in both grey and white matter volume over the four year time period. Furthermore, Salat et al. (2004) examined the thinning of the cerebral cortex across a range of different age groups to identify the areas of the brain most susceptible to loss in volume. The findings indicated that, in addition to an overall thinning of the cortex, the motor cortex exhibited the greatest rate of decline in relation to ageing. Taken together, these results indicate that loss of cortical volume increases with age and that the motor cortex is especially vulnerable to loss of matter.

Age-related loss of grey and white matter has been associated with decreased motor performance (Kennedy & Raz, 2005). Rosano et al. (2008) examined the relationship between grey matter volume and motor performance using magnetic resonance imaging and a gait-analysis task. The findings revealed that decreased grey matter was associated with poorer motor outcomes, such as impaired balance and a slower walking pace. Moreover, Zahr, Rohlfing, Pfefferbaum, and Sullivan (2009) reported that declines in white matter are associated with decreased performance across a range of different motor tasks. Using hand exterity tasks, a grooved pegboard task, and a balancing task, the authors observed that motor performance deteriorated wth age. This was attributed to changes in white matter associated with aging. Zahr et al. (2009) suggested that in addition to the loss

of white matter volume, the integrity of the remaining white matter deteriorates with age and further contributes to poorer motor outcomes (Zahr et al., 2009).

While age-related loss of brain volume is well-documented, it has been demonstrated that the number of neurons in the brain remains constant over the lifespan (Desrosiers et al., 1995; Pakkenberg & Gundersen, 1997; Resnick et al., 2003). Pakkenberg and Gundersen (1997) suggested that the number of neurons do not decrease with age per se, despite observing a 10% decline in the number of neurons across the lifespan. The 10% decline was, however, suggested to be a cohort effect resulting from the cross-sectional design of the study. The consensus among researchers is that decreased brain volume does not necessarily indicate neuron death (Ward, 2006). Research by Grady (2008) suggested that volume decrease is due to structural changes within the cortex, as neurons become more dense and white matter integrity declines.

Age Related Changes in Cortical Activation

Changes in brain function are typically observed by examining brain activation patterns using functional magnetic resonance imaging (fMRI; Grady, 2008). Age-related differences in brain activation patterns are evident for older adults whilst they perform motor tasks, compared to younger adults (Seidler et al., 2010). Older adults demonstrate over-activation (compared to younger adults) of cortical areas whilst performing motor tasks, whereby areas of the brain not typically associated with motor control become more active (Seidler et al., 2010). Two main theories have been proposed to account for this over-activation in older adults, the non-selective recruitment theory and the compensation theory (Seidler et al., 2010).

Non Selective Recruitment Theory

The non-selective recruitment theory proposes that the over-activation evident for older people performing motor tasks is a result of aging and reflects ‘inefficiency’ in the older brain (Logan, Sanders, Snyder, Morris, & Buckner, 2002; Riecker et al., 2006). It has been suggested that age-related cortical degeneration results in less functional specificity, such that given areas of the brain become less associated with a particular function. This results in ‘inefficiency’, as more areas of the older brain must be recruited to complete a given task (Seidler et al., 2010).

Riecker et al. (2006) examined non-selective recruitment theory by observing activation patterns in older people during varying speeds of a finger-tapping task. Higher speeds of tapping were assumed to represent a greater task difficulty, such that faster

tapping was more resource-demanding. The authors predicted that, if the over-activation was purposeful, then over-activation would increase with higher tapping frequencies in order to facilitate the movement. Riecker et al. (2006) observed that over-activation in older adults was constant during varying speeds of finger tapping, which was interpreted as support for the non-selective recruitment theory. However, the assumption that higher tapping speeds represents a greater task difficulty may be problematic. Finger tapping is a measure of motor speed and the usefulness of the measure is in its ability to determine how many taps can be completed in a given time (Christianson & Leathem, 2004; Jiménez-Jiménez et al., 2011; Meyer & Sagvolden, 2006). Finger tapping may only become difficult when the upper limits of a person's motor speed is reached. Therefore, performing at varying levels below this limit may not differ in terms of the demand placed upon cognitive resources. The results of the study should be interpreted with caution, as the finger tapping measure is not intended to be used as an indicator of resource demand.

Compensation Theory

Compensation theory suggests that cortical over-activation in older adults serves a compensatory purpose and reduces the impact of age-related loss of cortical volume (Seidler et al., 2010). A number of studies have presented findings in support of the compensation theory (Cabeza, Anderson, Locantore, & McIntosh, 2002; Heuninckx, Wenderoth, & Swinnen, 2008; Mattay et al., 2002). Harada, Miyai, Suzuki, and Kubota (2009) explored compensatory over-activation in the context of gait control in older adults. Three separate levels of walking intensity were assessed. The results of the study indicated that more intense walking resulted in increased activation of the prefrontal cortex of older adults, an area not typically activated during such a task. Furthermore, participants who demonstrated greater difficulty in walking also demonstrated greater over-activation. These findings indicated that increased walking difficulty was associated with increased over-activation in older adults. It is important to note that this was a correlational study, thus causality cannot be inferred. The findings are, however, consistent with the compensation theory as motor difficulty was positively related to over-activation, such that increased difficulty was associated with increased over-activation.

Heuninckx et al. (2008) examined whether cortical over-activation was due to compensation or non-selective recruitment during a motor task. It was hypothesised that if activation was compensatory, then increased activation would be associated with better motor performance. Conversely, if activation represented non-selective recruitment, then activation would be associated with poorer performance as it represents inefficiency in

neural transmission. It was found that better performance in the motor task was positively correlated with higher activation levels, particularly when the task was difficult. It was suggested that this finding was indicative of the compensatory role of over-activation, as increased activation was associated with better motor performance.

The Compensation Theory is the more widely accepted explanation for the different activation patterns seen in older adults (Seidler et al., 2010). A recent review of literature by Park and Reuter-Lorenz (2009) led them to suggest that increased activation in older brains serves an adaptive function and promotes improved performance across a range of tasks. Over-activation has been linked to better performance in memory, learning and motor tasks (Park & Reuter-Lorenz, 2009). Over-activation tends to occur in prefrontal areas of the brain, leading many researchers to suggest that such areas are responsible for compensatory mechanisms (Park & Reuter-Lorenz, 2009). Indeed, Heuninckx et al. (2008) reported that over-activation was confined to specific prefrontal areas, especially the dorsolateral prefrontal cortex (DLPFC). Such over-activation in prefrontal areas has been associated with improved motor performance in older adults (Park & Reuter-Lorenz, 2009). Prefrontal areas are typically associated with cognitive control rather than motor control (Seidler et al., 2010). The evidence would suggest, therefore, that older adults are more dependent upon primarily cognitive areas whilst completing motor tasks, in comparison to younger adults (Heuninckx, Wenderoth, Debaere, Peeters, & Swinnen, 2005).

Executive Functions

The prefrontal cortex is associated with higher order functioning and synthesises information from other cortical areas to achieve complex behaviours, such as directing and maintaining attention , anticipating events and adapting to changing circumstances (Miller, Freedman, & Wallis, 2002). These behaviours are typically described as ‘Executive Functions’ (EF; Elliott, 2003).

EF is a term used to describe a variety of complex cognitive processes (Elliott, 2003). EFs enable an individual to adapt to novel and demanding situations and to engage in goal directed behaviour (Huizinga, Dolan, & van der Molen, 2006). Intact EF is essential to the ability to plan, formulate a goal and implement goal directed strategies efficiently (Gilbert & Burgess, 2008; Jurado & Rosselli, 2007). EF is reliant upon the prefrontal cortex and individuals with prefrontal lesions often demonstrate impaired EF (Elliott, 2003; Huizinga & Smidts, 2010). Functional imaging studies have revealed that prefrontal areas of the brain are highly activated during tasks requiring EF (Stuss &

Levine, 2002). In a systematic review of EF, Stuss and Levine (2002) explains that the prefrontal cortex can be divided into two main areas, the ventral prefrontal cortex and the DLPFC. The ventral prefrontal cortex is associated with emotional processing and the understanding of stimulus reward relationships. The DLPFC is primarily responsible for spatial and conceptual reasoning processes associated with EF.

Carlin et al. (2000) examined the performance of people with prefrontal lesions on an EF task. The participants completed the Tower of London task, which is considered a measure of EF as it requires planning and goal directed behaviour. Those with prefrontal lesions had greater difficulty completing the task compared to the control group. Those with prefrontal lesions took longer and required more moves for successful completion of the task. As the difficulty of the task was increased, the differences between the two groups was more pronounced. The findings of this study support the notion that EFs are reliant upon intact prefrontal networks. These results are consistent with the findings of numerous studies in supporting a strong relationship between EF and prefrontal areas of the brain (Andres & Van der Linden, 2001; Mueller & Dollaghan, 2013; Nagahama, Okina, Suzuki, Nabatame, & Matsuda, 2005)

EF processes are thought to be necessary to function as an independently, as they enable an individual adapt to their ever-changing environment and effectively complete daily tasks (Jurado & Rosselli, 2007). A number of studies reveal age-related declines in EF, which has a profound impact upon the functional living skills of older people (Cahn-Weiner, Malloy, Boyle, Marran, & Salloway, 2000; Grigsby, Kaye, Baxter, Shetterly, & Hamman, 1998; Jurado & Rosselli, 2007). It has been proposed that those EFs most susceptible to age-related decline are spatial working memory (SWM), set-shifting and planning (Fisk & Sharp, 2004; Kessels, Meulenbroek, Fernández, & Olde Rikkert, 2010)

Spatial Working Memory

SWM is responsible for holding spatial information about one's environment, such as the location of an object, for future use (Nyberg, Lövdén, Riklund, Lindenberger, & Bäckman, 2012). Of all EFs, working memory is potentially the most sensitive to age-related neurological changes, with healthy adults demonstrating steady declines in working memory from the age of 20 onwards (Kane et al., 2004; Salthouse, 1994). SWM has been identified as particularly susceptible to decline in older age (Nyberg et al., 2012). Fiore, Borella, Mammarella, and De Beni (2011) examined whether SWM declines over the life span. Young (M = 27.8) and older (M = 68.8) participants completed a SWM task in

which they were required to recall the position of dots in a 5x5 matrix. The dots were presented one at a time for a period of one second and the participant had to recall the position of the last four dots. Older participants performed significantly worse than their younger counterparts, struggling to recall the positions of the dots accurately. Although research into SWM in older adults is not extensive, studies to date have been consistent in reporting a decline with age (Bopp & Verhaeghen, 2007; Cansino et al., 2013)

As previously indicated, movement in older adults is associated with increased recruitment of the prefrontal cortex (Heuninckx et al., 2008; Seidler et al., 2010)). The increased activation of prefrontal areas may be indicative of increased reliance upon EF to perform movements successfully (Heuninckx et al., 2008; Mattay et al., 2002). SWM contributes significantly to the ability to plan and execute successful movements (Anguera, Reuter-Lorenz, Willingham, & Seidler, 2011). Using fRMI, Anguera et al. (2011) examined activation patterns in older and younger adults whilst they learnt a new motor task. The results indicated that activation of areas involved in SWM, such as the DLPFC, were similar in older and younger adults. However, the acquisition of the new motor task was significantly slower for the older adults. The key difference between activation patterns was in the early stages of learning the new motor task. The younger participants demonstrated activation in areas associated with SWM (DLPFC), whereas older participants did not demonstrate such activation. The findings led the authors to suggest that early engagement of SWM contributed positively to the learning of a new motor task. The lack of early engagement, therefore, negatively impacted upon the ability of older adults to learn the new motor task. The findings of this study indicate the vital role of intact SWM for motor learning.

The prefrontal and parietal cortices are particularly susceptible to age-related grey and white matter atrophy, with both cortices demonstrating significant thinning with ageing (Salat et al., 2004). Furthermore, age-related dopaminergic degeneration occurs with ageing (Kaasinen et al., 2000). Some research suggests that movement and EF share the same dopamine circuit – as low levels of dopamine in the motor cortex correspond with low levels of dopamine in prefrontal cortex (van Dyck et al., 2008). Age-related prefrontal atrophy, coupled with dopaminergic degeneration, may act to diminish prefrontal resources and limit the availability of compensatory cognitive resources. Motor control in ageing may, therefore, be impacted via the reduced availability of compensatory cognitive resources, in particular the availability of EFs to help plan and organise goal-directed movements.

Transcranial Direct Current Stimulation

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique which is used to modify cerebral excitability by decreasing or increasing the firing rate of neurons (Utz, Dimova, Oppenländer, & Kerkhoff, 2010). Anodal (positive) stimulation depolarises neurons allowing them to fire more spontaneously, resulting in an increased firing rate (Utz et al., 2010) Cathodal (negative) stimulation hyperpolarises the neurons and decreases the firing rate of those neurons (Utz et al., 2010). The application of tDCS is considered to be easy and safe. Two electrodes are placed onto the scalp at the area of interest and a current of 1-2mA flows from the anode to the cathode stimulating underlying neural tissue (Been, Ngo, Miller, & Fitzgerald, 2007). Therefore tDCS can be used to depolarise or hyperpolarise neurons in an area of interest.

tDCS impacts upon a range of different behaviours, including memory and attention, depending upon electrode placement (Jacobson, Koslowsky, & Lavidor, 2012). A number of recent studies have reported that anodal stimulation of the motor cortex improves performance on motor tasks, whereas cathodal stimulation negatively impacts motor control (Boggio et al., 2006; Jeffery, Norton, Roy, & Gorassini, 2007; Stagg et al., 2009). Studies involving cognition have reported similar results, with anodal stimulation increasing performance and cathodal stimulation decreasing performance on a range of different tasks (Jacobson et al., 2012).

A recent study by Monti et al. (2008) is at odds with the general consensus of the literature (Jacobson et al., 2012). Monti et al. (2008) examined the impact that anodal and cathodal stimulation had upon a picture naming task. Monti et al. (2008) reported that cathodal stimulation increased performance on the picture naming task. Conversely, anodal stimulation did not impact upon performance at all. These results appear to be an anomaly and may be due to the study having no control group for comparison. Furthermore, the study used a between groups design in which group non-equivalence may have influenced results. The study also involved a small sample size (n=8), which consisted of a clinical stroke population. The use of a clinical population may add confounding factors, potentially skewing the results of the study.

Most research investigating tDCS has found that anodal stimulation has the ability to increase performance on tasks associated with the area of the brain being stimulated (Jacobson et al., 2012). Fregni et al. (2005) examined the impact that 10 minutes of 1 mA anodal tDCS over the left DLPFC had upon performance in an EF task. Fifteen participants aged between 19 and 22 years completed the study. Participants were randomly assigned to

a control group (sham tDCS) or an anodal tDCS group. Participants had to complete an *n*-back assessment of working memory (an EF). The task required participants to watch rapidly presented letters and to recall whether the last letter presented matched the letter presented three times prior. Participants who received anodal stimulation over the left DLPFC significantly improved in terms of their accuracy in comparison to the control group.

The therapeutic potential of tDCS has more recently been examined (Rothwell, 2012). tDCS is currently being considered for use in a range of disorders (for example, stroke, depression, schizophrenia, Parkinson's disease and chronic pain and the results are promising (Rothwell, 2012). Butler et al. (2013) examined the use of tDCS to improve motor control in stroke. They found that the application of anodal stimulation to the motor cortex significantly improved motor function. Overall, the therapeutic potential of tDCS is promising but further research is still required (Nitsche et al., 2005)

Research Rationale

It is increasingly apparent that EFs and motor control are intrinsically linked in healthy ageing. The Compensation Theory suggests that prefrontal areas support motor functioning in older adults by providing additional resources to complete motor tasks. These prefrontal areas are primarily associated with EF, and are not typically associated with motor control. The link between SWM and motor control raises the question of whether improved SWM is associated with improved motor control in healthy older adults. It has been established that anodal tDCS over DLPFC can improve EF (Fregni et al., 2005). In light of this, the present study examines whether anodal stimulation of DLPFC improves SWM and, consequently, fine motor control in older adults. If, as an EF involving DLPFC, SWM provides compensatory support for movement in older adults, then improved SWM should lead to improved FMC.

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Supplementary Material

Exploring Compensation Theory: The Impact of Non-Invasive Brain Stimulation on Spatial Working Memory and Fine Motor Control in Older Adults.

Dissertation submitted by

Leon Booth

November 2014

Extended Results

Missing Data and Outliers

Prior to analysis the data were visually inspected for errors. The data were then screened for missing values. Missing values analysis indicated that 3.4% of the whole data set was missing. Two participants did not have any post2 data and three participants did not complete the Purdue assembly task at post2. This is not a concern for GLMM, as the model can deal with missing values. Therefore, no data substitution method was used.

Examination of boxplots indicated that one participant was an outlier on the measures of fine motor control. As they were an influential outlier, their data were removed and the participant was not included in any subsequent analyses.

Assumption Testing for GLMM

Although no assumptions exist for GLMM for the purposes of experimental rigour assumptions tests associated with a traditional repeated measures ANOVA model are reported.

Normality. Normality tests were conducted for all of the variables separately at the pre, post1, and post2 time points.

For spatial working memory, the pre and post 1 time points the Shapiro-Wilk tests indicated that the assumption of normality was violated. Skewness and kurtosis measures were within acceptable parameters (+/- 1.96; Allen & Bennett, 2010). Visual inspection of the histograms and boxplots confirmed normal distribution. For the post2 time point the Shapiro-Wilk test indicated that SWM was normally distributed. It was noted that SWM at the pre time point resembled a bimodal distribution. However, as the subsequent time points confirmed that SWM was normally distributed in the population this was not considered to be an issue.

For Purdue assembly, Shapiro-Wilk was non-significant for all time points, indicating normality. Visual inspection of histograms in addition to skewness and kurtosis measures within +/-1.96 confirmed normality for Purdue assembly (Allen & Bennett, 2010).

For sequential tapping, Shapiro-Wilk indicated normal distribution of the sequential tapping task for all time points. Visual inspection of histograms and skewness and kurtosis measures also confirmed the normality assumption for sequential tapping.

Homogeneity of Variance. F*max* values were calculated for all of the variables. All scores were less than 10, indicating that all measures met the homogeneity assumption (Allen & Bennett, 2010).

Sphericity. Mauchly's test of sphericity was non-significant ($p = .345$) for the SWM task, indicating that the assumption of sphericity was met. For both the Purdue assembly and sequential tapping tasks the test was significant indicating that the assumption of sphericity was violated. To resolve this an auto regressive matrix was used in the GLMM for these measures. An auto regressive matrix accommodates for the violation of sphericity.

Assumption Testing for Bivariate Correlations

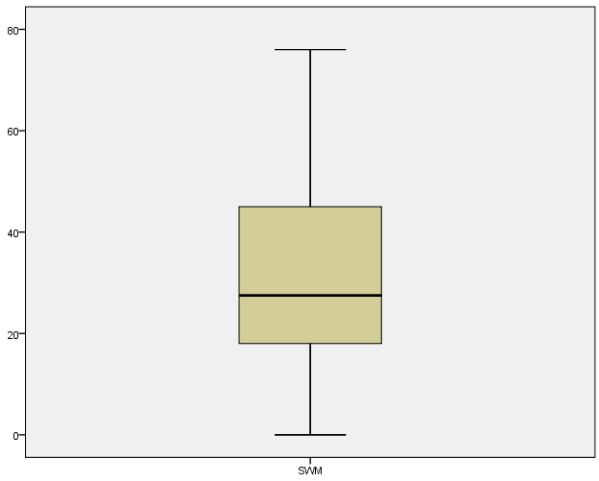
Normality. The normality tests were the same as conducted for GLMM for the pre time point. The Shapiro-Wilk test indicated that both the Purdue assembly and sequential tapping tasks were normally distributed. For SWM, the Shapiro-Wilk test indicated a violation of normality. Visual inspection of boxplots and histograms demonstrated normal distribution of SWM. Skewness and kurtosis measures were within +/- 1.96, indicating normality for SWM (Allen & Bennett, 2010).

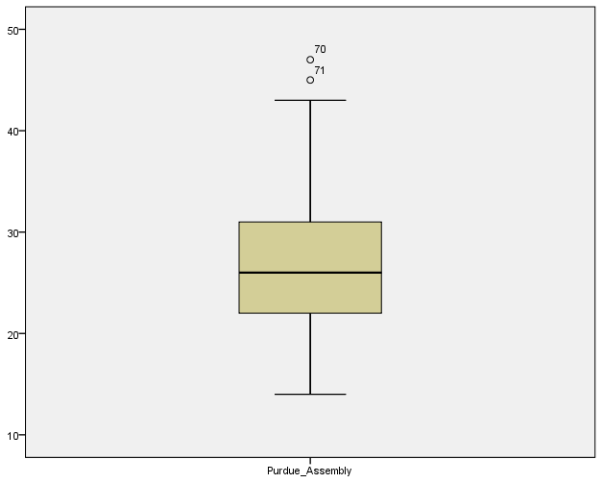
Linearity and Homoscedasticity. Visual inspection of scatterplots confirmed that the assumptions of linearity and homoscedasticity were met.

SPSS Statistical Analysis Output

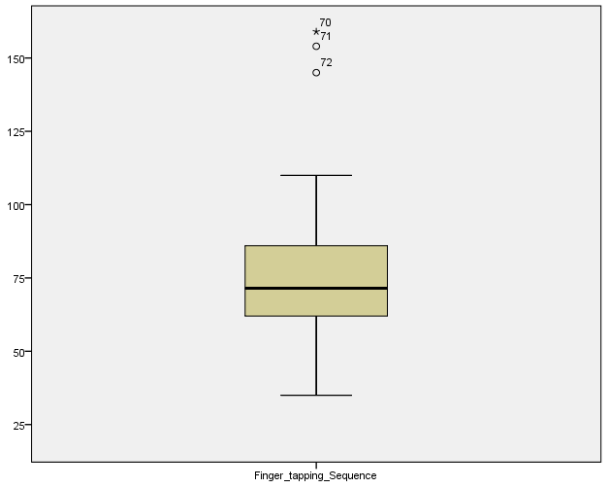
Initial Boxplots Indicating Outliers

Note: All subsequent analyses performed with the removal of outlier.





The two outliers represent the pre and post1 scores from the same participant



The three outliers represent the pre, post1, and post2 scores for the same participant which identified two outlier on the Purdue assembly.

Descriptive Statistics for Pre Time Point

Descriptives

			Statistic	Std. Error
SWM	Mean		34.29	3.412
	95% Confidence Interval for Mean	Lower Bound	27.29	
		Upper Bound	41.29	
	5% Trimmed Mean		33.52	
	Median		28.50	
	Variance		325.915	
	Std. Deviation		18.053	
	Minimum		9	
	Maximum		76	
	Range		67	
	Interquartile Range		33	
	Skewness		.650	.441
	Kurtosis		-.677	.858
Purdue_Assembly	Mean		24.75	.892
	95% Confidence Interval for Mean	Lower Bound	22.92	
		Upper Bound	26.58	
	5% Trimmed Mean		24.74	
	Median		24.00	
	Variance		22.269	
	Std. Deviation		4.719	
	Minimum		14	
	Maximum		36	
	Range		22	
	Interquartile Range		6	
	Skewness		-.029	.441
	Kurtosis		.306	.858
	Interquartile Range		19	
	Skewness		.093	.441
	Kurtosis		.287	.858

			Statistic	Std. Error
Finger_tapping_Sequence	Mean		70.39	3.199
	95% Confidence Interval for Mean	Lower Bound	63.83	
		Upper Bound	76.96	
	5% Trimmed Mean		70.49	
	Median		70.50	
	Variance		286.470	
	Std. Deviation		16.925	
	Minimum		35	
	Maximum		104	
	Range		69	
	Interquartile Range		19	
	Skewness		.093	.441
	Kurtosis		.287	.858

Normality Tests for Pre Time Point

Tests of Normality

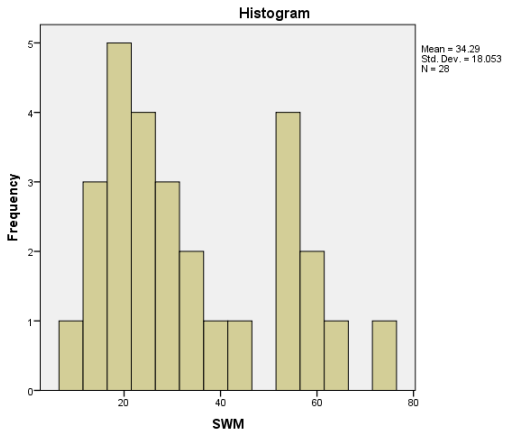
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
SWM	.165	28	.049	.920	28	.034
Purdue_Assembly	.147	28	.123	.975	28	.730
Finger_tapping_Sequence	.126	28	.200*	.961	28	.368

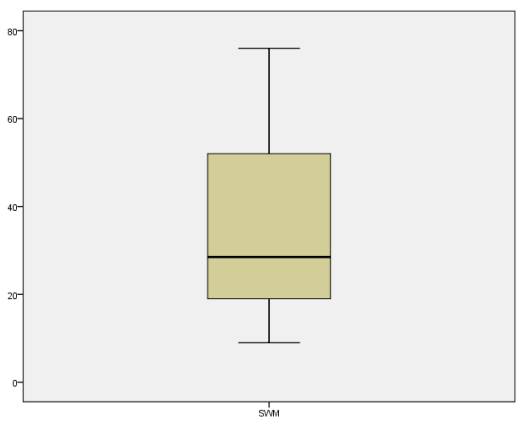
*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

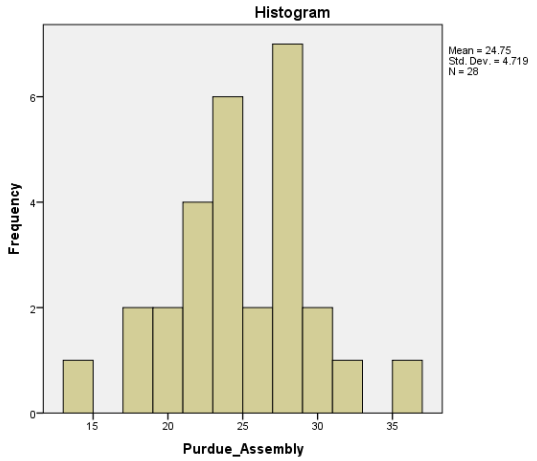
Box Plots and Histograms for Pre Time Point

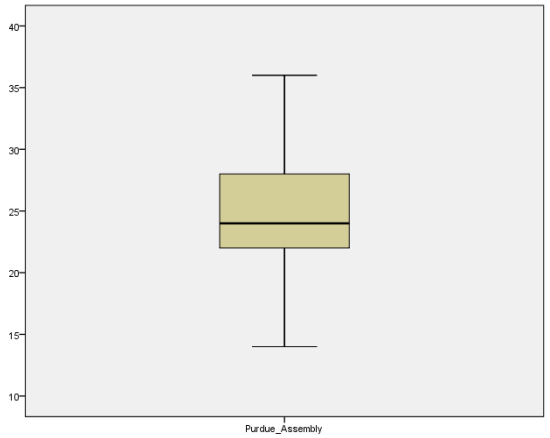
SWM:



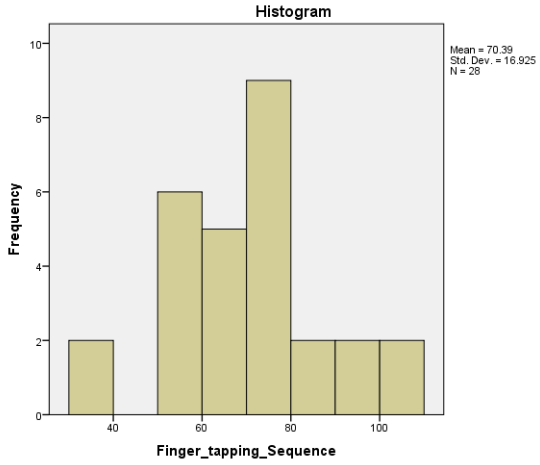


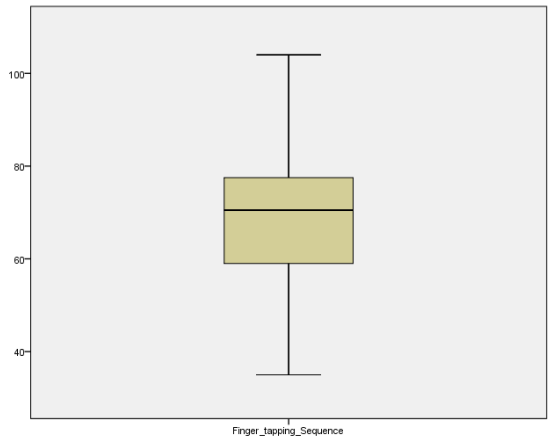
Purdue Assembly:





Sequential Tapping:





Descriptive Statistics for Post1 Time Point

Descriptives

			Statistic	Std. Error
SWM	Mean		30.86	3.951
	95% Confidence Interval for Mean	Lower Bound	22.75	
		Upper Bound	38.96	
	5% Trimmed Mean		30.09	
	Median		27.00	
	Variance		437.164	
	Std. Deviation		20.908	
	Minimum		0	
	Maximum		75	
	Range		75	
	Interquartile Range		36	
	Skewness		.733	.441
	Kurtosis		-.420	.858
Purdue_Assembly	Mean		27.04	.997
	95% Confidence Interval for Mean	Lower Bound	24.99	
		Upper Bound	29.08	
	5% Trimmed Mean		27.17	
	Median		27.00	
	Variance		27.813	
	Std. Deviation		5.274	
	Minimum		16	
	Maximum		35	
	Range		19	
	Interquartile Range		8	
	Skewness		-.353	.441
	Kurtosis		-.680	.858

			Statistic	Std. Error
Finger_tapping_Sequence	Mean		73.18	3.150
	95% Confidence Interval for Mean	Lower Bound	66.72	
		Upper Bound	79.64	
	5% Trimmed Mean		73.14	
	Median		69.00	
	Variance		277.856	
	Std. Deviation		16.669	
	Minimum		40	
	Maximum		105	
	Range		65	
	Interquartile Range		26	
	Skewness		.266	.441
	Kurtosis		-.407	.858

Normality Tests for Post1 Time Point

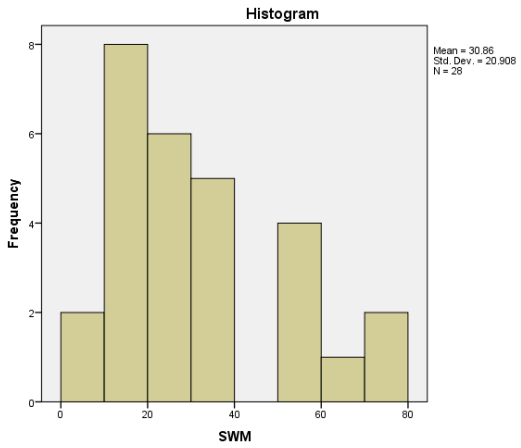
Tests of Normality

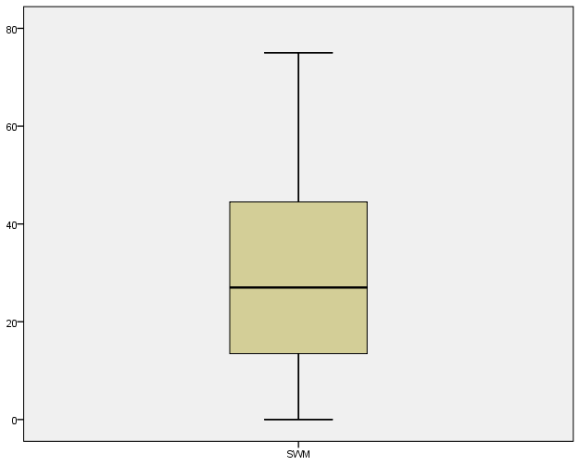
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
SWM	.157	28	.076	.918	28	.032
Purdue_Assembly	.148	28	.118	.950	28	.198
Finger_tapping_Sequence	.145	28	.140	.969	28	.548

a. Lilliefors Significance Correction

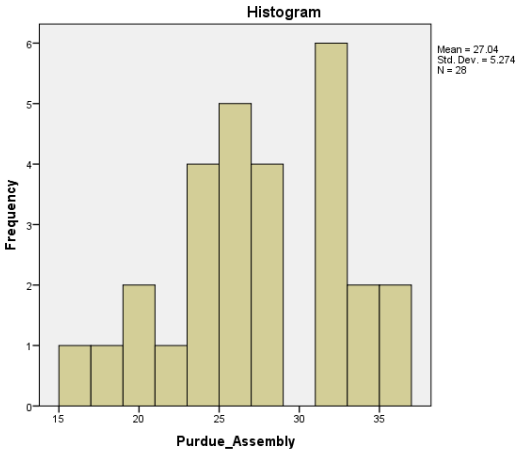
Box Plots and Histograms for Post1 Time Point

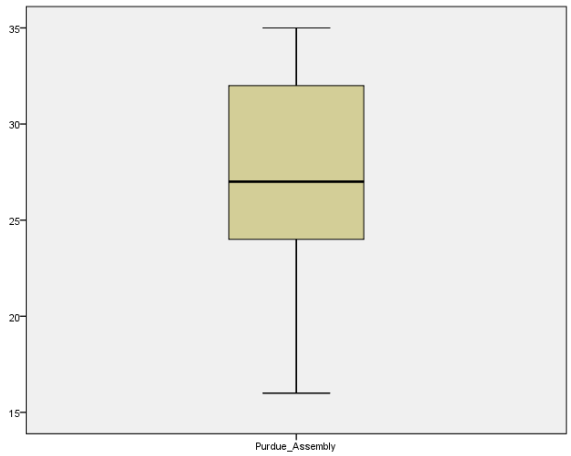
SWM:



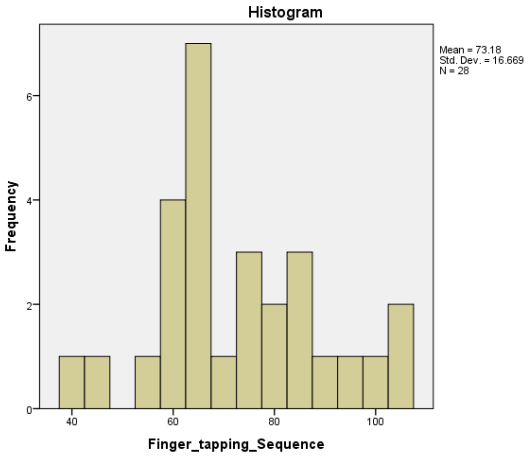


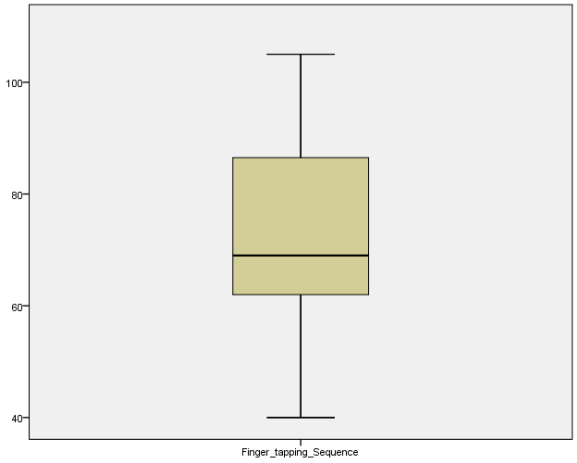
Purdue Assembly:





Sequential Tapping:





Descriptive Statistics for Post2 Time Point

Descriptives

			Statistic	Std. Error
SWM	Mean		31.30	3.568
	95% Confidence Interval for Mean	Lower Bound	23.90	
		Upper Bound	38.70	
	5% Trimmed Mean		31.29	
	Median		30.00	
	Variance		292.858	
	Std. Deviation		17.113	
	Minimum		3	
	Maximum		60	
	Range		57	
	Interquartile Range		27	
	Skewness		-.019	.481
	Kurtosis		-.960	.935
Purdue_Assembly	Mean		25.09	1.227
	95% Confidence Interval for Mean	Lower Bound	22.54	
		Upper Bound	27.63	
	5% Trimmed Mean		25.19	
	Median		25.00	
	Variance		34.628	
	Std. Deviation		5.885	
	Minimum		14	
	Maximum		34	
	Range		20	
	Interquartile Range		11	
	Skewness		-.114	.481
	Kurtosis		-.855	.935

			Statistic	Std. Error
Finger_tapping_Sequence	Mean		75.22	3.236
	95% Confidence Interval for Mean	Lower Bound	68.51	
		Upper Bound	81.93	
	5% Trimmed Mean		74.55	
	Median		74.00	
	Variance		240.905	
	Std. Deviation		15.521	
	Minimum		52	
	Maximum		110	
	Range		58	
	Interquartile Range		21	
	Skewness		.806	.481
	Kurtosis		.294	.935

Normality Tests for Post2 Time Point

Tests of Normality

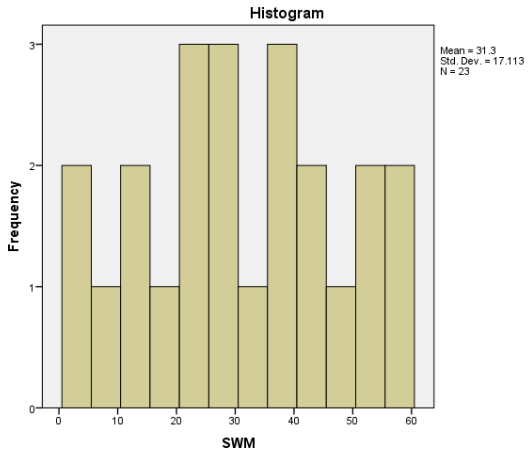
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
SWM	.086	23	.200*	.966	23	.597
Purdue_Assembly	.103	23	.200*	.961	23	.484
Finger_tapping_Sequence	.114	23	.200*	.942	23	.199

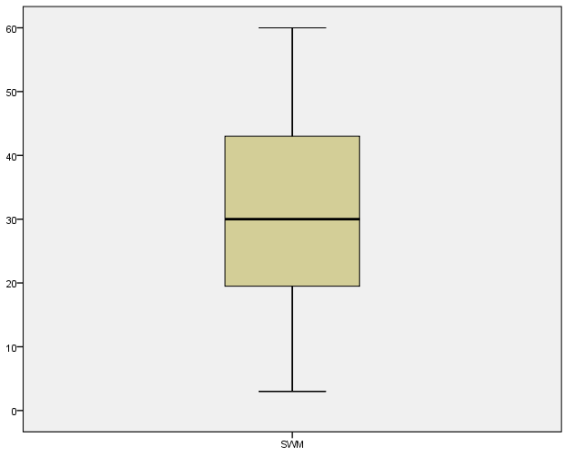
*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

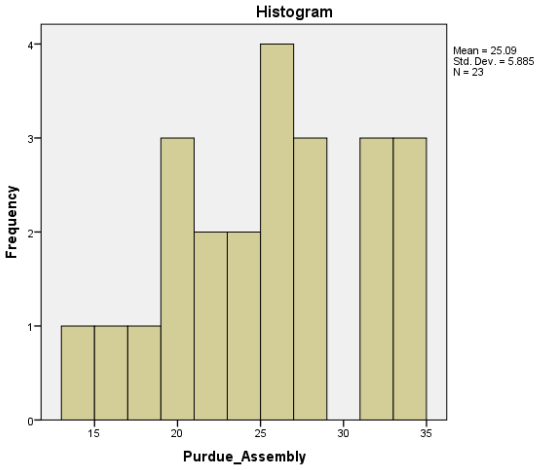
Box Plots and Histograms for Post2 Time Point

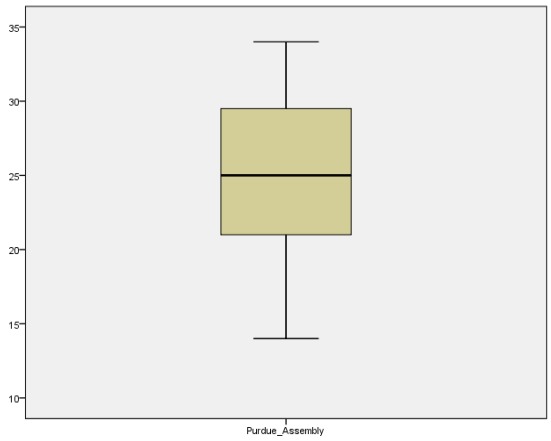
SWM:



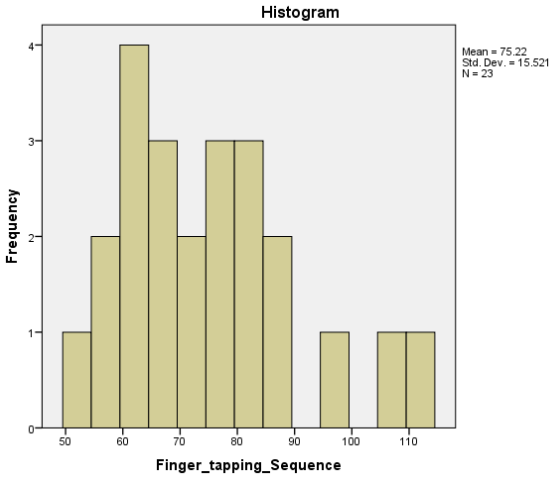


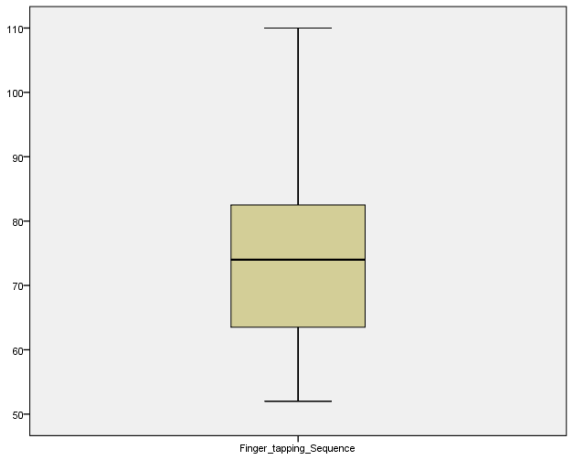
Purdue Assembly:





Sequential Tapping:





Sphericity Analysis for GLMM:

SWM:

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
SWMerrors	.912	2.126	2	.345	.919	1.000	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Group
Within Subjects Design: SWMerrors

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Purdue Assembly:

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
PurScore	.620	9.557	2	.008	.725	.801	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Group
Within Subjects Design: PurScore

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Sequential Tapping:

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
SeqScore	.658	9.618	2	.008	.745	.816	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Group
Within Subjects Design: SeqScore

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

GLMM Output

The GLMM does not provide an output per se, hence screenshots of the model are provided.

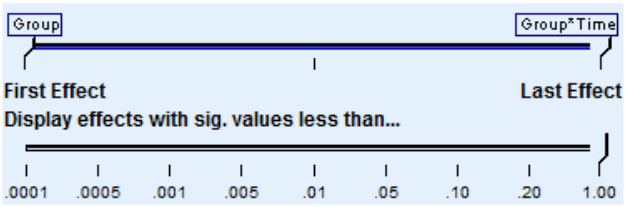
SWM:

Fixed Effects

Target:SWM

Source	F	df1	df2	Sig.
Corrected Model ▼	1.866	5	76	.110
Group	3.138	1	76	.081
Time	1.934	2	76	.152
Group*Time	0.424	2	76	.656

Probability distribution:Normal
Link function:Identity



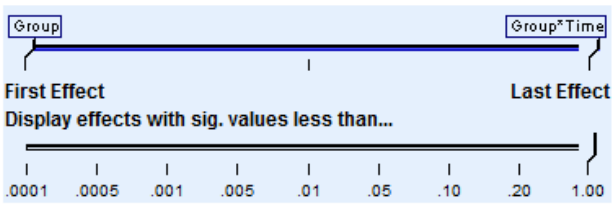
Purdue Assembly:

Fixed Effects

Target:Purdue_Assembly

Source	F	df1	df2	Sig.
Corrected Model ▼	5.388	5	73	.000
Group	0.240	1	73	.626
Time	10.201	2	73	.000
Group*Time	1.072	2	73	.348

Probability distribution:Normal
Link function:Identity



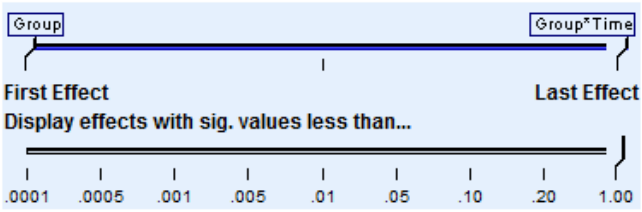
Sequential Tapping:

Fixed Effects

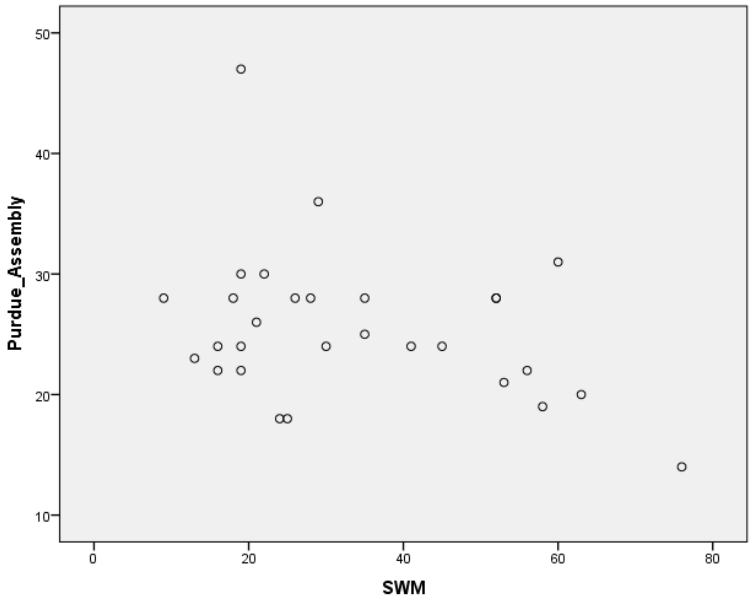
Target:Sequential_Tapping

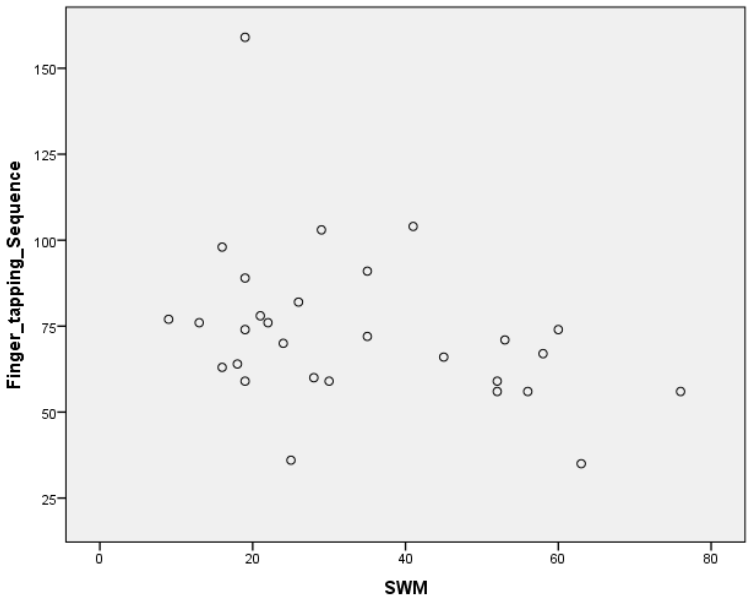
Source	F	df1	df2	Sig.
Corrected Model ▼	2.046	5	76	.082
Group	0.155	1	76	.695
Time	3.846	2	76	.026
Group*Time	1.436	2	76	.244

Probability distribution:Normal
Link function:Identity



Scatter Plots for Bivariate Correlations at Pre





Bivariate Correlations at Pre

Correlations

		SWM	Purdue_Assembly	Finger_tapping_Sequence
SWM	Pearson Correlation	1	-.329*	-.357*
	Sig. (1-tailed)		.041	.029
	N	29	29	29
Purdue_Assembly	Pearson Correlation	-.329*	1	.740**
	Sig. (1-tailed)	.041		.000
	N	29	29	29
Finger_tapping_Sequence	Pearson Correlation	-.357*	.740**	1
	Sig. (1-tailed)	.029	.000	
	N	29	29	29

*. Correlation is significant at the 0.05 level (1-tailed).

**. Correlation is significant at the 0.01 level (1-tailed).

Information sheet

PARTICIPANT INFORMATION SHEET

Project title: The Impact of Transcranial Direct Current Stimulation on Executive Functioning

Ethics approval reference: HR32/2013

Invitation

You are invited to participate in a research project investigating whether transcranial Direct Current Stimulation (tDCS) can impact upon executive functioning (your ability to plan and organize information). tDCS is a safe non-invasive brain stimulation technique which delivers low electrical currents to the brain through electrodes placed on the scalp.

Please take time to read the following information carefully. Ask us any questions if some part of the information is not clear to you or if you would like more information. Please ask any questions you have before you sign the consent form.

Who is the Chief Investigator (CI) of this study?

Dr Andrea Loftus and Dr Peta Dzidic, School of Psychology & Speech Pathology, Curtin University, are CIs on this study. The student researchers working on this study are Natalie Campbell and Leon Booth.

Why have I been invited to participate in this research?

You have been invited to participate in this study as you are over 60 years of age and have met the requirements for participation. You may decide to be in the study or not take part at all. If you do decide to take part in this study, you may stop at any time. However, before you decide, it is important that you understand why this research is being done and what it will involve. The following information will explain the study and assist you to decide whether or not to participate.

What are the aims of this study?

A number of recent studies have shown that non-invasive brain stimulation techniques may result in improvements in memory, learning and thinking. One such method is transcranial direct current stimulation (tDCS). This method stimulates the brain via an electrode on the scalp that transmits a weak direct current. tDCS is non-invasive and painless.

This study investigates whether tDCS can be used to promote change within an area of the brain that is responsible for executive functioning. Executive functioning refers to the ability to plan, organise and shift between different tasks. Everyday tasks such as writing a shopping list or remembering to attend a hospital appointment are examples of executive functioning. If tDCS is found to impact upon executive functioning, it could help our

understanding of how executive functioning can be improved and this can eventually lead to the development of interventions for those with executive control difficulties.

How long will I be in this study?
If you decide to participate in the study you will be asked to visit the School of Psychology at Curtin University for about 2 ½ -3 hours over two times, 2 weeks apart.

What is transcranial Direct Current Stimulation (tDCS) and how does it work?
The human brain is made up of billions of tiny neurons and electrical currents. All our actions and thoughts are dependent upon the firing and inhibition of these neurons. tDCS is the application of weak electrical currents (1-2 mA) to change the electrical activity of these neurons. tDCS works by altering the firing rates of the neurons. When the tDCS electrodes are placed on the scalp, the electrical change produced in the brain is exceedingly small, changing neuron excitability by only a fraction of a millivolt. The use of tDCS has not been associated with any adverse outcomes.

What will happen if I decide to be in this study?
If you decide to be a part of this study, the researcher will ask you some general medical questions to determine if you are suitable for tDCS. This can be done over the telephone or upon your arrival at the University if you prefer. If you are suitable for tDCS, the researcher will arrange a time that is convenient for you to come to the lab.

On arrival at the lab, the researcher will give an overview of the experiment and what is required of you and will ask whether you have any questions. Should you wish to participate in the study, you will then be invited to provide informed consent for participation. You will then be asked to sit in a comfortable chair for approximately twenty minutes.

This study will be completed within two testing sessions:
Session 1: Baseline measures of executive function and movement
You will be asked to sit in a comfortable chair and complete four different measures of executive control on a computer. No prior computer skills are required to complete these tasks. Before completing each task, verbal instructions and a demonstration will be provided by the researcher. Each task will take approximately 5 - 10 minutes. You will also be asked to recall a list of words which will be read out to you, which will take approximately 10 minutes. You will also be asked to perform some basic movement tasks. The researcher will then measure and attach two electrodes to your head – one just above the eye and one at the front left part of your head. These will be secured using specially designed headbands which will wrap around your head. tDCS will then be administered for 30 minutes, during which time the researcher will chat with you or, if you prefer, you can read one of our magazines. You will be offered light refreshments during this phase. After the tDCS, you will complete the same tasks as you did at the start of the session.

Session 2: Post-tDCS measures and interview

You will complete the same tasks as you did for Session 1. At this time you will also complete an interview where you will be asked to share your experiences of your memory and tDCS, this will take around 30 minutes.

You can terminate the study at any point without effect or explanation should you wish.

What are the benefits of my participation?

The study may not be of direct benefit to you; however the findings will potentially benefit individuals who have deficits in executive functioning. Your participation will provide us with a clearer understanding of how tDCS can aid in the improvement of executive function in general.

What can go wrong if I take part in this study?

This research project is not expected to pose any risk to you. There have been no long-lasting adverse effects associated with tDCS. The tDCS protocol to be used in this study has been employed by numerous researchers with no reports of subject discomfort or harm. The investigators will strictly adhere to the current international safety guidelines and precautions for the use of tDCS in the study.

Who will have access to my data?

Information which could identify you as an individual will not be published or reported. Only the combined results of all participants in the study will be published or reported. You will remain anonymous as you will only be identified by a code number. The coded data will be securely stored for at least five years, as prescribed by university regulations and will only be accessible to the study investigators.

Who has approved this study and does it meet ethical requirements?

The project will be carried out according to the National Statement on Ethical Conduct in Research Involving Humans (June 1999) produced by the National Health and Medical Research Council of Australia and according to the Good Clinical Practice Guidelines. This research project has been reviewed and approved by the Human Research Ethics Committee of the Curtin University (project number: HR32 / 2013)

Who can I contact about this study?

If you have any questions or concerns about this study, please contact the Chief Investigator/s on this project whose contact details are listed at the start of this information sheet.

Do I get to keep a copy of the Information Sheet and Consent form?
You will be given a copy of the Information Sheet to keep. If you decide to take part in this research you may request a copy of this signed consent form for your records also.

What if there is a problem and I want to make a complaint?

If you have any concerns of an ethical nature or complaints about the manner in which the research is conducted, please contact the Human Research Ethics Committee by telephoning (08) 9266 2784 or emailing hrec@curtin.edu.au. Alternatively, you may write to the Office of Research and Development, Curtin University of Technology, GPO Box U1987, Perth WA 6845).

Consent Form

Consent Form

Project:
The Impact of Transcranial Direct Current Stimulation on Executive Functioning

Ethics approval number:
HR32/2013

Chief Investigator:
Dr Andrea Loftus, School of Psychology & Speech Pathology, Curtin University

I (Participant's Name)_____ confirm that:

1. I have understood and completed the tDCS exclusion criteria checklist

2. I have been given clear information (verbal and written) about this study and have been given time to consider whether I want to take part.

3. I have been told about the possible advantages and risks of taking part in the study and I understand what I am being asked to do.

4. I have been able to ask questions about the study and its procedures and all questions have been answered satisfactorily.

5. I know that I do not have to take part in the study and that I can **withdraw at any time** during the study without any effect and without having to explain why.

6. I agree to take part in this research study and for the data obtained to be published provided my name or other identifying information is not used.

If you are unclear about anything you have read in the Information Sheet or this Consent Form, please speak to one of the Investigators before signing this Consent Form.

Name of Participant Signature of Participant

Date_____

This study has been approved under Curtin University's process for research with humans. This process complies with the National Statement on Ethical Conduct in Human Research (Chapter 5.1.7 and Chapters 5.1.18-5.1.21). For further information on this study contact the researchers named above or the Curtin University Human Research Ethics Committee. c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth 6845 or by telephoning 9266 9223 or by emailing hrec@curtin.edu.au.

tDCS Exclusion Criteria Sheet

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 (does not include anti-depressants or anti-anxiety drugs)

• 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 – if they have bad asthma, NO. But if it is controlled, then they must bring puffer with them.

• 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 – remove during tDCS.

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

Participant's name (printed) Participant's signature

Date:

Ethics Approval

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
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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 Consultation

STATISTICAL CONSULTATION FOR PSYCHOLOGY HONOURS STUDENTS 2014

Please complete this form, then email the form to Dr Robert (Bob) Kane and make an appointment time for you and your supervisor(s).

Student Name:

Thesis Title:

Supervisors:

Research Question

Can anodal tDCS improve spatial working memory and fine motor control in older adults?

Does a relationship exist between spatial working memory and fine motor control?

Hypotheses

H1a: The anodal group will show significantly greater reductions in SWM errors between the pre-test and post-test 1, and between the pre-test and post-test 2.

H1b: The anodal group will show significantly greater increases in assembly

H1c: The anodal group will show significantly greater increases in number of finger taps between the pre-test and post-test 1, and between the pre-test and post-test 2.

Sample Size Required Based on Power Analysis

Approximately 30

Sampling Strategy:

Participant to be recruited from a database of older adults who have previously indicated interest in research participation.

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

CANTAB Spatial working memory task
Purdue Pegboard (fine motor control)
Sequential finger tapping task (fine motor control)

Planned Analyses

Generalised linear mixed model

Specific Questions for Statistical Consultant

Would a GLMM be an appropriate statistical test for the circumstance of the study?
What would be the best means of examining the relationship between spatial working memory and fine motor control?

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 3 mixed design.

	Pre-test	Post-test 1 Immediately after stimulation	Post-test 2 Two weeks after stimulation
Anodal			
Sham			

Participants will be randomly allocated to the anodal and sham groups, and then tested on the outcome variables (SWM total errors, assembly score, & total number of finger taps) before, immediately after, and two weeks after stimulation.

Hypotheses for the first research question

You formulate the following hypotheses (which I've reworded for the GLMM):

Compared to the sham condition:

H1a: The anodal group will show significantly greater reductions in SWM errors between the pre-test and post-test 1, and between the pre-test and post-test 2.

H1b: The anodal group will show significantly greater increases in assembly scores between the pre-test and post-test 1, and between the pre-test and post-test 2.

H1c: The anodal group will show significantly greater increases in number of finger taps between the pre-test and post-test 1, and between the pre-test and post-test 2.

Hypothesis testing

Each hypothesis can be tested with a Generalised Linear Mixed Model (GLMM). The GLMM is implemented through SPSS's (Version 22) GENLINMIXED procedure. The GLMM represents a special class of regression model. The GLMM is 'generalised' in the sense that it can handle outcome variables with markedly non-normal distributions; the GLMM is 'mixed' in the sense that it includes both random and fixed effects. Your GLMM consists of one nominal random effect (participant), one categorical fixed effect (group [anodal versus sham]), one ordinal fixed effect (time [pre, post 1, post 2]), and the Group x Time interaction. Following a significant interaction, post-hoc Least Significant Difference (LSD) contrasts can be conducted across the simple main effects of time to isolate the source of the interaction.

Controlling for multiple statistical tests

In order to optimise the likelihood of convergence, a separate GLMM analysis should be run for each of the three outcome measures. Analysing each outcome independently of the others will of course inflate the familywise error rate. The per-test alpha will therefore need to be corrected to control the inflation. This normally involves dividing the traditional per-test alpha-level (.05) by the number of outcomes (3).

Statistical assumptions

For a repeated measures design such as yours, the traditional ANOVA model requires the following assumptions to be satisfied: Normality, homogeneity of variance, and sphericity. The GLMM 'robust statistics' option will generally take care of violations of normality and homogeneity of variance. Violations of sphericity can be accommodated by changing the covariance matrix from the default of compound symmetry to autoregressive. Also, GLMM is robust to unequal group sizes.

Participant attrition

When data are collected longitudinally, we have the problem of participant attrition (wave non-response). Wave non-response will normally reduce statistical power. Compared to the traditional statistical procedures for analysing behavioural change (e.g., repeated measures ANOVA), GLMM is less sensitive to participant attrition because it does not rely on participants providing data at every assessment point; the GLMM maximum likelihood procedure is a full information estimation procedure that uses *all* the data present at *each*

assessment point. This reduces sampling bias and the need to replace missing data. GLMM is able to use the data present at each assessment point because time (pre, post 1, post 2) is interpreted as a Level 1 variable that is nested within participant at Level 2.

Statistical power

Each of your hypotheses predicts a Group x Time interaction. Data from previous studies using outcomes similar to yours should be used to estimate the magnitude of these interactions. If these data aren't available, then all you can really do is estimate the number of participants required for an 80% probability of capturing a 'small to moderate' interaction (i.e., $f = .18$) between group (intervention, control) and time (pre, post 1, post 2) at your Bonferroni-adjusted alpha-level of .017. According to G*Power, the required sample size is 68 (34 in each group). I've opted for a 'small to moderate' interaction effect because two-way interactions tend to be on the 'small' side. If, by any chance, the two-way interaction turns out to be on the 'moderate to large' side ($f = .28$), then a sample size of 30 will cut it (15 in each group). As argued in the previous section, unlike repeated measures ANOVA, GLMM does *not* rely on participants providing data at every assessment point; GLMM uses all the data present at each assessment point thereby reducing the impact of subject attrition on statistical power.

The *F*-values and *t*-values output by GLMM can be converted into effect sizes by applying the appropriate formulae.

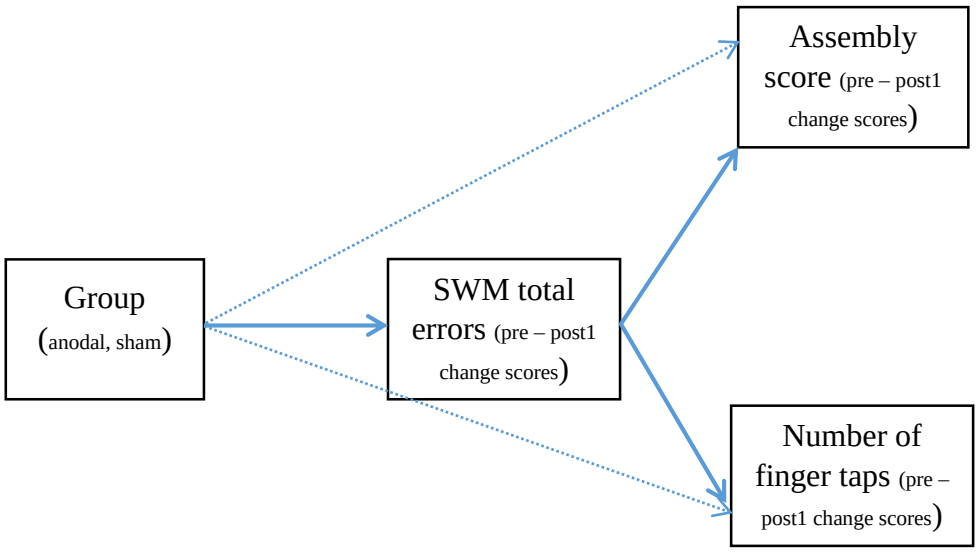
Hypotheses for the second research question

I can't remember whether we agreed on a mediation hypothesis here. I'll assume that we did.

H2: At post-test 1, anodal stimulation impacts FMC via SWM.

Hypothesis testing

H2 proposes the following mediation model:



This simple mediation model can be readily tested with LISREL 8.8. It's necessary to show that the model fits the data before examining the significance of the pathways; and (despite what some researchers say) it's necessary to show that the *indirect* pathways are significant before testing mediation.

NB:
At our meeting, we talked about using reliable change (RC) scores. Unless we have reliability estimates for our outcomes, however, RC scores cannot be computed. For your outcomes, reliability can be estimated from test-retest correlations – but I doubt this information is available. You'll therefore need to analyse the raw change scores.

Sample size estimation

It has been recommended that we have at least 5 participants for each *free* parameter in the path model (Kline, 2005). A free parameter is a parameter that must be estimated from the sample data. Your mediation model has nine free parameters. According to Kline's rule-of-thumb, a minimum sample size for testing this model would be 35 (22 in each group).

Assumption testing

Multivariate normality

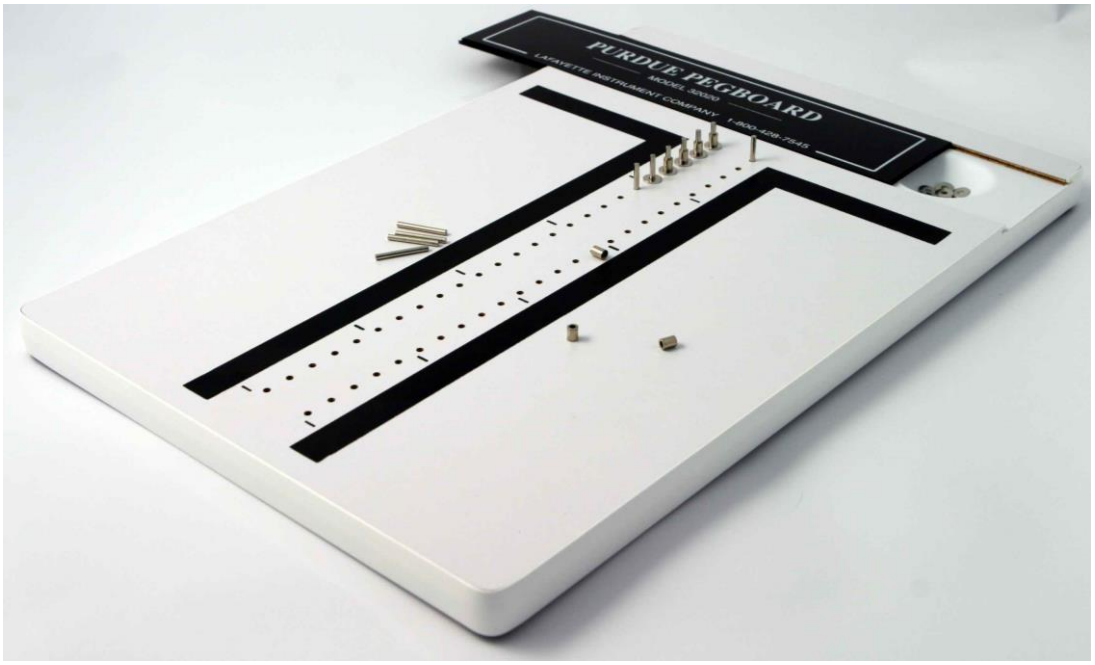
Path analysis assumes that the variables being analyzed are *multivariate normal* (Kline, 2005). LISREL will test for multivariate normality. If the assumption is violated, and it almost always is, the chi-square statistic that is normally used to derive the fit statistics will be inflated (Joreskog & Sorbom, 2004). In these circumstances, Joreskog and Sorbom recommend deriving the fit statistics from a version of chi-square that corrects for the inflation. The Satorra-Bentler chi-square, available through LISREL, provides such a statistic (Joreskog, 2005).

Linearity

Path analysis also assumes that the bivariate relationships among the variables are *linear* rather than *curvilinear*. The most straight-forward way to test for linearity is to examine the scatterplots of the bivariate relationships. If there are no obvious curvilinear trends, then we can assume that the linearity assumption has been met.

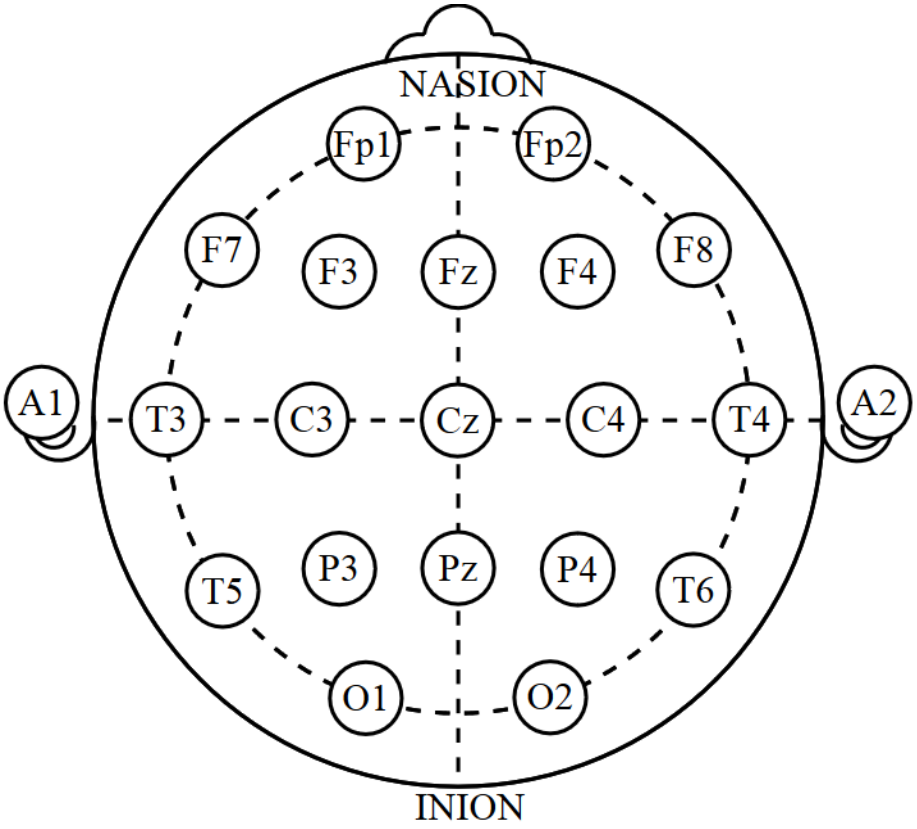
Note: The second research question was changed to explore the relationship between SMW and FMC. This is because it would be unrealistic to recruit and test 35 participants within the scope of the current study. Therefore for the second hypothesis a bivariate correlations were performed in place if the mediation model.

Purdue Pegboard Task



Note: The participant had to create a series of assemblies working their way down the vertical line of holes. Each assembly began by the insertion of a peg into the board with the dominant hand, then placing a washer on the peg, followed by a collar, and finally another washer to complete the assembly**.** The participant created as many assemblies as possible in one minute.

International 10-20 System for placement of Scalp Electrodes



References

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