Exploring the effects of rhythmic afferent alpha and gamma range electrical stimulation on processing mechanisms in a tone discrimination dual-task paradigm

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ABSTRACT

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Neural oscillations are the changes in the action potentials and the local field potentials (LFPs) of the central nervous system (CNS). Synchrony is when cell populations in different parts of the brain are activated together to achieve a task. The synchrony of brain oscillatory activity could modulate information processing. Synchrony of different oscillatory frequencies can have effects on cognition, motor skills and behaviour. Faster reaction times are correlated with neural oscillations in the alpha (8-12 Hz) or gamma (30-80 Hz) ranges. Rhythmic afferent electrical stimulation in these ranges could influence neural oscillators for speed of processing or task organization. Our aim is to identify how rhythmic electrical stimulation influences performance in a dual-task paradigm using postural and reaction time tasks. Twelve subjects had a transcutaneous nerve stimulation (TENS) protocol applied to their median nerve, in 5 frequency conditions while discerning between two auditory stimuli and maintaining stable balance. Center of pressure (CoP) data were collected under 3 postural conditions. Reaction times, response correctness, CoP excursion and range were measured. There was a main effect of TENS frequency on reaction time; reaction times were longer during a 10 Hz TENS condition. There was a main effect of postural condition; the eyes closed, sway referenced condition had larger excursion and range. Alpha-range TENS lengthened reaction times and had an effect on postural dual-task performance. Further research could identify how afferent rhythmic stimulation affects processing mechanisms.

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Contribution of Authors

Justin Dionne and Dr. Richard Courtemanche developed the study concept and design. Justin Dionne performed the data acquisition. Justin Dionne, Dr. Richard Courtemanche and Dr. Nancy St-Onge developed and revised the analytical methods. Justin Dionne analyzed the data with the supervision of Dr. Richard Courtemanche and Dr. Nancy St-Onge. Justin Dionne, Dr. Richard Courtemanche interpreted the results. Justin Dionne created the draft of the thesis and manuscript documents. Dr. Richard Courtemanche provided critical revision of the manuscript. All authors discussed results and contributed to the final version of the manuscript.

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List of Abbreviations

C8:	Cervical Nerve Root 8
CNS:	Central Nervous System
CoP:	Center of Pressure
EEG:	Electroencephalogram
EMG:	Electromyogram
EC:	Eyes Closed
EO:	Eyes Open
LFP:	Local Field Potential
MEG:	Magnetoencephalogram
mTENS:	Micro Transcutaneous Electrical Nerve Stimulation
RMS:	Root Mean Square
RSVP:	Rapid Serial Visual Presentation
rTMS:	Repetitive Transcranial Magnetic Stimulation
SOT:	Sensory Organization Test
SR:	Sway Referenced
tACS:	Transcranial Alternating Current Stimulation
TBI:	Traumatic Brain Injury
tDCS:	Transcranial Direct Current Stimulation
TENS:	Transcutaneous Electrical Nerve Stimulation
TMS:	Transcranial Magnetic Stimulation

CHAPTER 1: General Introduction

A dual-task paradigm, where two tasks are performed concomitantly causes increased attentional demands. During a dual-task paradigm we often see decreases in performance such as longer reaction times; this is due to our ability to allocate task-related attention (Pashler, 1994; Tombu & Jolicœur, 2003). We have a finite amount of attentional resources that can be used at any given time, according to a capacity sharing model (Pashler, 1994). This produces a splitting of resources, causing a decrease in the performance of the tasks. The amount of attention attributed to each task can be controlled by the individual and can be voluntarily modified in time. In the following sections we will explore several topics which used together could help to develop a methodology to allow us to improve our ability to use these attentional resources. In the following sections we will go over: neural oscillations in cognition, entrainment of internal timing mechanisms, electrical stimulation of the nervous system, postural stability, reaction time in dual-task and we will end on the objectives and hypotheses of this study.

Neural Oscillations in Cognition and Motor Tasks

Schnitzler and Gross (2005) present the contribution of neural oscillations to information processing in the brain. These appear to serve as a neural population recruitment mechanism for engaging the neurons, insuring their communication into functional networks. Briefly, these oscillations could serve to control the timing of action potentials, which are communicating signals within networks. While the contribution to the oscillatory signals could be shared by both membrane potentials and action potentials, the changes in cell populations can be recorded at the level of the local field potentials (LFPs), or from the electroencephalogram (EEG) or a magnetoencephalogram (MEG). In this section, neural oscillations in terms of frequency bands, synchrony and entrainment will be discussed.

Neural oscillations have proven to be a widely studied topic in the neurosciences, in their capacity to serve a functional purpose. Specifically, they could favor synchrony, and bring together cell populations in different parts of the brain, that are activated together to achieve a task (Schnitzler & Gross, 2005). This raises the question as to what happens when the brain shows more, or less, synchronous activity, in terms of the processing of information, and the specificity of the brain regions. Previous research suggests that increases in synchronous activity have a positive influence on cognitive tasks such as a visuo-motor matching task (Hummel & Gerloff, 2004). This information could be used to develop technology or procedures using technology to improve cognitive ability.

Synchrony could be specific to certain frequency bands, and differentially affect motor skills and behaviour. The main frequency bands subdivisions from EEG and LFPs are: theta (4-8 Hz), alpha (8-12 Hz), beta (12-30 Hz) and gamma (>30 Hz) (Buzsaki, 2006). Theta-band oscillations have been attributed to the encoding and retrieval of memory whereas gamma oscillations have been attributed to working memory, processing of attended stimuli and other cognitive functions such as facial recognition (Ward, 2003). Stronger gamma band oscillations have been correlated with faster response times to a simple reaction time task (Gonzalez Andino, Michel, Thut, Landis, & Grave de Peralta, 2005). These suggest that gamma band oscillations are important in attentional processing. Beta oscillations have mainly been attributed to motor execution and imagery (Kühn et al., 2005). Alpha oscillations have been attributed to attentional suppression and focusing (Gonzalez Andino et al., 2005; Ward, 2003). The alpha band is a viable candidate for the optimal frequency to entrain for the study of attentional processes. An example of findings for alpha-wave synchronization is that the sensorimotor cortex local field potentials are coherent with muscle EMG in the frequency range of 6-9 Hz (Schnitzler & Gross, 2005). Other findings have shown similar results in terms of alpha wave synchronicity. The synchronous activity found when doing a visuo-motor matching task was found to be in the 7-13 Hz range as well (Hummel & Gerloff, 2004). Research has explored the alpha frequency range in terms of expertise rather than performance (Del Percio et al., 2009). Del Percio et al. (2009) found that alpha waves were lower in expert athletes when compared to non-athletes in a simple upright standing task involving double leg and single leg standing. They suggested that this was due to the phenomena of neural efficiency, in which experts would require less power of alpha waves due to more efficient neural communication. Alpha waves have also been found to be affected in pathology (Roche et al., 2004; Thompson, Sebastianelli, & Slobounov, 2005). Roche et al.

(2004) compared matched controls to a traumatic brain injury (TBI) group in a Go/NoGo task in which EEG was taken. They found that the TBI group had more variable alpha power and that when alpha power was decreased, reaction times lengthened. This suggests that alpha band synchronization and desynchronization is abnormal in a TBI population and that these mechanisms are needed for proper functioning of certain cognitive processes (Roche et al., 2004). Individuals with TBI have decreased EEG amplitudes across the delta, theta, alpha and beta spectrums, which may suggest impaired allocation of resources involved in attention (Thompson et al., 2005). Taken together these findings suggest that neural oscillatory frequency is involved in cognitive and motor processes and that they may be useful in the development of treatments for people with impairments in cognitive processing ability and motor control.

Entrainment of Internal Timing Mechanisms

It seems clear that the synchronization of neural oscillations is a strong factor for the improvement of cognitive processing, an aspect of which speed of processing can be measured by reaction time. Recently Stefanics et al. (2010) found that the more predictable a stimulus, the faster the reaction time. In their study, fast reaction times correlated with the peak of the phase of delta wave oscillations, which could relate performance and synchrony of neural oscillations. Lakatos et al. (2008) studied if predictable stimuli could cause the entrainment (or phase-locking) of neural oscillations through the applied stimulus in macaque monkeys. Predictable stimuli entrained neural oscillations to the frequency of the stimuli (Lakatos, Karmos, Mehta, Ulbert, & Schroeder, 2008). A study by Ronconi et al. 2016, found that rhythmic auditory stimulation with the goal of increasing alpha band rhythmicity increased task performance, but could also be improved with stimulation at other frequencies.

Properly timed stimuli do seem to have the capacity to entrain neural oscillations, if at the appropriate frequency. This is supported by multiple studies exploring the effects of different types of stimulations and frequencies on task performance (Del Percio et al., 2007; Joundi, Jenkinson, Brittain, Aziz, & Brown, 2012; Kayser, McNair, & Kayser, 2016; Linkenkaer-Hansen, Nikulin, Palva, Ilmoniemi, & Palva, 2004; Ronconi, Pincham, Cristoforetti, Facoetti, & Szucs, 2016; Stefanics et al., 2010). One study used transcranial alternating current stimulation (tACS) at 20 Hz and 70 Hz during a Go/No-Go task (Joundi et al., 2012). 20 Hz stimulation impaired motor performance in both Go and No-Go task where 70 Hz stimulation improved motor performance on Go trials and had no effect on No-Go trials. Motor performance is similarly affected by beta and gamma stimulation (Moisa, Polania, Grueschow, & Ruff, 2016). Moisa et al. 2016 found that when using tACS of the dorsomedial prefrontal cortex, motor performance, in terms of movement initiation, was improved by gamma band stimulation and impaired by beta range stimulation. Power in task-specific frequency bands have been shown to have an effect on sensory evidence which is hypothesized to be the cause of influences on choice during a cognitive task and the reason behind task specific improvements with prestimulus (Kayser et al., 2016). Alpha range (10 Hz) audio-visual stimulation before a cognitive motor task increased the power of alpha waves, as well as reaction times and number of correct responses in both non-athletes and athletes (Del Percio et al., 2007). This is also supported by a study by Linkenkaer-Hansen et al. (2004), who found that performance of a reaction time task could be improved by the use of a 10 Hz prestimulus. In their study, the alpha band frequency (10 Hz) had a higher correlation with the improved reaction times than other frequency bands (Linkenkaer-Hansen et al., 2004). The studies above identify a specificity of the alpha band frequency in being optimal for enhancing speed of processing, and lowering reaction times during performance of a sensorimotor task.

Electrical Stimulation of the Nervous System

A particularly useful method to stimulate the nervous system in a spatially and temporally controlled manner is through electrostimulation. One device which can stimulate the nervous system is a Transcutaneous Electrical Nerve Stimulator (TENS) unit, controlled by a clinician or experimenter. TENS has traditionally been used to modulate pain. By sending electrical pulses through large nerve fibers, the electrical stimulation inhibits the pain signal originating from small nerve fibers of nociceptors, blocking its travel up to the brain (Sluka & Walsh, 2003). Devices such as TENS stimulators affect electrically responsive tissues, of which nervous tissue is of course one of the most responsive. Electrical stimulation of different targets has provided varying methodologies; other examples include the stimulation of nervous tissue through direct intracortical microstimulation (in the case of the capacity to do this in an invasive manner), transcranial direct current stimulation (tDCS) or using transcranial magnetic stimulation (TMS). tDCS can improve posture and gait control during a dual-task paradigm (Zhou et al., 2014). This study found that stimulation of the left dorsolateral prefrontal cortex helped to improve posture and gait control when performed simultaneously to a cognitive task. TMS has been used extensively in research and clinical work, some studies have used TMS applied in a repetitive manner, which could be linked to an influence on neural oscillations (Paus, Sipila, & Strafella, 2001; Schindler et al., 2008). The use of theta burst stimulation has been successful in creating entrainment of neural oscillations (Schindler et al., 2008). TMS has also been able to stimulate neural oscillations through the use of single and paired-pulse TMS (Paus et al., 2001). Those authors also used a TENS unit-like electrical stimulator to compare the effects of centrally stimulated muscles to peripherally stimulated muscles. To identify the effects of those stimulation methods on the central nervous system, EEG measures could be combined with this type of stimulation. While they used this method mainly to remove artefacts from their TMS results, it brings forward the question whether neural oscillations can be modulated through the stimulation of peripheral afferent nerves.

The stimulation of afferent nerves for treatment and rehabilitation has been done in the context of TENS usage, which has also included non-pain related applications (van Dijk, Scherder, Scheltens, & Sergeant, 2002). Electrical stimulation has previously been shown to stimulate the central nervous system through afferent nerves in animals (Dutar, Lamour, & Jobert, 1985). Afferent rhythmic stimulation of the spinal cord has been found to be helpful in alleviating motor deficits in a primate model of Parkinson’s disease (Santana et al., 2014) and may be helpful in human Parkinson’s disease (de Andrade et al., 2016). Afferent rhythmic stimulation may also help motor function in spinal cord injury (Ievins & Moritz, 2017). TENS itself has been used to treat cognitive disorders such as neglect hemianesthesia (Vallar, Rusconi, & Bernardini, 1996), dementia and Alzheimer's (Scherder, Bouma, & Steen, 1995; Scherder, Bouma, & Steen, 1992; Scherder, Van Someren, & Swaab, 1999; Scherder & Bouma, 1999). TENS was found to be similar to vestibular stimulation as both improved tactile perception in persons with neglect hemianesthesia. In the treatment for Alzheimer's disease TENS has been found to improve long-term visual memory and verbal fluency. These effects may be achieved by TENS stimulation of the central nervous system (CNS), it is proposed that these effects may be achieved by stimulation of the hippocampus via TENS (Scherder et al., 1995; Scherder et al., 1992; Scherder & Bouma, 1999; Scherder et al., 1999). TENS stimulation of the median nerve is also proposed to activate the anterior cingulate cortex (van Dijk et al., 2002). TENS however, lacks the precision to stimulate areas, such as the hippocampus, specifically, the effect more likely results from a widespread stimulation of the CNS affecting the hippocampus as well as many other brain areas. Although TENS has never been used to entrain neural oscillations, in the specific goal of enhancing performance of a cognitive task, its capacity to affect the central nervous system permit to hypothesize a central effect of TENS stimulation. It was shown that a breath-controlled TENS paradigm has the ability to produce activation of the alpha band frequency as measured by EEG (Salansky & Fedotchev, 1994). Microcurrent TENS applied at the right lower leg has been found to stimulate Delta band oscillations in the left frontal cortex (Li, Li, Li, & Wang, 2014). TENS applied to the extensor digitorum before a finger movement task decreases MEG readings at the somatosensory cortex (Murakami et al., 2010). These findings taken together indicate that the use of TENS to entrain neural oscillations is plausible. TENS also appears to be more effective when its frequency coincides with the EEG frequency of the subject (Salansky, Fedotchev, & Bondar, 1998). The search for the optimal frequency seems important, and our current knowledge would identify the alpha and gamma ranges as candidates for optimal entrainment of neural oscillations to improve cognitive processing ability due to their involvement with attention (Gonzalez Andino et al., 2005; Ward, 2003).

Postural Stability

To properly evaluate if TENS of an afferent nerve can speed up reaction time, it is preferable to identify tasks when reaction time is already long. One situation that has been used to manipulate reaction time length is a dual-task paradigm, where one of the two tasks is a reaction-time task (Ross et al., 2011). A dual-task paradigm involves performing two tasks concomitantly, thus increasing attentional demands. Longer reaction times are produced, due to our finite ability to allocate task-related attention (Pashler, 1994; Tombu & Jolicœur, 2003). This is because we have a finite amount of attentional resources that can be used at any given time, according to a capacity sharing model (Pashler, 1994). In the next section we will discuss the two components of dual-task in terms of a postural task and a cognitive task, as well as how dual-task is affected in pathologies of the nervous system.

Postural control is generally defined as the body's ability to maintain stability and orientation (Chaudhry, Bukiet, Ji, & Findley, 2011; Paillard & Noé, 2015; Palmieri, Ingersoll, Stone, & Krause, 2002). The stability aspect involves maintaining the body's center of gravity within its base of support, because when it exits the base of support we become unstable and will fall unless we take a step. By measuring the center of pressure (CoP), many variables can contribute to the assessment of postural stability, for example: excursion, velocity, range or root mean square (RMS) amplitude. CoP is the center of the forces we distribute on the ground by standing (Chaudhry et al., 2011; Paillard & Noé, 2015; Palmieri et al., 2002). Excursion measures the total movement of the CoP. Velocity is the total movement of the CoP, relative to time. Range is the difference between the maximum and minimum displacement in a given direction. RMS amplitude measures the average displacement around the mean CoP. Large excursion and velocity values have been attributed to decreases in postural stability. Large RMS amplitudes also identify a decrease in postural stability (Paillard & Noé, 2015; Palmieri et al., 2002). To collect these measurements, specific tools are needed. One widely used tool is the force platform. These are used in many protocols for research studying postural stability (Chaudhry et al., 2011;

Guskiewicz, Perrin, & Gansneder, 1996; Paillard & Noé, 2015; Palmieri et al., 2002; Resch, May, Tomporowski, & Ferrara, 2011; Ross et al., 2011).

Many research protocols to assess the involvement of different sensory systems use a force platform. One of these protocols is the Sensory Organization Test (SOT) which has been used to assess postural control in many situations (Resch et al., 2011). The SOT involves several conditions that challenge the subject's sensory system, manipulating visual and kinesthetic input. This is done by swaying either the platform or the visual surround with the subject having his eyes either opened or closed (Resch et al., 2011). Guskiewicz et al. 1996 used an SOT-like protocol by using a foam pad, a dynamic platform and a visual conflict dome to challenge the subject. The SOT has been validated for determining whether or not postural dysfunction is present (Ross et al., 2011). The SOT has also been used in dual-task paradigms to assess balance capabilities of concussed individuals while performing an auditory switch task (Resch et al., 2011). Resch et al. 2011 found that balance measures were not affected during dual-task, but that individuals had longer reaction times when performing both tasks together. There are multiple lines of research that identify effects of dual-task paradigms on gait, balance and posture (Courtemanche et al., 1996; Lajoie, Teasdale, Bard, & Fleury, 1993; Li et al., 2010; Silsupadol et al., 2009). Courtemanche et al. 1996 studied how gait control differs in diabetic neuropathic persons compared to healthy nondiabetic, nonneuropathic controls. Lajoie et al. 1993 investigated the effects of prioritization of postural or reaction time tasks under conditions of differing difficulty, in healthy young adults. Li et al. 2010 studied the effects of cognitive dual-task training in healthy older adults. Silsupadol et al, 2009 looked at the effects of single-task training compared to dual-task training in older adults. Dual-task paradigms have been used in research involving task prioritization and difficulty (Jehu, Desponts, Paquet, & Lajoie, 2015; Remaud, Boyas, Lajoie, & Bilodeau, 2013). These studies found that task prioritization was a contributing factor to postural performance. Specifically, when subjects prioritized the postural task, postural measures where worse than when the other task was prioritized (Jehu et al., 2015). This effect seems to be contingent on task difficulty in a healthy young population as the same effect was only found during challenging tasks (Remaud et al., 2013). Therefore, we may see differences in postural measures and allocation of attention during more difficult postural conditions.

Reaction Time in a Dual-Task Paradigm

A dual-task paradigm can include a cognitive component. This cognitive component, for example, can measure proficiency in verbal memory or reaction time (van Dijk et al., 2002). A measure of cognitive processing speed, reaction time can be integrated into a dual-task paradigm to address attentional mechanisms (Jehu et al., 2015; Pashler, 1994; Tombu & Jolicœur, 2003). Generally, reaction time tasks involve a stimulus triggering a response by the subject; the reaction time is the delay between the application of the stimulus and the response initiation, usually measured in milliseconds. Reaction time can be attributed to the processing speed of the CNS, which is affected by attentional allocation mechanisms (Catena, van Donkelaar, & Chou, 2011). Our tone discrimination task uses two tones that are played in quick succession and the subject must respond whether the tones are same/different using either a vocal response or the push of a button. Weiner 1973 assessed the difficulty of this task by relating the difference in frequency of the tones to the reaction time. Reaction times lengthened if the stimuli were more similar; this was attributed to the difficulty of the task (Weiner, 1973). Task difficulty is not the only factor affecting reaction time, task prioritization is another factor involved in reaction time. It has been found that reaction time in a dual-task paradigm is improved by prioritization of the reaction time task over the other task (Jehu et al., 2015). Age and certain specific pathologies also contribute to the individual differences in performance (Catena et al., 2011; Li et al., 2010). The elderly population has deficits in balance (Li et al., 2010). Li et al. 2010 found that training in dual-task settings can improve motor control in this group. Traumatic brain injury (TBI) is an example of pathology where postural stability is impaired (Guskiewicz et al., 1996) and reaction time is affected (MacFlynn, Montgomery, Fenton, & Rutherford, 1984).

Rationale

For our experiment we wanted to investigate if TENS stimulation at 10 Hz and 55 Hz could have an effect on processing mechanisms. We decided on a dual-task paradigm involving both a postural task and a tone discrimination task, because this would lengthen the reaction time, allowing us to more easily detect an effect on this variable. We chose to do a double leg standing task for posture as it is fairly common in the literature (Guskiewicz et al., 1996; Paillard & Noé, 2015; Palmieri et al., 2002). We chose specifically to use an SOT-like condition as this would vary the difficulty (Catena et al., 2011; Chaudhry et al., 2011; Li et al., 2010) and thus increase attentional demand in both dual-task and postural single-task (Guskiewicz et al., 1996; Lajoie et al., 1993; Remaud et al., 2013). During the performance of the postural task we did not expect differences in performance between varying TENS conditions as the TENS was applied on the upper body (on the right side) and its main goal was to affect the reaction time task. Reaction time tasks are very adaptable: many types of stimuli and responses can be paired together and presented to the subject. However, in our context, the choice of the reaction time task must not interfere with the postural task; for this reason, we chose a tone discrimination task, as it is independent of visual stimulation, permitting to leave vision for the postural performance. Our experiment is novel: TENS has not been used to affect performance in a dual-task paradigm; for a first study we chose to apply it to a young and healthy population. We focused on task difficulty in dual-task to lengthen reaction times without task prioritization, in a young healthy population.

Objectives and Hypothesis

Through neural oscillation, TENS and dual-task paradigms it seems it may be possible to enhance the postural stability of an individual as well as attenuate the lengthening of reaction times in a dual-task setting. The use of TENS in this manner has not yet been attempted, but its implications could prove useful. TENS is also widely used by clinicians and is well tolerated in the healthy population as well as elderly and pathological populations, with the exceptions of certain contraindications such as pacemakers (Scherder, Van Someren, Bouma, & vd Berg, 2000; van Dijk et al., 2002). The use of TENS in this way could help to develop new protocols for the assessment and the eventual treatment of deficits in reaction time and postural stability.

Objectives

Our study investigated if the stimulation at alpha and gamma frequencies by TENS could attenuate the lengthening of reaction time during a dual-task paradigm, in a healthy population.

Hypotheses

Our hypotheses were as follows: TENS stimulation at 10 Hz and 55 Hz will improve reaction time for the tone discrimination task in a dual-task paradigm; no difference in postural measures (excursion, range, maximum velocity and RMS) will be significant between differing TENS conditions; and there will be no significant effect of Sham TENS conditions on reaction time.

CHAPTER 2: Rhythmic afferent alpha range electrical stimulation disrupts processing mechanisms in a tone discrimination dual-task paradigm

Rhythmic afferent alpha range electrical stimulation disrupts processing mechanisms in a tone discrimination dual-task paradigm

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Abstract

Brain oscillatory activity could pace our capacity to process information. Brain stimulation in the alpha (8-12 Hz) and gamma (30-80 Hz) ranges influences information processing. Rhythmic afferent input also has the capacity to entrain central oscillatory processes: we propose to study how afferent rhythmic electrical stimulation influences performance in a posture/tone discrimination (TD) dual-task paradigm. Twelve subjects (7F, 5M, 23 +/- 1.86 years of age, healthy) received transcutaneous electrical nerve stimulation (TENS) to their right median nerve, in 5 conditions: no stimulation, 10 Hz, 10 Hz sham, 55 Hz and 55 Hz sham, while performing a TD task (finger movement) with their right hand and while performing a postural task [maintaining stable upright balance on a force platform with eyes open (EO), eyes closed (EC) and eyes closed/sway-referenced (SR)]. For the TD task, reaction time and response correctness were evaluated, and for the postural task, center of pressure (CoP) excursion, range, maximum velocity and root-mean-square were measured. For the TD task, we saw no significant differences of response correctness across conditions, but there was a stimulation effect on reaction time, longer with 10 Hz stimulation, compared with others. There was a main effect of postural condition (for excursion and range, SR > EO, EC conditions). Overall, alpha-range afferent stimulation slowed reaction times in dual-task performance, likely interfering with endogenous rhythms that facilitate processing speed. Rhythmic afferent stimulation could further serve to probe mechanisms of timing and control in dual-task and overall performance.

Introduction

Multiple lines of evidence point to the fact that gait, balance and postural control are influenced by the performance of secondary tasks, which is especially true for individuals with potentially limited information processing resources (Courtemanche et al., 1996; Lajoie et al., 1993; Li et al., 2010; Silsupadol et al., 2009). Voluntary control of cognitive resources and controlling attentional processes is at the center of optimized information processing when performing multiple tasks simultaneously. This optimization is the focus of ongoing work across motor control and cognition research for specific neural activity biomarkers. One of those is the expression of oscillatory activity facilitating information processing. Neural oscillations are produced by the combined electrical activity of interacting neuronal networks (Buzsaki & Watson, 2012; Schnitzler & Gross, 2005), which appear in a variety of behaviors such as in sensory analysis, sensorimotor or cognitive tasks (Buzsaki, 2006; Buzsáki, Logothetis, & Singer, 2013). The performance of specific time-constrained tasks, such as a choice reaction-time task, has been associated with the expression of neural oscillations in parietal and frontal areas at a variety of frequencies, including alpha and gamma (Helfrich, Herrmann, Engel, & Schneider, 2016; Hummel & Gerloff, 2004; Stefanics et al., 2010; Womelsdorf et al., 2007). The optimization of such oscillatory activity can be related to performance aspects such as processing speed, such that trials yielding shorter reaction times were found to coincide with greater neural oscillatory synchronization(Hummel & Gerloff, 2004), and even that oscillatory activity predicts response correctness in the case of a somatosensory spatial attention task (Haegens, Handel, & Jensen, 2011) or a temporal order task (Takahashi & Kitazawa, 2017).

To verify causally if these oscillations and their synchrony are functionally relevant, stimulation in the nervous system can be performed to evaluate their effects on behavior; as such, these neural oscillations can be entrained through the use of electrical stimulation devices (Paus et al., 2001; Salansky & Fedotchev, 1994; Schindler et al., 2008; van Dijk et al., 2002), which include transcranial magnetic stimulation (TMS) (Thut et al., 2011), transcranial direct current stimulation (tDCS) (Zhou et al., 2014), and transcranial alternating current stimulation (tACS)

(Moisa et al., 2016). What has been seldom used for this purpose is trancutaneous electrical nerve stimulation (TENS), which is customarily used to stimulate afferent nerves or nearby cell bodies as a pain modulation device (Sluka & Walsh, 2003). However, it does have potential to entrain neural oscillatory activity (van Dijk et al., 2002), and stimulation of afferent pools can modify neural dynamics in disease (Fuentes, Petersson, & Nicolelis, 2010; Fuentes, Petersson, Siesser, Caron, & Nicolelis, 2009; Santana et al., 2014). In our case, TENS units have the advantage of being small, lightweight, and optimal for stimulating afferent neural pools in an active posture/balance task.

Functionally, neural oscillations and coherence may be involved with the processing of attention (Gonzalez Andino et al., 2005; Siegel, Donner, Oostenveld, Fries, & Engel, 2008; Ward, 2003). One particular strategy to probe attentional demands is by using a dual-task paradigm, where two tasks are performed concomitantly. In an example of a balance task complemented by a reaction-time task, reaction times are affected by the dual-task setting, due to finite attentional resources to allocate (Pashler, 1994; Pashler & Sutherland, 1998; Tombu & Jolicœur, 2003). These attentional resources are limited for particular periods of time, according to a capacity-sharing model (Pashler, 1994; Pashler & Sutherland, 1998), and this task competition produces a reallocation of resources, affecting the overall performance in the tasks. The amount of attention attributed to each task can be controlled voluntarily in a time-dependent manner by the individual, in order to suit the overall context requirements. In a postural stability / reaction time task dual-task situation, the needs for allocation of attention to the postural stability task are fulfilled at the expense of the reaction-time task, where subjects show lengthened reaction times (Catena et al., 2011; Lajoie et al., 1993; Li et al., 2010; Resch et al., 2011).

In this study, we propose to use TENS to a sensory nerve to provide a temporal synchronization signal that can alter brain synchronization for task performance. This “neural entrainment” could also influence the efficiency of dual-task processing, by increasing or decreasing the length of reaction times during a dual-task situation. Our aim is to identify how electrical stimulation influences performance in a dual-task paradigm involving postural and reaction time tasks. This study would lead to further knowledge into the central mechanisms for optimizing movement, as they could be related to internal timing mechanisms and the allocation of attention.

Materials and Methods

Participants

Twelve healthy young adults (n=12, 7 women and 5 men; 23+-1.86 years, 169.91 +- 12.48 cm) participated in this study. No participants reported lower limb injuries in the past 3 weeks prior to data collection, or the use of pace-makers/defibrillators, neurological or vestibular conditions. Participants did not report any visual deficiency except for the wearing of corrective glasses/contacts which they wore during the experiment, and they did not report any hearing deficiency. Participants were informed of the nature and aim of the study prior to signing the consent form. This experimental protocol was approved by the Concordia Human Research Ethics Committee.

Experimental procedures

Participants visited the research laboratory for a single session, during which single-task (postural tasks or tone discrimination task, alone) and dual-task trials (postural tasks and tone discrimination task, performed together), all of which were performed under five TENS electrical stimulation conditions. Stimulation order and task order were randomized to avoid an order effect (Table 1 of the Appendix provides an example of trial order). Participants were given a rest period of 30-60 seconds between trials and a rest time of 2-3 minutes between blocks of trials (e.g., changing stimulation parameters or from single-task to dual-task). All trials were exactly 30 seconds long. A total of 90 trials were recorded (45 dual-task/posture + tone discrimination, 30 single-task/posture, 15 single-task/tone discrimination), given across all postural and electrical stimulation conditions). Fig. 1 shows details of the experimental protocol apparatus and design.

Postural task

The postural task measures were done using the dual-force platform in the NeuroCom Equitest CRS Balance Master system (NeuroCom International Inc., Clackamas, OR, USA), focusing on classical postural measures (Chaudhry et al., 2011; Paillard & Noé, 2015). An illustration of the apparatus is given in Fig. 1B. Each participant performed three postural conditions adapted from the sensory organization test (SOT): (1) eyes open, fixed platform (EO); (2) eyes closed, fixed platform (EC); and (3) eyes closed, sway-referenced platform (SR). For the last condition, the platform rotated in the antero-posterior direction (toes down – toes up, respectively) equivalent to the change in position of the CoP, meaning set to 1.0 to replicate the parameters of its corresponding SOT condition. The visual display on the NeuroCom was turned off throughout. Three 30 second trials of each postural condition were performed. Each participant was allowed one practice trial of 20 seconds for each postural condition before data collection began. For safety purposes participants were harnessed to prevent falling. The order of postural conditions was randomly determined during each set of conditions. Force plate data were recorded at a sampling rate of 100 Hz, and low-pass filtered (Butterworth 10 Hz) in both directions to avoid lagging.

Tone discrimination task

The tone discrimination task was an auditory task consisting in the differentiation of pairs of tones, where participants were asked to identify whether the two tones from a pair were the same or different. Participants were allowed to practice the task once before data collection, standing on the floor next to the NeuroCom device. The tones used were 1000 Hz, 1040 Hz and 1080 Hz. They were chosen to be 40 Hz apart from each other as this pitch difference has been shown to challenge pitch perception and yield reaction times near 500 ms long without large numbers of errors (Weiner, 1973). These tones and each individual pairing were pseudo-randomly generated and equally distributed over the 21 tone pairs for every 30 second trial. A trial consisted in 750 ms silence followed by a tone pair with tones being 250 ms each and an inter-tone time of 150 ms. A schematic representation of the data acquisition process and hardware interconnections is given in Fig. 1C; a sample period from a trial tone sequence, and associated responses, is shown in Fig. 1D. Participants responded by applying pressure to finger switches attached to their middle and index fingers, applying pressure to the index finger for tone pairs they found as "same" and to the middle finger for tone pairs found to be "different". Movement of the fingers did not mechanically affect the postural control. The response time (the delay between the beginning of the second tone and the finger switch response) and the percentage of errors (correct identification of same/different pairs) of participants were computed from these responses.

Electrical Stimulation

Electrical stimulation was applied using the Eclipse+Digital TENS machine (Empi Canada Inc., Mississauga, ON, Canada). Self-adhesive TENS electrodes were placed on the right side with an electrode medial to the biceps brachii at the mid-biceps level and lateral (right side) to the T1 vertebrae. Fig. 1A shows the relative location of the stimulation sites. These include both a superficial location of the median nerve as well as the C8 nerve root from which it originates, allowing for both a distal and a proximal stimulation point. The stimulation of the median nerve innervates the index, middle finger and thumb which was chosen as these fingers are involved in the tone discrimination task response to the auditory stimulus. Participants were allowed to experience the TENS before performing the trials. The intensity of TENS was determined as being 30-50% along the length of a visual analog scale ranging from no sensation to pain and was therefore classified as strong but non-painful and was similar for each participant; this intensity was also too low to trigger finger movements. TENS began 10 seconds before each task and was ended within 10 seconds of task completion. TENS was given according to five conditions: two rhythmic conditions, (1) one at 10 Hz stimulation (10 Hz, 100 µs, continuous setting), and another (2) at 55 Hz Stimulation (55 Hz, 100 µs, continuous setting); two sham conditions, one (3) being a 10 Hz Sham (set at 14 Hz, 100 µs, modulated rate setting which varies the frequency, producing a non-rhythmic average 10 Hz rate), and (4) a 55 Hz Sham (set at 80 Hz, 100 µs, modulated rate setting, producing a non-rhythmic average 55 Hz rate); and finally (5) a control condition (no stimulation). The modulated rate setting consists of a 60% frequency decrease over 9 steps, followed by an increase back up to the original value in 9 steps. This takes a total cycle time of 6 seconds. The sham conditions thus consisted in non-rhythmic versions of the matching conditions, and while the average stimulation rates were equal, they differed in their lack of a rhythmic component. The order of TENS conditions was random, and the subject was not informed as to which condition was being applied. Behaviorally, the only condition which was more obviously different from the others was the no-stimulation condition.

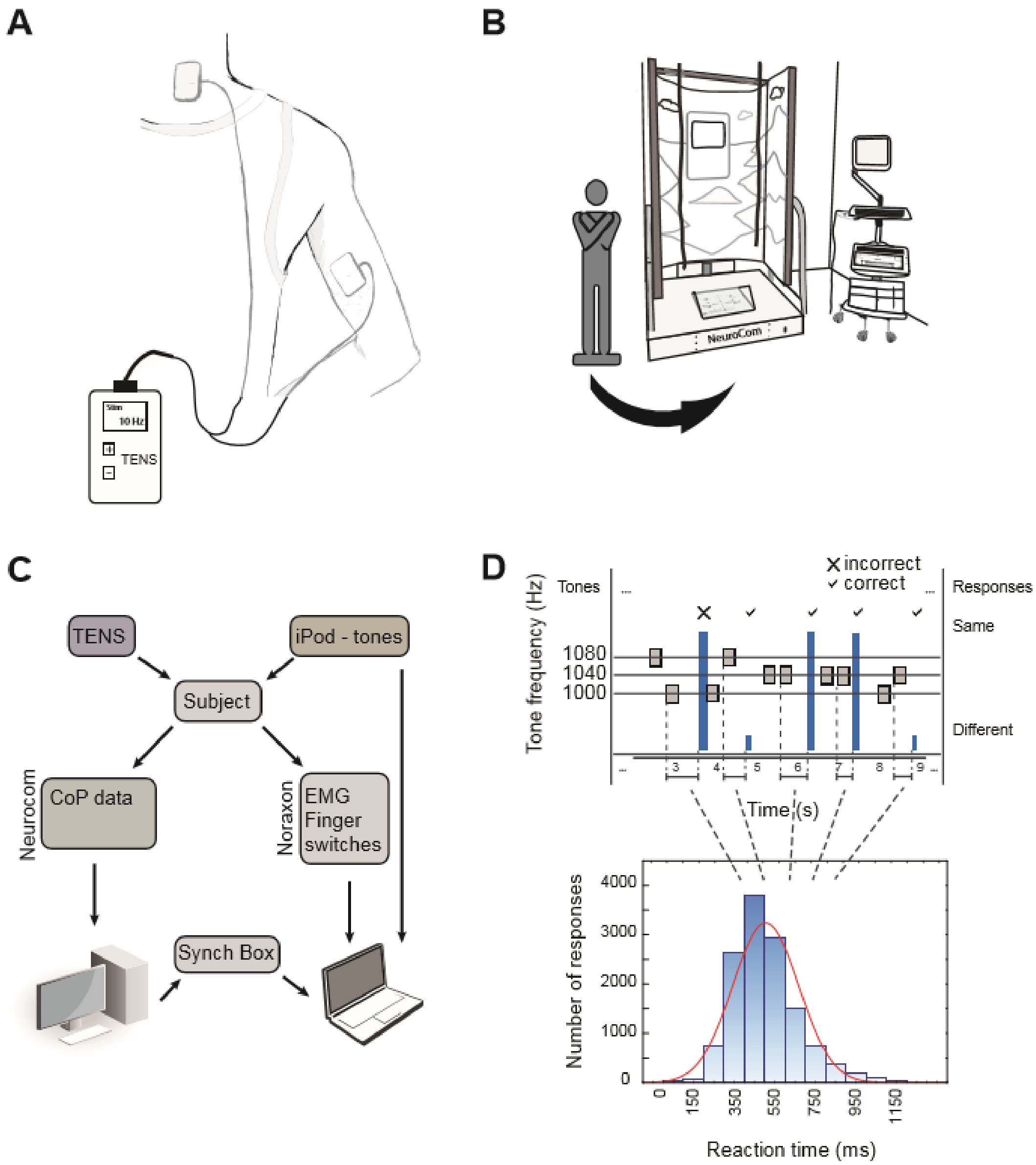

Figure 1. Methods and Setup. **A**. Electrode position for the TENS machine used to stimulate the median nerve. **B**. Participant hand position and balance platform for the postural task. **C**. Connectivity diagram of equipment setup. **D**. Representation of the tone discrimination task with tones (grey blocks) and responses (blue bars), as well as a frequency analysis of all reaction time response measures.

Data and statistical analysis

For force-plate measures, the medio-lateral and antero-posterior excursion, range, maximum velocity and root mean square (RMS) were taken as outcome measures. Separate analyses of variance (ANOVAs) with repeated measures were done for medio-lateral and antero-posterior excursion, range, maximum velocity and RMS. For most of the force-plate data which did not show a normal distribution, the data was transformed to allow the use of parametric statistical tests. The data transformations used consisted of the log10(x) transform (for medio-lateral excursion, range, maximum velocity as well as antero posterior excursion, range, and maximum velocity) and square root (x) transform (for medio-lateral RMS). Repeated-measures ANOVAs were used for the statistical analyses of reaction time and response correctness. Categorical factors were: postural condition (EO, EC, SR), task level (single or dual), stimulation type (control-none, 10 Hz, 10 Hz sham, 55 Hz, 55 Hz sham) and response correctness (correct or incorrect, for RT only). When relevant, Tukey post-hoc tests were used to explore significant components of the main effects or interactions. Statistical significance was set to $p<0.05$.

Results

Of the 12 participants whose data we collected, 11 completed all 90 trials, and the remaining subject completed 69/90 trials. This latter corpus of trials was varied and complete enough to be included in our data analyses. The database was first scanned for outlier values. During the tone discrimination task 510/13746 (3.71%) were omissions (not responded), 292/13746 (2.12%) were reaction times shorter than 250 ms and 35/13746 (0.25%) were reaction times longer than 1150 ms. The removed data accounts for 837/13746 (6.09%). These reaction times were excluded for being too short or because they would overlap with the following tone pairs. This left for 12909 valid tone discrimination responses, of which incorrect responses (where the tone pair category was inaccurately answered) accounted for 1607/12909 (12.45%) of all responses, leaving 11302/12909 (87.55%) responses that were correct overall. After a trial by trial scan through the data, no data was removed from CoP platform data.

Tone discrimination performance

For the tone discrimination task, there was no main effect for reaction time between single and dual-task conditions ($F(1, 39) = 0.03599$, $p = 0.85053$) and there was no main effect across postural conditions EO, EC and SR ($F(2, 56) = 1.0573$, $p = 0.35421$). There was no main effect of TENS condition on response correctness ($F(4, 108) = 1.6758$, $p = 0.16$). There was a main effect of TENS condition in both single ($F(4, 72) = 2.9584$, $p = 0.02541$) and dual-task ($F(4, 236) = 3.4546$, $p = 0.00913$). In single task reaction times were significantly longer in the 10 Hz condition (573 ms +/- 35 ms). In dual-task reaction times were significantly in the 10 Hz condition (550 ms +/- 15 ms).Because the effects were similar, we collapsed across single and dual-task, all 3 postural conditions (EO, EC and SR) as well as correct and incorrect responses. With the collapsed conditions a main effect of stimulation type was found on reaction time ($F(4,296) = 6.1874$, $p < 0.001$). Reaction times were significantly longer during the 10 Hz condition (555 ms +/- 15 ms). . There was also an interaction correctness x stimulation type on reaction time. Incorrect reaction times were longer for 10 Hz and 55 Hz conditions, while only the reaction times for stimulation at 10 Hz were longer for correct responses. There was also a difference in reaction time between correct and incorrect responses ($F(1, 74) = 5.9373$, $p= 0.01723$). Reaction times were longer for incorrect responses (554 ms +/- 16 ms) compared to correct responses (500 ms +/- 14 ms). Fig. 2 shows the main results for the reaction time component of the tone-discrimination task.

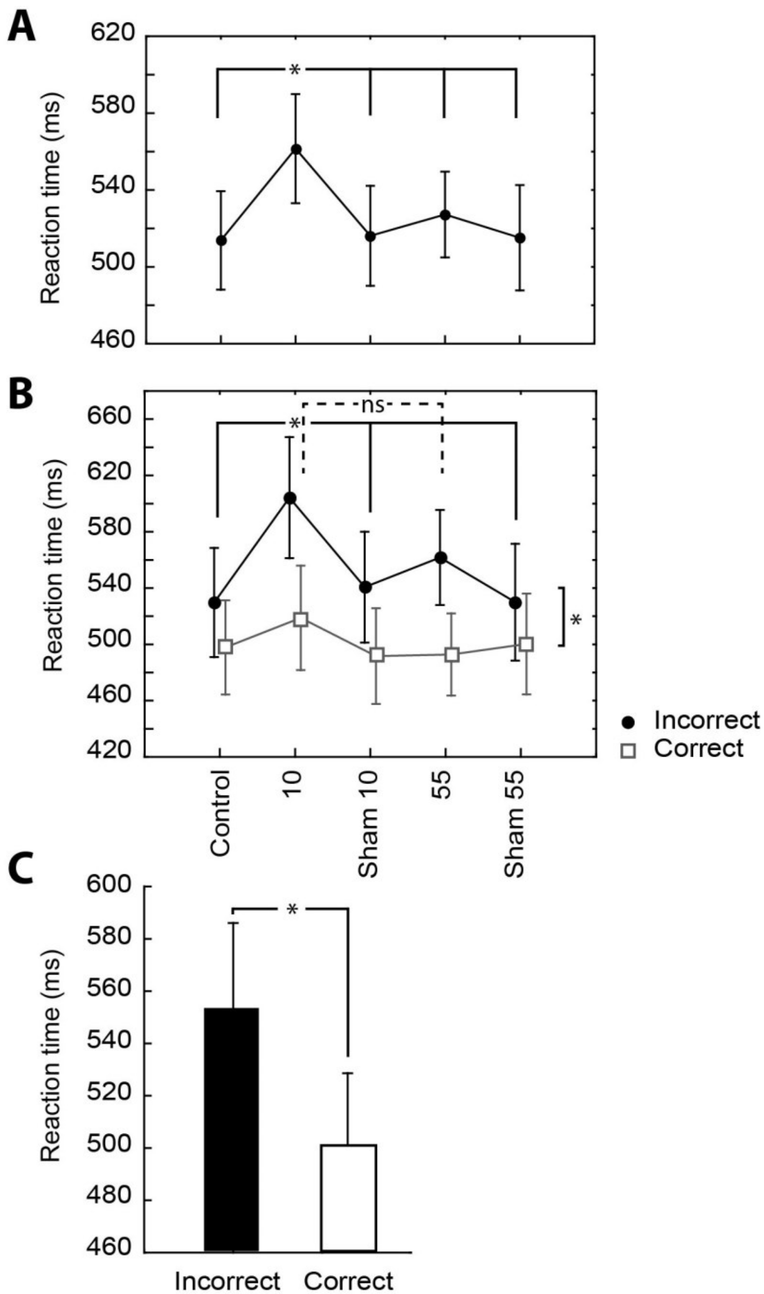

Figure 2. Reaction Time and Response Correctness. **A**. 10 Hz stimulation caused slower reaction times for the tone discrimination task. **B**. Reaction Time by Response Correctness interaction, incorrect responses were longer than correct responses. 10 Hz and 55 Hz stimulation caused slower reaction times for incorrect responses and 10 Hz stimulation caused slower reaction times for correct responses. **C**. Reaction times were slower in incorrect responses than in correct responses.

Postural performance

Performing in single or dual-task situation affected the overall postural performance for antero-posterior excursion ($F(1,318) = 4.4733$, $p < 0.05$), range ($F(1,318) = 13.107$, $p < 0.001$), maximum velocity ($F(1,318) = 12.446$, $p < 0.001$) and medio-lateral range ($F(1,318) = 4.9761$, $p < 0.05$). In most cases (except antero-posterior range) single-task performance had higher values (higher excursion and range, faster max velocity) compared to dual-task performance. There was an interaction of task level x posture condition for antero-posterior excursion ($F(2, 318) = 3.1024$, $p < 0.05$) and range ($F(2,318) = 5.6476$, $p < 0.01$).

We found a main effect of postural condition on most CoP variables, the exception being medio-lateral RMS. There was a main effect of postural condition on medio-lateral excursion ($F(2,318) = 94.9$, $p < 0.001$), range ($F(2,318) = 37.021$, $p < 0.001$), maximum velocity ($F(2,318) = 36.746$, $p < 0.001$), antero-posterior excursion ($F(2,318) = 603.46$, $p < 0.001$), range ($F(2,318) = 912.77$, $p < 0.001$), maximum velocity ($F(2,318) = 290.47$, $p < 0.001$) and RMS ($F(2,318) = 45.545$, $p<0.001$). In the SR postural condition, excursion, range, and maximum velocity (medio-lateral & antero-posterior), and antero-posterior RMS values were greater comparatively than in the EO and EC conditions. This was the true for all 5 different stimulation types (control, 10 Hz, 10 Hz sham, 55 Hz and 55 Hz sham), in both single and dual-task trials. The main effects and interactions associated with the postural conditions for excursion are illustrated in Fig. 3.

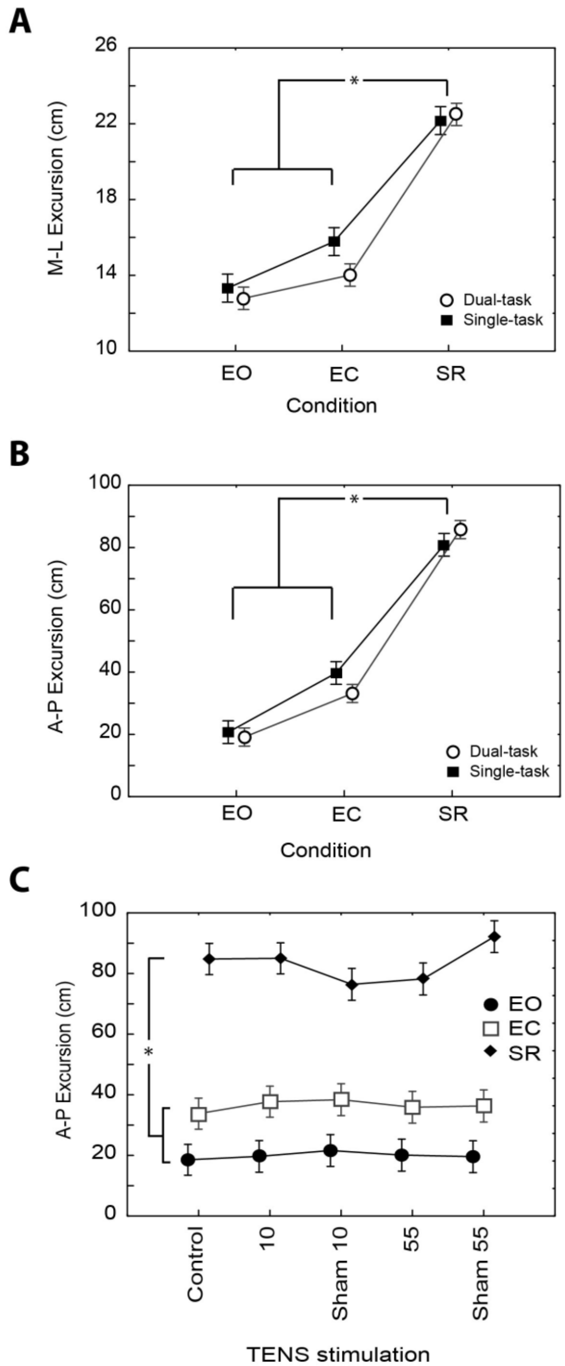

Figure 3. Effects and Interactions of Neurocom Condition on the Postural Task. **A**. Medio-Lateral excursion in a Task by Neurocom interaction, SR is significantly different to the other conditions in both single and dual task situations. **B**. Antero-Posterior excursion in a Task by Neurocom interaction, SR is significantly different to the other conditions in both single and dual task situations. **C**. Antero-posterior excursion in a TENS by Neurocom analysis. Excursion

during SR is significantly higher for all TENS conditions. Single and dual-task trials are combined for this analysis.

We also looked at the triple interaction (task level x stimulation type by postural condition), for medio-lateral excursion ($F(8,845) = 0.58$, $p = 0.79$), antero-posterior excursion ($F(8,845) = 0.76$, $p = 0.63$), range ($F(8,845) = 0.59$ $p = 0.79$) and maximum velocity ($F(8,845) = 1.04$, $p = 0.41$), RMS ($F(8,845) = 0.20$, $p = 0.99$). Though not significant, this shows a relative difference between the SR condition and the EO and EC conditions. This is shown in Fig. 4. The triple interactions for medio-lateral range, maximum velocity and RMS were not significant, for these variables the SR condition was not as prominently affected as in the antero-posterior variables of the same measures.

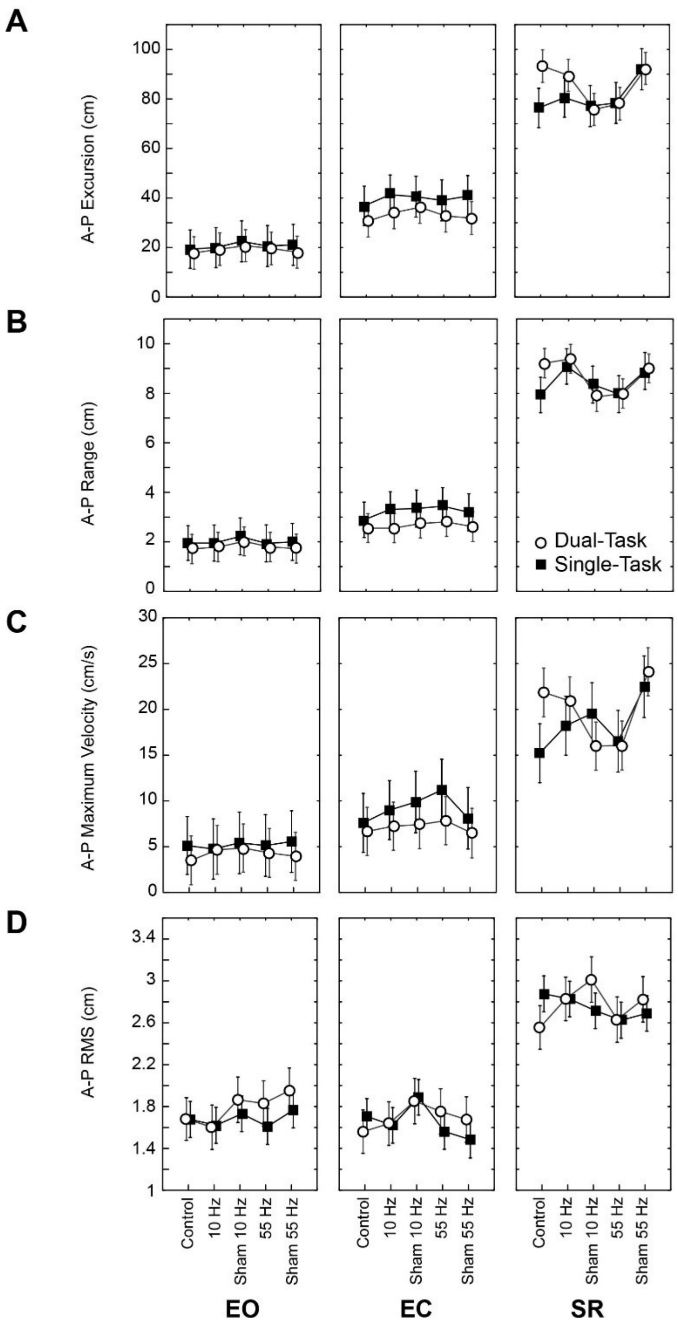

Figure 4. Trends of Postural Condition on the Postural Task. **A**. 3-way interaction of task TENS and Neurocom conditions on antero-posterior excursion. Excursion is increased in SR, and also has different trends than in EO and EC. **B**. 3-way interaction of task TENS and Neurocom conditions on antero-posterior range. Range is increased in SR, and also has different trends than in EO and EC. **C**. 3-way interaction of task, TENS and Neurocom conditions on antero-posterior maximum velocity. Maximum velocity is increased in SR, and also has different trends than in EO and EC. **D**. 3-way interaction of task, TENS and Neurocom conditions on antero-posterior RMS. RMS is increased in SR, but seems to follow a similar trend to EO and EC.

Discussion

This study aimed to determine whether rhythmic or non-rhythmic TENS at different frequencies could influence somatosensory afferent pathways and oscillatory integration mechanisms in a dual-task paradigm. More likely to affect the reaction time of the finger task as somatosensory TENS was embedded within its sensorimotor loop, we predicted a rhythm-specific effect on accuracy in judgment or in reaction time in our tone-discrimination task, and maybe even have a spillover effect on postural performance. We found that there was a specific effect of 10 Hz rhythmic TENS on the tone discrimination task. We will first address the lack of effect of TENS on postural variables, and then the frequency-specific interference in the tone discrimination task, likely by disturbing central resources and attentional allocation through oscillatory integrative mechanisms, likely due to a phase-specific asynchrony.

Dual-task effect on posture

Our hypothesis concerning the performance of the postural portion of our dual-task was that electrical stimulation of the median nerve in the arm would likely have no major effect on postural performance, as balance can be maintained as a priority in a dual-task context (Resch et al., 2011). In our case, upper-limb TENS stimulation had no effect on CoP measures such as excursion, velocity, range and RMS, which are commonly used in the assessment of postural stability(Palmieri et al., 2002). However, the single- vs. dual-task context showed an effect, as CoP measures in single-task showed more sway when compared to dual-task (antero-posterior excursion, range, maximum velocity and medio-lateral range), consistent with previous results showing that postural performance decreases when the focus of attention is posture (Jehu et al., 2015). The postural condition also showed an effect, where the EO and EC were similar, and the SR condition was the most destabilizing, regardless of TENS stimulation frequency. The SR condition provides the subject unreliable information for two sensory systems (somatosensory and visual), and likely then is more difficult than the other two conditions, involving removal of visual information (EC) or fully useful information (EO). We thus confirm that postural task difficulty has an effect on dual-task performance in healthy young adults (Plummer-D'Amato et al., 2012; Remaud et al., 2013). In our asymptomatic young subjects, overall postural performance was maintained at a high level throughout all trials, both in dual-task and single-task.

10-Hz stimulation during task performance disrupts information processing

Our findings show that reaction times are slowed by rhythmic alpha-range stimulation of afferent nerves, but not by rhythmic gamma frequency stimulation or dysrhythmic stimulation at the alpha and gamma frequencies. This is contrary to our initial hypothesis: instead of facilitating neural processing, this 10 Hz stimulation disrupted the information processing mechanisms, whether it be stimulus identification (sensory encoding or perceptual analysis), response selection or response programming. Physiologically, afferent stimulation in the alpha range could disrupt the natural balance of central alpha to gamma oscillations attributed to attention (Gonzalez Andino et al., 2005; Kühn et al., 2005; Ward, 2003). Since only rhythmic alpha stimulation caused lengthened reaction times, this rhythmic component appears key to time management in sensorimotor processing. Alpha band EEG power in higher level brain regions of the frontoparietal network decreases prior to visual, somatosensory and auditory stimuli detection with improved performance in a cognitive discrimination task (Haegens et al., 2011; Kayser et al., 2016; Leske et al., 2015). In our experiment alpha waves in the frontoparietal network are likely present and affected by alpha range TENS. Our study aimed to entrain the oscillations, using continuous TENS to boost rhythms to affect internal information processing mechanisms. This is a novel use of TENS, and represents a cost-effective and promising sensory intervention to affect performance. However, our results suggest that continuous entrainment is likely ineffective to enhance processing speed when handling multiple tasks. Different electrical stimulation period parameters may be more appropriate to achieve an improvement in reaction time performance. For example, prestimulation yielded improvements in cognitive task performance (Del Percio et al., 2007; Linkenkaer-Hansen et al., 2004; Ronconi et al., 2016; Zhou et al., 2014). Zhou et al. (2014) used transcranial direct stimulation (tDCS) over the left dorsolateral prefrontal cortex for a time period of 20 min immediately prior to a dual-task paradigm, improving performance in postural and cognitive tasks. Other studies implemented a prestimulus immediately prior to the detection of the task stimulus. Del Percio et al. (2007) used a 1-min flickering 10 Hz audiovisual stimulation immediately prior to the task performance; Linkenkaer-Hansen et al. (2004) used index finger electrical stimulation during a prestimulus oscillation window of 1 second (to the task stimulus not the electrical stimulation); Ronconi et al. (2016) used a 2 second rhythmic auditory stimulation immediately prior to rapid serial visual presentation (RSVP) task. In addition, performance enhancement has been shown in when alpha TMS is given in a manner coordinated with MEG-recorded alpha rhythms in the parietal lobe (Thut et al., 2011). These types of prestimulation seem effective at improving reaction time performance.

Moreover, predictable stimuli can induce faster reaction times (Stefanics et al., 2010), and entrain neural oscillations (Lakatos et al., 2008). In their study, Lakatos et al. (2008) presented macaque monkeys with rhythmic audio-visual stimulation requiring them to respond to either audio, visual or both stimulation signals. Neural oscillations that were in-phase with the attended rhythmic stimuli, be it audio, visual or both, were enhanced in processing, while those that were out-of-phase produced a decrease in processing efficiency. Continuous afferent alpha stimulation may disrupt this mechanism, by imposing an external rhythm out of phase with the natural alpha rhythm. Afferent stimulation could thus cause an artificial increase in alpha rhythmicity throughout the tone discrimination task, which could negatively affect performance prior to the stimulus detection. In addition, alpha and theta EEG activity are prominent in a perturbation recovery postural task (Mierau et al., 2017), showing that our externally imposed TENS rhythm might have fallen out of phase with this ongoing rhythm, affecting dual-task performance as well. The phenomenon of "rhythmic interference" has been demonstrated during stimulation using tACS coupled with EEG (Helfrich et al., 2014a; Helfrich et al., 2014b; Polanía, Nitsche, Korman, Batsikadze, & Paulus, 2012). Synchronized stimulation, in phase with neural oscillations, improved task performance; stimulation out of phase with neural oscillations was detrimental to task performance, for 6 Hz (Polanía et al., 2012), 10 Hz (Helfrich et al., 2014a) and 40 Hz (Helfrich et al., 2014b) stimulations. Our use of TENS to influence the afferent somatosensory pathway may have caused a similar effect of disruption as when stimulated out of phase. This could be solved by optimizing the timing of afferent stimulation to certain parts of the trials, as to phase-selectively excite the internal rhythms rather than merely boost alpha power. This phase specificity in processing is similar to what had been observed in active somatosensory sensing (Ahissar, Haidarliu, & Zacksenhouse, 1997; Ahissar & Assa, 2016), and it means active seeking rhythms might subserve improved neural processing and reaction time performance. In this context, an improvement of our paradigm would alter the timing of our stimulation and its phase adaptation with brain rhythms, most probably in sensorimotor areas; enhanced excitability linked with stimuli would lead to better stimulus detection rather than continuous electrical stimulation, which likely arrived in a relatively unadapted manner during execution of the reaction time task. The timing of stimulation would need to be timed with endogenous sensorimotor rhythms, and internal communication-through-coherence frequency carriers (Fries, 2015). We could then potentially take advantage of slow-rhythm plasticity mechanisms. In an optimal experiment, we could use EEG to identify the timing of the subjects' neural oscillations and match our stimulation time with phasic peaks of cortical activity (Johnson, Hamidi, & Postle, 2010; Veniero, Vossen, Gross, & Thut, 2015).

Rhythmic stimulation effects on attention and movement initiation

Electrical stimulation methods, such as tACS, can alter motor performance, targeting the primary motor cortex with rhythmic stimulation in beta (20 Hz) and/or gamma (70 Hz) ranges (Joundi et al., 2012; Moisa et al., 2016; Pogosyan, Gaynor, Eusebio, & Brown, 2009). These studies show a decrease in speed of movement initiation when beta stimulation is applied during task execution. Joundi et al. (2012) and Moisa et al. (2016) also found that gamma-band stimulation increased speed of movement initiation. We found a lengthening effect for reaction time that could relate to a change in movement initiation speed due to rhythmic stimulation in the alpha range.. A major difference, though, can be related to the specificity of stimulation focus, as our TENS using an afferent nerve likely stimulated a more widespread area than rTMS, tDCS, or tACS would. The path was likely from the afferent median nerve up to the cuneate nucleus, coursing up to the ventral posterior lateral nuclei of the thalamus, and landing in the primary and secondary sensory cortices (Gardner & Johnson, 2013). Of course, at each node we can expect divergence, with the effect of including the thalamic intralaminar nuclei (which are less specific and would cause more widespread transmission), and also affecting other sensorimotor areas concomitantly. Therefore, our afferent nerve stimulation in the alpha band may have also affected many areas in the frontal and parietal lobes in affecting movement initiation.

We also selected a dual-task paradigm to introduce a competition for attentional resources, where one of the two tasks included a reaction time (Ross et al., 2011). In this context, longer reaction times are produced, due to subjects' finite ability to allocate task-related attention (Pashler, 1994; Tombu & Jolicœur, 2003). The amount of attentional resources that can be used are finite at any given time; multiple models of attention could explain this, from single-channel filter theories, early- or late-filter theories, detailing a resource bottleneck during stimulus identification or response selection. Multiple resource theories, or flexible allocation of capacity theories, where there is a communal pool of resources for all tasks, could also help to explain this effect (Pashler, 1994). We have found that a flexible allocation of capacity lends itself well to our results, as our stimulation might have affected the allocated portion of attentional capacity: rhythmic TENS in the alpha range had a negative effect on the allocation of these finite resources. TENS stimulation at this frequency could impair the rhythm-controlled flexibility of the allocation algorithm of these resources, while much less likely have produced a change in task prioritization (Remaud et al., 2013), as participants were instructed to complete both tasks to the best of their abilities, with no specific focus on either task. However, the tone discrimination task requires more controlled processing while the postural task processing is more automatic (Schmidt & Lee, 2005). In our paradigm, the postural task can be performed with relatively less attention than the tone discrimination task, which requires perceptual processing, decision-making, and response selection for each tone pair. This may be affected differently in more demanding postural tasks. As attention has been related to brain rhythmicity in sensory and top-down monitoring regions (Engel, Fries, & Singer, 2001; Engel & Fries, 2010; Hummel & Gerloff, 2004), the passage from one task to the other could be based on neural resources that are controlled by intrinsic rhythmic networks; the rhythmicity we introduced could have decreased processing efficiency. Alpha-band EEG activity decreases preceding events, and natural rhythmicity can serve to translate vigilance into an optimal motor response (Breska & Deouell, 2017). Disturbing tactile 10-Hz rhythms would be especially deleterious to spatiotemporal mechanisms in the parietal lobe affecting perception and spreading further along the information processing networks (Takahashi & Kitazawa, 2017).

Conclusion: Use of afferent system stimulation to affect central rhythms

One of the limitations of the current protocol is that we did not measure electroencephalographic (EEG) activity during postural control. However, from a technical standpoint, measurement of standing and walking EEG still represents a challenge, due to the movement-related artefacts (Gramann et al., 2011; Gwin, Gramann, Makeig, & Ferris, 2011; Mierau et al., 2017), and as such, this was outside of the scope of the current study, but remains in the plans. Specific to our experimental design, we were also mindful of the capacity of TENS stimulation to generate bioelectric artefacts. On counterpoint, a strength of our study design is that we have used afferent nerve stimulation to probe central processing, potentially disturbing less central local circuits than by using centrally targeted rTMS, applied to specific nodes in the network. Apart from being more amenable to the study of sensorimotor behavior while standing on a force platform, this approach influences the dual-task processing by imposing an afferent rhythm to the sensorimotor networks, challenging the central processing "tempo" and timing for optimal sensory sampling. In addition, our protocol uses dual-task allocation, with a task requiring continuous sampling of the environment (the postural task), intermixed with one which has discrete events (responding to the tone discrimination demands). This information processing context links the continuous with the discontinuous, calling upon rhythmic sensorimotor loops, and a sampling-specific perceptual process (Ahissar et al., 1997; Ahissar & Assa, 2016). Afferent system rhythmic input modulation has not been overly studied, but it might have long-term benefits vs. disease. It has been successfully used in the context of rhythmic stimulation of the spinal cord in Parkinson's Disease (where network rhythmicity is pathophysiologically altered) (de Andrade et al., 2016; Fuentes et al., 2010; Fuentes et al., 2009; Santana et al., 2014), and some recent approaches focus on transcutaneous spinal cord stimulation (Ievins & Moritz, 2017). Here, we appropriated the low-cost (and well-used) TENS rhythmic stimulation techniques to probe the central networks in the standing human. Part of the value of such an approach partially resides in its portable, inobtrusive nature, but also in its capacity to probe the central sampling processes. Eventually, such an approach should be paired with ambulatory EEG techniques, in order to assess with precision of the effects on localized brain rhythms, event-related potentials, and multi-site coherence. In addition to promising value for Parkinson's Disease, it could also be eventually be used to address the pathophysiology of essential tremor (Popa et al., 2013; Raethjen & Deuschl, 2012), neuropsychiatric illnesses (Buzsaki & Watson, 2012), in "disrythmias" [(Llinas, Ribary, Jeanmonod, Kronberg, & Mitra, 1999; Schulman et al., 2011), including those related to chronic pain (Alshelh et al., 2016; Walton, Dubois, & Llinás, 2010), a usual condition for TENS stimulation] and other afflictions affecting brain rhythms [e.g., concussion (Barr, Prichep, Chabot, Powell, & McCrea, 2012)]. In essence, this paradigm appears to be promising in probing the sensorimotor vs. cognitive interface, and the underlying neural resources.

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CHAPTER 3: General Discussion

General Discussion

To recap, we found a main effect of TENS condition for reaction time, where 10 Hz rhythmic TENS caused longer reaction times. We also found that incorrect responses had longer reaction time than correct responses. This was also true for an interaction between response correctness and TENS condition, where 10 Hz and 55 Hz rhythmic TENS had longer reaction times in incorrect responses than sham conditions or no TENS. For postural measures we found a main effect of postural condition. The SR condition had increased measures or excursion, range, maximum velocity and antero-posterior RMS when compared to the EO and EC conditions. There was also an interaction of task and postural condition where values in single task were greater than dual-task values for antero-posterior excursion and maximum velocity. In the following section we will discuss the limitations of our experiment and future experiments that are related to it and could benefit the scientific community.

Limitations

The main limitation of our current research is the lack of EEG measures to verify the effect of our TENS protocol. EEG is a commonly used test used in research to investigate and verify brain activity with electrical stimulation (Johnson et al., 2010; Li et al., 2014; Salansky et al., 1998; Salansky & Fedotchev, 1994; Schindler et al., 2008; Thut et al., 2011; Veniero et al., 2015). Based on previous research it is plausible that TENS could help entrain neural oscillations at the rhythms stimulated (Li et al., 2014; Paus et al., 2001; Salansky & Fedotchev, 1994) but this is not confirmed in our study and we can only use reaction time to gauge effects on internal timing mechanisms. Our current results suggest that these neural oscillations are disrupted rather than aided by the stimulation. This could be due to the disruption of natural neural rhythms specifically in terms of alpha-band activity and temporal information processing (Breska & Deouell, 2017; Takahashi & Kitazawa, 2017). With the use of EEG, we could verify if and how neural oscillations were disrupted. Phase of stimulation is a factor that could be taken into account with regards to disruption of neural oscillations. This phase effect (rhythmic interference) has been displayed during stimulation using tACS coupled with EEG (Helfrich et al., 2014a; Helfrich et al., 2014b; Polanía et al., 2012). Stimulation in phase with neural oscillations increased performance while stimulation out of phase with neural oscillations impaired task performance. A visual representation of stimulation with phase is shown in Fig. 5.

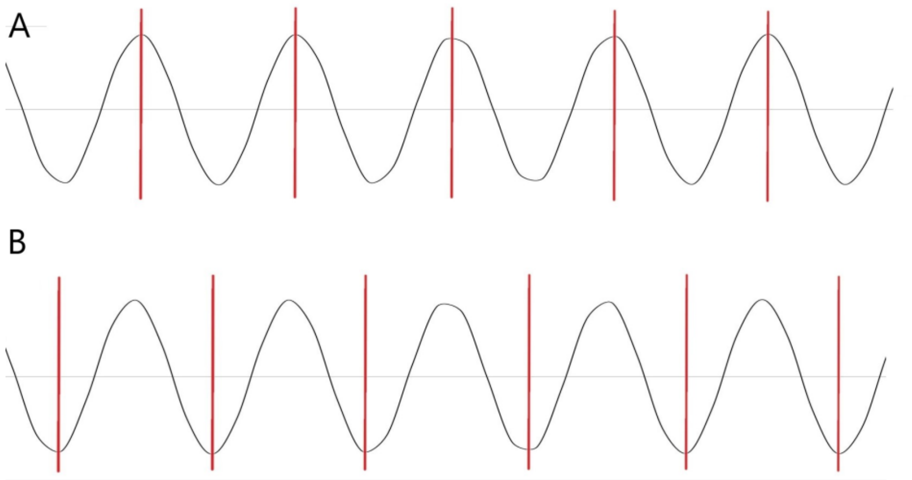

Figure 5. Stimulation phase representation. **A**. Stimulation in phase with neural oscillations, where the stimulation occurs at the peaks. **B**. Stimulation out of phase with neural oscillations, where the stimulation occurs at the troughs.

Initially an EEG pilot had been planned for this project. However due to time constraints and other complications this was not possible. The use of EEG to explore the effects of a similar TENS protocol is discussed further in the future experiments section.

A second limitation to this study was the exclusion on EMG data for analysis. EMG data was collected but due to large amount of artefact and time constraints for the completion of my master's thesis this data was not fully analyzed. This data could help us to identify any involvement of movement initiation with regards to choice reaction time. This would be done by identifying the time difference between EMG data and finger switch data. Therefore, allowing us to identify the effects of TENS stimulation on both of these and further differentiate the associated effects; though limited, the appendix includes a short section where select trials were analyzed in this way.

A third limitation of our study was the sample size. We had 12 participants (n=12) included within this study, however due to interpersonal variability in terms of reaction time and postural stability our data was not normally distributed. A larger sample size could potentially have helped to solve this problem; however, it is unclear how many more participants would be needed to properly achieve this goal.

Future Experiments

Using the current experiments data two interesting sets of analyses could be done. First, we could analyze EMG data to determine if EMG reaction times and Finger Switch reaction times differed. This would further allow us to discover whether movement initiation was affected by our TENS procedure. As mentioned previously a limited version of this analysis is provided in the appendix. The second analysis would be to compare postural position on the platform with reaction time performance. This would give us a better idea of the effect of our postural task in terms of attentional allocation, as we might be able to correlate reaction time improvements or deficits in relation to postural position and/or sway. Future experiments could also encompass other lines of research not explored in the scope of our current experiment.

One such line of research to be explored is a pathological population, for example traumatic brain injury (TBI). TBI is a pathology that can affect both postural stability and cognition. For example, individuals with TBI have slower reaction times up to six weeks after their injury when compared to a healthy population (MacFlynn et al., 1984). One type of TBI is a concussion. Concussions are defined as: "[...] a complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces" (McCrory et al., 2009). Amongst other deficits, individuals affected by a concussion have impairments in postural stability (Guskiewicz et al., 1996) as well as abnormal brain electrical activity (Barr et al., 2012).

Individuals with TBI are even more challenged in a dual-task situation. In the case where one of the tasks is to maintain the steadiest balance possible, and the other task is a reaction time task, the subject needs to choose the proper allocation of resources to each task, namely attentional resources. Individuals with TBI seem to prioritize balance over cognitive performance; when they have a better postural stability their reaction times are slower (Catena et al., 2011). Prioritization of postural stability in the allocation of attention has also been reported for a healthy population; in this case, balance was maintained during a dual-task situation, while reaction times were lengthened (Resch et al., 2011). This prioritization could be a safety mechanism to prevent falls when the posture control mechanisms are challenged. This attentional shift is influenced by the difficulty of the cognitive task (Plummer-D'Amato et al., 2012). It is plausible that dual-task training could also aid individuals with TBI to recover postural stability. This type of training has been shown to be effective in helping elderly persons, another population that has deficits in reaction time and postural stability (Li et al., 2010).

TBI is an excellent example of a pathological population that could benefit from dual-task training or even an electrical stimulation paradigm. A future experiment would be to explore the effects of such a paradigm on a population with deficits in reaction time and internal timing mechanisms. It is possible that though not very effective in a healthy young population, where internal timing mechanisms are normal, electrical stimulation could be beneficial in a population where neural oscillations and internal timing mechanisms are impaired such as in TBI (Roche et al., 2004).

One further experiment would be to investigate the use of our TENS and dual-task paradigm with EEG. EEG with our current task would, however, come with some complications. The movement related artefact from standing and moving (Gramann et al., 2011; Mierau et al., 2017) involved with our dual-task paradigm would cause difficulty in analyses of EEG results. Using the tone discrimination task at rest in conjunction with EEG would be more effective in helping to identify the role of TENS stimulation on neural oscillations. Optimally several frequency ranges could be tested. This would be useful in confirming that TENS stimulation of an afferent nerve can entrain neural oscillations at different frequencies as well as helping to stipulate which ranges of stimulation are beneficial or disruptive to natural neural oscillatory rhythms. Studies using EEG with TENS have been previously done (Li et al., 2014; Salansky & Fedotchev, 1994) but not with a cognitive task. Other types of stimulation have been used to investigate this type of effect for example Zhou et al. 2014 who used tDCS in a similar manner. It would be interesting to view the effects of a protocol involving TENS with a cognitive task using EEG measures.

Conclusion

To conclude our study found that the use of rhythmic TENS stimulation had an effect on internal timing mechanisms when applied during a dual task paradigm. The effect was performance impairment in regards to reaction time. We believe this to be due to the disruption of the normal rhythms of internal timing mechanisms associated with attentional resource management. Further research of this effect is necessary to determine the exact cause of performance impairment and leads us to believe that an adjustment of the stimulation type or timing could yield performance enhancing effects.

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Appendix

The following appendix contains:

- Table 1 (describes the order of trial randomization to further describe the methodology)
- Preliminary analysis of EMG data and statistics.

Task	TENS	Trial Block 1	Trial Block 2	Trial Block 3
Dual-task	10 Hz (Sham)	SR	EO	EC
		EC	EC	EO
		EO	SR	SR
Dual-task	Control	EC	EO	EO
		SR	EC	SR
		EO	SR	EC
Single-task (posture)	55 Hz (Sham)	EC	EC	
		EO	SR	
		SR	EO	
Single-task (tone)	10 Hz	Trial 1	Trial 2	Trial 3
Dual-task	55 Hz	SR	EO	SR
		EO	SR	EO
		EC	EC	EC
Single-task (posture)	10 Hz	EC	EC	
		EO	EO	
		SR	SR	
Single-task (posture)	10 Hz (Sham)	SR	EO	
		EC	SR	
		EO	EC	
Dual-task	10 Hz	EO	EO	EC
		EC	SR	EO
		SR	EC	SR
Single-task (tone)	Control	Trial 1	Trial 2	Trial 3
Single-task (posture)	Control	EO	EO	
		SR	EC	
		EC	SR	
Single-task (tone)	10 Hz (Sham)	Trial 1	Trial 2	Trial 3
Dual-task	55 Hz (Sham)	EO	EO	EC
		EC	SR	EO
		SR	EC	SR
Single-task (posture)	55 Hz	SR	EO	
		EC	EC	
		EO	SR	
Single-task (tone)	55 Hz	Trial 1	Trial 2	Trial 3
Single-task (tone)	55 Hz (Sham)	Trial 1	Trial 2	Trial 3

Table 1 Trial order example. Trial blocks (for dual-task and single-task posture) consisted of 1 trial of each postural condition: EO, EC and SR for a total of 3 trials per trial block. Table was completed from left to right (in dual-task and single-task posture, all three postural conditions of a trial block were completed before moving to the next trial block). The order of performance was randomized for columns of: task (dual-task, single-task posture and single-task tone discrimination), TENS condition (control, 10 Hz, 55 Hz, 10 Hz sham and 55 Hz sham) as well as at trial blocks 1,2 and 3 (randomized in dual-task and single-task posture at each trial block for postural conditions: EO, EC, SR).

Note: This is an example of the trial order for a participant; all participants had different trial orders (randomized as described above).

EMG data:

Electromyogram data was collected for the *extensor digitorum* and *flexor digitorum* muscles of the forearm to determine when movement was initiated. In the following section I will provide limited preliminary analyses of EMG data. This includes data from the results of 515 matched reaction times from 27 trials of 3 participants. EMG data was filtered using a 10 – 350 Hz butterworth zero-lag filter. We first calculated a baseline threshold (mean + 2 standard deviation) on a 100 – 200 ms window before the 2nd audio tone of each pair in the filtered signal. To identify EMG burst onsets, we found the time where a 25 ms window envelope surpassed the baseline threshold and then starting from that point we identified when a 5 ms window envelope surpassed the threshold and designated that time point as the EMG burst onset (Figure 6). Data was analyzed by dependent samples t-tests comparing EMG reaction times to finger-switch reaction times. This was done by comparing the timing of EMG burst onsets to their corresponding finger-switch presses (Figure 7).

Results:

There was a significant difference between EMG reaction time and finger switch reaction time $t(514) = 52.78$, $p<0.05$ with an average difference of 53 ms +/- 23 ms. All EMG reaction times were shorter than finger-switch reaction times.

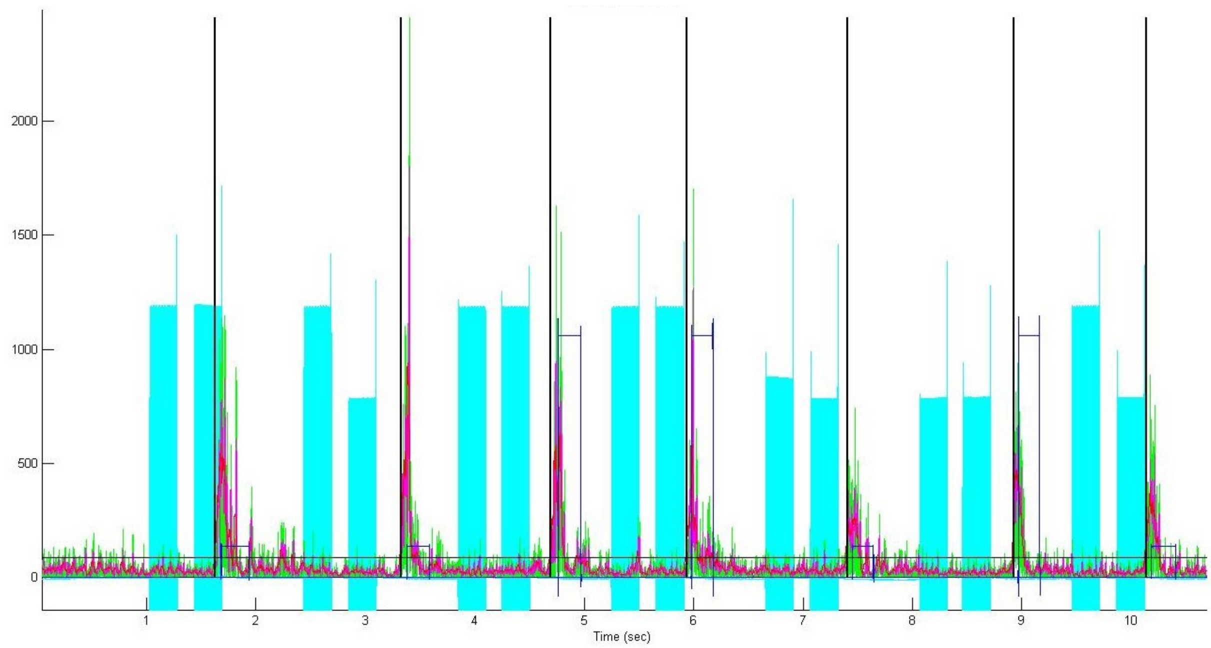

Figure 6 EMG Sample Data. The vertical axis displays EMG amplitude. This figure includes tones (cyan), finger-switches (blue), filtered EMG (green), EMG with a 25 ms envelope (red), and EMG with a 5 ms envelope (pink). Black vertical lines before EMG bursts denote EMG onset for the task.

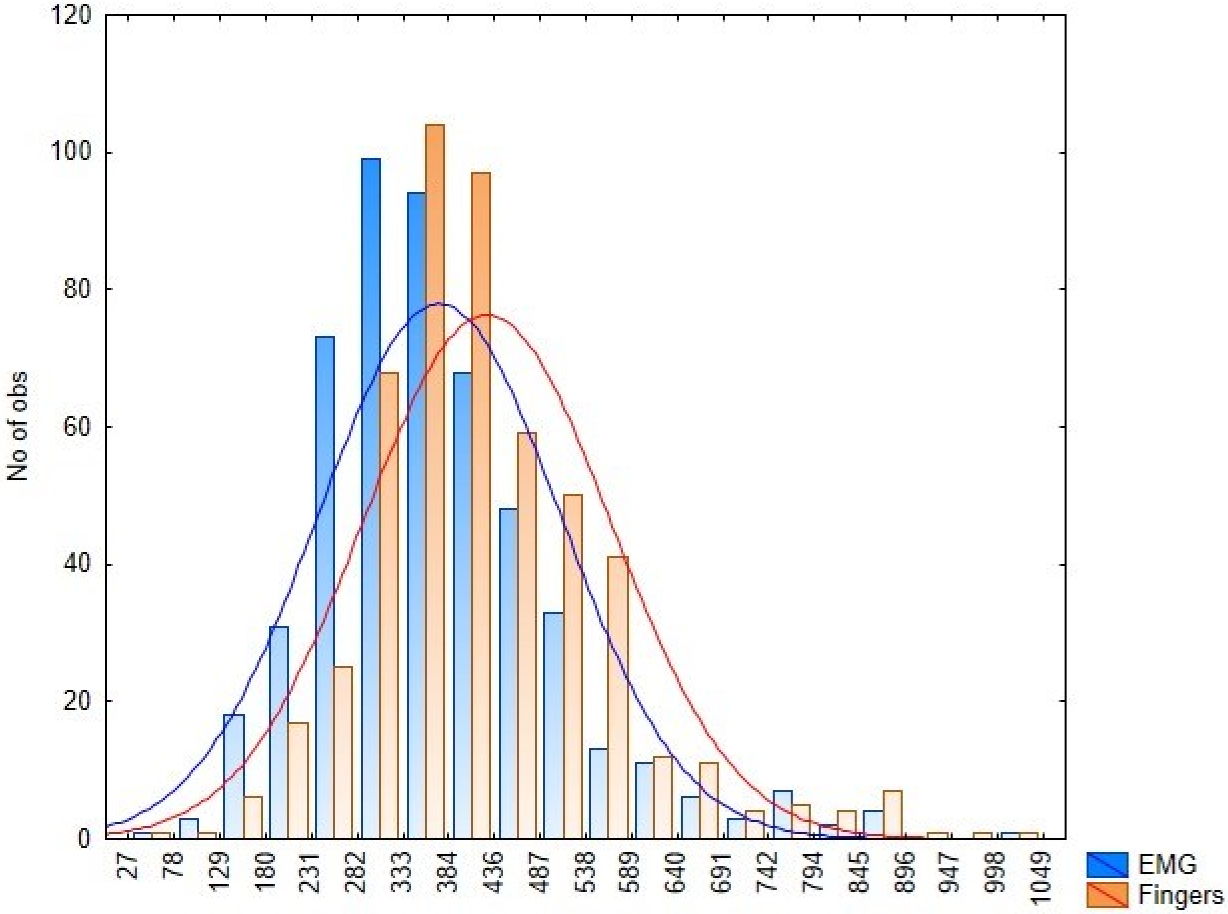

Figure 7 Reaction Time Comparison Histogram. Here we present a frequency distribution histogram of both EMG and finger-switch reaction times with associated lines of normal fit. The horizontal axis displays reaction time in seconds. All reaction times are matched with dependent samples.