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Effects of transcranial direct current stimulation of the motor cortex on cycling time trial performance and prefrontal cortex activation

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University of Northern Iowa

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EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION OF THE
MOTOR CORTEX ON CYCLING TIME TRIAL PERFORMANCE AND
PREFRONTAL CORTEX ACTIVATION

An Abstract of a Thesis
Submitted
in Partial Fulfillment
of the Requirements for the Degree
Master of Arts

Abigail Hope Auten
University of Northern Iowa
May 2021
ABSTRACT

Transcranial direct current stimulation (tDCS) is a neuromodulatory technique that delivers low levels of a constant current via scalp electrodes to specifically targeted areas of the brain. The effects of tDCS on whole-body exercise performance has been of interest in recent literature. **Purpose:** To investigate if tDCS, administered via Halo Sport, influences time trial performance in trained cyclists, and if changes in exercise performance are associated with prefrontal cortex (PFC) activation and/or muscle oxygenation (SmO$_2$). **Methods:** Twelve recreationally trained cyclists volunteered to participate in two 10km time trials following 20 minutes of tDCS or a sham condition. **Results:** T-tests showed there was no significant difference in performance (time to completion or watts) or physiological measures (Bla’, HR, SmO$_2$, PFC oxygenation) between the Halo and sham conditions. **Conclusion:** These results indicate that the application of tDCS via Halo Sport does not induce changes in exercise performance or related physiological parameters during a 10km cycling time trial.
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has been approved as meeting the thesis requirement for the Degree of Master of Arts

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CHAPTER ONE
INTRODUCTION

The limiting factors of exercise performance have been the focus of many current and past exercise science research discussions (e.g. Amann, 2011; Neyroud et al., 2014; Schillings et al., 2003). During continuous submaximal exercise, the ability of the skeletal muscle fibers to contract and the excitability of motor neurons projecting from the central nervous system are significantly decreased (Taylor et al., 2016). To accommodate for this reduction in force or power output, the output signals from the motor cortex of the brain to the periphery (i.e., skeletal muscle) must be increased to generate enough force to maintain exercise intensity. Supraspinal fatigue can be described as a reduction in motor cortical neuronal drive or the lack of ability to generate output from the motor cortex, and in combination with peripheral factors (i.e., changes at or distal to the neuromuscular junction) can cause muscular fatigue. Previous research has suggested that the development of supraspinal fatigue is often coupled with changes in the excitability of the motor cortex (Angius et al., 2015).

A multitude of electrical and magnetic stimulation techniques have been developed and extensively researched to modulate excitability and output signals from the motor cortex (Rossini et al., 2015). Increasing the output from the motor cortex can delay the onset of supraspinal fatigue and likely improve exercise capacity (Huang et al., 2019). Of these techniques, transcranial direct current stimulation (tDCS), and specifically its’ effects on physical performance have gained much interest in current literature (e.g. Baldari et al., 2018; Mesquita et al., 2019; Okano et al., 2015). tDCS is a
neuromodulatory intervention that delivers low levels of a constant current to specifically targeted areas of the brain, such as the motor cortex, which create excitability changes (Okano et al., 2015). tDCS is a non-invasive stimulation technique that is affordable and easy to administer. Halo Sport is a commercial tDCS device that mimics traditional over the ear headphones, to provide comfort and convenience. Halo Sport uses weak currents sent through surface electrodes of the scalp and aims to stimulate both sides of the motor cortex (Huang et al., 2019). This neuromodulatory technique has been deemed safe, resulting in mild to no adverse side effects (Brunoni et al., 2012). For these reasons, interest in tDCS’ potential ergogenic effects on physical performance has increased greatly.

There has been considerable research done on the impact of tDCS on single-joint isometric exercise with tDCS and whole-body exercise just recently being investigated. Unlike single joint exercise, whole-body exercise incorporates multiple muscle groups and better imitates real-life sporting competition. It has been extensively reported that fatigue, whether due to peripheral or central factors, is one of the main factors contributing to the cessation of exercise. One of most common biomarkers of peripheral muscle fatigue is the concentration of lactate in the blood (Finsterer, 2012). Therefore, measuring blood lactate following each time trial may offer an insight into the degree of peripheral fatigue observed following a self-paced cycling time trial. In fact, it has been shown that peak blood lactate was higher following a 4 km time trial in comparison to either a 20 km or 40 km time trial, possibly indicating a greater degree of peripheral fatigue following shorter, higher intensity time trials (Thomas et al., 2015). Another
commonly used marker of oxidative energy production and thus peripheral muscle fatigue is oxygen saturation in the working skeletal muscles which can be measured by near-infrared spectroscopy (NIRS). NIRS technology is non-invasive and measures the association between the absorption of light by oxyhemoglobin and deoxyhemoglobin (Pratt, 2018). It has been reported that a cyclist’s power output is inversely related to muscle oxygen saturation during exercise (Crum et al., 2017). Therefore, oxygen desaturation occurs at higher intensities and power outputs of exercise (including time trials) as the skeletal muscles are utilizing more oxygen in order to meet the increased demands of exercise (Bhambhani, 2004). Perhaps, tDCS might allow for reduced oxygen saturation in the working skeletal muscle, resulting in increased workload.

Excellence in sport performance not only requires a high level of physical capability, but also mental capability. Previous neuroimaging studies have reported that, during whole body aerobic exercise, the prefrontal cortex (PFC) increases neuronal activation (as measured by brain oxygenation via functional NIRS (fNIRS)) during submaximal aerobic exercise (up to approximately 80% of peak ability) but then decreases when intensity reaches a very hard or maximal effort (Rooks et al., 2010). More specifically, at very high or maximal intensities of exercise where competitive exercise may take place, there may be a shift in resources from areas required for cognitive function to areas required for motor control and maintenance of vital function (e.g., thermoregulation) (Dietrich & Sparling, 2004). This shift in resources may explain the reduction in PFC activation during very high intensities of aerobic exercise. While the effect of tDCS on changes in PFC activation during whole body aerobic exercise is not
well understood, noninvasive fNIRS is a commonly used tool which would allow investigation into these changes. The advantages of fNIRS is that it is also portable and provides live feedback regarding physiological changes associated with brain activity. This may provide us with mechanistic insight into how tDCS can alter PFC activation during competitive exercise.

Therefore, the present study seeks to evaluate if tDCS (Halo Sport) influences exercise time trial performance in trained cyclists. An additional objective is to explore if the change in exercise performance is associated with changes in PFC and muscle oxygenation. Results may provide important insights into the mechanisms of how tDCS influences both competitive exercise and brain and muscle activity, and further allow sports performance personnel to identify and utilize appropriate techniques to improve competitive performance.

The novelty of this study is the utilization of fNIRS brain imaging technology in observing PFC activation during competitive cycling following application of tDCS. This will be the first known study to report these results that will extend our understanding of the neurophysiological changes that may accompany use of tDCS.

Research Questions and Hypothesis

1. What is the impact of tDCS on time trial performance of recreationally trained cyclists?

   Hypothesis 1: tDCS will positively affect performance by decreasing time to complete a 10km time trial.
It has been reported that administration of tDCS can increase time to exhaustion on cycling and treadmill tests (Angius et al., 2018; Lattari et al., 2018; Park et al., 2019; Vitor-Costa et al., 2015).

Hypothesis 2: tDCS will positively impact performance by making exercise feel less effortful (i.e., a reduction in RPE).

It has been reported that tDCS can create a downward trend in RPE in cycling and treadmill tests (Angius et al., 2018; Angius et al., 2015; Okano et al., 2015; Park et al., 2019).

2. What is the effect of tDCS on brain and muscle oxygenation during a 10km cycling time trial?

Hypothesis 1: tDCS will not significantly increase brain oxygenation during a 10km cycling time trial.

To date, there has been no research on PFC activation during competitive whole-body exercise following application of tDCS on the motor cortex.

Hypothesis 2: tDCS will not significantly decrease muscle oxygenation during a 10km time trial.

To date, there has been no research on muscle oxygenation during competitive whole-body exercise following application of tDCS on the motor cortex.
Variables

Independent Variables

tDCS administered via Halo Sport
No tDCS (sham condition)

Dependent Variables

Time to completion – time required for a task to be completed
Heart Rate (HR) – number of heartbeats per unit of time
Blood Lactate (Bla\(^{-}\)) – the concentration of lactate in the blood
Ratings of perceived exertion (RPE) – subjective measure of exercise intensity
Muscle Oxygenation (SmO\(_2\)) – amount of oxygen available in skeletal muscle tissue
Brain Oxygenation - amount of oxygen available in cerebral tissue

Limitations

The following are possible limitations of the current study:

1. This study will ask that participants refrain from exercising within 24 hours of each trial and participants may choose not to adhere to these suggested exercise restrictions.
2. The study sample will consist of trained middle-aged male cyclists from the Cedar Falls area, ages 18-45. Therefore, the results of this study may not apply to individuals who are untrained or outside of the age range.
3. Brain and muscle oxygenation will be assessed in limited cortical and muscular regions using a superficial measurement technique. Therefore, our results may differ from those of studies using more global and invasive measures of oxygenation or other brain and muscle regions during exercise.
CHAPTER TWO
LITERATURE REVIEW

Introduction

In recent literature, there have been many discussions about the limiting factors that lead to the cessation of exercise (Amann, 2011; Neyroud et al., 2014; Schillings et al., 2003). Fatigue during exercise is generally thought of as a decrease in muscle performance, shown as a decreased ability to produce power and force (Allen et al., 2008). A common belief in exercise physiology is that the discontinuation of exercise is caused by fatigue originating in the skeletal muscle due to depletion of energy substrates or build-up of metabolites (Hunter et al., 2003). However, a more current approach is that fatigue originates in the central nervous system which decreases neural drive to the muscle (Wan et al., 2017). For this reason, the brain is being explored as a potential determinant of regulating exercise performance.

Transcranial direct current stimulation (tDCS) is a neuromodulatory technique that delivers low levels of a constant current via scalp electrodes to specifically targeted areas of the brain (Okano et al., 2015). This technique is non-invasive and can safely change the excitability of the neurons in the brain and impact functional plasticity (Huang et al., 2019). The change in excitability is dependent on both the position and polarity of the stimulation (Jacobson et al., 2012). Anodal stimulation generates a depolarization of the resting membrane potential of the cortical neurons, increasing neural firing and excitability, whereas cathodal stimulation hyperpolarizes cortical neurons, causing decreased cortical excitability (Tortella, 2015). tDCS has gained popularity as a brain
stimulation technique because it is easy to administer, inexpensive, and generally well-tolerated with, at most, mild adverse side-effects reported. Such adverse side effects associated with tDCS are itching, tingling, minor headache, and discomfort (Brunoni et al., 2012). The effects of tDCS are greatly dependent on placement of the electrodes (montage), size of the electrodes, current intensity, and duration of stimulation. Electrical stimulation of the brain has been a technique used for centuries and was first explored in clinical settings to see the ergogenic effects of stimulation on neuropsychiatric disorders such as; depression, drug addiction, bipolar disorder, chronic pain, stroke rehabilitation, and many more (Brunoni et al., 2012). More recently, this technique has been used to increase speed and accuracy in cognitive tasks and to improve fine motor skills in domains such as music and cognitive functioning (e.g. Cerruti & Schlaug, 2009; Jacobson et al., 2012; Waters-Metenier et al., 2014). In addition, using tDCS as an ergogenic tool to increase strength and power, as well as improve endurance performance has gained popularity with scientific researchers in recent years (e.g. Baldari et al., 2018; Park et al., 2019; Vitor-Costa et al., 2015).

Past Studies Using tDCS

As mentioned above, tDCS has long been used in clinical research as a tool to treat and reduce the symptoms of various neurologic and psychiatric disorders. After ten consecutive, 20 minute sessions of tDCS to the left dorsolateral prefrontal cortex, depressive symptoms of participants with depressive disorder decreased and remained lowered for a month after stimulation (Tortella, 2015). A study done on patients with schizophrenia delivered tDCS stimulation once a day for ten consecutive days.
Researchers used a tDCS montage of anodal stimulation of the prefrontal cortex and cathodal stimulation of the right supraorbital area. Results showed a beneficial change in the positive and negative syndrome scale (a medical scale used to assess severity of symptoms in schizophrenia patients). Additionally, studies done using cathodal stimulation on the left temporo-parietal junction have showed improvements in auditory hallucinations (Tortella, 2015). Another study applied cathodal tDCS once a day for ten consecutive days to the pre-supplementary motor area and saw a significant decrease in mean Yale-Brown Obsessive Compulsive Scale (used to ask about obsessive thoughts and symptoms of OCD) scores in participants with obsessive compulsive disorder (D’Urso et al., 2016). In addition to reducing the negative effects of the aforementioned neural disorders, this brain stimulation technique is also being examined as a means of improving cognitive performance across a number of cognitive domains. Cerruti and Schlaug (2009) found that stimulation of the prefrontal cortex (PFC) can improve performance on a complex verbal problem-solving task. Hsu et al. (2021) found that tDCS stimulation over the dorsolateral PFC improved multi-tasking performance by reducing cost (by up to 20%) and these improvements lasted for up to one hour post-stimulation. tDCS has also recently been used as a tool in the music domain to improve motor learning with difficult musical sequences. Waters-Metenier et al. (2014) found that tDCS applied to the motor cortex led to faster and more synchronized execution of finger movements in piano players. A review done by Jacobson et al. (2012) on the effects of tDCS in motor and cognitive domains noted that motor changes occur more frequently than cognitive changes. Taken together, the results of the above-mentioned studies
provide evidence that tDCS has been used across a wide variety of human participants and has the ability to positively alter one’s motor and cognitive function.

Efforts to understand the physiological mechanisms of tDCS is of vital importance to establish tDCS as an ergogenic aid for various therapeutic, exercise performance, motor, and cognitive outcomes. Here, we focus on acute tDCS administration and its effects on whole-body exercise performance.

Studies Done with tDCS and Whole-Body Exercise

Interest in the potential exercise performance benefits of tDCS on strength, power, and endurance has grown greatly in recent years. Many studies have been conducted examining tDCS and single-joint isometric exercise and reported beneficial results (e.g. Abdelmoula et al., 2016; Frazer et al., 2016; Hazime et al., 2017). After tDCS stimulation, Abdelmoula et al. (2016) found increases in contraction length of the elbow flexor and extensor muscles and Hazime et al. (2017) reported an increase in maximal voluntary contraction of the external and internal rotator muscles of the shoulder. Additionally, Frazer et al. (2016) observed an increase in wrist flexor strength after the application of tDCS. Although single-joint isometric exercises allow for a more controlled environment and investigation into the physiological reasons for fatigue associated with a single small muscle group, whole-body exercise represents a more realistic view of sporting competition with activation of multiple larger muscle groups. That said, there are limited studies completed on tDCS and whole-body exercise such as running and cycling. Of the literature available on tDCS and whole-body exercise, the results related to exercise performance appear to be inconsistent and often with faulty
methodological design. **Table 1** below displays a summary of the most important investigations into acute tDCS administration on healthy participants and whole-body exercise performance over the past 10 years (2011-2020). Variables of interest in these studies are both subjective (influenced by personal feelings) and objective (not influenced by personal feelings; facts). Subjective variables include ratings of perceived exertion (RPE) and perceived pain (PAIN). Objective variables include heart rate, time to exhaustion, blood lactate, peak and mean power outputs, and sport specific performance variables such as kick speed in taekwondo. Vitor-Costa et al. (2015) recruited 11 male participants to perform an incremental cycling test to voluntary exhaustion after 13 minutes of
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tDCS stimulation to the left and right motor cortex. Although there were no changes in hemodynamic responses between sham and anodal tDCS, there was an increased time to exhaustion and a trend for lower RPE ($p = 0.07$) following tDCS administration. The trend for lower RPE suggests that tDCS stimulation of the motor cortex could make the exercise feel easier for a relative intensity. In agreement with these findings, Angius et al. (2018) reported an increase in time to exhaustion and decreased RPE on an incremental cycling test after application of 10 minutes of tDCS to the bilateral motor cortex and ipsilateral shoulder. The results of this study also showed no change in hemodynamic responses. Similarly, 20 minutes of tDCS applied to the left dorsolateral prefrontal cortex (DLPFC) and the right orbitofrontal cortex of 14 males increased time to exhaustion on a constant-load cycling test, however, there was no change seen in RPE (Lattari et al., 2018). Angius et al. (2015) applied 10 minutes of tDCS to the left motor cortex and right DLPFC to 16 males before a constant load cycling test. There was no change in time to exhaustion reported, however, after a cold pressor test there was a significant reduction in the ratings of pain reported in comparison to the sham condition. Okano et al. (2015) administered tDCS to the temporal and insular cortex of 10 males prior to an incremental cycling test. Following anodal tDCS there was a near 4% increase in mean peak power throughout exercise and a slower increase in heart rate and RPE in comparison to the sham condition. The authors suggest that increasing the excitability of the insular cortex may have been the reason behind the lower RPE and overall improvement in exercise performance. Sasada et al., (2017) applied stimulation to the lumbar spinal cord and the motor cortex for 15 minutes. Following this stimulation, participants performed a 30-
second all-out Wingate anaerobic test, and similar to the previous findings by Okano et al. (2015), there was a significant increase in peak mean power throughout exercise (Sasada et al., 2017). In contrast, tDCS applied to the temporal cortex and vertex of the brain of 14 males showed no change in peak power during a constant load cycling test (Barwood et al., 2016). This study also saw no changes in time to exhaustion, RPE, or heart rate. Taking a different approach to previous studies, Baldari et al. (2018) examined performance on a ramp protocol treadmill test after the application of tDCS to the motor cortex of 13 males and found no change in time to exhaustion, RPE, or heart rate. Unlike studies on cycling and running, Mesquita et al. (2019) looked into the impact of tDCS applied to both sides of the motor cortex and ipsilateral shoulder of 19 male and female taekwondo athletes. Application of tDCS worsened performance of these athletes in frequency speed of kick testing, showed no change in countermovement jumps, and increased RPE. tDCS procedures and methodologies differ throughout these studies in terms of placement of electrodes, duration of stimulation, type of exercise, and variables examined. Although there is conflicting evidence as to the true effects of tDCS on exercise performance, the aforementioned studies suggest that application of weak stimulation to the brain has the potential to positively alter both subjective and objective variables during whole-body exercise. That said, the exact physiological mechanisms which have a direct impact on altering such subjective and objective variables during exercise are currently unknown.
Halo Sport

Halo sport is a commercial tDCS device that delivers weak direct currents to the scalp through surface electrodes, also called primers. Currents can range from two to three mA for a selected period of time (usually 20 minutes) and are easily controlled through the headset. Halo sport is a headset that mimics traditional over-the-ear headphones for comfortability and to specifically target the motor cortex. The motor cortex is located in the rear part of the frontal lobe and contains many interconnected neurons, the main function of the motor cortex is to produce neural signals or output that controls the execution of movement throughout the entire body. It has been contended that Halo Sport has the ability to change excitability of these neurons within the motor cortex, and thus, positively impact the fluidity and efficiency of human movement. Increasing excitability would allow neurons from this area of the brain to easily build connections and boost motor drive by increasing output to the skeletal muscles. Improved motor drive could result in performance benefits such as improved focus, decreased perceptions of difficulty, increased power output, and longer exercise duration. Halo Sport is beginning to be used during rehabilitation and competition but the scientific backing for its’ impact on physical performance remains ambiguous (Huang et al., 2019).

Currently, only two studies have been completed utilizing Halo Sport as a tDCS device to explore the potential benefits whole-body exercise performance. Huang et al. (2019) administered 20 minutes of 2mA stimulation to the motor cortex using the Halo Sport headset. Nine healthy male participants received stimulation while resting in a chair with closed eyes prior to performing a 5-minute warm up on the ergometer bike.
Participants then performed five 6-second sprints on the bike with 10% of body mass applied to the front pedal. Results showed a significant increase in mean peak power \( (p = .07) \) throughout exercise along with a trend of decreased heart rate. There was no change in peak power or any other physiologic response. Park et al. (2019) administered the same 20 minutes of 2mA stimulation using Halo Sport, however, participants received 15 minutes of stimulation while warming up and 5 minutes while resting. Twelve healthy male participants then performed a constant-load test to volitional failure. Participants ran at a pace corresponding with 80% of their previously determined maximum oxygen consumption value \( (\text{VO}_{2\text{max}}) \). Results showed that time to exhaustion (TTE) was significantly longer after the application of tDCS, however, there were no changes in cardiorespiratory responses such as heart rate (HR), ratings of perceived exertion (RPE), oxygen consumption \( (\text{VO}_2) \), and pulmonary ventilation (VE). These studies done by Huang et al. (2019) and Park et al. (2019) had contrasting methodology in terms of when stimulation was administered, the type of exercise performed, and physiological variables examined. The only common variable recorded between these studies was HR. Huang et al. (2019) saw a decreased trend for HR throughout exercise while Park et al. (2019) saw no changes in HR throughout exercise. Other variables such as peak and mean power, TTE, and RPE were not common between these two Halo studies. Although, these studies are considerably different in methodologies and results, evidence supports the argument that Halo could be beneficial for improving exercise performance.
Possible Mechanisms and Limitations

Previous studies done using tDCS have had methodology and tDCS procedures that vary widely that have produced inconsistent results. tDCS montages generally consist of an anode and a cathode but placement of these electrodes often differs between studies (Vitor-Costa et al., 2015). Angius et al. (2016) did a study comparing two common tDCS electrode montages and correlated results on a TTE test. The cephalic electrode montage chosen had the anodal electrode positioned over the motor cortex and the cathodal over the prefrontal area. The extracephalic electrode montage had the anodal electrode over the motor cortex and the cathodal electrode over the right shoulder. Results showed that the extracephalic montage was more successful in increasing TTE and decreasing RPE (Angius et al., 2016). Electrode montage, along with stimulation intensity and duration, number of sessions, and intervals between tDCS sessions can have an influence on overall performance outcomes (Brunoni et al., 2012). tDCS procedures and devices are not standardized worldwide, and devices can easily be made with standard lab equipment. For this reason, there are large numbers of devices with different technologies and set ups being used in scientific research (Brunoni et al., 2012). Other tDCS procedures can vary due to discrepancies in when the stimulation is administered. Generally there have been two methods used; it can be applied before exercise while the Participants are relaxed (Angius et al., 2015; Huang et al., 2019; Okano et al., 2015) or while the participants are warming up (Park et al., 2019). Further, some studies do not specify what the participants are doing while receiving stimulation and therefore, optimal tDCS procedures and methodologies are still being determined today.
Precise mechanisms through which tDCS works are still unknown but there are several proposed mechanisms. The primary effect of tDCS is thought to be a modulation of resting membrane potentials, likely facilitating activation of a specific cortical area (e.g., motor cortex), increasing output and reducing the effects of fatigue. In addition, previous research has shown that there is decreased activation of input to the prefrontal cortex during higher intensities of exercise (Rooks et al., 2010) therefore, individuals may have an added ability to activate other brain regions such as the motor cortex and shift resources to this area after tDCS stimulation. Moreover, extra resources would allow for increased neural drive and further reduce fatigue. Studies have also shown that anodal and cathodal tDCS can increase and decrease neuronal activity, respectively, likely as a result of changes in membrane polarization. If motor cortex excitability does increase following anodal tDCS stimulation, it may lead us to believe that there is an increase in neural efficiency. More specifically, there is less motor cortex input (afferent feedback from the muscle) for a given output (used in motor unit recruitment). This possible mechanism might also explain why there is a lower RPE for a given change in cycling power or running speed. In addition, tDCS stimulation could initiate alterations at the periphery. For example, stimulation may result in a calcium influx and different levels of N-methyl-D-aspartic (NMDA) receptors. Different calcium concentrations result in different synaptic modulation, specifically, higher concentrations can result in long term potentiation (LTP)-like plasticity (Yavari et al., 2018). This would increase the ability of the nervous system to make changes and adapt easily to exercise stimuli by adjusting functions and connections (Mateos-Aparicio & Rodríguez-Moreno, 2019). This
may allow for increased utilization of oxygen within the skeletal muscle, resulting in
greater work capacity at high intensities and resulting in improved exercise performance.
Another possibility is the modification of activation of (NMDA) acid receptors (Park et
al., 2019). The NMDA receptor is a specific type of glutamate receptor, glutamate is an
excitatory neurotransmitter and plays an important role in the functioning of the central
nervous system (Newcomer et al., 2000). The feeling of pain is a huge factor in exercise
tolerance, and it is commonly believed that pain experienced during exercise is due to
accumulation of metabolites (e.g. hydrogen ions, potassium, or lactate). Peripheral
muscle nociceptors that detect these built-up metabolites are classified as group III and
IV afferents. These afferents project signals to brain areas such as the somatosensory
cortex and the thalamus where it is perceived as pain (Angius et al., 2015). tDCS
montages targeted at these specific areas of the brain may be able to induce a sense of
reduced effort and difficulty and result in less exercise-induced pain and better exercise
tolerance (Park et al., 2019).

Conclusions

Although the balance may swing in favor of tDCS as a promising tool to be used
for ergogenic purposes, there are many questions left unanswered. To date, no studies
have been done to monitor the activity of brain or muscle oxygenation following
stimulation of tDCS. Studies done on brain oxygenation during exercise have shown a
rise in cerebral oxygenation during low to moderate exercise intensities and a decline at
hard to maximal exercise intensities. The rise of cerebral oxygenation is said to be related
to the hemodynamic responses associated with low to moderate intensity exercise, such
as increased cardiac output (Rooks et al., 2010). Central fatigue is characterized as a reduction in performance of factors in the central nervous system, usually proximal to the neuromuscular junction (e.g. the brain, spinal cord, and peripheral nerve). Central fatigue may be evoked by low brain oxygenation caused by inadequate oxygen delivery or a low-pressure gradient driving diffusion from the capillaries to the mitochondria. Insufficient brain oxygenation may depress cortical excitability and potentially impact performance (Smith & Billaut, 2010). Peripheral fatigue is attributed to other factors unrelated to the spinal cord or brain, such as those of skeletal muscle fibers. Studies done on levels of muscle oxygenation during exercise have reported that muscle oxygenation decreases progressively when exercise intensity increases and levels off near maximal power outputs (Belardinelli et al., 1995; Y. Bhambhani et al., 2001; Bhambhani, 2004; Grassi et al., 1999). Perhaps tDCS stimulation may impact muscle oxygenation and allow further utilization at the skeletal muscle level. In conclusion, it seems as though investigation into the Halo sport headset and its’ impact on exercise performance as well as changes in brain and muscle oxygenation during exercise is warranted.
CHAPTER THREE
METHODS

Study Design

All participants served as their own control in a placebo-controlled, counterbalanced, crossover study with a repeated measures design. The participants visited the lab on three separate occasions. On the first occasion, participants completed an 8-minute submaximal bike test on a Monark stationary bike at the same time of the day as the 10km time trials to eliminate any effects of circadian variations. On the two other occasions the participants performed a 10km cycling time trial following stimulation of a 20-min Halo Sport session either with (Halo) or without (sham) electrical current delivered to the primers. During stimulation, participants were seated, quiet, and relaxed while listening to music of their choosing. All trials were separated by at least 72 hours but no more than 10 days. Participants were wearing brain (fNIRS) and muscle (Moxy) oxygenation devices during both time trials. See Figure 1 for a detailed outline of the study design, including duration between exercise testing sessions.
Figure 1. Detailed outline of Study

Participants

All participants were informed of the study protocol approved by the University of Northern Iowa’s Institutional Review Board (IRB) before obtaining written consent prior to participation in the study. Following IRB approval, recruitment flyers were posted. Twelve male, recreationally trained cyclists were recruited. All participants were active (no less than 30 min∙day$^{-1}$, 3 days∙week$^{-1}$, for at least 3 consecutive months) and were between the ages of 18 and 45 years. See Table 2 for subject demographics. All participants were administered a health history questionnaire which indicated that no subject had a history of musculoskeletal injuries, metabolic, cardiovascular or pulmonary disease, mental disorders/diseases, or were on medications during the study. Participants were asked to refrain from alcohol, caffeine, and physical activity for 24 hours before testing sessions. Participants were instructed to consume a meal of similar nutritional composition at the same time interval prior to all trials.
Table 2. Subject Demographics. *Data are expressed as means ± standard deviations. cm = centimeters, kg = kilograms, kg/m² = kilograms per meter squared, ml/kg/min = milliliter per kilogram per minute*

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>BMI (kg/m²)</th>
<th>Body Fat (%)</th>
<th>Estimated VO₂ max (ml/kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25.5 ± 7.8</td>
<td>181.7 ± 5.9</td>
<td>85.9 ± 12.3</td>
<td>25.7 ± 3.0</td>
<td>15.3 ± 7.0</td>
<td>41.5 ± 5.0</td>
</tr>
</tbody>
</table>

Anthropometric and Body Composition Measurements

Prior to the first testing session, height (cm) and body weight (kg) was measured using a stadiometer and floor scale, respectively. Upon arrival for the first exercise testing trial (submaximal bike test), body fat percentage was also determined using bioelectrical impedance analysis (InBody 720).

Exercise Testing and Screening

All submaximal bike testing was performed on a Monark stationary bike (Ergomedic 828 E, Monark Exercise, Vansbro, Sweden) while wearing a Polar heart rate monitor (V800, Polar Electro Inc., Woodbury, NY, USA). The test began with a three-minute warm-up at 50 watts and then the intensity was increased to 150 watts and participants were asked to maintain 60 rpm for the duration of 5 minutes. Heart rate was recorded at the cessation of the test and prediction equations were used to estimate VO₂max (Fox, 1973). A 2km familiarization of the time trial was also performed following the submaximal bike test to ensure participants understood the protocol and felt comfortable with the cycling intensities, and self-paced nature of the work intensity in the time trials. After a minimum of 72 hours following the submaximal bike test, participants returned to
the exercise laboratory for one of the following two counter-balanced trials: tDCS (Halo) or no tDCS (sham).

**Time Trial Task**

Immediately after either tDCS via Halo or sham stimulation, participants performed a self-selected warm up. To assess endurance performance, participants performed a 10km time-trial test on a VeloTron bike (VeloTron RacerMate, RacerMate Inc., Seattle, WA, USA). VeloTron bikes have a fully adjustable frame to fit multiple users and generates variable load ranges from 5 to 2000 watts, selected by the user.

After a five minute, self-selected warmup, participants started the 10km cycling time trial under as consistent environmental conditions as possible. All time trials began from a standing start at a gear ratio of 53 x 17 and were completed using a virtual flat (i.e. zero gradient) course programed into the VeloTron software. Participants were asked to complete the time trial as quickly as possible, manipulating gearing as needed. Total time needed to complete the 10km time trial was recorded from the VeloTron software. Overall RPE was also collected 10 minutes after exercise has ceased to provide an accurate quantification of session load (Uchida et al., 2014).

**Blood Lactate and Heart Rate**

A blood lactate [Bla’] measurement (Lactate Plus, Nova Biomedical, Waltham, WA, USA) was collected immediately post-exercise as a proxy of the intensity of that particular trial. All [Bla’] samples were collected at the earlobe using a lancing device, obtained in duplicate and averaged for analysis. Heart rate was also continuously measured...
throughout all trials using a Garmin heart rate monitor (HRM-Dual, Lenexa, KS, USA), which was integrated with the Moxy NIRS device.

**Halo Sport Procedures**

The Halo Sport headset itself is similar in appearance to an audio headset. The headset has foam electrodes (termed primers) which will be wetted prior to use to initiate the electrical current with the scalp. The headset will be positioned over the vertex of the head, with the primers lying across the top of the head, from ear to ear. The aim will be to stimulate both (left and right) sides of the motor cortex. The maximum energy output will be 2.2 mA and will be controlled by the Halo application on an iPhone or iPad.

Prior to exercise, participants were seated in a chair, in a resting state. The Halo Sport headset was correctly positioned on the head of participant and the electrical current will be turned to 2.0 mA over the course of 30 seconds. In the active Halo group, 2.0 mA was maintained for 20 minutes. In the sham group, intensity was ramped down after 30 seconds. This procedure is similar to previous studies done using Halo Sport (Huang et al., 2019; Park et al., 2019).

**Functional Infrared Spectroscopy Recording Procedures**

Prefrontal cortex (PFC) oxygenation was measured using a dual wavelength (760 and 850 nm), portable fNIRS system (OctaMon, Artinis Medical Systems) during both time trial sessions. This device has been previously used to illustrate ecological validity during self-paced running (Smith & Billaut, 2010). Four LED optodes (transmitters) and one receiver were placed over the right and left PFC regions (RPFC and LPFC; 4x2 configuration). Optode placement is based on the modified international
electroencephalogram 10/20 system (Orihuela-Espina et al., 2010). The fNIRS cap was located 2 centimeters (cm) above the nasion and centering on the Fpz location (distinctly depressed area directly between the eyes, just superior to the bridge of the nose). A source-detector distance of 3.5 cm was used, which is recommended as an optimal distance to detect cortical activity among adults (Herold et al., 2018; Orihuela-Espina et al., 2010). Short separation channels were not implemented in the current study due to potential for additional error in data analyses (Santosa et al., 2018). The signal sampling rate was 10 Hz. In order to reduce possible disruptions in signals such as movement or heart rate, a moving 2-second average filter was applied to all raw data. Neural activity induces changes in blood flow to activated areas of the brain. When blood flow is increased in activated areas of the brain, local supply of oxygen is greater than consumption – which was shown through a higher concentration of oxyhemoglobin and decreased concentration of deoxyhemoglobin (Herold et al., 2018).

Muscle Oxygenation Procedures

During both Halo and sham 10km time trials, a Moxy NIRS monitor (Fortiori Design, Minnesota, USA) was placed on the dominant legs’ vastus lateralis (VL) – distal part of the VL muscle belly (10-15 cm above the proximal border of the patella) (Billaut & Buchheit, 2013). The monitor was attached following cleaning with an alcohol wipe and secured with a double-sided adhesive disk and covered by a dark athletic tape to reduce intrusion of light (Paquette et al., 2019). The Moxy monitor position on the participant’s skin was marked to ensure the monitor was placed on the same site in the following testing session. A moving 5-second average was applied on the raw muscle O₂
saturation (SmO\textsubscript{2}) signal to reduce the noise created by movement (Rodriguez et al., 2018). During exercise, SmO\textsubscript{2} represents the balance between O\textsubscript{2} delivery and O\textsubscript{2} extraction by the muscle (Ferrari et al., 2011). Minimum and maximum SmO\textsubscript{2} are the absolute lowest and highest 5-second average SmO\textsubscript{2} reached during either of the 10km time trial sessions (Halo or sham). Minimum and maximum SmO\textsubscript{2} values were determined from the lowest and highest observed values throughout the entire Halo or sham time trials for each participant. All SmO\textsubscript{2} values were normalized, so that 0 and 100\% represent these minimum and maximum SmO\textsubscript{2} of the participant, respectively. SmO\textsubscript{2} values are presented in these normalized values in the results section of the main manuscript. McManus et al. (2018) provided evidence that in this subject group, both MOXY and PortaMon produce physiologically credible tissue oxygen saturation index measures during rest and exercise.

Statistical Analysis

In previous research studies in which the Halo Sport device was used to enhance exercise performance in healthy adults, researchers reported significant results (p < 0.05) with a total of 9 (Huang et al., 2019) and 12 participants (Park et al., 2019) in crossover studies with repeated measures design. Therefore, we aimed to include a larger sample than those described in these previous studies (e.g. Barwood et al., 2016; Lattari et al., 2018; Okano et al., 2015) to ensure accurate analysis of the effects of the Halo Sport intervention. All results are expressed as means ± standard deviation. Brain and muscle (SmO\textsubscript{2}) oxygenation changes from baseline within each time trial (Halo and sham) were analyzed using data from the LPFC (fNIRS channels 1-4 averaged) and RPFC (fNIRS
channels 5-8 averaged) and VL muscle, respectively. Paired t-tests were used to compare Halo and sham 10km time to completion, overall RPE, immediately post-exercise blood lactate, SmO₂ and PFC regions (left and right) for O₂Hb and tHb. Data was analyzed using GraphPad Prism 9.0.2.
CHAPTER FOUR

RESULTS

Performance Measures

Time to Completion

A t-test revealed that there was no significant difference ($p = 0.92$) in time to complete a 10km cycling time trial between Halo and sham conditions (17.58 ± 1.88 min; 17.68 ± 1.92 min) (shown in Table 3).

fNIRS

Prefrontal Cortex Oxygenation

As shown in Figure 2, t-tests were used to compare oxygenated hemoglobin (O$_2$Hb) and total hemoglobin (tHB) in the right prefrontal cortex (RPFC) and the left prefrontal cortex (LPFC) between Halo and sham conditions. Results showed no significant difference ($p = 0.70$) in average RPFC oxygenation (26.85 ± 24.10 μmol, 23.18 ± 17.96 μmol) and no significant difference ($p = 0.98$) in average LPFC oxygenation (13.53 ± 3.84 μmol, 13.56 ± 4.18 μmol) between conditions. Additionally, results showed no significant difference ($p = 0.86$) in average LPFC tHB (18.63 ± 5.17 μmol, 18.23 ± 5.44 μmol) and no significant difference ($p = 0.73$) in average RPFC tHB (40.87 ± 39.86 μmol, 35.46 ± 30.65 μmol) between conditions.
Muscle Oxygenation

A t-test revealed that there was no significant difference ($p = 0.40$) in average muscle oxygenation between Halo and sham conditions, shown in Figure 3 below (18 ± 9 percent, 23 ± 15 percent).
Physiological Parameters

Heart Rate

Despite the application of tDCS, average HR did not show a significant difference ($p = 0.74$) compared to sham conditions (163.5 ± 17.2 bpm, 160.9 ± 20.1 bpm).

Blood Lactate and Rate of Perceived Exertion

There was no significant difference ($p = 0.78$) observed in overall RPE between Halo and sham conditions (16.20 ± 1.99, 15.95 ± 2.03). Lastly, we analyzed the effects of tDCS on post-exercise BLa- levels and found no significant difference ($p = 0.56$) between Halo and sham conditions (10.66 ± 2.47 mmol, 9.99 ± 2.88 mmol). These results are displayed in Table 3 below.
Table 3. Results of Halo and sham BLa-, RPE, HR, Time

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Halo</th>
<th>sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLa- [mmol]</td>
<td>10.66 ± 2.46</td>
<td>9.98 ± 2.88</td>
</tr>
<tr>
<td>RPE</td>
<td>16.20 ± 1.99</td>
<td>15.95 ± 2.03</td>
</tr>
<tr>
<td>HR [bpm]</td>
<td>163.5 ± 17.2</td>
<td>160.9 ± 20.1</td>
</tr>
<tr>
<td>Time [min]</td>
<td>17.58 ± 1.88</td>
<td>17.67 ± 1.92</td>
</tr>
</tbody>
</table>

Data are presented as means ± standard deviations. Mmol = millimoles, bpm = beats per minute, min = minutes.
CHAPTER 5
DISCUSSION

The major finding in this study was that 10km cycling time trial performance was unaffected by tDCS via the Halo Sport device. Results confirm some previous findings showing that tDCS has minimal effect on exercise performance and related physiological parameters (e.g. Angius et al., 2018; Baldari et al., 2018; Barwood et al., 2016). In addition, it was shown that both PFC and muscle oxygenation of the vastus lateralis were maintained over the entire portion of this self-paced, 10km time trial. Moreover, brain and muscle oxygenation show similar trends, whereby PFC and SmO$_2$ are well maintained and do not hinder or help self-paced exercise. That said, this study provides novel evidence to suggest that PFC oxygenation and SmO$_2$ are well preserved during time trial cycling following Halo Sport administration when the intensity of exercise is free to vary in response to external and internal physiological cues.

Interest in the potential ergogenic effect of non-invasive brain stimulation has grown in the recent years and although there are various studies using tDCS and exercises, there are few focusing specifically on the Halo Sport device. Initial research focuses on single-joint isometric exercises, however whole-body exercise better simulates actual sporting competition. Therefore, whole-body exercise may be a more accurate method for assessing the ergogenic effects of tDCS on exercise performance. Of those studies done on whole-body exercise, results are inconsistent. Park et al. (2019) found increased time to exhaustion during a constant load treadmill test after tDCS (21.18 ± 7.13 mins; 18.44 ± 6.32 mins; $p = 0.01$). Similarly, Vitor-Costa et al. (2015) also saw
increased time to exhaustion during an incremental cycling test, with no other significant results in other parameters (HR, RPE, Power output). However, this study found no significant difference in time to complete a 10km cycling time trial. Our results are similar to those of Barwood et al. (2016) who observed no changes in performance measures (time to exhaustion or power output) during a 20k time-trial following anodal tDCS (time to completion: 36 min 21 sec ± 52 sec in sham, 36 min 21 sec ± 88 sec in Halo; power output: 197 ± 12 W in sham, 197 ± 20 W in Halo). Additionally, Angius et al. (2015) found no significant difference ($p = 0.06$) in a time to exhaustion task between tDCS and sham conditions (16.58 ± 8.49 min, 14.68 ± 8.62 min). One possible explanation for the ineffectiveness of tDCS on sport performance may be that results are dependent on the experimental environment, duration and intensity of stimulation, and electrode configuration or placement on the head. Additionally, Halo Sport is a commercially made tDCS device that allows minimal adjustments to these factors (Huang et al., 2019).

To the author’s knowledge, no studies have investigated the relationship between tDCS, PFC oxygenation, and whole-body self-paced exercise. This study found an increase in activation from baseline but no changes in average left and right PFC $O_2$Hb or tHB and no related time-trial performance changes between Halo and sham conditions. There is evidence that submaximal aerobic exercise increases activation of the PFC, as suggested by increases in $O_2$Hb and tHb saturation (Rupp & Perrey, 2007). Therefore, oxygenation of the PFC seems to be related to the intensity of exercise, when compared to the baseline period. Nonetheless, the effect of Halo Sport on any intensity parameters
or cortical oxygenation remains unclear. Our results are similar to those of Muthalib et al. (2013) who found no changes in levels of PFC activation with the application of anodal tDCS over the right motor cortex and no significant changes in an isometric contraction task of the elbow flexors. Additionally, Huang et al. (2019) found that 20-min of tDCS over the LPFC does not affect HR, RPE, or EEG during a 20-min self-paced time-trial in male cyclists. It is possible that through repetition and experience, the act of self-pacing becomes more automatic and requires less thought and less activation in the area of the brain used for processing.

Similarly, no studies have investigated the effects of transcranial direct current stimulation on muscle oxygen saturation. This study found similar values for average muscle oxygen saturation between Halo and sham conditions. As expected, muscle saturation decreased progressively throughout the time-trial task and recovered quickly after the cessation of exercise. These responses of muscle oxygen saturation during whole-body exercise have been well documented (e.g. Belardinelli et al., 1995; Rupp & Perrey, 2007). Belardinelli et al. (1995) observed that oxygen saturation in the vastus lateralis decreased progressively during an incremental VO$_{2\text{max}}$ test. They further observed that SmO$_2$ decreased rapidly during a medium work rate range and leveled off when nearing VO$_{2\text{max}}$ or very hard work rates. Rupp and Perrey (2007) noted similar results in local muscle oxygen saturation in the vastus lateralis during a maximal time to exhaustion cycling test. In tandem, these results suggest that during moderate and hard intensities of exercise there is a discrepancy between local muscle O$_2$ delivery and utilization. Rupp and Perrey (2007) further observed an increase in deoxygenated
hemoglobin (HHb) which may indicate a limitation in delivery of O$_2$ to the working muscles rather than an inability to utilize available O$_2$.

Our study also found no effect on cardiorespiratory (HR) or physiological (Bla-) response during the 10km time trial with the application of tDCS. These results are similar to those of Park et al. (2019) who found no change in HR responses during a constant load treadmill test after 20 minutes of Halo stimulation. Additionally, there are various studies that found no changes in HR responses during different exercises tasks following tDCS (e.g. Baldari et al., 2018; Barwood et al., 2016; Vitor-Costa et al., 2015). However, results of studies investigating tDCS and exercise related cardiovascular responses are conflicting. Okano et al. (2015) saw a decreased HR trend following anodal tDCS during an incremental exercise test. The autonomic nervous system and cardiac responses are regulated by both sympathetic and parasympathetic neural pathways. Parasympathetic pathways are said to regulate HR during rest and exercise at lower intensities, whereas at higher intensities, HR becomes controlled by sympathetic pathways. This may indicate that the intensity of a 10km time-trial at full effort triggered a mostly sympathetic HR response, which may be unaffected by tDCS. Also, previous studies have reported no effect of tDCS on HR during exercise intensities that are near VO$_{2}\text{max}$ (Barwood et al., 2016). This study further found no significant difference in post-exercise blood lactate levels between Halo and sham conditions. Similarly, Barwood et al. (2016) found similar blood lactate results following a 20km time trial after tDCS (9.96 ± 3.29 mmol, 8.08 ± 3.21 mmol). Although this study observed no significant
difference in levels of blood lactate between Halo and sham conditions, these results indicate that this 10km time trial was a high intensity task.

Results of studies investigating tDCS and RPE are inconsistent. Okano et al. (2015) found RPE to increase more slowly following anodal tDCS stimulation over the temporal cortex. However, our study showed no difference in RPE after stimulation. Barwood et al. (2016) and Vitor-Costa et al. (2015) found similar results for RPE during time to exhaustion cycling tasks after tDCS. These results may indicate that the motor cortex is not related to perceptual responses, rather perceptions of effort may be regulated by different parts of the brain (e.g. insular cortex, thalamus). Further, Angius et al. 2018 found no changes in perceptions of pain in a time to failure task following anodal stimulation of the motor cortex. Many factors have been proposed as to why perceptions of effort and pain may be insensitive to the analgesic effects of tDCS such as attentional focus, release of endogenous opioids or catecholamines, and supraspinal inhibitory mechanisms.

There are several limitations to the current study that should be noted. Several studies using tDCS to target specific areas of the brain have shown promise, however, Halo Sport is a commercially made device that does not allow for many adjustments. Due to anatomical differences between participants, it is possible that stimulation via Halo Sport may have not targeted the motor cortex and may have influenced other areas of the brain. Additionally, this study focused on recreationally trained males, ages 18-45. Our results may not translate to other populations as tDCS may have different effects on more novice or elite individuals, females, or different age groups. Lastly, this study used a
10km time trial to measure performance. It is possible that tDCS would produce different results with different modes of exercise or different distances.

The results of this study indicate that the application of tDCS through Halo Sport has no effect on 10km time trial performance and related physiological parameters in recreationally trained male cyclists. Future research done using tDCS should examine the potential long-term impact of training using tDCS on exercise performance, the potential benefits of tDCS on different modes and intensities exercise, and the potential differences between different populations (e.g. females, younger/older adults). Additionally, the impact of tDCS on decision making and accuracy during sport situations may be of interest.
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