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Effects of Long-Term Use of Anodal tDCS on Working Memory

Comparing the difference in performance between active and sham anodal tDCS on a dual n-back task over 11 sessions.

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Abstract

This study observes the effects of repeated use of anodal transcranial direct current stimulation over 11 sessions of training on a dual n-back task. Participants (14) in an active stimulation group were compared to a sham stimulation group (12). The dual n-back task used was an adaptive program that increased and decreased the difficulty ('n' level) in response to performance. The difficulty level and the number of correct and erroneous responses were recorded in order to look at the progress rates between groups. The study did not find any lasting significant effects in the comparison of the two groups, except for one significant result of less mean auditory erroneous responses made by the control group. The study supports the data found by past meta-analysis of tDCS studies on working memory by showing that there is no significant improvement in performance following anodal tDCS stimulation.

Preface

Transcranial direct current stimulation has in the past two decades come out of obscurity and become a topic of study due to its neuromodulatory effects and low risk of adverse effects. Studies with a clinical approach hope to use tDCS as a tool for cognitive improvement and enhancement and as an alternative or addition to pharmacological treatments. Beyond this a few commercial companies have popped up offering tDCS devices and DIY instructions for use in a myriad of applications ranging from increased energy during the day to better performance on video games. As such a few studies have observed an increase in performance on a verbal working memory task when using anodal tDCS yet none so far have attempted to see what would happen after repeated use. This study will be attempting to explore this avenue of tDCS stimulation. I would like to use this opportunity to thank Stig Hollup my supervisor, Kyrre Svarva for helping with SPSS statistics, Eva Langvik for offering advice on statistical method, and Adrianna Slyk-Sokol for her help.

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1. Introduction to Transcranial Direct Current Stimulation (tDCS)

Transcranial Direct Current Stimulation (tDCS) is a method of non-invasive neuromodulation that has recently seen a rise in popularity due to its simple equipment, easy procedure and low level of risk. Originally having been experimented with over 200 years ago, tDCS has only been considered a possibly useful technique for both clinical and cognitive purposes in the past two decades. The equipment uses two electrodes to create a current flow which modulates cortical activity. Current flows from the positive electrode, named the anode, to the negative electrode, named the cathode. The electrical fields created through this process influence cortical activity in their respective ways, the anode increasing activity while the cathode reducing activity. Various studies have attempted to use tDCS, finding results ranging from altered cognitive performance to changed behavior.

Since its original conception tDCS has been applied to various clinical and cognitive contexts. Initially used to alter mood, the device has since been applied to a variety of conditions. tDCS has been used on depression, pain and chronic pain syndrome, aphasia and dementia amongst other disorders. tDCS has also been used in an attempt to modulate cognitive performance. Studies have used stimulation on working memory, motor learning and attention. Due to the low risk of adverse effects and relative ease of use and set up, tDCS is hoped to be a valid alternative to pharmacological treatment and an aid in various clinical and cognitive contexts.

Included in the tDCS equipment are two electrodes, a battery powered device that delivers constant current and two possible modifications allowing for observation of the current strength, such as an ammeter, and software or a switch to modulate current strength. The device uses small batteries and studies use varied current strengths, with a minimum of 0.6mA and a maximum of 2mA being recommended. The minimum strength is suggested because any lower amount is thought to be too weak to pass through the resistance caused by bone and tissue, a study by Nitsche & Paulus (2000) found that this was the minimum current strength required in order to influence motor evoked potentials (MEP) using anodal tDCS. The maximum of 2mA is a suggested safety level as skin irritation may occur above this level. The electrodes used are suggested to be at a minimum of 25cm^2 but range up to 35cm^2 (Nitsche et al. 2008). The reason for this is to properly and uniformly disperse the current

along a larger surface area and not focus it into a small one. A smaller point of focus may lead to irritation and skin damage. Often studies write up their current strength in mA/cm^2 to reflect the current intensity over surface area.

As a side note it is worth mentioning that tDCS has entered the commercial sector, with companies offering various devices claiming beneficial effects for anything from increased energy to better performance in video games. On top of this DIY (do it yourself) websites and videos have popped up on the internet informing readers and viewers on how to put together, acquire and use tDCS equipment for various purposes. As tDCS is proposed to affect cognitive performance through influencing neural functioning, there is potential for adverse effects and problems arising from improper use. As such it is important to explore the effects that tDCS has on both brain and behavior. This study will observe the effects of tDCS ranging over a set of 11 sessions on working memory.

2. Neurological Basis for tDCS

The premier question for whether or not tDCS actually has any significant effect, is if tDCS has an actual neurological influence. If tDCS does not actually change the excitability of neurons in the targeted areas, then it is in no way effective in its purpose. As such tDCS uses a low current strength, too weak to elicit action potentials in neurons as Transcranial Magnetic Stimulation (TMS) or Transcranial Electric Stimulation do. The current fields must therefore have some different form of modulating excitability.

The anode and cathode cause two different types of static fields; the anode creates a positive field while the cathode creates a negative one. These fields change the availability of positively charged ions in the respective sites through the properties of a regular electric circuit. Negative ions flow from the cathode to the anode changing the concentration of charged ions under the electrodes.

Originally evidence for the influence of electric currents on neurons was observed in animal slice studies by Purpura & McMurtry (1964). The study observed a difference in excitability based on the strength of the current and current type applied. Anodal stimulation increased activity while cathodal decreased it. Stimulation of an area will also leave a lasting effect that

continues beyond the stimulation session, with the duration depending on the strength and duration of stimulation (Stagg & Nitsche, 2011).

It has already been said that tDCS is not strong enough to cause action potentials, instead tDCS is said to change the membrane potential of the neurons under its field of effect (Fregni, et al., 2005). The membrane potential is shifted depending on the electrode type towards depolarization or hyperpolarization, meaning that the neurons in the affected area are more sensitive towards input. This has several implications for how the affected neurons perform. A good example of the mechanisms that are modified is the NMDA receptor which reacts to membrane potential in order to open its ion channels.

Initially the neurological basis for tDCS was observed using ion gate blockers. Nitsche, et al., (2003) used Carbamazepine, a sodium channel blocker, Flunarizine, a calcium channel blocker and Dextromethorphane, a NMDA antagonist and observed significant effects from all three drugs. Participants having been given Carabamazepine and Flunarizine did not have the excitability changes associated with anodal tDCS, although the membrane potential level of the stimulated area had been raised, the drugs prevented any differentiation from occuring as a result of the stimulation. By blocking gates for positively charged ions the authors of this study showed that anodal tDCS works through the manipulation of available ions.

Dextromethorphane being an NMDA antagonist showed a different result. As the duration of the activity increase of anodal tDCS continues beyond the stimulation period, it has been proposed that tDCS elicits a form of long term potentiation (LTP). The use of the NMDA antagonist removed the LTP like effect that follows anodal stimulation. Furthermore, the long lasting effect of cathodal stimulation also disappeared when the NMDA receptor was blocked. This is an interesting observation as it suggests what mechanisms may be at root.

The NMDA receptor is a specific type of receptor that requires changes in the membrane potential in order to activate. NMDA receptors are a type of glutamate receptor that reacts to N-methyl-D-aspartate. The receptor is permeable to Ca^{2+} Na^+ and K^+ and it has a special mechanism that requires both membrane voltage to increase and Glutamate to be present to activate. During resting membrane potential, the NMDA channel is blocked by a tightly bound extracellular Mg^{2+}. During depolarization the Mg^{2+} is repulsed by electrostaticity. This opens the channel to both Na^+ and Ca^{2+}. A cell's excitatory postsynaptic current is generally

influenced by the charge flow from AMPA receptors at resting potential. When depolarization occurs and the NMDA channel is opened, a larger charge flow occurs. NMDA receptors play a significant role in the late and slow phase of excitatory postsynaptic current and potentials. The Ca^{2+} that enters the postsynaptic cell is also important because it functions as a trigger for a biochemical signal. LTP is dependent on signaling cascades such as the CaMK II (Calcium-calmodium-dependant protein kinase II) signaling cascade, which in term is dependent on the availability of Ca^{2+} in the cell. (Hudspeth, Jessell, Kandel, Schwartz, & Siegelbaum, 2013)

While the mechanisms of the NMDA channel help understand how anodal tDCS can cause an increase in activity, it does not exactly explain why cathodal tDCS loses its long term effect following the use of Dextromethorphane. Nitsche et, al., (2003) suggest that the disappearance of the long term activity change following cathodal stimulation is due to reduced presynaptic firing and a lowered membrane potential level. Stagg, et al., (2009) found supporting evidence to this, finding that there was a reduction in glutamate in cathodal stimulated areas. This result was proposed to occur due to a reduction in activity which caused a reduction in glutamate synthesis from glutamine.

The results of the Nitsche, et al., (2003) study show the two phases of tDCS stimulation, one the alteration of ion availability that leads to increased or decreased activity and the long term effects that follow. Furthermore, the study implicates the NMDA receptors which play an important role in long term potentiation and depression (LTP & LTD).

As both LTP and LTD are implicated in the long term side effects of tDCS it is worth discussing how these two states may come about. In the first part of their study, Fritsch et al., (2010) used anodal direct current stimulation (DCS) on mouse primary motor cortex (M1) neurons. Testing the synaptic efficacy of the stimulated neurons following a 15-minute session at 0.75mV/mm the authors found an increase in activity even 30 minutes after stimulation offset. The authors observed that anodal DCS in conjunction with repeated activation promoted the secretion of the neurotrophin Brain-Derived Neurotrophic Factor (BDNF) leading to an increase in the TrkB phosphorylation. BDNF is crucial in the neuronal growth process and requires an influx of calcium ions.

The second part of the study looked at how anodal tDCS would influence BDNF and TrkB knockout mutated mice. If their observations from the first part of the study were any indication of the underlying mechanisms involved in tDCS, the mutant mice should not show any increase in activity following stimulation. This is exactly what was observed suggesting that LTP following anodal tDCS is associated with calcium influx causing secretion of BDNF and signaling cascades.

The final part of the Fritsch, et al., (2010) enlisted human participants with a genetic predisposition BDNF Val66Met polymorphase. In this condition the secretion of BDNF is reduced by between 18 and 30%. Participants with this reduced BDNF production showed worse learning rates following tDCS stimulation compared to the normal control group.

All of this data shows that tDCS works on a few mechanisms that underlie neuronal growth, in similar fashion to natural long term potentiation and depression.

The study looked at behavioral differences in humans by also observing the effect of tDCS on a learning task in participants who were genetically predispositioned with BDNF Val66Met polymorphase. In this condition the secretion of BDNF is reduced by approximately 18-30%. After a 5-day period with stimulation, Met participants had a lower performance rate on the learning task than control participants.

While this data goes far as to explaining the mechanisms of anodal stimulation cathodal stimulation is less understood. Nitsche, et al., (2003) as well as Nitsche, et al., (2004) showed that NMDA antagonists, ion channel blockers and GABA agonists do not mediate the effects of tDCS. While glutamate levels do change in response to this form of stimulation there is no direct evidence of the involvement of GABAergic neurotransmitters (Stagg, et al., 2009).

It has already been mentioned that the glutamatergic system is influenced through cathodal stimulation, but dopaminergic system also appears to play a crucial role in the long term effects of cathodal stimulation. Through the administration of L-DOPA (a precursor to dopamine) Kuo, et al., (2008) observed a prolonged long term effect. In support of this Nitsche, et al., (2006) showed that administering a D_2 receptor antagonist completely removed the long term hyperpolarization effect. Neither of these studies observed any additional differences in activity, meaning that the availability of dopamine did not further

reduce activity beyond that which the cathodal stimulation would. Acetylcholine was also found to increase the long term effects Kuo, et al., (2007). A final feature of cathodal stimulation that may be mentioned is that it has been shown to influence the production of caspase, which is a known factor in cell apoptosis (Kook, et al., 2013).

There are a few other interesting observations that have been made that hint at the mechanisms of tDCS. One is the duration of stimulation. While initially tDCS requires a few minutes of stimulation at a relative current density in order to trigger its long term effect, too long stimulation can cause a reversal of the effect. Monte-Silva, et al., (2013) observed that stimulation with tDCS for 13 minutes caused altered activation rates in neurons, doubling the duration of the stimulation to 26 minutes resulted in a reversal of long term effects. Peculiarly, Batsikadze, et al., (2013), observed that amplitude also played an important role. Cathodal stimulation at 1mA resulted in the regular long term excitability reduction. Doubling the strength on the other hand caused long term excitability increase. Whether or not these results are caused by the electrical properties of the circuitry or it is related to how neurons react to the altered membrane potential is unknown.

To summarize, tDCS has two main effects. Primarily a short term increase or decrease in activity depending on the respective form of stimulation used. This short term effect has to do with change in ion flow and a neuron's membrane potential, either through hyper- or depolarization. Secondarily a long term effect that continues for a period after stimulation offset. In anodal stimulation it is associated with NMDA receptors and LTP and promotes secretion of neurotrophins. In cathodal stimulation it is associated with LTD effect that is modulated by the dopaminergic and cholinergic systems and influences the production of caspase.

3. Safety aspects of tDCS

It has already been touched upon earlier in this paper that there are certain guidelines for tDCS. These are in place because electricity does have several properties that may lead to adverse or damaging effects if used wrongly.

Although tDCS is a non-invasive procedure it may cause damage to body tissue. The use of electricity on skin may cause an electrochemical reaction, creating toxins that will aggravate the affected area. In order to make sure the risk of this is reduced the electrodes used should have a protective barrier, such as saline soaked sponges. This does not completely remove the possibility of damage or discomfort occurring at higher levels of electric stimulation. The current density of the electrodes should lie within 0.06 mA/cm^2 as there are reports of significant skin irritation occurring around this strength (Nitsche et al., 2008). The density level of the current should be calculated by using dividing the strength of the current by the size of the electrode.

$$\text{Example: 2mA / 30cm} = 0.0667\text{mA/cm}^2.$$

Even so it may be beneficial to screen participants for skin diseases or conditions which may be more sensitive to electrical stimulation.

Another worry of using tDCS is the possibility of modification of proteins and amino acids or generating toxins within neural tissue. No studies have reported any such occurrence and it is suggested that the skin, cranium and the perfusion of the brain work as protective barriers against such dangers Nitsche, et al., (2008). Another danger that is worth considering is the possibility of excitotoxicity occurring due to the increase in activity. It is considered improbable for activity levels to raise high enough for excitotoxicity to become a danger. This approach lies in the properties of the electrical fields that are used in tDCS. The current, as mentioned earlier, is not strong enough to elicit action potential, it alters the membrane potential of the affected area in order to make it more or less likely for a neuron to fire. The neurons will therefore only more efficiently react to any excitatory signals entering the stimulated area and activity cannot raise outside of the physiological range.

While there is no expected danger of excitotoxicity for healthy persons, there is a potential that certain groups may experience detrimental effects by using tDCS. If there are large quantities of glutamate available when NDMA receptors may open to allow greater amounts of Ca^{2+} enter the cell and may eventually lead to the production of free radicals that are toxic to a cell. For diseases such as Huntington's where NMDA receptors are already overly active, the additional use of tDCS may be further damaging. Any study wanting to perform tDCS stimulation should therefore screen its participants for any neurological disorders that may be aggravated by the use of tDCS.

A study by Liebetanz, et al., (2009) did show damage to neural tissues through use of tDCS. The study found that it is first when using a current density of 142.9 A/m^2 for a duration of 10 min resulted in lesions to rat brains. The authors explain that this level is far above the recommended amount and should never be applied to any human studies. The study also explained that a danger when using any electrical current is that heat is a side effect. If cortical temperatures were to increase to 43°C neural damage may occur. The Study did show that this level of heat could only be achieved well above suggested safe parameters.

tDCS being a non-invasive procedure for stimulation can be considered safe in that it poses no direct damage to any tissue within the recommended safety parameters. There are of course aspects that must be considered for it to not have adverse effects but following the correct guidelines has proven to be quite safe for those exposed to stimulation.

Poreisz, et al. (2007) looked into the possible adverse effects of tDCS on both healthy subjects and patients with various ailments. The study attempted to see what problems may arise from using tDCS and whether certain groups were more at risk than others. The study utilized data from 567 tDCS session. Healthy participants, stroke patients, migraine patients and tinnitus patients were all included in the data. The results showed that the most prevalent negative effect of tDCS was a mild tingling under the stimulated area. 70.6% of participants in the studies used expressed feeling this effect. The second and third most prevalent effects were fatigue and mild itching. These were felt by 35 and 30% of participants respectively. tDCS resulted in headaches for 11.8% of participants in the study. A group of participants amounting to less than 3% experienced some level of nausea or insomnia. Mostly there were no differences in the experience of tDCS between the healthy and patient groups. Though effects occurred more often in one group than the other. Healthy participants experienced, more often than their patient counterparts, the tingling sensation associated with electronic stimulation. Headaches on the other hand are a more common side effect in the patient group.

The study by Poreisz, et al. (2007) furthermore reported that no long term effects were found. The study concluded that while there were adverse effects within both patient and healthy groups, the effects were relatively minor. The authors go on to suggest that by using proper safety measures, following the guidelines that have been suggested and making sure that the equipment is properly prepared, tDCS stimulation is safe for both patients and healthy

participants. They do note though, that it is worth screening participants that may experience worse adverse effects and that may be effected in an unethical manner.

Studies on tDCS have so far mainly focused on a short time frame of tDCS use. Some studies have looked at repeated uses. Loo, et al., (2012) looked at the repeated use of tDCS over 15 sessions over 3 weeks. They tested on 64 patients with diagnosed depression attempting to improve mood by using an experimental group and a sham group. They found that the experimental group experienced an improvement in their mood compared to sham and also performed better on attention and working memory on a task. The test did report that one participant with bipolar disorder experience a period of Hypomania in correlation with the tDCS stimulation. There were also reports of lesser effects such as itching and redness on skin under the stimulated area. There were also reports of such experiences as fatigue, nausea, blurred vision and other unpleasant experiences but these were limited to a minority.

Another study by Palm, et al., (2011) looked at therapy resistant depression. Over 2 weeks they applied sham and active anodal stimulation. The study found no improvements in the experimental compared to sham groups. The authors did conclude that they observed changes in the PANAS subscales used for testing which they suggest may mean that tDCS influenced emotion regulation. The authors also theorized that more sessions could eventually show a significant improvement. Neither study reported any significant adverse effects as a result of stimulation.

The possibility that there the effects of tDCS may somehow continue to increase over time is worth investigation. Not only may it have clinical implications, but it may also be a tool for training cognitive processes.

4. tDCS Findings

tDCS has been used in quite a few different contexts. As mentioned before the device has been used on depression, some studies have looked into any potential benefits for aphasia, there have been studies observing performance on various cognitive tasks. The areas to which tDCS is being applied is growing with time.

One of the most studied applications of tDCS is in conjunction with motor learning or simply to observe the effects of electrical currents on neurons. Studies have used both humans and animals for the various observations. The studies tend to apply anodal stimulation to the M1. The results point towards increased learning speeds during and after stimulation (Fritsch, et al., 2010; Liebetanz, et al., 2002; Nitsche, et al., 2000; Nitsche, et al., 2003; Quartarone, et al., 2007). One of the first studies to look at the effects of tDCS on the M1 was performed by Nitsche, et al., (2000). The study looked at excitability changes following both cathodal and anodal stimulation and found differences of up to 40%. A good supporting study was performed by Lang, et al., (2004). They used human participants to show an increase in motor evoked potentials, following anodal tDCS, of approximately 32%. When stimulating with cathodal tDCS the reduction in activity was approximately 27%. The study also found that the cathodal stimulation after effect lasted an average of 40 minutes, while anodal stimulation lasted shorter. Furthermore, Boggio, et al., (2006a) observed improved motor function of the non-dominant hand following anodal tDCS stimulation of the M1.

Nitsche, et al., (2003) observed the differences between stimulating premotor, M1 and prefrontal cortices with anodal, cathodal and sham stimulation. The study used 15 minutes of stimulation time at a strength of 1mA. The study also used an implicit motor learning task and a serial reaction time task. Standard results of increased and decreased stimulation occurred for the respective stimulation types. With the increase in excitability, both reaction time and motor learning was also improved when stimulating the M1 but not the other cortical regions.

The authors theorized that the anodal stimulation worked as a form of "noise reduction" allowing for the required neural cells to fire at an increased rate and leading to better performance. While these results are interesting in themselves, the study has implications for how tDCS may be used as a tool. Not only does it improve cognitive functioning, it can also be used as an experimental tool for observing the behavioral results of stimulating various cortical areas during task performance. Such an approach would help classify various cortical regions and explain how they are involved in cognitive processes. The currently discussed study helps maintain that the M1 is a critical cortical region for motor learning.

Put together these studies make up a back bone for tDCS studies and are widely quoted in subsequent tDCS studies. The finding that behavioral changes occur as a result of tDCS stimulation is what has spurred the search for other applicable areas.

Keeping in mind the exploratory possibilities of tDCS, Quartarone, et al., (2007) used it to observe how neurons in participants with amyotrophic lateral sclerosis (ALS) reacted to tDCS compared to healthy participants. Stimulating for 7 minutes at 1mA the study observed the standard increase in activity in healthy participants. The study did not see any altered rates of activity amongst participants with ALS using either anodal or cathodal stimulation. The authors discuss several possibilities for why this may have occurred. One proposal is that the pathology of the disease influences the underlying mechanisms of tDCS. Differences in motoneuron membrane, altered glutamate transmission and higher thresholds are all offered as reasons. The authors express that more studies must be conducted in order to find the true underlying cause.

As mentioned earlier tDCS has been applied to cognitive performance. Notably working memory has been a focal point of tDCS studies (Andrews, et al., 2011; Boggio, et al., 2006b; Fregni, et al., 2005; Ohn, et al., 2008). Fregni, et al., (2005) used 1mA anodal stimulation on the dorsolateral prefrontal cortex (DLPFC) during a 3 back memory task. The 3 back memory task is a variation of the n-back memory task, it requires a participant to constantly update their working memory with the three most recent stimuli of a longer sequence. Every time a specific stimulus repeats itself following 2 other stimuli in the sequence the participant must give the correct response (a more detailed explanation of the n-back will be given later). The task used letters shown on a screen. While the stimulation lasted 10 minutes the task itself took approximately 5 minutes to perform and was performed during the final 5 minutes of the stimulation. Performance was compared between an experimental condition and a sham condition. The experimental condition showed better performance and made less errors on the working memory task compared to the sham controls.

Another interesting finding is brought by Boggio, et al., (2006b). The study builds on the results found by Fregni, et al., (2005) by applying anodal tDCS to the left DLPFC (LDLPFC). The study differs though as the participants were all diagnosed with Parkinson's disease. The authors found that stimulating the LDLPFC was associated with increased performance compared to sham or to stimulation of other areas. The study shows what has

become somewhat of a trend in tDCS studies, improvement of cognitive functioning in participants with cognitive deficits or at risk groups.

Andrews, et al., (2011) utilized a slightly different testing paradigm in order to underline one of the defining mechanisms of tDCS. They used 3 conditions for testing, a sham condition, a stimulating at rest and a stimulating during task performance. The three conditions account for a possible placebo effect, stimulation when the cortical region is not specifically activated by a task and stimulation when the cortical region is activated by the task. The study found that performance was improved on an n-back task but only for the final experimental condition where the task was performed during stimulation.

While these individual studies show a positive correlation between anodal tDCS stimulation and task performance, a meta-analysis performed by Brunoni, et al., (2014) found less supportive evidence. The study compared sham, repetitive transcranial magnetic stimulation (rTMS) and active tDCS stimulation on the DLPFC. The study found 12 applicable studies covering 33 experiments and observed that while tDCS compared to sham did show increased performance on reaction time (RT), amount of correct responses and less mistakes, a meta-regression including rTMS showed that tDCS was only associated with improved RT.

Stimulation of the DLPFC has also found its way to a more clinical context (Brunoni, et al., 2012). Boggio, et al., (2007) attempted to see whether stimulating the DLPFC of participants with diagnosed with major depressive symptoms. The authors chose this approach due to the notion that activation of higher order cognitive functions located in the prefrontal cortex would cause a top down effect and lessen depressive symptoms. Considering the minimal adverse effects and low risk of tDCS the device is hoped to become a reliable form of treatment that can be used instead or together with pharmacology. The authors tested participants using the Hamilton Depression Rating Scale and the Beck Depression Inventory. The study is one of the few to utilize tDCS for recurring sessions, stimulating participants for 10 sessions in total over a period of 2 weeks. Participants in the experimental condition expressed a greater reduction in depressive symptoms lasting up to a 1-month period after finishing treatment. The authors suggested further investigation of tDCS as a tool for treating depression was warranted.

An interesting point to keep in mind from the above discussed study is that the experience of reduced symptoms lasted for up to a month after treatment was finished. This may suggest an exponential effect where repeated stimulation sessions cause a top down effect that continues to influence behavior and cognition longer than any single session could.

There are other results worth mentioning. Fecteau, et al., (2007) used a combination of both cathodal and anodal stimulation over the left and right DLPFC respectively to reduce risk taking behavior. Monti, et al., (2008) observed that when applying cathodal stimulation to stroke patients suffering from aphasia, word recall and naming was improved. Williams, et al., (2010) performed a different type of study to the previous ones by using tDCS to increase performance of non-dominant limbs and reducing activity in cortical regions of dominant limbs in an attempt to help stroke patients with rehabilitation. Zhu, et al., (2015) also found that using cathodal tDCS over the LDLPFC resulted in increased performance in learning on a golf putting task.

The most common criticism of tDCS is the low sample sizes and small number of studies available for determining how significant the effect of tDCS is. Studies often recruit less than 20 participants and utilize different testing procedures. Attempting to observe how effective tDCS is in a meta-analysis, Kalu, et al., (2012) included 96 active and 80 sham courses. A systematic review of the studies shows that active stimulation was more effective than sham in improving depressive symptoms. Unfortunately, a meta-regression showed no significant correlations. On the other hand, Bastani, et al., (2012) found more positive results in their meta-analysis, reporting that stroke patients benefited significantly from tDCS stimulation.

When considering generally positive results from tDCS stimulation, it is difficult to understand why meta-regressions repeatedly find no significant correlations. This is worrying, but the authors of the meta-analysis maintain that given more data and more studies utilizing a similar experimental paradigm, a significant effect can be found.

The current study will be following in the footprints of past studies attempting to see the effects of anodal tDCS stimulation on the LDLPFC while participants perform an N-Back task.

5. Working Memory

Working memory (WM) is a proposed cognitive construct that temporarily holds a limited amount of information for processing and manipulation. It is a necessary ability for human functioning and is suggested to be involved in a variety of behavior. During a task WM functions as a temporary store for relevant information. When learning a phone number for the first time, WM is involved in holding the digits until they are either released, after being written down for example, or replaced by other information. It is often used synonymously with short-term memory, though a distinction should be made.

WM can continuously be updated and the contents changed, while at times this is the result of a willing process, it is most commonly the direct result of the limitations.

Both time and capacity are the two factors which limit WM. The most well-known example of WM's capacity limitation can be found in the article "The magic number seven, plus minus two." by Miller (1956). WM has since been the focus of various papers that have attempted to observe the limitations and functioning with varying results, finding differing capacities that are dependent on various factors such as information type, information unit size and shared characteristics (Conwan, 2012).

Several theories have since been proposed as to how WM works and what distinct functions can be attributed to it. In 1974 Baddeley & Hitch proposed a model of WM, splitting it into subcategories that each pertained to a specific aspect ascribed to WM. A visuospatial sketchpad, for storage and manipulation of visual information. A phonetic loop, that stores and manipulates auditory information and a central executive, which controls the WM system and relays information between WM and long term memory. In order to better explain data from various WM tests which could not be fully be explained by the original model, Baddeley (2000) later added an additional component named the episodic buffer which worked as a back-up store between the central executive, long-term memory and the other WM components.

Other theories have since examined WM from a different perspective, Conwan (1998) proposed WM as an extension of both long term and short term memory. The information represented in WM is seen in this perspective as a subset of representations in long term

memory. WM has also an additional component in the form of attentional focus. This component is what limits WM and sets a maximum capacity for the amount of long term representations that can be maintained at once.

A red line that follows through all the WM theories and approaches shows that WM is not considered to be a unitary function, it has several components that together make up the whole. The theories acknowledge such aspects as an attentional or monitoring component and a split between visual or auditory modality. Various studies have confirmed that WM can be split amongst sensory types, specifically the difference between visual and auditory WM has been well studied. Various experiments have gone so far as to show that different test modality types lead to activation in different cortical areas (Smith, & Jonides, 1997; Crottaz-Herbette, Anagnoson & Menon, 2004).

There is also evidence for WM being split within modality Courtney, et al., (1996) show that different cortical areas are activated during two visual WM tasks utilizing different stimulus types, in this case spatial location or object type. Other studies have supported these findings (Smith, & Jonides, 1997)

This distinction between various types of WM will be quite relevant for the current study as the task that is utilized during experimentation is a dual n-back with both auditory and spatial modalities.

A fairly novel approach towards WM can be seen in Miyake and Friedman's (2000; Miyake & Friedman, 2012) article on latent variable analysis of executive functions. Within it Miyake and Friedman identify a component of WM that they term "updating and monitoring of WM representations" or "updating" for short. Through latent variable analysis of various tasks said to measure updating and monitor, mental set shifting and prepotent response inhibition functions Miyake and Friedman found that these three forms of executive function were distinct. The functions were found to correlate to some degree, but not significantly enough to warrant a unitary perspective. As such this approach has given the updating and monitoring aspects of WM statistical construct validity as a separate executive function.

6. Role of the DLPFC

It was earlier mentioned that working memory and short term memory are often mentioned synonymously. This approach is becoming largely invalid as more and more evidence is piling up for distinction between the two. Smith and Jonides (1997) observed a difference in cortical activity depending on the purpose of memorized information. If information was simply to be stored for a short duration, it would activate posterior parietal regions, an area hence designated as a temporary store. When information was to be monitored and manipulated, the dorsolateral prefrontal cortex (DLPFC) was activated. Hence the split between simple store and area of manipulation is a reasonable step to take.

Smith and Jonides are not the only ones to observe such differences. Studies have found that the DLPFC is activated when the working memory load surpasses a certain threshold or requires manipulation (Eldreth, et al., 2006) and is thought to largely be responsible for WM capacity (Kane, & Engle, 2002). Eldreth, et al., (2006) observed that the DLPFC was activated in response to the increase in memory load, suggested to aid in memory-consolidation. The study found different neural substrates for retention and for manipulation, with the DLPFC increasing activation as a result of memory load and the ventrolateral prefrontal cortex showed greater activation during manipulation. The study utilized a visual delayed response task during which participants were to remember words in a list. These results were supported by data gathered for a review of neurological components of working memory by Linden (2007).

Although these studies support the role of the DLPFC in working memory, the exact function it encompasses is less understood. While Eldreth, et al., (2006) experienced an increase in association with memory load, the area is suggested to play a role in processing relationships between information in working memory (Blumenfeld, et al., 2011). A review of literature lead Courtney et al., (2007) to propose that the DLPFC was central in updating, maintenance, shifting and resistance to distractor interference.

The above mentioned studies observed the activation of the DLPFC through fMRI studies, while this is a valid approach to observe whether or not an area activates during task performance, it does not express the functional role which an area plays. A more practical approach towards observing the role of the DLPFC was performed by Osaka, et al., (2007).

Using Transcranial Magnetic Stimulation (TMS) Osaka, et al., found that targeting the left DLPFC by TMS to disrupt the activity of this region resulted in reduced recalled words in a reading span task. These results are supportive of the DLPFC being involved in memory load and retention.

Other studies have found supportive evidence with a similar study design, Basso, Ferrari & Palladino (2010) found that stimulating both left and right DLPFC with TMS resulted in reduced accuracy on a WM tasks as the WM load increased. Feredoes, et al., (2011) found that DLPFC was activated during a working memory tasks in response to distractors, causing the authors to suggest that the DLPFC activates in order to prevent distractions from the ongoing task. The study found that disrupted activation of DLPFC caused increased activity in posterior visual regions when distractors were involved.

Additionally, a review by Balconi, (2013) of studies using TMS in association with WM tasks reported that using TMS on the DLPFC had an effect on neural efficacy (ratio between accuracy and response time). Applying TMS to the LDLPFC causes disruptions in performance on verbal WM tasks. Also that the left DLPFC, and not the right DLPFC, plays an important role on verbal tasks. This data supports the notion that the LDLPFC is implicated in verbal fluency, (Hudspeth, et al., 2013).

As such the specific role of the DLPFC is disputed, yet all imaging and TMS studies have found that the DLPFC plays an important role in WM. The literature does suggest that various tasks may activate different regions of the PFC, though the n-back task does activate the DLPFC (Blokland, et al., 2008). Rodriguez-Jimenez, et al., (2009) also found that the left DLPFC showed greater activation during an auditory n-back task than during a visual one.

The current study will be observing the effects of tDCS on WM. As such it will follow in the footsteps of past tDCS studies using a similar study setup. A dual n-back using both verbal and visual stimuli will be used and will show whether or not the stimulation of the left DLPFC will result in altered performance in both, either or none of the modality types.

The study will be able to test the effects of tDCS on the DLPFC in both visual and auditory WM.

The current study will be utilizing a similar experimental setup to previous studies. An N-Back task will be used to test participants during anodal tDCS stimulation to the LDLPFC. There will be some variation compared to previous studies. Due to the long term nature of this study the n-back task will be adaptive and grow in difficulty. Beginning at a level of 2-back difficulty will increase as participants perform well by adding to the number of letters back one must remember (3-back, 4-back, etc…). The program used for the n-back task will record both correct and wrong responses offering a better overview of the performance of participants. The program will also utilize both spatial and auditory stimuli, and record performance (correct, wrong) for both of these modalities. This is to observe whether tDCS stimulation of the LDLPFC will cause better performance in either modality.

7. Current Study

As such the study allows for several hypotheses. A) tDCS stimulation will result in a difference in performance on the n-back task. B) tDCS will have a lasting effect altering performance over time. C) Participants in the experimental condition will perform differently in the amount of correct and wrong responses compared to participants in the control condition. D) tDCS stimulation will improve the performance of participants on the verbal aspect of the task more than on the spatial aspect of the task.

8. Method

In this study 27 participants were recruited to perform an n-back task while experiencing active or sham anodal tDCS over the LDLPFC. One participant withdrew from the study due to lack of time. Participants performed in total 11 sessions of tDCS. Initially the experiment included using EEG recordings before and after n-back training and completion of the 11 sessions but this part was dropped due to lack of time from participants and technical problems with the EEG equipment.

8.1.   Participants

Participants were both males and female students at the Norwegian University of Science and Technology NTNU, between the ages of 21 and 28. All participants sign a consent form and were allowed to withdraw from the experiment at any point. Participants were also monitored

for any discomfort that may have occurred during stimulation. Participants were told about the possible adverse effects of tDCS and asked to withdraw from the study if they knew of any condition they might have which would be negatively impacted by the experiment.

8.2. tDCS Equipment and Parameters

The tDCS equipment used included a power source using a 9 Volt battery with a variable voltage device allowing to change current strength. An ammeter was included in the circuit to observe current strength. The electrodes ended in $25cm^2$ sponges and were attached to the head using adaptable cloth mesh headgear. A saline solution was used to soak the sponges before placement on the head.

The current strength was set at 1.5 mA for a current density of $0.6mA/cm^2$. The participants were monitored at all times for any adverse effects and were told to stop if they experienced any discomfort. The stimulation session lasted for a total of 13 minutes.

The anode was placed over the LDPFC (Brodmann areas 9 and 46) and the cathode was placed on the contralateral side of the head supraorbitally where it would not influence any cortical regions.

8.3. N-Back Task

The n-back task is an updating working memory task, often used to test working memory capacity, that requires participants to remember a 'n' amount of past stimuli from a sequence of stimuli presented one at a time. When the current stimulus is the same as the stimulus that is 'n' amount earlier in the sequence the participant must give the correct response. The 'n' is presented as a number such as "2-back" or "3-back" task. This number explains how many letters in the sequence must be remembered.

Example:
During a 2-back task the following sequence is shown: e f j w j j p q e r e
The participant would press the response button on the second 'j' and third 'e' to show that the letter was repeated with the correct spacing.

The task version used for this study was a computer program installed on a laptop named the MindSparke Brain Fitness Training Program (see Appendix B), developed by MindSparke. It is an adapting dual n-back task meaning that it uses both spatial and auditory stimuli simultaneously and adapts the 'n' level to the performance of the participant.

The program shows a large black square at the center of the screen, this square is split into a 3 by 3 grid. A smaller white square appears briefly in one of the 9 spots at a time. The program also vocalizes letters. Both modalities are done simultaneously and so participants must hold both auditory letters and the spatial location of the white square in mind. When the participant was to give a response they had to press the "l" key for auditory and the "a" key for visual.

The task is administered in 25 minute sessions with 20 trials per session. During each trial there can be a maximum of 6 correct responses per modality for a total of 12 correct responses. When the participant performs well at a 'n' level and manages to give 10 correct responses and a max of 2 erroneous responses the program increases the difficulty level. The participant is therefore continuously challenged and will never reach a "ceiling" in task performance.

The program also shows statistics for task performance over the course of the sessions once the participant is done with all 20 trials of a session. Performance feedback is therefore shown to all participants and they are able to see their progression from session to session.

8.4.   Procedure

The participant was sat down in front of the laptop and initially allowed 3 practice trials to make sure that they understood the task. Participants then put on the headgear with the attached electrodes and were told to begin the task. While the participants worked on the task the tDCS device was turned on and slowly ramped up from 0 to 1.5 mA over the course of 30 seconds. Participants would then perform the task during stimulation for a duration of 13 minutes. For the duration of the stimulation period the device and participant were monitored to make sure that the current strength remained stable and that the participant was not experiencing any discomfort. The tDCS device and ammeter were both turned away and

hidden from participants so they would not be distracted or able to see what was going on with the equipment.

After 13 minutes the tDCS device was ramped down to 0 over a duration of 30 seconds and the headgear was removed between trials. The participants would continue to perform the task until all 20 trials were completed. A session may be completed on 25 minutes but the participants may take breaks between trials and so the duration of the session may last as long as 30 minutes. Once the participant was finished with all 20 trials they were free to leave.

Participants in the control group experienced sham stimulation. This means that the tDCS equipment was attached to them just as it would be in the experimental condition, and the current strength was ramped up to 1.5 mA, but following this the device was slowly ramped down again without the participants knowing. The reason for this is to elicit the tingling sensation that is common for stimulation and convince that stimulation is actually occurring. The total duration of stimulation is limited to 1 minute, a duration that is not long enough to elicit any effects.

Initially participants were to perform 20 sessions every other day during weekdays. These parameters had to be changed as the duration of the experiment caused scheduling conflicts for the participants. The amount of sessions was reduced to 11 and the sessions were adapted to when participants were available meaning that they performed anywhere from 1-5 sessions during weekdays generally over a duration of 2 months.

8.5.   Statistical calculations

All statistical calculations were performed using SPSS Statistics version 24. The raw data was put through SPSS Syntax Editor (see Appendix B) in order to calculate the mean levels of 'n', auditory and visual correct responses and auditory and visual erroneous responses that participants achieved per session.

Once all the mean values were calculated data was organized in order to allow for processing through SPSS Statistics. Novel variables were created by weighting auditory and spatial correct and erroneous responses with related 'n' values. Correct responses were multiplied by the related 'n' value, meaning that a correct response at n=2 is valued as 2, while a correct

response at n=6 is valued as 6. For the erroneous responses the weighting values were reversed, meaning that an erroneous response at n=2 was valued as 6, while an erroneous response at n=6 is valued as 2. The value is multiplied by the amount of correct and erroneous responses. If a participant performs a mean of 3 correct responses at n=3 their result for that session would be 9.

Multivariate ANOVA (MANOVA) was performed on the data set in order to find significant differences between the two groups.

9. Results

The first observation that will be made is the level of difficulty which the participants managed to achieve over the course of the 11 sessions. The mean 'n' values for control and experimental groups are represented in **Graph 1** showing the rate of progression of participants over the 11 sessions. Both the plot lines are increasing as participants get more proficient with lower 'n' levels and progress to more difficult segments. All participants significantly improved from session 1 to session 11 (A paired samples t-test has shown significance, *t(25) = -9.1, p < 0.000. d = -2.291, r = -0.753*). The two plotlines are closely related showing neither group is performing significantly better than the other over the course of the experiment. A MANOVA test showed no significant differences between groups in any of the 11 sessions.
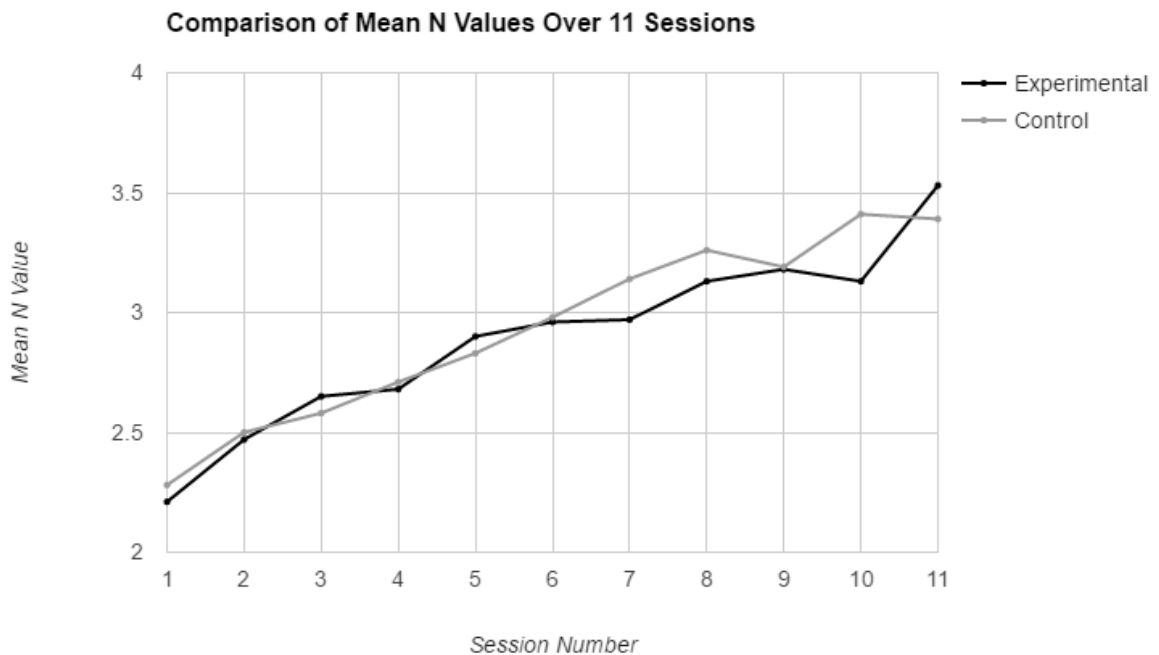
Graph 1: Comparison of the mean 'n' values over 11 sessions between experimental and control group.

Graph 2a shows the experimental and control correct responses in both spatial and auditory modalities. The responses are weighted through 'n' value meaning that the higher the 'n' value the higher the value of the correct response. This shows that there is little difference between the conditions as both the experimental and control groups perform equally over time, both groups improved with the correct responses performed over time. MANOVA analysis showed no significant differences between groups on either spatial or auditory correct responses. The results also show a progression in performance for participants. A paired samples t-test shows that all participants perform significantly better at session 11 than session 1 on both spatial ($t(25) = -9.915, p < 0.000, d = 2.261, r = 0.749$).

Graph 2b shows the mean amount of correct responses made without any weighting. A between-subjects ANOVA shows that there is no significant difference between groups on the amount of correct responses they make. A paired samples t-test shows that there is no difference in the amount of correct responses made over time for the auditory modality. There is a significantly different amount of correct responses made in the spatial modality from the first to last session ($t(25) = -3.549, p = 0.002, d = -0.836, r = -0.386$).

Graph 2a: Comparison of weighted correct responses done over 11 sessions. Correct responses at a higher 'n' value are weighted higher than correct responses at lower 'n'.
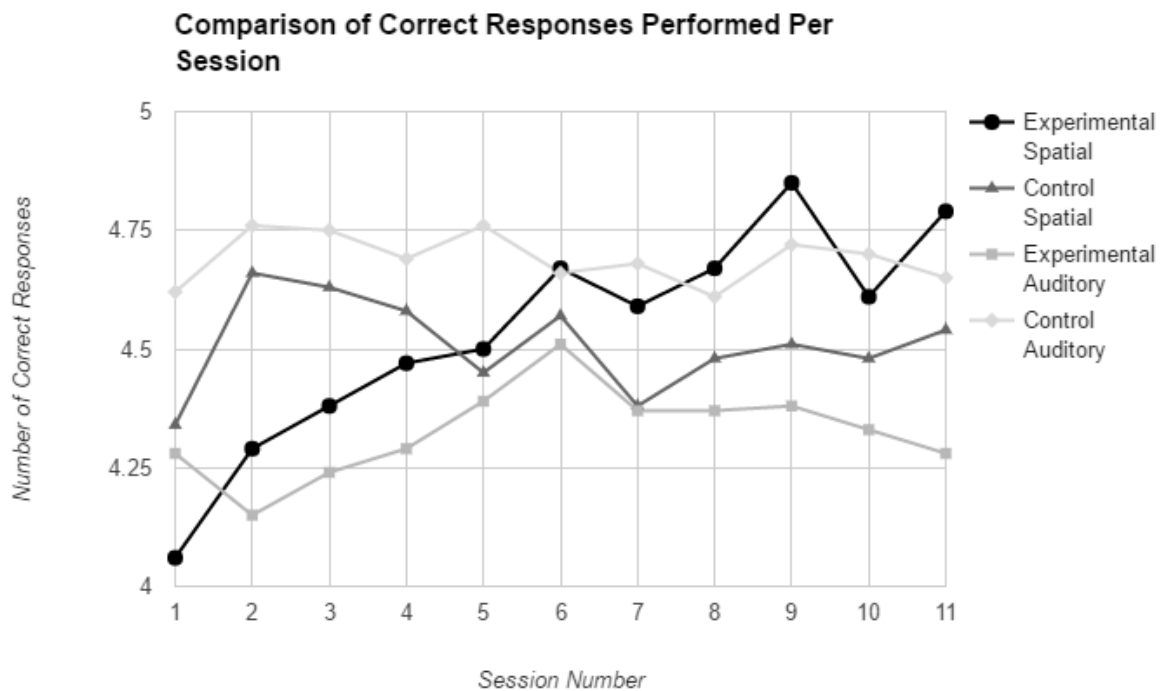
Graph 2b: A comparison of the amount of correct responses performed over 11 sessions.

Graph 3a shows the differences in misses in both spatial and auditory modalities for the duration of all 11 sessions. The graph uses the weighted results showing performance over

time. As the difficulty increases the misses are valued less. Higher scores on the misses show worse performance. The spatial modality shows a slowly decreasing rate of performance meaning more erroneous responses made. The auditory modality shows an increase in performance over time. The difference in performance from session 1 to session 11 was found to be significant for both spatial ($t(25) = 6.627, p > 0.000, d = 1.672, r = 0.641$) and auditory ($t(25) = 6.184, p > 0.000, d = 1.572, r = 0.618$).

A MANOVA analysis showed a small significant difference in performance at week 9 in the spatial modality ($F(1, 24) = 5.103, p = 0.033, d = 0.897, r = -0.409$). Participants in the experimental condition performed better than their control counterparts achieving a lower weighted score.

A small significant difference was found for week 11 in the auditory modality. Control group participants performed better than their experimental counterparts ($F(1, 24) = 4.934, p = 0.036, d = 0.868, r = 0.398$).

Graph 3b shows the mean amount of erroneous responses made for all sessions. A between-subjects ANOVA shows that there is only a significant difference between groups for the auditory modality ($F(1, 24) = 10.769, p = 0.003, d = 1.298, r = 0.544$). Two paired samples t-tests show that participants perform significantly different from session 1 to session 11 in the spatial modality ($t(25) = 4.658, p < 0.000, d = 1.141, r = 0.495$) and in the auditory

modality ($t(25) = 3.420$, $p = 0.002$, $d = 1.285$, $r = 0.541$).
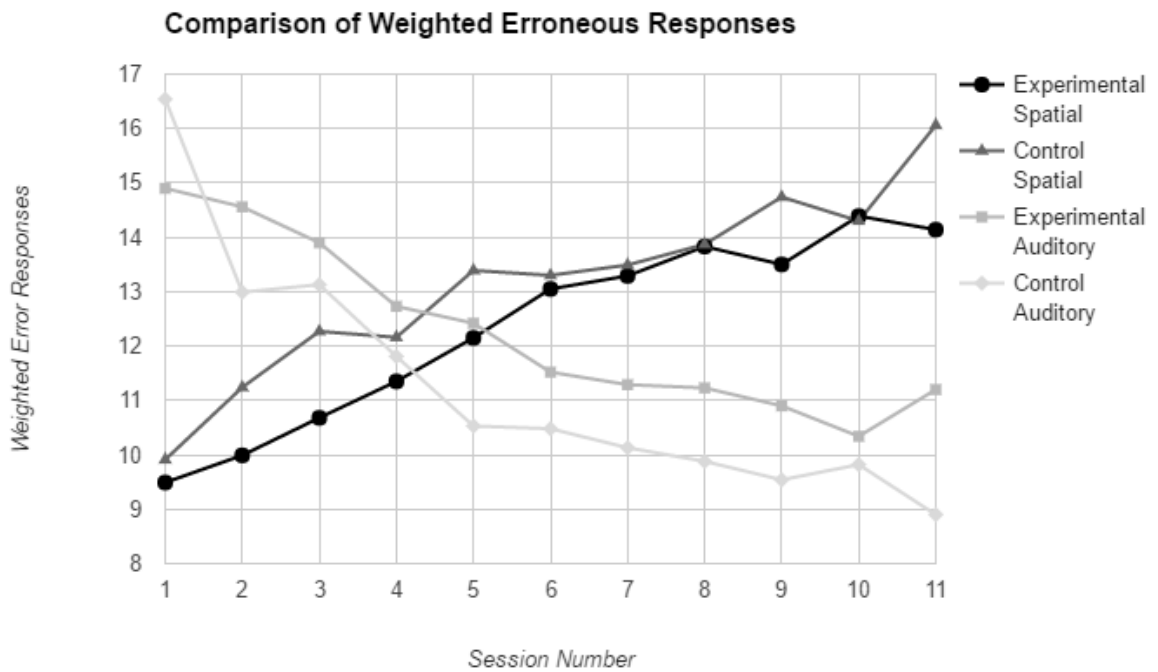
Graph 3a: Comparison of erroneous responses done over 11 sessions. Erroneous responses at higher 'n' values are weighted less than correct responses at lower 'n'.
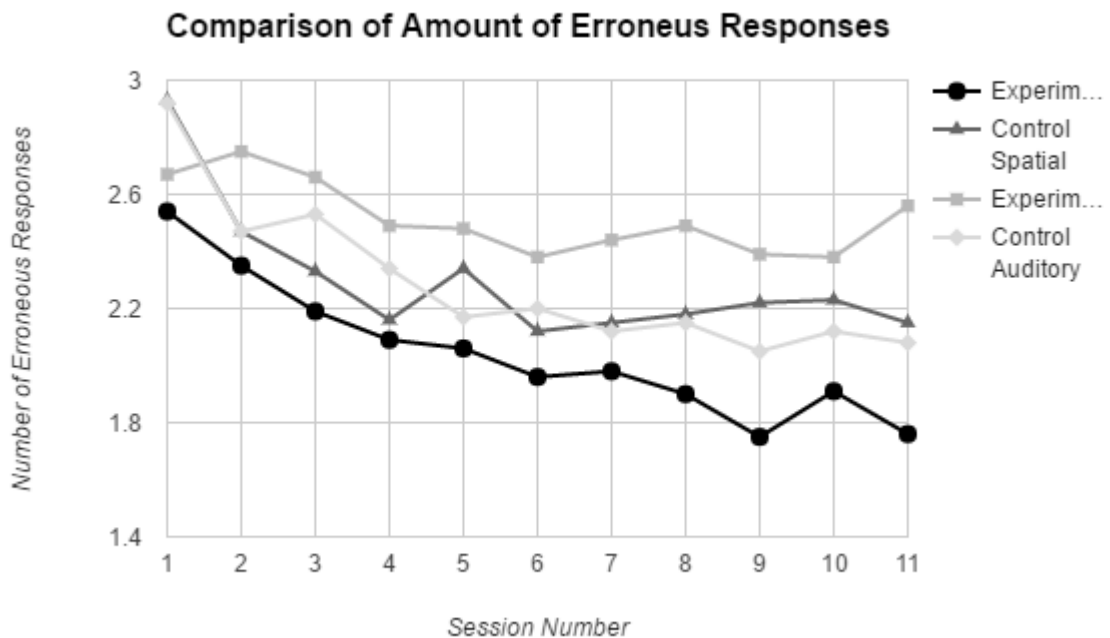
Graph 3b: Comparison of the amount of erroneous responses over the course of the 11 sessions.

10. Discussion

This study set out to observe the long term effects of anodal tDCS stimulation over the LDLPFC on working memory. An experimental design using a dual n-back test and 11 tDCS sessions was used in order to test four hypotheses. A) tDCS stimulation will result in a difference in performance on the n-back task. B) tDCS will have a lasting effect altering performance over time. C) Participants in the experimental condition will perform differently in the amount of correct and wrong responses compared to participants in the control condition. D) tDCS stimulation will improve the performance of participants on the verbal aspect of the task more than on the spatial aspect of the task.

The data gathered for this experiment was put through a SPSS in order to observe the statistical results and see how the participants performed. The final graphs that were presented in the results section were created using Google Spreadsheet. The reason for including weighted scores for both the correct and erroneous responses is to better show the progress in performance that participants make from session to session. While the amount of responses in themselves do show a certain level of progression from the first to last session they are unrepresentative of the difficulty level and the correct responses are limited to a max of 6. The weighted scores include the parameter of difficulty by using the 'n' levels and show much clearer progression rates.

A few difficulties arose during the course of this study. Due to scheduling problems and technical difficulties participants could not regularly attend sessions. The participants could perform anything from 1-5 sessions a week over the course of 2 months. This irregular attendance was seen in both groups but may have had an influence on the progress rates that were observed. Furthermore, in order to fit the schedule of the participants the sessions were not performed at the same time of day, and could occur early, late or before or after classes. The participants therefore did not have a stable fatigue or attentional level and this could have had an influence on the performance of participants. Although this does lend to a more ecologically valid study, poorer or better performance in a specific week may have been the result of an easier or more difficult schedule and less fatigue.

Participants who took part in this study improved their performance on the dual n-back task over time. The significance scores showed that there was an increase in performance over time in the majority of tested parameters. The only score that remained unimproved from session 1 to session 11 was the amount of auditory correct responses. This figure appears fairly stable over time and there is no significant difference between groups.

There were few significant differences between groups found in this study. The mean 'n' score was the same for participants and the MANOVA results show that there was no session where the results for either group would vary enough to be considered significantly different. The statistically significant between-group results were found for total amount of errors made, for difference in performance on erroneous responses on week 9 in the spatial modality and on week 11 for the auditory modality. These specific results show better performance and less mean erroneous responses in the control group for auditory modality and better performance on erroneous responses for the spatial modality in the experimental group.

Initially it will be interesting to look at the mean 'n' scores and the results for this. As is fairly obvious from the graph, the participants are improving over time and achieving higher levels of difficulty. Neither the experimental or control group perform significantly better at any point of the experiment. This result is not in accordance with the individual studies that report better performance of the experimental group compared to the control. It does support the findings of the meta-analysis which found no significant difference between sham and active stimulation (Brunoni, et al., 2014; Kalu, et al., 2012). This experiment, as most tDCS experiments, is limited in sample size and this may have had an influence on the results and not allowed for any statistical differences to arise. Another difference between this and previous studies is the use of a dual n-back task. The previous tasks have kept a very homogenous modality by mainly using verbal stimuli. This study did have a verbal aspect but it was performed simultaneously with a spatial aspect, it is not outside of reason that the two modalities may have caused somewhat of an interference that eliminated any obvious effects that stimulation may have had.

The LDLPFC is after all associated mostly with the verbal fluency within working memory. As the task demands that participants switch between verbal and spatial information perhaps activity in the LDLPFC differed compared to a task in which only verbal stimuli would be used. Anodal tDCS functions by raising the membrane potential and making it easier for

neurons to fire. If activity in the LDLPFC was disrupted due to the multiple modalities of the task, then the effect of tDCS could be reduced.

As such the results for correct responses continues to show no difference between groups. Experimental participants did not perform statistically different from their control counterparts. Performance continues to increase for both modalities and in mean amount of correct responses increases for the visual responses, but remains stable for the auditory ones. While the mean amount of correct responses for auditory remains stable from session 1 to session 11, the weighted scores show that participants are constantly progressing in their performance in this modality.

The erroneous responses show a similar trend. While two significantly different results did occur for the erroneous performance of participants, these results occur only once and do not continue beyond a single session. The lack of recurrence may be explained through a combination of the small sample size and the varying mental state participants were in.

The interesting result from this data set is the higher level of mean erroneous responses in the auditory modality for participants in the experimental condition. This result is surprising as it does not correlate with past studies that found anodal tDCS having a positive influence on performance in the auditory modality. The poor results could not be explained due to tDCS parameters as they were both held to mimic past experiments. This effect did not carry over into the weighted scores and looking at the erroneous performance of participants shows that only in the final week is there a significant difference. Neither of these results have any clear cut explanation though it could be possible that tDCS and the task type caused an interference effect and lead to more erroneous responses. The meta-analysis performed by Brunoni, et al., (2014) does say that only reaction time was shown to significantly increase in participants with tDCS stimulation. Perhaps stimulation of the LDLPFC causes a higher tendency to respond by reducing inhibitory factors. The prefrontal cortical regions have been shown to exhibit an inhibitory effect (Bahrami, 2007) on more posterior regions, perhaps the application of tDCS to the LDLPFC caused participants to be less inclined to prevent a response when they were unsure. More research would have to be done to see whether this could be a possibility.

Another interesting result that was found in this study is that participants perform poorer on the visual modality than on the auditory modality as difficulty increases. Participants in both conditions scored lower in the auditory modality over time while they scored higher in the spatial modality over time. This suggests that there are innate mechanisms contributing to better performance in the auditory domain than the visual one over time. Whether this is a result of the working memory aspect or more basal functions is unclear.

11. Conclusion

This study did not find supportive evidence for an influence of anodal tDCS stimulation over a longer period on working memory. It did not even show any immediate effect. This may have resulted from several factors. Previous studies generally used a 3-back test meaning that the level of difficulty was already set fairly high. While some studies have shown that increased load leads to increased activity in the DLPFC perhaps the current study used too low difficulty levels to elicit a response. While this may seem less likely as the experiment did eventually reach a higher level of difficulty, the adaptive nature of the training program used means that difficulty levels may have fallen during the course of a single session enough to mask the effects of tDCS.

This study as such shows neither detrimental or positive effects coming from the use of tDCS and can be considered supportive of the meta-analysis studies that have found no significant effect from using anodal tDCS to alter performance. Through conversation with the participants it was clear that tDCS did have some basic influence on behavior though this was not recorded as it was not part of the study focus. Participants did express feelings of poorer concentration and slightly increased energy levels though these were limited to the first three sessions following which such effects were not experienced again.

There were several aspects of this study that could have hampered any effect from becoming visible, from the erratic session schedule to the nature of the dual n-back task compared to a single one. Future studies of the same ilk should perhaps limit themselves to a single modality and use less adaptive software that would not allow for a reduction in difficulty level following poor performance. Although the use of dual n-back could be considered more ecologically valid as often times information in day to day life is relayed in more than one

modality. The scheduling used should also be more rigid and of course the sample size should be larger as it may help in reducing any random significant results from occurring. Additionally, there is the possibility that the electrodes used in this study were slightly too small to give a full effect. Generally, studies utilize 35cm^2 electrodes while this study utilized 25cm^2 electrodes. Additionally, it is unlucky that the EEG aspect of this study had to be discounted as the data may have shown some interesting results that might have aided in the understanding of the behavioral results.

Effects from long term use of tDCS should not be discounted as this study does have several inconsistencies that may have been very critical in the final results.

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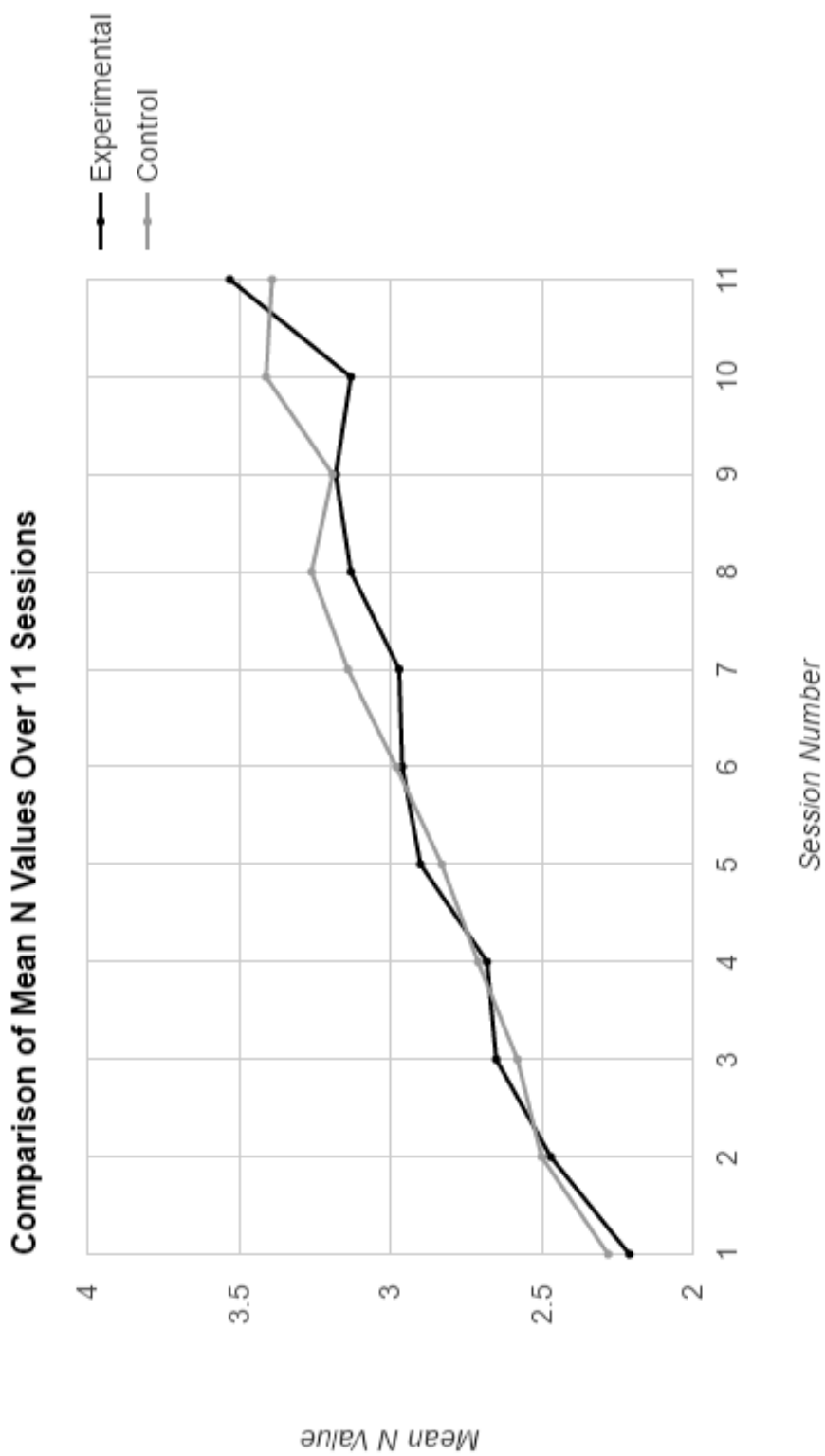
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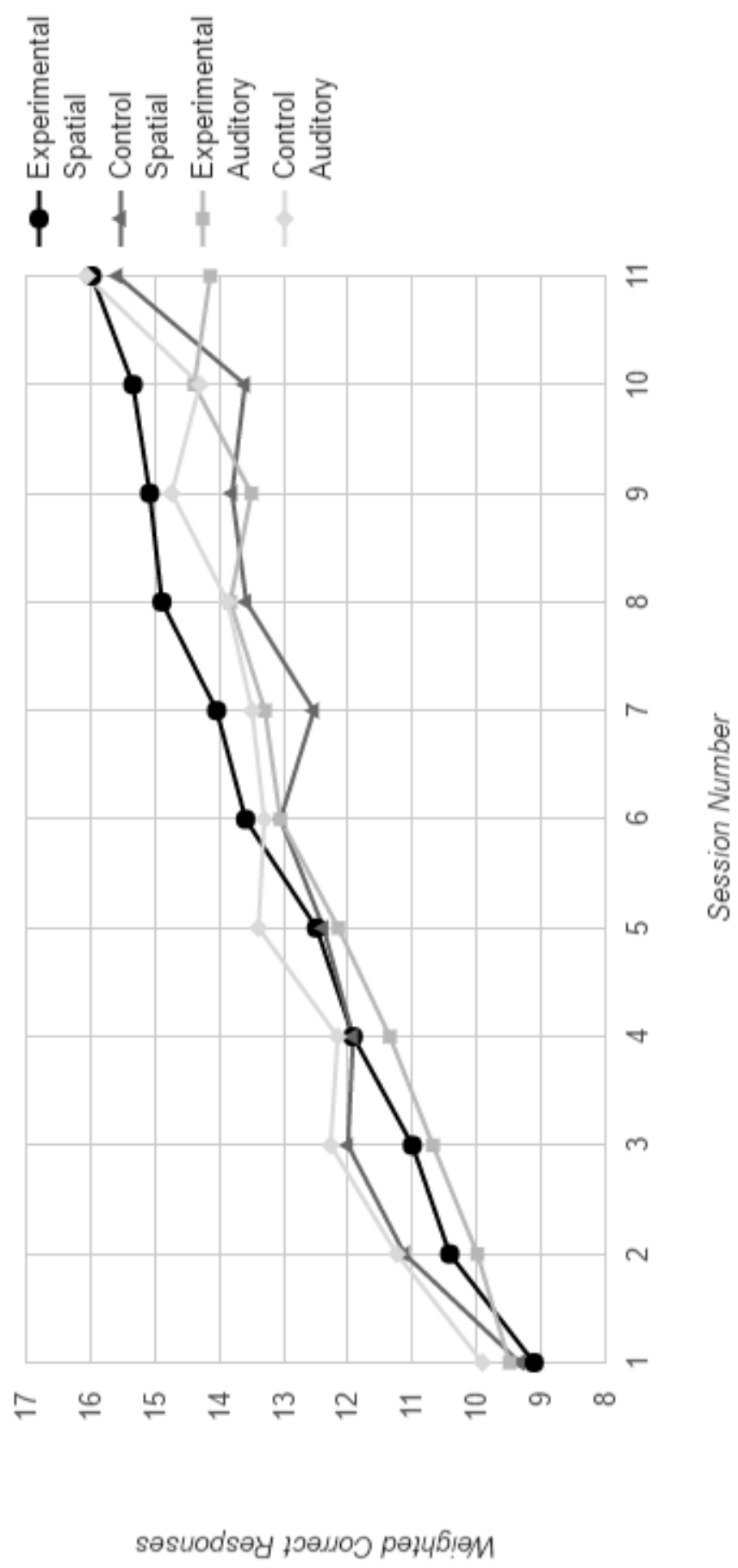
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Appendix A - Graphs

Comparison of Mean N Values Over 11 Sessions

Comparison of Weighted Correct Responses

Weighted Correct Responses

Session Number

Experimental Spatial
Control Spatial
Experimental Auditory
Control Auditory

Comparison of Amount of Correct Responses

Legend:
- Experimental Spatial
- Control Spatial
- Experimental Auditory
- Control Auditory

Number of Correct Responses

Session Number
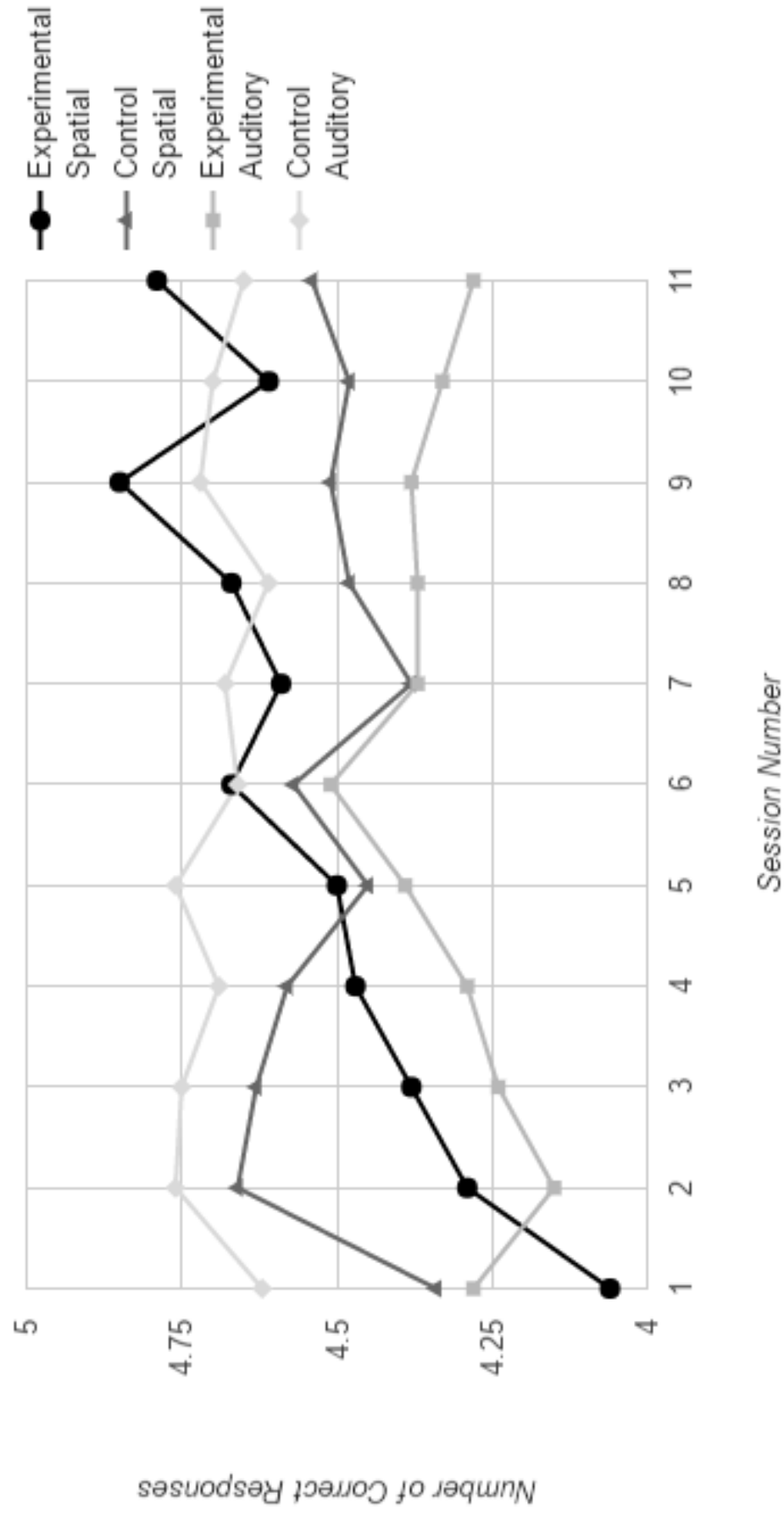
Comparison of Weighted Erroneous Responses

Weighted Error Responses

Session Number

Experimental Spatial
Control Spatial
Experimental Auditory
Control Auditory
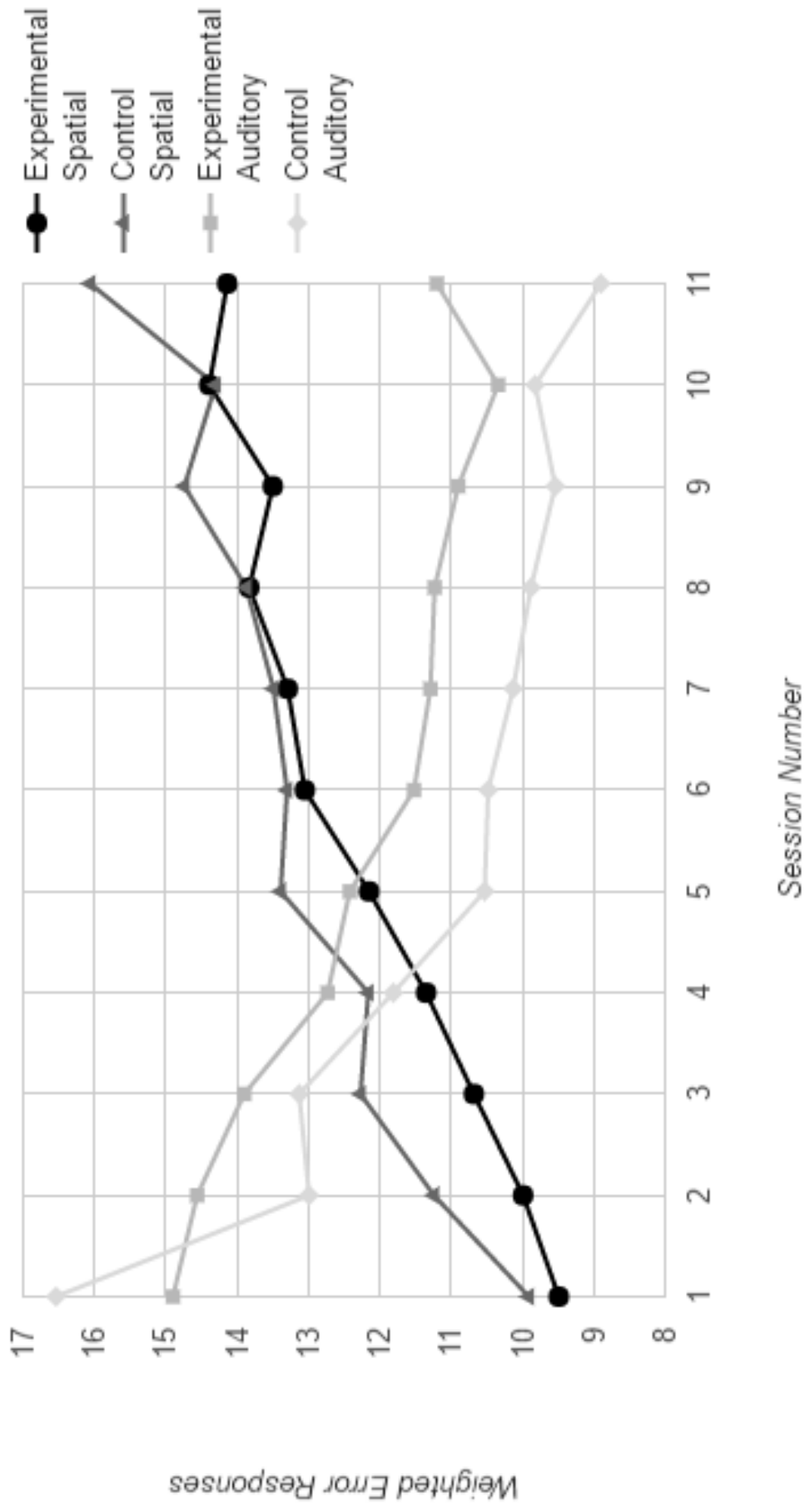
Comparison of Amount of Erroneus Responses

Number of Erroneous Responses

Session Number

Experim...
Control
Spatial
Experim...
Control
Auditory
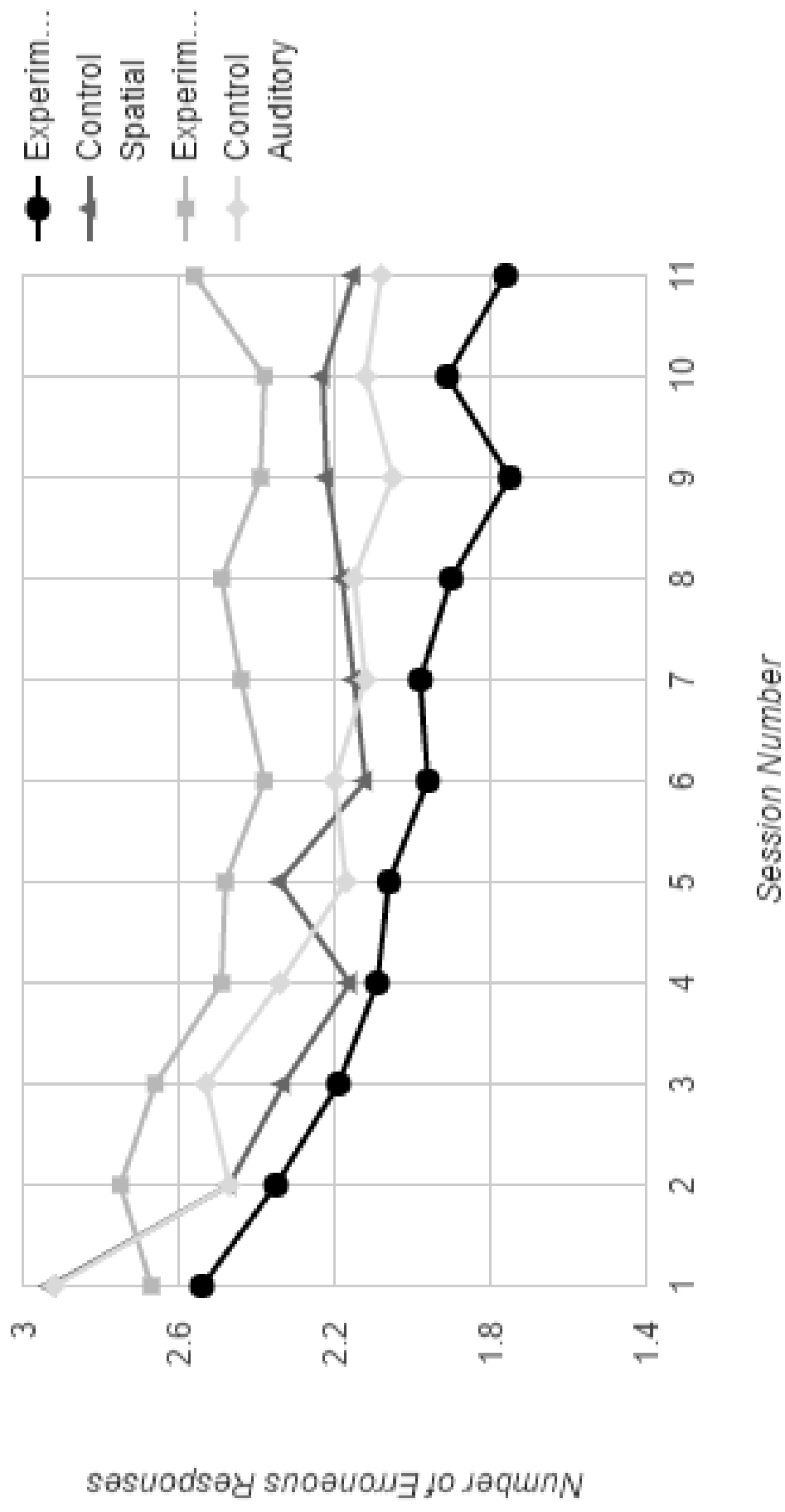
Appendix B - Mindsparke Brain Fitness Training & SPSS Statistics Syntax

MindSparke Brain Fitness Training

http://www.mindsparke.com/

Example of how the training looks on screen:
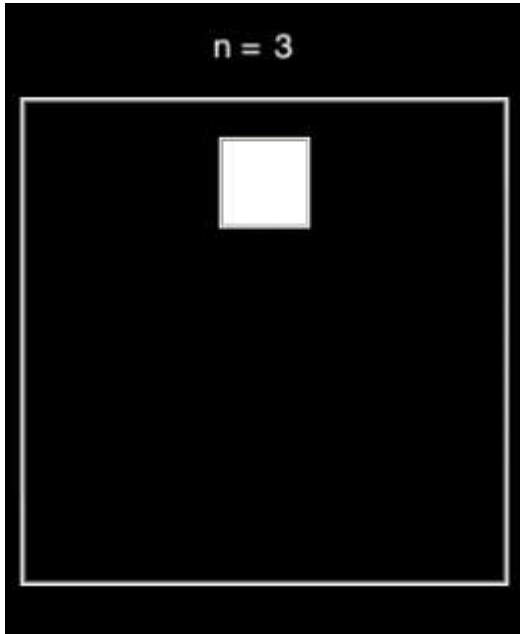
SPSS Syntax:

* Encoding: UTF-8.
* Restructure the file from long to wide.
* Person shall be the case with subcategories
* for all the variables for 11 sessions.

* Open the file

get file 'F:\Folder\Experimentdata.sav'.

*Remove empty data points.

sel if (not(sysmis(ID))).

* Make an inverted n variable
* to multiply with the error responses

compute Ninv = 8-N.
exec.

* Weight all the correct and error responses with respective n or ninv.

```
compute Vhits_Poeng = visualhits * N.
compute Vmiss_Poeng = visualmisses * Ninv.
compute Ahits_Poeng = auralhits * N.
compute Amiss_Poeng = auralmisses * Ninv.
exec.
```

* Aggregate to get an average of all the trials
* within each session.

```
agg out *
/break Groupnr ID Sessionnr
/Nmin = min(N)
/Nmax = max(N)
/NMean = mean(N)
/VhitsM = mean(visualhits)
/VmissM = mean(visualmisses)
/AhitsM = mean(auralhits)
/AmissM = mean(auralmisses)
/Vhits_MPoeng = mean(Vhits_Poeng)
/Vmiss_MPoeng = mean(Vmiss_Poeng)
/Ahits_MPoeng = mean(Ahits_Poeng)
/Amiss_MPoeng = mean(Amiss_Poeng).
exec.
```

* Save the result as a temporary file.

```
sav out 'F:\OliverS\tmp.sav'.
```

```
*******************************************************************************.
*******************************************************************************.
*******************************************************************************.
```

* Now restructure the file so you get
* one case per person.

```
get file 'F:\Folder\tmp.sav'.
```

* Remove the decimals from sessionnr.

```
format Sessionnr (f2).
```

```
SORT CASES BY ID Sessionnr.
CASESTOVARS
```

```
 /ID=ID
 /INDEX=Sessionnr
 /GROUPBY=INDEX.

* now we have a row of data per person.
* save the restructured file.

sav out 'F:\Folder\experimentdata restructured.sav'.

**************************************************************************.
**************************************************************************.
**************************************************************************.

* Perform t-tests to compare group 1 and 2
* at session 1 and 11.

get file 'F:\Folder\Experimentaldata restructured.sav'.

T-TEST GROUPS=groupnr(1 2)
 /MISSING=ANALYSIS
 /VARIABLES=Nmin.1 Nmax.1 NMean.1 VhitsM.1 VmissM.1 AhitsM.1 AmissM.1
Vhits_MPoeng.1
   Vmiss_MPoeng.1 Ahits_MPoeng.1 Amiss_MPoeng.1
 /CRITERIA=CI(.95).

T-TEST GROUPS=groupnr(1 2)
 /MISSING=ANALYSIS
 /VARIABLES=Nmin.11 Nmax.11 NMean.11 VhitsM.11 VmissM.11 AhitsM.11
AmissM.11 Vhits_MPoeng.11
   Vmiss_MPoeng.11 Ahits_MPoeng.11 Amiss_MPoeng.11
 /CRITERIA=CI(.95).

**************************************************************************.
**************************************************************************.
**************************************************************************.

* We aggregate the file now to receive
* one case per group.

get file 'F:\OliverS\2016-09-28-TDCS-BRED.sav'.

agg out *
/break groupnr
/Nmin.1 = mean(Nmin.1)
/Nmax.1 = mean(Nmax.1)
```

```
/NMean.1 = mean(NMean.1)
/VhitsM.1 = mean(VhitsM.1)
/VmissM.1 = mean(VmissM.1)
/AhitsM.1 = mean(AhitsM.1)
/AmissM.1 = mean(AmissM.1)
/Vhits_MPoeng.1 = mean(Vhits_MPoeng.1)
/Vmiss_MPoeng.1 = mean(Vmiss_MPoeng.1)
/Ahits_MPoeng.1 = mean(Ahits_MPoeng.1)
/Amiss_MPoeng.1 = mean(Amiss_MPoeng.1)
/Nmin.2 = mean(Nmin.2)
/Nmax.2 = mean(Nmax.2)
/NMean.2 = mean(NMean.2)
/VhitsM.2 = mean(VhitsM.2)
/VmissM.2 = mean(VmissM.2)
/AhitsM.2 = mean(AhitsM.2)
/AmissM.2 = mean(AmissM.2)
/Vhits_MPoeng.2 = mean(Vhits_MPoeng.2)
/Vmiss_MPoeng.2 = mean(Vmiss_MPoeng.2)
/Ahits_MPoeng.2 = mean(Ahits_MPoeng.2)
/Amiss_MPoeng.2 = mean(Amiss_MPoeng.2)
/Nmin.3 = mean(Nmin.3)
/Nmax.3 = mean(Nmax.3)
/NMean.3 = mean(NMean.3)
/VhitsM.3 = mean(VhitsM.3)
/VmissM.3 = mean(VmissM.3)
/AhitsM.3 = mean(AhitsM.3)
/AmissM.3 = mean(AmissM.3)
/Vhits_MPoeng.3 = mean(Vhits_MPoeng.3)
/Vmiss_MPoeng.3 = mean(Vmiss_MPoeng.3)
/Ahits_MPoeng.3 = mean(Ahits_MPoeng.3)
/Amiss_MPoeng.3 = mean(Amiss_MPoeng.3)
/Nmin.4 = mean(Nmin.4)
/Nmax.4 = mean(Nmax.4)
/NMean.4 = mean(NMean.4)
/VhitsM.4 = mean(VhitsM.4)
/VmissM.4 = mean(VmissM.4)
/AhitsM.4 = mean(AhitsM.4)
/AmissM.4 = mean(AmissM.4)
/Vhits_MPoeng.4 = mean(Vhits_MPoeng.4)
/Vmiss_MPoeng.4 = mean(Vmiss_MPoeng.4)
/Ahits_MPoeng.4 = mean(Ahits_MPoeng.4)
/Amiss_MPoeng.4 = mean(Amiss_MPoeng.4)
/Nmin.5 = mean(Nmin.5)
/Nmax.5 = mean(Nmax.5)
```

```
/NMean.5 = mean(NMean.5)
/VhitsM.5 = mean(VhitsM.5)
/VmissM.5 = mean(VmissM.5)
/AhitsM.5 = mean(AhitsM.5)
/AmissM.5 = mean(AmissM.5)
/Vhits_MPoeng.5 = mean(Vhits_MPoeng.5)
/Vmiss_MPoeng.5 = mean(Vmiss_MPoeng.5)
/Ahits_MPoeng.5 = mean(Ahits_MPoeng.5)
/Amiss_MPoeng.5 = mean(Amiss_MPoeng.5)
/Nmin.6 = mean(Nmin.6)
/Nmax.6 = mean(Nmax.6)
/NMean.6 = mean(NMean.6)
/VhitsM.6 = mean(VhitsM.6)
/VmissM.6 = mean(VmissM.6)
/AhitsM.6 = mean(AhitsM.6)
/AmissM.6 = mean(AmissM.6)
/Vhits_MPoeng.6 = mean(Vhits_MPoeng.6)
/Vmiss_MPoeng.6 = mean(Vmiss_MPoeng.6)
/Ahits_MPoeng.6 = mean(Ahits_MPoeng.6)
/Amiss_MPoeng.6 = mean(Amiss_MPoeng.6)
/Nmin.7 = mean(Nmin.7)
/Nmax.7 = mean(Nmax.7)
/NMean.7 = mean(NMean.7)
/VhitsM.7 = mean(VhitsM.7)
/VmissM.7 = mean(VmissM.7)
/AhitsM.7 = mean(AhitsM.7)
/AmissM.7 = mean(AmissM.7)
/Vhits_MPoeng.7 = mean(Vhits_MPoeng.7)
/Vmiss_MPoeng.7 = mean(Vmiss_MPoeng.7)
/Ahits_MPoeng.7 = mean(Ahits_MPoeng.7)
/Amiss_MPoeng.7 = mean(Amiss_MPoeng.7)
/Nmin.8 = mean(Nmin.8)
/Nmax.8 = mean(Nmax.8)
/NMean.8 = mean(NMean.8)
/VhitsM.8 = mean(VhitsM.8)
/VmissM.8 = mean(VmissM.8)
/AhitsM.8 = mean(AhitsM.8)
/AmissM.8 = mean(AmissM.8)
/Vhits_MPoeng.8 = mean(Vhits_MPoeng.8)
/Vmiss_MPoeng.8 = mean(Vmiss_MPoeng.8)
/Ahits_MPoeng.8 = mean(Ahits_MPoeng.8)
/Amiss_MPoeng.8 = mean(Amiss_MPoeng.8)
/Nmin.9 = mean(Nmin.9)
/Nmax.9 = mean(Nmax.9)
```

```
/NMean.9 = mean(NMean.9)
/VhitsM.9 = mean(VhitsM.9)
/VmissM.9 = mean(VmissM.9)
/AhitsM.9 = mean(AhitsM.9)
/AmissM.9 = mean(AmissM.9)
/Vhits_MPoeng.9 = mean(Vhits_MPoeng.9)
/Vmiss_MPoeng.9 = mean(Vmiss_MPoeng.9)
/Ahits_MPoeng.9 = mean(Ahits_MPoeng.9)
/Amiss_MPoeng.9 = mean(Amiss_MPoeng.9)
/Nmin.10 = mean(Nmin.10)
/Nmax.10 = mean(Nmax.10)
/NMean.10 = mean(NMean.10)
/VhitsM.10 = mean(VhitsM.10)
/VmissM.10 = mean(VmissM.10)
/AhitsM.10 = mean(AhitsM.10)
/AmissM.10 = mean(AmissM.10)
/Vhits_MPoeng.10 = mean(Vhits_MPoeng.10)
/Vmiss_MPoeng.10 = mean(Vmiss_MPoeng.10)
/Ahits_MPoeng.10 = mean(Ahits_MPoeng.10)
/Amiss_MPoeng.10 = mean(Amiss_MPoeng.10)
/Nmin.11 = mean(Nmin.11)
/Nmax.11 = mean(Nmax.11)
/NMean.11 = mean(NMean.11)
/VhitsM.11 = mean(VhitsM.11)
/VmissM.11 = mean(VmissM.11)
/AhitsM.11 = mean(AhitsM.11)
/AmissM.11 = mean(AmissM.11)
/Vhits_MPoeng.11 = mean(Vhits_MPoeng.11)
/Vmiss_MPoeng.11 = mean(Vmiss_MPoeng.11)
/Ahits_MPoeng.11 = mean(Ahits_MPoeng.11)
/Amiss_MPoeng.11 = mean(Amiss_MPoeng.11).
exec.

sav out 'F:\Folder\Experimentaldata 2group.sav'.
```