UNDERSTANDING OCCIPITOPARIETAL ALPHA OSCILLATIONS AND ENHANCING SUSTAINED ATTENTION USING ELECTROENCEPHALOGRAPHY AND TRANSCRANIAL ALTERNATING CURRENT STIMULATION

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ACKNOWLEDGEMENTS

I would first like to thank the Defence Science and Technology Laboratory (DSTL), which provided funding for this PhD. In particular, I express my gratitude to Dr. Annalise Whittaker from DTSL for her constant help throughout this project. Secondly, I would like to thank the Department of Experimental Psychology, and my two supervisors: Prof. Roi Cohen Kadosh and Prof. Nick Yeung. The immense support and trust that was given to me during my time at Oxford made the completion of this PhD an absolute pleasure. Lastly, I would like to express my gratitude to the city and university of Oxford. The opportunity to spend four years in such a beautiful and engaging place has been one of the greatest privileges of my life. The memories I have made here, of engaging conversations with fellow researchers, of dream-like walks around the historic architecture of the city, and of weekend rambles in the lush countryside that surrounds it, will no doubt stay with me for many years to come.

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January 2018, Oxford

RATIONALE AND PRIMARY AIMS

People are often required to perform monotonous tasks for long periods. Under such conditions, attention commonly deteriorates over time, causing impairments in performance of critical tasks (Mackworth, 1956). It is therefore imperative that researchers develop effective methods for identifying and preventing attentional deteriorations before they occur.

Such impairments in attention are commonly accompanied by changes in the amplitudes of electroencephalographic (EEG) activity in different frequency bands (Clayton, Yeung, & Cohen Kadosh, 2015). Perhaps most notably, reductions in visual concentration are associated with increases in the amplitude (or 'power') of alpha oscillations (defined as 7 – 13 Hz activity recorded maximally over occipitoparietal cortex) (Foxe & Snyder, 2011; O'Connell et al., 2009). However, in contrast to such findings, alpha oscillations have also been associated positively with a range of neurocognitive processes that appear central to sustained attention (e.g. top-down control and perceptual stability; Clayton, Yeung, & Cohen Kadosh, 2017). I therefore predicted at the beginning of this project that, if one could experimentally manipulate EEG alpha power, it should be possible to bring about significant modulations of visual attention task performance.

It has been reported previously that such experimental manipulation of neural oscillations can be achieved using rhythmic, non-invasive brain stimulation. For example, transcranial alternating current stimulation, which involves application of oscillating electrical fields to the brain, has been found enhance occipitoparietal alpha power when delivered over posterior cortex at ~10 Hz (alpha-tACS; Helfrich et al., 2014; Neuling, Rach, & Herrmann, 2013). This form of stimulation has also been found to exert reliable effects on cognitive task performance (e.g. Kar & Krekelberg, 2014; Müller, Vellage,

Heinze, & Zaehle, 2015). I therefore chose to deliver tACS across the experiments of this project, at various frequencies during the performance of sustained attention tasks. The central purpose of these experiments was to determine whether tACS would influence sustained attention task performance. However, given the previously mentioned variability with which alpha oscillations have been found to covary with processes of visual attention, I also hoped that manipulating alpha power with tACS would allow me to better understand the causal involvement of alpha oscillations in visual attention.

ABSTRACT

This project studied the effects of 10-Hz (alpha)-tACS, delivered over occipitoparietal cortex, on sustained attention. Poor performance on all visual tasks used in this project had previously been associated with increased EEG alpha power. I therefore assumed that alpha-tACS would reliably impair visual task performance. However, my results did not support this prediction. In my first two experiments (Chapters 4 & 5), alpha-tACS was found to reduce the slope of deteriorations in task performance that otherwise occurred during control-tACS (i.e. sham- and 50-Hz-tACS). In my third experiment, an auditory control task indicated that such effects are specific to the visual domain (Chapter 6). Furthermore, in a fourth experiment, in which tACS was delivered during a visual task where performance naturally *improved* over time, alpha-tACS was conversely found to limit the slope of such improvements (Chapter 7). Therefore, regardless of whether task performance improved or deteriorated naturally over time, alpha-tACS seemed to exert a consistently stabilising effect on visual attention. I tested this hypothesis in my fifth experiment, in which alpha-tACS was delivered during an audiovisual switching task. I assumed that, if alpha-tACS stabilises visual attention, this stimulation should impair switching between visual tasks, but leave switching from visual to auditory tasks unaffected. In contrast to this prediction, alpha-tACS was not found to influence visuovisual vs. audiovisual switching. However, alpha-tACS was found to exert a trend-level, impairing effect on visuoauditory switching accuracy, suggesting that this stimulation may help to focus visual attention by preventing transitions of attention away from the visual domain (Chapter 8). A final experiment indicated that 4-Hz-tACS exerts weak, but descriptively similarly effects on visual task performance to those observed during alpha-tACS in my first two experiments (Chapter 9). Throughout these studies, tACS was found to have highly variable and inconsistent effects on EEG power. Overall, these results provide intriguing evidence to suggest that low-frequency tACS can be used to stabilise performance on a range of visual attention tasks. However, the usefulness of

tACS for purposes of cognitive enhancement in real-world settings may be limited by the small magnitudes of its influence on both brain activity and behaviour.

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LIST OF COMMON ABBREVIATIONS

aCTET	Auditory Continuous Temporal Expectancy Task
EEG	Electroencephalography
ERP	Event-related potential
tACS	Transcranial Alternating Current Stimulation
tES	Transcranial Electrical Stimulation
vCTET	Visual Continuous Temporal Expectancy Task

CHAPTER 1 – SUSTAINED ATTENTION

Sustained attention, defined as the endogenous maintenance of cognitive focus for an extended period of time under non-arousing conditions (Roberton & Garavan, 2004), is of crucial importance in the modern world. Nevertheless, we struggle to maintain our attention, often with grave consequences. Fatigued clinicians commit medical errors (Taylor-Phillips et al., 2014), inattentive lifeguards permit drownings (Schwebel, Lindsay, & Simpson, 2007), and unfocused train drivers cause major collisions by ignoring stop signals (Edkins & Pollock, 1997). Furthermore, the causes of such lapses in attention are only partially understood.

In one of the earliest studies on sustained attention, Mackworth (1956) showed that participant errors on attentionally demanding tasks increase significantly following prolonged task performance (i.e. > 30 minutes). Often referred to as the *vigilance decrement*, this cognitive decline has since been widely replicated across a range of tasks (e.g. Basner & Rubinstein, 2011; Helton et al., 2005; Wascher et al., 2014). However, only a few interventions have been shown to reliably limit the extent of these declines. Some of the most effective interventions include administration of pharmacological agents like caffeine, amphetamines, and methylphenidate (Koelega, 1993). Unfortunately, such treatments can cause negative side effects and physiological damage with repeated use. Consequently, the development of safer and more effective alternatives is clearly needed. It is assumed in this thesis that the development of such alternatives will come through improved neuroscientific understanding of sustained attention.

In this chapter, I give an overview of current research on this topic. I first review the different experimental tasks and measures used to study sustained attention. I then describe some of the factors known to influence the stability of attention (i.e. both within-

and between-subjects factors), as well as the different psychological theories about why sustained attention deteriorates over time. I finish by discussing the neural systems that are thought to play important roles in sustained attention. I focus first on the different brain regions and networks that have been suggested to facilitate the different constituent processes of sustained attention. I then discuss the possible roles played by cortical oscillations in these constituent processes.

EXPERIMENTAL PARADIGMS OF SUSTAINED ATTENTION

Sustained attention is a psychological concept that most people have some understanding of from their own experience. Most of us can remember times when we have had to focus our attention on boring subjects for long periods of time. However, from the perspective of academic research, sustained attention can only be studied and understood by measuring performance on specific, cognitive tasks. In this section, I review the different varieties of cognitive tasks used for this purpose. For each variety, I give a brief description of their defining features, as well as their fundamental strengths and weaknesses.

Rare responding tasks

The traditional way of studying sustained attention is to measure participant responses (e.g. reaction times and error rates) to infrequent and temporally unpredictable signals over extended periods of time (see p.19). In some paradigms, subjects are asked to respond to targets that are presented only sparsely and between long intervals of stimulus-absence. Consequently, subjects must remain consistently vigilant throughout the task despite receiving no intermittent sensory input. One example of these kinds of ‘vigilance tasks’ is the 'Psychomotor Vigilance Task' (Dinges & Powell, 1985). Here, participants are required to maintain focus on a blank screen and respond as quickly as possible to randomly timed visual events. In contrast, it is also common for

sustained attention paradigms to display stimuli *continuously* over the course of a task, but with the instruction that participants respond only to a rare and specific subset (i.e. 'targets'), and not to the rest (i.e. 'non-targets'). In other words, participants have to make a decision about the higher-level features (rather than just the presence) of stimulus on every trial. A classic example of this kind of paradigm is the 'Continuous Performance Task' (Rosvold, Mirsky, Sarason, Bransome, & Beck, 1956). This task has many variants but generally requires subjects to monitor long and random sequences of stimuli (e.g. letters, or numbers) for the occurrence of predefined targets (e.g. 'X', or '3'). Another example is the 'Continuous Temporal Expectancy Task' (O'Connell et al., 2009), in which subjects are presented with a continuous stream of images. ~90% of these images are presented for 800 ms, while the other ~10% are presented for a longer period of time. Subjects are required to press a button whenever they notice that one of these longer images has been presented.

Key strengths of these 'rare responding tasks' are their capacity to induce performance decrements when performed for long periods (e.g. Ballard, 2001), as well as their good test-retest reliability in healthy individuals (Cornblatt, Risch, Faris, Friedman, & Erlenmeyer-Kimling, 1988; Hahn et al., 2014). They also have high ecological validity, given the common importance of monitoring for infrequent targets in many real world tasks that require sustained attention (e.g. checking luggage scans for rare weapons). Of relevance to this point is the finding that performance on the Psychomotor Vigilance Task can predict fatigue related declines on a simulated airport luggage-screening task (Basner & Rubinstein, 2011). Nevertheless, rare responding tasks do suffer from some clear weaknesses.

These tasks must generally be performed for long periods of time to induce performance deteriorations. Paradigms like the Continuous Performance Task can even suffer from floor effects in error rates of healthy adults (e.g. Aman, Vamos, & Werry,

1984; Ballard, 2001; Kahn et al., 2012). In other words, participants often do not make large numbers of errors on these tasks. To counter this problem, researchers have tried to make these tasks harder. For example, versions of the Continuous Performance Task have been used in which targets are redefined as specific sequences of stimuli rather than single events (e.g. 'X's followed by 'A'; Ballard, 2001). Due to their increased difficulty, these tasks are less prone to floor effects than simpler paradigms (Kahn et al., 2012). However, they inevitably make significant demands of working memory resources *in addition* to sustained attention. They therefore complicate efforts to study sustained attention in isolation. In addition though, perhaps the most significant limitation of rare responding tasks is that they sample subject behaviour only infrequently and therefore do not facilitate analysis of moment-to-moment fluctuations in vigilance, or an understanding of the frequencies at which these fluctuations occur (Robertson, Manly, Andrade, Baddeley, & Yiend, 1997).

Rare inhibiting tasks

In contrast to this last weakness of rare responding tasks, a number of paradigms have been designed that sample subject behaviour much more frequently. I refer to these as '*rare inhibiting tasks*'. Rapid sampling of behaviour is achieved with these tasks by requiring participants to respond to all stimuli *except* rare targets (in contrast to responding exclusively to targets). This leads to repetitive participant responding that rapidly becomes mindless and, in theory, increases the likelihood that participants will fail to inhibit their responding to targets (Robertson et al., 1997). Such lapses are known as ‘commission errors’. A classic example of a rare inhibiting task is the '*Sustained Attention to Response Task*' (SART: Robertson et al., 1997), which requires subjects to respond to all stimuli in long stream (e.g. letters, or numbers) other than a specific subset (e.g. 'X', or '3').

The improved temporal resolution of rare inhibiting tasks has enabled researchers to study the behavioural predictors of lapses in attention (e.g. reaction time variability; see p.21) Rare inhibiting tasks can also induce vigilance decrements when performed for sufficiently long periods of time (Grier et al., 2003; Helton et al., 2005) and can lead to fluctuations in performance in shorter forms (~10 minutes). This has allowed for neuroimaging analysis of 'on' vs. 'off' task epochs (i.e. periods of good vs. bad sustained attention; Esterman, Noonan, Rosenberg, & Degutis, 2013; O'Connor, Manly, Robertson, Hevenor, & Levine, 2004). More generally though, rare inhibiting tasks have decent test-retest reliability (intraclass-correlation coefficient for RTs and error rates of 0.72; Soreni, Crosbie, Ickowicz, & Schachar, 2009), and have received good external validation. Performance on the SART correlates with self-reports of attentional and cognitive failures in everyday life (Robertson et al., 1997; Smilek, Carriere, & Cheyne, 2010). Nevertheless, rare inhibiting tasks again suffer from some key weaknesses.

For example, similar to simple rare inhibiting tasks, rare inhibiting tasks tend not to cause overall deteriorations in attention when performed for brief periods. Improvements in SART performance over time have even been reported (Helton, Kern, & Walker, 2009). This makes it difficult to determine whether such short tasks are good experimental analogues of real world situations (in which declines are prevalent). It is important to note that a version of the SART, called the '*Gradual Onset Continuous Performance Task*' (gradCPT; Rosenberg, Noonan, DeGutis, & Esterman, 2013) has been suggested to alleviate this problem. In this task, transitions between stimuli are gradual rather than abrupt, and thus naturally grab attention to a lesser extent. However, even ignoring this issue, rare inhibiting tasks also suffer from the more unique problem that it is unclear to what extent they assess response control in addition to sustained attention. For example, when participants are questioned about the causes of their commission errors, they commonly blame a failure of motor control (or an 'errant hand') rather than lapses of attention (Cheyne, Carriere, & Smilek, 2009). Furthermore, speed-

accuracy trade-offs have been reported to have a significant influence on SART performance, with commission errors increasing with faster response times (Seli, Jonker, Cheyne, & Smilek, 2013). This suggests that errors on rare inhibiting tasks may better reflect changes in motor impulsivity and inhibition than sustained attention.

Continuous responding tasks

Sustained attention can also be studied using tasks that require responses on every trial, regardless of stimulus features or identities. I refer to these tasks as 'continuous responding tasks'. One of example of this paradigm is the rapid serial visual presentation (RSPV) task used by J. S. Macdonald, Mathan, and Yeung (2011). Each trial of this task consists of the presentation of a rapid (10 Hz) stream of white noise images in which an embedded target image is briefly presented on 50% of trials. Following each of these stimulus streams, participants have to report whether they saw the target, as well as their confidence in this judgement. In the study by J. S. Macdonald et al. (2011), participants were required to perform this task repeatedly for a long period of time (i.e. > 25 minutes). This allowed for the analysis of slow fluctuations in error rates and task focus. Another example of a continuous responding paradigm is the task used by Wascher et al. (2014). Here, participants were presented on each trial with two peripheral bars. One of these bars quickly changed colour following its presentation and participants were required to classify this colour change with either a left or right button press (for red vs. blue changes). This means that, on some trials (known as 'incongruent trials'), participants had to respond to left-side bars with their right hand, or vice versa (which has been shown to tax cognitive control processes; e.g. X. Liu, Banich, Jacobson, & Tanabe, 2004). Again, this task requires continuous focus for an extended period, allowing for the assessment of declines and fluctuations in attention through the analysis of task accuracy and response times.

As with all previously described tasks, continuous responding tasks lead to vigilance decrements over time when performed for long periods. Furthermore, as they require continuous responding from participants (in a similar fashion to rare inhibiting tasks), they again enable analysis of fluctuations in sustained attention with decent temporal resolution. However, they also have a more unique advantage. On tasks in which targets are rare, vigilance decrements over time can be driven simply by participants understanding that targets are presented rarely. This leads them to develop a growing preference for not responding with increasing time on task, otherwise known as a 'conservative response bias' (see p.22). However, as the probability of a specific categorisation response being correct (e.g. target present vs. absent) is 50% on the previously described, continuous responding tasks, it seems unlikely that participants performing these tasks would develop such a preference for one response over another. As a result, fluctuations in performance on continuous responding tasks, in comparison to fluctuations on both rare responding and inhibiting tasks, may be less likely to reflect changes in response strategy and more likely to reflect true variations in sustained attention.

THE BEHAVIOURAL MEASURES OF SUSTAINED ATTENTION

The previous section focused on the different cognitive tasks used to study sustained attention. However, performance of these tasks can be assessed using a number of different measures (e.g. task errors, reaction times, self-reports of attentional focus). In this section, I review the strengths and weaknesses of each of these measures for the purpose of studying sustained attention.

Errors

Changes in sustained attention over time have perhaps been most commonly measured as changes in either the total number or proportion of errors committed by an

individual within a specific window of time. These errors are defined primarily as 'omission errors' (i.e. failing to respond to targets), or 'commission errors' (i.e. failing to inhibit responses to targets). In support of the validity of this measure, error rates are often reported to increase with time on task in both rare responding and inhibiting tasks of sufficiently extended duration. Furthermore, given that efforts to improve sustained attention can perhaps be best characterised as attempts to limit human error during extended cognitive performance, this measure could be argued to be the most appropriate in applied vigilance research. Nevertheless, error rates do suffer from the important weakness that they are largely uninformative on tasks where performance is very good. For example, on simple versions of the Continuous Performance Task, floor effects are commonly observed in the error rates of healthy adults (Helton et al., 2009). This makes it difficult to assess subtle intra- or inter-subject variations in sustained attention.

Reaction times

An alternative measure is reaction times (RTs). RTs have the advantage of not suffering from floor effects, but still rising in parallel with error rates with increasing time on task (e.g. Lieberman, Coffey, & Kobrick, 1998). RTs are often slowed in patients with traumatic brain injury (Rosvold et al., 1956) and schizophrenia (Lenzenweger, 2001), which are both clinical populations known to suffer from impaired sustained attention. RTs have also been shown to be negatively related vigilance levels, determined using EEG (Minkwitz et al., 2011). It could therefore be argued that, like error rates, RTs are negatively related to vigilance. However, this position has not been consistently supported, with rapid rather than slow RTs also being associated with increased error rates in both rare responding (Halperin et al., 1988) and rare inhibiting tasks (Seli et al., 2013). This could be explained by RTs being the product of multiple independent cognitive processes. For example, it has been suggested that the relationship between

fast reaction times and error rates may reflect motor hyperactivity and impulsivity more than inattention (Halperin et al., 1988). However, even ignoring this issue, RTs can additionally be argued to be a poor measure of attention for the purely statistical reason that they are often positively skewed rather than normally distributed (Leth-Steensen, Elbaz, & Douglas, 2000). This means that the central tendency measure (or mean RT) will often only coarsely summarise true RT distributions.

Reaction time variability

A different approach is to focus instead on the variability of RTs – particularly in the case of rare inhibiting tasks in which a wealth of RT data is collected. Supporting its validity as a measure of sustained attention, RT variability has been reported to rise with error rates with increasing time on task (Rosenberg et al., 2013). RT variability is also commonly increased in patients with traumatic brain injury (Segalowitz, Dywan, & Unsal, 1997), ADHD (Castellanos et al., 2005), and focal frontal damage (Stuss, Murphy, Binns, & Alexander, 2003) (although see Molenberghs et al., 2009). Furthermore, RT variability can predict subjective reports of attentional focus (Bastian & Sackur, 2013) and has been used to divide gradCPT task performance into error-prone 'off-' and less error-prone 'on-task' epochs. Specifically, periods of low RT variability were associated with reduced task errors (Esterman et al., 2013). Overall then, RT variability appears to be decent measure of sustained attention, allowing valid assessment with good temporal resolution. However, as RT variability can only be calculated from performance on tasks with near-continuous subject responding, this measure suffers from the limitations of both rare inhibit and continuous responding tasks (see p.16 & 18). It is also important to note that RT variability can be calculated in a number of ways (e.g. standard deviation, coefficient of variation), with each having different reliabilities and exhibiting different relationships with other performance measures (Flehmig, Steinborn, Langner, Scholz, & Westhoff, 2007).

Sensitivity (d') and Response Bias (ß)

Moving back to the discussion of error rates, there is an implicit assumption that variations in error rates during a vigilance task reflect general changes in the attentional focus of an individual. However, according to signal detection theory, the performance of an individual on such a task can be described using two separate parameters: 1) their capacity to detect the occurrence of targets (known as 'sensitivity'; d'), and 2) their likelihood of responding to a target when it is presented (known as 'response bias'; *ß*) (Macmillan & Creelman, 1991). Changes in either parameter can influence overall task performance. Of course, if a person becomes less sensitive to target stimuli, their task performance will suffer. However, as shown in Figure 1 (p.22), declines in target detection rates on a vigilance task can also reflect gradual shifts towards more conservative response biases over time.

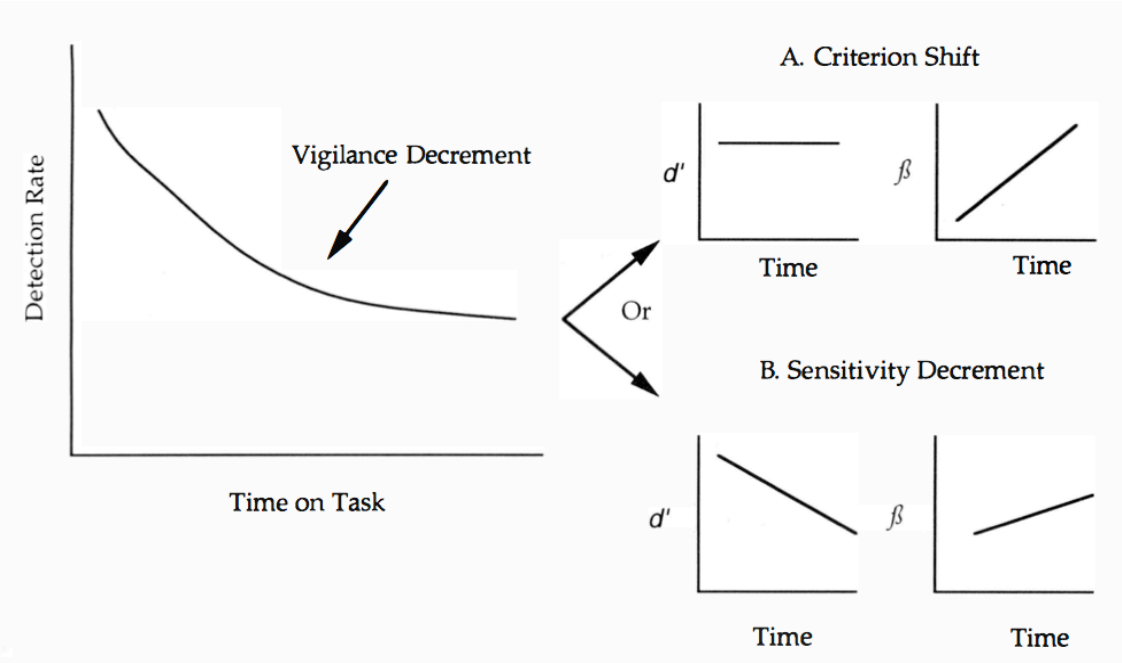


Figure 1 – Vigilance decrements and signal detection theory. Declines is detection rates over time can be caused by either a shift towards a more conservative response bias, or a decline in perceptual sensitivity (taken from Parasuraman, Warm, & See, 1998).

Interestingly, such isolated changes in response bias have been observed in tasks with low-target probability (Davies & Parasuraman, 1982; Singh, Tiwari, & Singh, 2007). Consequently, increasingly conservative response biases over time may reflect an increasing realisation of the rarity of target presentations and a desire to maximise task accuracy while minimising cognitive effort. This is important, particularly in research aiming to improve sustained attention, as it may be that an intervention that leads to improved performance on a vigilance task does so by affecting response bias rather than sensitivity. Of relevance to this point is the observation that, in a study of the effects of transcranial direct current stimulation on sustained attention task performance, researchers observed effects on response bias but not sensitivity (Nelson, McKinley, Golob, Warm, & Parasuraman, 2014). The main implication of such findings is that, to comprehensively measure changes in vigilance performance, it is important, when possible, to run a signal detection analysis of the performance of each subject, calculating their individual d' and *ß* values from the different ratios of hits (i.e. correct responses/inhibitions to targets) and false alarms (i.e. incorrect responses/inhibitions to non-targets) (Macmillan & Creelman, 1991).

Introspective self-assessments

In contrast to these objective measures of vigilance, fluctuations in sustained attention can also be measured by collecting participant self-assessments of their attentional focus. One way of doing this is to ask subjects to spontaneously report when they feel that their mind has wandered off-task (sometimes referred to as the 'self-caught' method; e.g. Braboszcz & Delorme, 2011; Cunningham, Scerbo, & Freeman, 2000). However, as this relies on a high degree of self-awareness, a more commonly used approach is to present participants with probes during task performance, which asks them to report their attentional focus at that point in time (so called '*probe-caught*' method). These probes are mostly commonly displayed at random moments (e.g. one

every 30-90 seconds; Kam et al., 2011; Smallwood, Beach, Schooler, & Handy, 2008). They can record attention responses in categorical form (e.g. 'on-' vs 'off-task'; Kam et al., 2011) or on a continuous rating scale (Kirschner, Kam, Handy, & Ward, 2012). Importantly, the use of this kind of approach is supported by the relative unambiguity of introspective self-reports as a measure of attention (compared to more objective measures like RT variability). The use of self-reports is also supported by evidence that these reports can predict the excitability of primary sensory cortex (Kam et al., 2011; Smallwood et al., 2008), and objective vigilance task performance (Kirschner et al., 2012) (although not in Kam et al., 2011). Nevertheless, these methods again have a number of weaknesses. For example, introspective judgements are usually only collected infrequently (e.g. at the end of 30-90 second task blocks; Kam et al., 2011). It is therefore unclear to what extent they accurately reflect attentional focus in moments immediately prior to report submission. One commonly taken approach is to assume that all trials between 12 and 15 seconds preceding probe onset were performed in the same attentional state (Kirschner et al., 2012; Smallwood et al., 2008). However, this appears to be fairly random definition and inevitably means that the attentional state at performance can only be known about a small minority of trials. This leads to significant removal of data from the final analysis and a reduction in statistical power. As an alternative, these reports can be collected more frequently (e.g. once every 10 seconds; J. S. Macdonald et al., 2011). However, as such consistent reminders of attentional focus are not presented in real-life situations, it is unclear to what extent this kind of repetitive sampling limits the ecological validity of a vigilance study. Furthermore, it has been found that giving people short breaks during sustained attention tasks (e.g. to report their subjective attentional states) can significantly diminish vigilance decrements (Ariga & Lleras, 2011).

THE PSYCHOLOGY OF SUSTAINED ATTENTION

So far, I have addressed the different strengths and weaknesses of various methodologies used to study sustained attention. In the following section, I focus on information that has been gained from these methods. I begin by discussing the different within- and between-subjects factors that influence the stability of sustained attention. I then discus the different psychological models that have been proposed to explain why sustained attention tends to deteriorate over time.

Factors that influence the stability of sustained attention

Within-subjects factors

Studies have repeatedly found that sustained attention capacities are affected by the psychological state of an individual during task performance. In particular, sustained attention can be impaired when subjects are tested in sub-optimal conditions. For example, RTs and error rates on vigilance tasks are significantly greater following extended sleep deprivation (Asplund & Chee, 2013; Doran, Van Dongen, & Dinges, 2001; Lim & Dinges, 2008; Loh, Lamond, Dorrian, Roach, & Dawson, 2004). RTs and error rates are also increased when testing occurs very late at night or early in the morning (i.e. 1am and 7am) (Manly, Lewis, Robertson, Watson, & Datta, 2002). However, such effects appear to depend on the chronotypes of individual subjects, with vigilance impairments greater in 'evening' types during morning testing, but in 'morning' types during evening testing (Carciofo, Du, Song, & Zhang, 2014; Lara, Madrid, & Correa, 2014). This could relate to fluctuations in their levels of arousal. For example, a number of studies have associated decrements in vigilance performance with a decline in physiological arousal (Pattyn, Neyt, Henderickx, & Soetens, 2008). However, in addition to these more biologically-rooted influences, cognitive factors like motivation have also been demonstrated to have a significant effect on the magnitude of vigilance

decrements. For example, A. Bonnefond, Doignon-Camus, Hoeft, and Dufour (2011) found that accuracy on an extended Erickson flanker task could be significantly improved by telling subjects that their performance would be evaluated online by a nearby research assistant. Similarly, Tomporowski and Tinsley (1996) found that deteriorations in vigilance performance were more pronounced in subjects who received no financial reward for their participation, compared to those who received full payment.

Between-subjects factors

Performance on sustained attention tasks is also influenced by a range of endogenous factors that vary between-subjects, rather than within. For example, youth (Filley & Cullum, 1994), intelligence (Carter & Swanson, 1995; Swanson & Cooney, 1989) and academic achievement (Whitten Campbell, D'Amato, Raggio, & Stephens, 1991) have all been positively associated with sustained attention capacities. Furthermore, Rose, Murphy, Byard, and Nikzad (2002) found that false alarm rates on a vigilance task correlated positively with measures of trait-extraversion ($r = 0.181$) and negatively with conscientiousness ($r = -0.275$). Individual differences in the psychological trait of 'boredom proneness' (assessed using the *Boredom Proneness Scale*) have also been found to predict vigilance task performance (Kass, Vodanovich, Stanny, & Taylor, 2001)

The psychological practices of individuals similarly influence their attentional capacities. For example, individuals who play video games have been found to perform better on vigilance tasks than those who do not (Schmidt et al., 2013; Schmidt, Teo, Szalma, Hancock, & Hancock, 2012). Of relevance to this point is the finding that cortical processing of task-irrelevant visual objects is reduced among video games players during sustained attention task performance (assessed with steady-state evoked potentials using electroencephalography; Mishra, Zinni, Bavelier, & Hillyard, 2011).

Meditation has also been associated widely with improved attentional control. This is particularly true of 'focused attention' meditation, in which great importance is given to the practice of sustaining voluntary attention on a chosen object. For example, individuals trained in focused attention meditation for 4-12 weeks have been found to exhibit increased perceptual sensitivity on sustained visual discrimination tasks, compared to non-trained controls and those instructed only in progressive muscle relaxation (MacLean et al., 2010; Semple, 2010). It therefore seems likely that individuals who regularly perform these kinds of mental exercises will be perform better than the general population on tasks of sustained attention.

Why does attention deteriorate over time? Fatigue, or boredom?

In the previous sections, I described the methods used to measure deteriorations in sustained attention, and the different factors that influence these deteriorations. However, why does sustained attention deteriorate in the first place? One of the conventional ways of describing deteriorations in attention task performance over time is as the product of mental fatigue. Like muscles after exercise, top-down attentional processes are thought to tire with extended use, leading to a reduction in an individual's capacity to control their attention following prolonged cognitive performance (Kahneman, 1973; Matthews, Davies, Westerman, & Stammers, 2000). This view is supported by findings of positive correlations between vigil duration and subjective ratings of cognitive workload (Dember et al., 1993; Warm, Dember, & Hancock, 1996). This view is also supported by evidence of reductions in medial cerebral blow flow velocity during extended target monitoring that, importantly, are not observed during passive viewing of identical visual streams (Shaw et al., 2009; Warm, Matthews, & Finomore, 2008). I refer to this perspective from here on as the '*resource depletion account'*. However, this is not the only explanation of why attention deteriorates over time. Deteriorations in vigilance performance have also been described as the product of under-stimulation. More

specifically, the prolonged and monotonous nature of sustained attention tasks has been suggested to cause a reduction over time in cortical arousal, goal focus, and on-task thought (Ariga & Lleras, 2011; Robertson, Galloway, & Hawkins, 1999; Robertson et al., 1997). Such reductions in on-task thought could reflect periods of mindlessness, in which people do not direct their attention towards anything in particular. However, when people fail to direct their attention to an external task, they most commonly refocus on self-generated thoughts (Smallwood & Schooler, 2006). It therefore seems more likely that deteriorations in task performance due to disengagement reflect periods of 'mind-wandering'. I therefore refer to this perspective from here on as the '*mind-wandering account*'.

These contrasting perspectives often make different predictions about the effects of certain manipulations on sustained attention task performance. In principle, therefore, the veracity of these competing theories can be directly assessed. For example, one approach is to study how performance deteriorations are affected by task difficulty. In general, studies taking this approach have reported more significant vigilance decrements when people perform demanding tasks (Helton & Russell, 2011b; Helton & Warm, 2008; Smit, Eling, & Coenen, 2004). For example, a vigilance task requiring people to identify degraded visual stimuli causes larger deteriorations in performance than a task with highly perceptible stimuli (Helton & Warm, 2008). Such findings appear to support the resource depletion account, which predicts that difficult tasks should increase demands on attentional resources, and therefore impair vigilance task performance by increasing mental fatigue. This is in contrast to the mind-wandering account, which predicts that increased task difficulty should reduce boredom, and therefore improve task performance through increased task engagement. However, in contrast to this view, it has been suggested that impaired task performance on difficult tasks is still consistent with the mind-wandering account. This is because, if mind-wandering occurs during a difficult task, this would have a more negative effect on

performance than if the task was easy (Smallwood & Schooler, 2006). Therefore, it seems that this line of research has not been able to conclusively distinguish between the resource depletion and mind-wandering accounts of vigilance decrements (Thomson, Besner, & Smilek, 2015).

Another approach is to study how vigilance performance is affected by the presentation of arousing/engaging stimuli. As such stimuli should naturally capture attention, it is predicted by the resource depletion account that they should place additional demands on an already tiring attentional system, accentuating mental fatigue and impairing vigilance performance. However, the exact opposite is predicted by the mind-wandering account, which assumes that arousing/engaging stimuli would improve vigilance performance by preventing boredom and task-disengagement. The predictions of the resource depletion account have received some support. For example, worse performance is observed on vigilance tasks when irrelevant stimuli with negative emotional valence are presented during task performance (Head & Helton, 2012; Helton & Russell, 2011a; Ossowski, Malinen, & Helton, 2011). However, in contrast to such findings, there is also evidence that task-irrelevant auditory stimuli can prevent deteriorations in auditory vigilance (Davies, Lang, & Shackleton, 1973). Furthermore, one study of an air-traffic control task found that deteriorations in performance over time were reduced when participants performed an “engaging” vs. “standard” version of the task. The “engaging” version required subjects to click on all incoming aircraft, increasing participant engagement with the task (Pop, Stearman, Kazi, & Durso, 2012). Consequently, it again seems that this line of research again cannot conclusively distinguish between the two competing models of vigilance decrements (Thomson et al., 2015). Researchers have therefore attempted to create new models of sustained attention that can better describe the diversity of findings in the literature.

Alternative perspectives – resource-control and opportunity costs

In trying to address these problems of both the resource depletion and mind-wandering accounts, Thomson et al. (2015) proposed the '*resource-control*' model of sustained attention. In contrast to the resource depletion and mind-wandering accounts, which generally view vigilance decrements as the product of over- vs. under-stimulation, this model makes a number of fundamental assumptions. Firstly, it assumes that the mental resources available for all cognitive processes (i.e. both on- and off-task; depicted on the y-axis of Figure 2; p.31), as well as the mental resources needed for a specific cognitive task (depicted by the dotted line in Figure 2), are fixed over time. The model also assumes that the default state of an individual is self-generated thought (i.e. mind-wandering) and that this default state occupies mental resources that could otherwise be dedicated to a sustained attention task. This default state of mind-wandering can be inhibited by executive control processes, which direct attention towards the sustained attention task. However, with increasing time on task, levels of executive control deteriorate, increasing the amount of mental resources that will be reoriented automatically to mind-wandering. When there are not sufficient mental resources for completion of the attention task, performance of that task will suffer. With further time on task, executive control will deteriorate even more, the amount of cognitive resources dedicated to mind-wandering will increase further, and greater impairments in task performance will be observed.

Thomson et al. (2015) argue that this model can explain a wide variety of findings in the sustained attention literature. For example, the model can explain why sustained attention tasks are subjectively effortful, as reductions in a person's executive control over time when they are trying to perform a difficult task would understandably result in a feeling of increased mental workload. The model also appears to explain why more significant deteriorations in performance are observed on difficult vs. easy tasks. This is

because a greater proportion of mental resources must be dedicated to hard vs. easy tasks and, therefore, any loss of resources to mind-wandering due to deteriorations in executive control will inevitably impair performance of difficult tasks more significantly than easy ones. In addition, the model can explain why deteriorations in task performance are reduced when tasks naturally engage attention (e.g. as in Pop et al., 2012). This is because, when people perform naturally engaging tasks, they do not need to engage as much executive control to prevent mind-wandering. Consequently, any deterioration in executive control over time will influence performance of engaging tasks less than those requiring high levels of executive control.

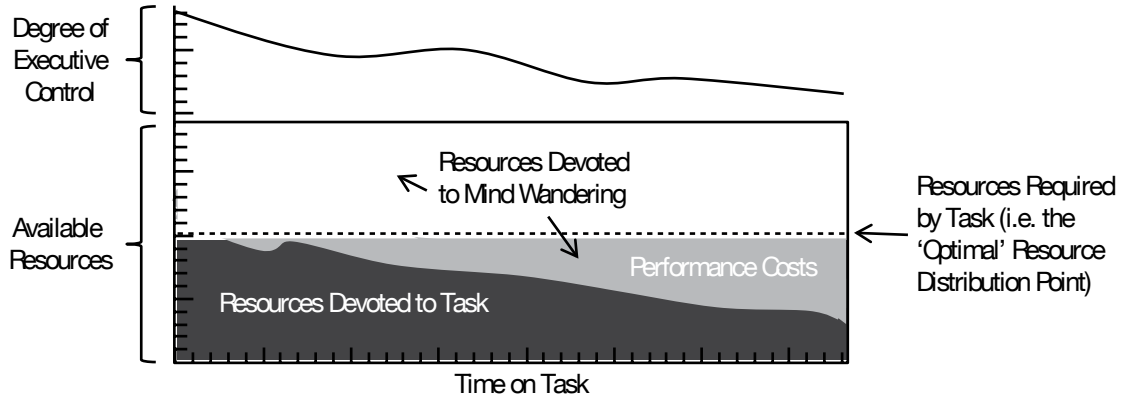


Figure 2 – The resource-control model of vigilance decrements. The total amount of attentional resources is fixed over time (depicted on the y-axis). The amount of resources needed to perform a given, sustained attention task is also fixed (the dotted line). The default state of an individual is internally-directed thought (i.e. mind-wandering). With increasing time on task, levels of executive control reduce, meaning that more and more attentional resources are devoted to mind-wandering (the combination of the white and light grey portions). When not enough resources are devoted to the sustained attention task (the decreasing dark grey portion), task performance suffers (the light grey portion beneath the dotted line) (taken from Thomson et al., 2015).

This model therefore provides an appealing synthesis of the resource depletion and mind-wandering theories of vigilance decrements. However, the model still has an important weakness: although it can explain the limits of an individual's *capacity* to perform a given cognitive task, it does not say anything about the processes that make a

person *choose* to perform that task. This issue is addressed in a model recently proposed by Kurzban, Duckworth, Kable, and Myers (2013). This model again assumes that the amount of mental resources available for all cognitive processes is fixed over time. Importantly, therefore, not all mental processes can be performed simultaneously. This is referred to as the problem of *simultaneity*. Given this limitation, an individual must decide which of a range of cognitive processes they wish to dedicate their cognitive resources to. This is referred to as the problem of *prioritisation*. Such prioritisation will inevitably require the assignment of costs and benefits (i.e. value) to candidate options. Specifically, while an individual may place a certain value on a given cognitive task, this value will be contrasted with the summed value of performing other tasks that are prevented by that given task. The cost of performing the given task over alternatives is called the '*opportunity cost*'. In general, it is assumed that people will endeavor to minimize opportunity costs. Furthermore, it is assumed that, when a person performs a boring task, the subjective value of alternative tasks will increase over time, increasing the opportunity costs of maintaining focus on the given task. Such increased opportunity costs will then increase the subjective feeling of mental effort, as well as the likelihood that the person will switch their attention to more appealing alternatives (i.e. impairing task performance). This model represents an important shift from resource-based models of sustained attention, to ones focused more on internal motivations. From an evolutionary perspective, it makes sense that organisms that are able to maximise their time spent on rewarding activities will gain a reproductive advantage over those that cannot. Nevertheless, the model does have some weaknesses. For example, it has been suggested that there are many situations in which opportunity costs will be high, but in which no significant sense of subjective mental effort is experienced (e.g. sitting next to a friend in a restaurant who is eating a meal you wish you had ordered) (Kool & Botvinick, 2013).

THE NEUROSCIENCE OF SUSTAINED ATTENTION

These kinds of psychological models do a decent job of describing the conditions in which sustained attention deteriorates over time. In doing so, these models commonly make reference to concepts like 'mental resources' and 'executive control'. However, while these concepts have a common sense, intuitive appeal, they are of limited use for researchers wishing to understand the neural mechanisms that support sustained attention. Neuroscientific models of sustained attention have therefore tended to deconstruct concepts like 'executive control', and theorised about the different roles played by neural systems in various, constituent processes of executive control.

For example, early models proposed that sustained attention relies on activity within so-called anterior and posterior attention systems. In particular, prefrontal regions were suggested to exert prolonged control over perceptual processing via relays in parietal cortex (Posner & Petersen, 1990; Sarter, Givens, & Bruno, 2001). These models have received support from lesion studies (Rueckert & Grafman, 1996, 1998). However, it has been argued that frontoparietal systems do not support sustained attention by performing unitary operations, but rather engage in multiple cognitive functions simultaneously (Stuss, Shallice, Alexander, & Picton, 1995). This elaborated model is supported by neuroimaging evidence that, during sustained attention task performances, activation is distributed across numerous, functionally separable brain networks (e.g. Langner & Eickhoff, 2013). Within this framework, sustained attention is argued to depend on three control functions: 1) monitoring and evaluation of ongoing cognitive processes, 2) energisation of task-relevant processes, and 3) inhibition of task-irrelevant processes (Stuss et al., 1995). Sustained attention in the visual domain, for example, would therefore rely on monitoring of current attentional focus, enhanced processing of relevant visual inputs, and inhibition of distracting stimuli. I dedicate the

following sections to discussing the neural systems that are most likely responsible for each of these cognitive processes.

Monitoring of behaviour

As stated above, the first process is the monitoring of cognition and behaviour. To maintain good performance over the course of a vigilance task, subjects must be able to identify the occurrence of errors (e.g. failed responding to target presentations) and adjust their perceptual / motors systems accordingly. This process has been proposed to depend crucially on the dorsal anterior cingulate cortex (dACC) (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004). Activity in this region increases following the commission of errors (Debener et al., 2005; Yeung, Botvinick, & Cohen, 2004) and during tasks that require the exertion of significant behavioural control (Braver, Barch, Gray, Molfese, & Snyder, 2001; Kerns et al., 2004). Activity in the dACC has also been found to diminish with extended vigilance performance, along with increases in reaction times (Coull, Frackowiak, & Frith, 1998; Lim et al., 2010), and is widely reported in neuroimaging studies of vigilance (Langner & Eickhoff, 2013). Furthermore, damage to the dACC is strongly associated with impaired sustained attention task performance (Alexander, Stuss, Shallice, Picton, & Gillingham, 2005; Shallice, Stuss, Alexander, Picton, & Derkzen, 2008).

Activation of task schema

Following the identification of mind-wandering and errors, is it necessary that task-relevant schemas are effectively reactivated, and that this activation is appropriately sustained. In the case of vigilance tasks, this process most likely involves the promotion of activity in attention-related cortical areas like the intraparietal sulcus (Langner & Eickhoff, 2013), which is suggested to play a strong role in the implementation of top-down attentional signals (Corbetta & Shulman, 2002). Lesion studies have commonly

linked this kind of continuous, top-down activation of task-relevant processing to activity in right medial prefrontal cortex (mPFC) (Alexander et al., 2005; Shallice et al., 2008). However, neuroimaging research has more recently promoted the involvement of a distributed 'cingulo-opercular network' in this process. For example, activity in this network has been strongly associated with the maintenance of sustained cognitive focus (Sadaghiani & D'Esposito, 2014; Sestieri, Corbetta, Spadone, Romani, & Shulman, 2014). Cingulo-opercular network activity has also been found to increase before successful target classifications in an auditory vigilance task (Sadaghiani, Hesselmann, & Kleinschmidt, 2009).

Inhibition of rival task schemas

Lastly, in addition to the activation of task-relevant schemas, it is important that distracting, task-*irrelevant* schemas are effectively inhibited. This is demonstrated by findings that sustained attention task performance is impaired during periods of increased activity in the default mode network (Drummond et al., 2005; Weissman, Roberts, Visscher, & Woldorff, 2006), amygdala (Fleck et al., 2012), and task-irrelevant sensory cortex (e.g., visual cortex during an auditory vigilance task; Sadaghiani et al., 2009). Such inhibition of task-irrelevant processes has again been linked with frontal structures (Geng, 2014; Shimamura, 2000). For example, during attention-demanding tasks, medial frontal and dorsolateral prefrontal activity has been shown to predict suppression of activity in regions encoding distracting stimulus features (Danielmeier, Eichele, Forstmann, Tittgemeyer, & Ullsperger, 2011; Suzuki & Gottlieb, 2013). Activations in these regions are also consistently reported across vigilance neuroimaging studies (Langner & Eickhoff, 2013).

THE ROLES OF NEURAL OSCILLATIONS

Sustained attention therefore appears to rely on the combined engagement of multiple cognitive processes, through the activity of distributed neural networks. However, the constituent processes of sustained attention cannot be described simply by the turning 'off' and 'on' of distinct brain areas. Instead, cognitive processes appear to rely on the *types* of activity that occur in these areas. For example, various cognitive processes have been suggested to depend on rapid fluctuations in neural activity, known as 'neural oscillations' (Buzsáki, 2006). These oscillations occur within specific brain regions, and within specific frequency bands. In the following sections, after giving a more detailed description of what neural oscillations are, I discuss the ways in which such rhythms might contribute to sustained attention. Note that much of this discussion is taken verbatim from a paper I published recently in *Trends in Cognitive Sciences* (Clayton et al., 2015).

What are neural oscillations and how are they measured?

Neural oscillations are observed in all animals and are thought to reflect rhythmic activity of large populations of neurons (Musall, von Pfostl, Rauch, Logothetis, & Whittingstall, 2014). This rhythmic firing causes fluctuations in cortical local field potentials that can be measured using implanted electrodes (e.g., intracranial electroencephalography) or scalp detectors (e.g., electroencephalography/ magnetoencephalography) (Figure 3A; p.37). The spectral composition of these fluctuations, and therefore the characteristic rhythmicity of neural activity, can be determined by transforming recorded electrophysiological data into the frequency domain using techniques like the Fourier transform. This approach allows estimation of the contribution of individual frequencies to the analysed signal (Figure 3B; p.37). In the case of cognitive electrophysiological research, frequencies are divided into spectral

bands with distinct functional associations: delta (1 – 4 Hz), theta (4 – 8 Hz), alpha (8 – 14 Hz), beta (14 – 30 Hz), and gamma (> 30 Hz) (Figure 3C; p.37).

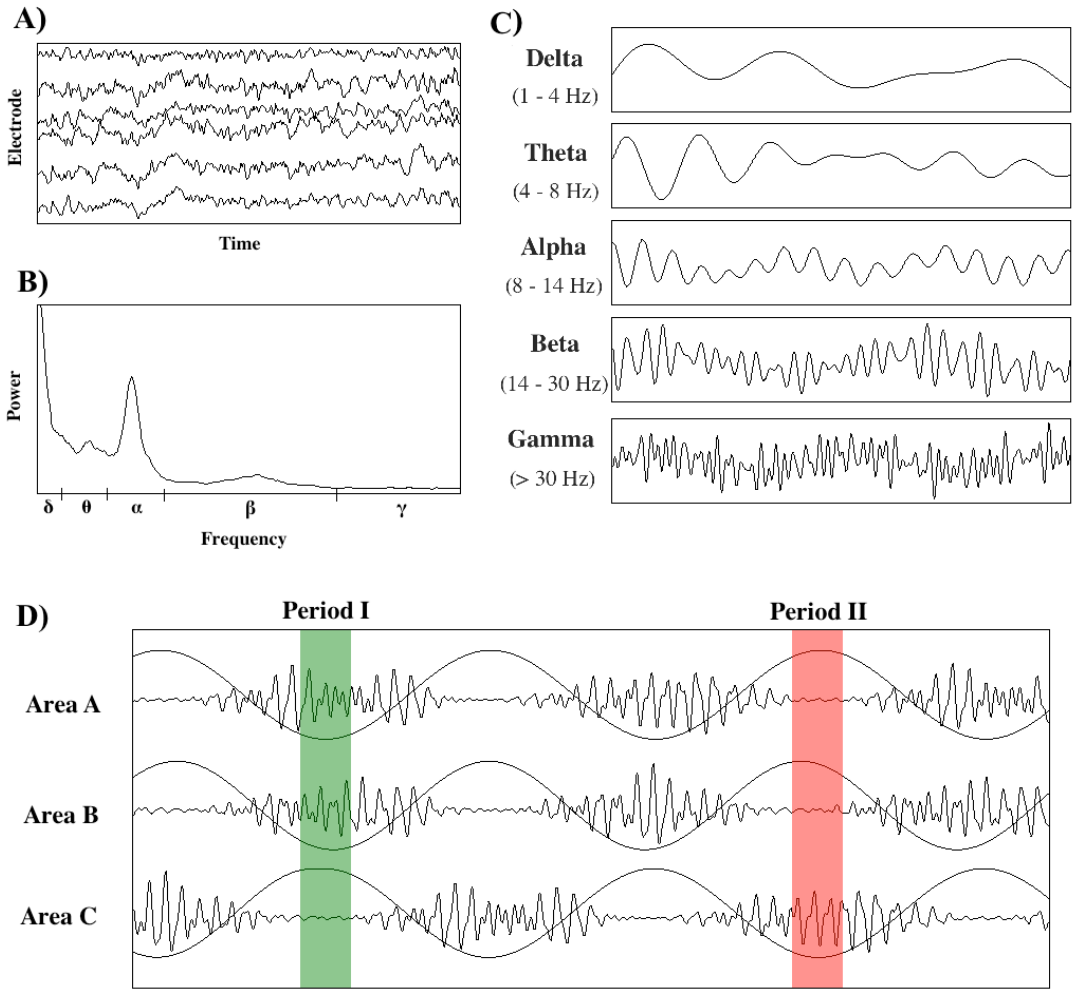


Figure 3 – An illustration of what cortical oscillations are, how they are analysed, and how they interact with each other. A) EEG data recorded from six electrodes positioned on the scalp. B) A plot of the power of specific oscillatory frequencies in a sample of eyes-closed, resting state EEG data (δ = delta, θ = theta, α = alpha, β = beta, γ = gamma). C) Electrophysiological data band-pass filtered in the delta, theta, alpha, beta, and gamma bands. D) Electrophysiological data recorded from three different cortical areas demonstrating both the modulation of gamma power by low-frequency oscillations, and the mechanisms by which oscillatory phase synchronisation between regions can facilitate and inhibit long-range neural communication (as in Periods I and II, respectively) (taken from Clayton et al., 2015).

Oscillations are thought to be prevalent in neural systems in part because they facilitate communication between neural populations (Buzsáki, 2006). One way they could do this is through phase synchronisation. Phase synchronisation involves the adjustment and maintenance of the phase relationship between oscillating neural populations. As shown in Figure 3D (p.37), neural populations can oscillate in phase or out of phase with each other. When in phase, communication between two areas is facilitated as action potentials from one area (Area A) arrive during the excitable phase of the other (Area B) and thus have enhanced post-synaptic impact (Period I). When oscillating out of phase, however, communication is prevented as actions potentials from one area (Area C) will arrive when the other (Area A) is inhibited (Period II). Due to conduction delays in long-range transmission of neural impulses, communication between brain regions is suggested to be optimal when partner areas are synchronised at low frequencies (Buzsáki, 2006; von Stein & Sarnthein, 2000).

Such low-frequency oscillations have been shown to modulate the power of high-frequency oscillations (Canolty et al., 2010; Oehrn et al., 2014; von Stein & Sarnthein, 2000). This is also shown in Figure 3D (p.37), in which the power of gamma oscillations depends on the phase of ongoing theta oscillations. Specifically, gamma power is greatest during theta troughs and lowest during theta peaks. This effect is known as power-phase coupling. Given the suggested role of low-frequency oscillations in long-range neural communication (Buzsáki, 2006; von Stein & Sarnthein, 2000), and of high-frequency oscillations in the synchronisation of local neural activity (Buzsáki, 2006), power-phase coupling between high and low frequencies provides a potential mechanism for the control of localised neural processing by distributed brain networks (Canolty et al., 2010; von Stein & Sarnthein, 2000).

Frontomedial theta: monitoring and control

I now describe some of the ways in which neural oscillations may contribute to the constituent processes of sustained attention. Theta oscillations (4 – 7 Hz) over medial prefrontal regions (frontomedial theta; fm-theta) is commonly been found to increase in power during sustained attention tasks, along with error rates and reaction times (Boksem, Meijman, & Lorist, 2005; Wascher et al., 2014). This suggests an association between this rhythm and the development of mental fatigue. Supporting this view, fm-theta power has therefore been used as an indicator of deteriorated attention (Lal & Craig, 2001). However, despite this negative association, there is evidence that fm-theta may in fact play a positive role in attentional control.

For example, fm-theta power has been shown to increase significantly following the presentation of rare 'oddball' stimuli (Mazaheri & Picton, 2005; Missonnier et al., 2006). 'Oddballs' are defined as target stimuli that occur rarely during a continuous stream of standard, non-target stimuli. Fm-theta power has also been found to increase during reorientations of auditory attention (Ahveninen, Huang, Belliveau, Chang, & Hamalainen, 2013), and prior to accurate performance on prolonged cognitive tasks (Oehrn et al., 2014; Wascher et al., 2014). This suggests a positive association between fm-theta power and the engagement of attention. Fm-theta power has also been found to increase following both negative task feedback (van de Vijver, Ridderinkhof, & Cohen, 2011) and the commission of errors on a range of tasks (Cavanagh, Zambrano-Vazquez, & Allen, 2012; van Driel, Ridderinkhof, & Cohen, 2012). Such power increases predict subsequent enhancements in post-error reaction time slowing (Cavanagh & Shackman, 2014). Consequently, fm-theta may also play important roles in cognitive monitoring and control processes (Cavanagh & Frank, 2014).

Consistent with this hypothesis, magnetoencephalography (MEG) (Ishii et al., 2014) and intracranial EEG studies (Oehrn et al., 2014) have localised fm-theta oscillations to dorsomedial prefrontal and anterior cingulate cortices. These areas are key hubs of the executive control and cingulo-opercular networks, respectively. In addition, theta oscillations in superficial layers of medial prefrontal cortex have recently been suggested to support cognitive monitoring and control processes by promoting integration of thalamocortical inputs and detection of conflict between current and intended behaviours (Cohen, 2014b). Together, this evidence provides a partial explanation for why fm-theta has been associated with both increased cognitive control over short time scales, and reduced attention following prolonged cognitive engagements (Mazaheri & Picton, 2005; Missonnier et al., 2006). Specifically, it suggests that increased fm-theta power during fatigue-related declines in sustained attention may reflect detection of mismatch between current and desired levels of attention. This detection may cause reactive engagement of cognitive control processes. However, when cognitive resources are depleted, these processes may be unable to refocus attention and, therefore, to improve task performance. Put simply, increased fm-theta power during prolonged cognitive engagements may be analogous to the revving noises of a tired motorcar trying to climb a steep hill.

Phase synchronisation, and long-range transmission of information

For theta-driven, cognitive monitoring systems to exert significant control over attention, they must communicate within attention-related brain networks. Posterior medial prefrontal cortex is hypothesised to exert such control by coordinating its activity with lateral prefrontal cortex, which, in turn, transmits modulatory signals to low-level, sensorimotor areas (A. W. MacDonald, 3rd, Cohen, Stenger, & Carter, 2000; Ridderinkhof et al., 2004). Recent evidence suggests that this prefrontal coordination is facilitated by theta-band phase synchronisation. For example, electroencephalography

(EEG) studies have commonly observed increased theta-band phase synchronisation between medial and lateral prefrontal areas following both negative task feedback (van de Vijver et al., 2011), and the commission of errors during sustained attention tasks (Cavanagh, Cohen, & Allen, 2009; van Driel et al., 2012). Similar results were also reported in a human intracranial EEG study in which posterior medial and lateral prefrontal activity was recorded invasively while patients performed a response conflict task (Oehrn et al., 2014). Here, theta phase synchronisation between these two regions increased significantly on correctly classified trials and during periods of high response conflict. In addition, the phase of posterior medial prefrontal theta oscillations modulated gamma power in lateral prefrontal cortex (an example of power-phase coupling; Figure 3D; p.37), and the strength of this gamma-theta coupling predicted improved performance on subsequent trials. Together, this evidence supports the role of theta-band prefrontal communication in the direction of cognitive control.

For these prefrontal activities to modulate sensorimotor processing, they must then be communicated to posterior brain areas. This communication may also be facilitated by long-range, low-frequency (< 14 Hz) phase synchronisation. Increased low-frequency phase synchronisation between frontal and posterior areas is commonly observed during the orientation of attention (Brázdil et al., 2013; Daitch et al., 2013; Dombrowe & Hilgetag, 2014), and has been found to predict improvements in attention following momentary attentional lapses (Cohen & van Gaal, 2013; Cohen, van Gaal, Ridderinkhof, & Lamme, 2009). Furthermore, during sustained attention tasks, fronto-posterior phase synchronisation in the alpha band has been found to decrease with cognitive fatigue (J. P. Liu, Zhang, & Zheng, 2010; Sun, Lim, Kwok, & Bezerianos, 2014) and to increase during periods of participant-assessed 'on-task' performance (Kirschner et al., 2012). Simultaneous EEG-fMRI recordings have revealed a positive association between this alpha-band, fronto-posterior phase synchronisation and haemodynamic activity in the executive control network (Sadaghiani et al., 2012). Global alpha power

has also been linked with increased activity in the cingulo-opercular network (Sadaghiani et al., 2010). Collectively, this evidence implicates large-scale, oscillatory synchronisation in the coordination of attention-related brain networks.

Gamma (>30 Hz) oscillations: promotion of task-relevant activity

According to the neurocognitive theory proposed by Stuss et al. (1995), sustained attention also depends on continuous activation of task-relevant activity. This function may be achieved via the generation of localised gamma oscillations in task-relevant cortical areas. Gamma oscillations in sensory cortices have often been linked with enhanced attention to sensory inputs. Increased gamma power in occipito-parietal cortex has been associated with improved visual oddball task performance (Akimoto et al., 2013; Reinhart, Mathalon, Roach, & Ford, 2011). Similarly, gamma power in auditory areas is increased during extended auditory attention tasks (Ahveninen et al., 2013; Potes, Brunner, Gunduz, Knight, & Schalk, 2014). These gamma modulations in sensory cortex are strongly influenced by the activity of cognitive control systems. One study found that, although gamma power increased in macaque visual cortex during deployment of attention to visual inputs, removal of lateral prefrontal cortex significantly attenuated this gamma enhancement (Gregoriou, Rossi, Ungerleider, & Desimone, 2014). Transcranial magnetic stimulation of lateral prefrontal cortex was also recently shown to modulate occipital gamma power during a visuospatial attention task (Marshall, O'Shea, Jensen, & Bergmann, 2015). In addition though, gamma oscillations have also been associated with activation in non-sensory cortices. For example, enhanced cognitive control following identification of response conflict is associated with increased gamma activity (as well as gamma-theta power-phase coupling) in lateral prefrontal cortex (Oehrn et al., 2014). Furthermore, in an intracranial EEG study, increased gamma power was observed during a visuomotor task in a range of frontal and posterior brain areas previously identified as being positively involved in this task (Ramot et al.,

2012). In summary then, gamma oscillations may support processes of sustained attention by facilitating local processing in many diverse regions of the brain.

SUMMARY

In this chapter, I described the different cognitive tasks and measures used to study sustained attention. I then discussed some of the key findings of studies using these methods, as well as the main psychological models used to explain why sustained attention tends to deteriorate during prolonged cognitive tasks. I finished by discussing the possible contribution of different neural systems to the constituent processes of sustained attention. This discussion focused first on distinct brain areas and networks, and finished with a focus on neural oscillations. However, this last section did not discuss the possible roles played by neural oscillations in an important process of sustained attention: inhibition of rival task schemas. I will argue in the next chapter that such processes of inhibition may be facilitated by alpha oscillations in sensory cortices. However, despite these strong associations with inhibition, alpha oscillations have also been linked with a much wider range of cognitive processes. I dedicate the next chapter to the discussion of these broad associations.

CHAPTER 2 – ALPHA OSCILLATIONS AND VISUAL ATTENTION

Most features of electrical brain activity are difficult to identify in live recordings. For example, some of the neural oscillations discussed in the previous chapter (e.g. fm-theta, long-range phase synchronisation) require statistical manipulations and averaging over many trials to be clearly distinguished from noise. Nevertheless, when people close their eyes, a clear and sustained oscillation reliably emerges in EEG recordings, with maximum amplitude over posterior brain regions and within a frequency range of approximately 7 – 13 Hz. These prominent rhythms are known as 'alpha' oscillations. Increases in their power commonly accompany reductions in cognitive activity, supporting the view that alpha oscillations primarily reflect processes of attentional disengagement (Lundqvist, Herman, & Lansner, 2013; Pfurtscheller, Stancák, & Neuper, 1996). Furthermore, alpha oscillations have commonly been found to increase in amplitude immediately before the commission of errors on sustained attention tasks (e.g. Chaumon & Busch, 2014; O'Connell et al., 2009). Nevertheless, this does not mean that alpha oscillations do not contribute to processes of sustained attention.

For example, it has been suggested that alpha may facilitate the suppression of cognitive processes that are irrelevant to ongoing tasks, supporting maintenance of attention to that task (Clayton et al., 2015). However, recent studies have also suggested that, in addition to their association with reduced visual processing (Pfurtscheller et al., 1996), alpha oscillations may support neurocognitive functions that are central to the engagement of visual attention (Sadaghiani & Kleinschmidt, 2016; Sherman et al., 2016; Piantoni et al., 2017). Given these strong associations with attention, as well as their predominance in EEG recordings, alpha oscillations seemed to be an ideal form of brain activity to focus on in this project. Specifically, it seemed likely that experimental modulation of alpha rhythms had the potential, more than other neural oscillations, to generate changes in sustained attention that could be useful in real-world settings. In

addition though, given the previously mentioned uncertainty around the contribution of alpha oscillations to attention, I also believed that a project focused on alpha oscillations had another basic, scientific purpose: to provide greater clarity on the ways in which cognitive processes might be supported by these dominant rhythms of the human brain.

In this chapter, I give an overview of current evidence on the associations between alpha oscillations and visual attention. I focus first on the different neural mechanisms thought to contribute to the generation of alpha oscillations. Then, after addressing the possibility that these rhythms serve no purpose in cognitive functioning at all, I describe how alpha appears to contribute to visual processing by exhibiting at least five distinct 'characters': those of the inhibitor, perceiver, predictor, communicator, and stabiliser. Before continuing, it should be noted that, in addition to visual regions of the brain, alpha oscillations are observed in auditory (Leske et al., 2014), sensorimotor (Haegens et al., 2015), and prefrontal areas (Supp, Siegel, Hipp, & Engel, 2011), as well as the hippocampus (Schürmann, Demiralp, Başar, & Başar Eroglu, 2000), and brain stem (Barman & Gebber, 2007). To avoid confusion, I focus exclusively in this chapter on alpha oscillations recorded maximally over posterior brain regions, or localised to occipitoparietal cortex. From here on, the term 'alpha oscillations' will refer only to these posterior rhythms. Note also that the majority of the chapter is taken from an article I recently published in the *European Journal of Neuroscience* (Clayton et al., 2017).

THE GENERATORS OF ALPHA

Oscillations can be generated by a diverse range of neurobiological mechanisms, from cyclical processes occurring in individual neurons, to network effects that are observed over larger spatial scales (Buzsáki, 2006; Wang, 2010). Furthermore, in addition to being expressed across many regions of the brain (e.g. Haegens et al., 2015), alpha oscillations have been recorded in the firing patterns of a range of neuronal

cell types (Wang, 2010; Womelsdorf, Valiante, Sahin, Miller, & Tiesinga, 2014). Such findings indicate that alpha oscillations are most likely generated by variety of neural processes. Nevertheless, existing evidence suggests that certain brain areas and neural circuit types are more likely than others to play significant roles in generating alpha rhythms.

For example, alpha oscillations have long been associated with activity in the thalamus (Berger, 1929). Support for this view comes from evidence that thalamic lesions profoundly diminish alpha oscillations (Lukashevich & Sazonova, 1995; Ohmoto et al., 1978), and that changes in electroencephalographic (EEG) alpha power covary with haemodynamic activation in the thalamus (Goldman, Stern, Engel Jr, & Cohen, 2002; Z. Liu et al., 2012). Electrophysiological recordings also reveal strong coherence between alpha oscillations in visual cortex and the thalamus (Chatila, Milleret, Rougeul, & Buser, 1992; Lőrincz, Kékesi, Juhász, Crunelli, & Hughes, 2009). Specifically, the phase of alpha has been found to correlate with the spiking activity of thalamocortical neurons in anterior layers of the lateral geniculate nucleus (Chatila et al., 1992; Lőrincz et al., 2009). These neurons are thought to facilitate transfer of visual information to cortex and cluster their spiking around the peaks and troughs of ongoing alpha oscillations (Figure 4; p.47). The rhythmicity of these thalamocortical neurons, and the phase position at which they fire, is strongly influenced by phasic inhibition from interneurons in the lateral geniculate nucleus (Lőrincz et al., 2009). Alpha oscillations in both interneuron and thalamocortical activity in the lateral geniculate may also be coordinated by local circuits that are connected by gap junctions, producing sustained cycles of activity at alpha frequencies (S. W. Hughes et al., 2011). Consequently, it seems that alpha oscillations are generated by a range of interconnected processes in the thalamus, and that these rhythms may be used to segment visual inputs into distinct subgroups (Lőrincz et al., 2009). However, there is also evidence that alpha oscillations are generated in large part by cortical activity.

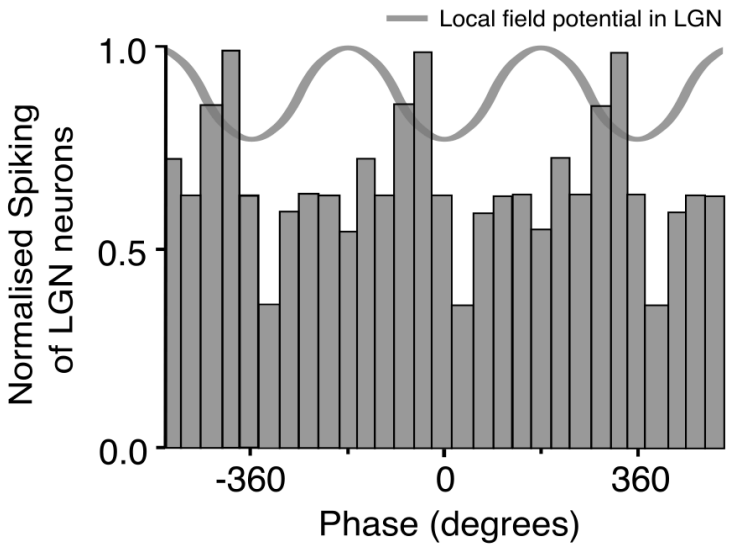


Figure 4 – Thalamic spiking is phase-locked to alpha. Normalised spike rates of thalamocortical neurons are displayed for the different phase positions of an ongoing alpha oscillation. This oscillation is observed in local field potentials recorded in the lateral geniculate nucleus (LGN; grey line). Subsets of thalamocortical neurons are shown to cluster their firing around the trough of the ongoing alpha oscillation. Note that other groups of thalamocortical neurons (not shown here) conversely exhibit maximum firing around the peak of ongoing alpha (adapted from Lőrincz et al., 2009).

This point is evidenced by the finding that pyramidal neurons from deep layers of cortex exhibit rhythmic firing at alpha frequencies when isolated from the thalamus in *in vitro* preparations (Silva, Amitai, & Connors, 1991). Furthermore, while laminar recordings of visual cortex *in vivo* have identified generators of alpha oscillations in all layers of cortex (Bollimunta, Chen, Schroeder, & Ding, 2008), greater alpha synchrony has often been observed in deep vs. superficial layers (Figure 5; p.48) (Buffalo, Fries, Landman, Buschman, & Desimone, 2011; van Kerkoerle et al., 2014) (although see Haegens et al., 2015). The hypothesis that cortex plays an independent role in alpha generation is also supported by the finding that alpha oscillations exhibit stronger coherence between cortical areas than they do between cortex and the thalamus (Da Silva, Van Lierop, Schrijer, & Van Leeuwen, 1973). In particular, alpha power in diverse regions of posterior cortex has been found to correlate most significantly with the

structural and functional connectivity of those regions with primary visual cortex (Hindriks et al., 2015). Alpha may even represent an intrinsic rhythm of visual cortex given that transcranial magnetic stimulation of this region evokes oscillations mostly in the alpha band, whereas stimulation of more anterior regions evokes only higher frequency rhythms (Rosanova et al., 2009). Consequently, although alpha oscillations are generated in large part by activity in the thalamus, they are also strongly influenced by activity in posterior cortical regions. Alpha oscillations therefore reflect a complex product of both thalamocortical and corticocortical interactions in visual cortex. It should therefore be unsurprising that alpha oscillations have been intimately linked with many functions of visual processing. I dedicate the following sections to discussing these associations.

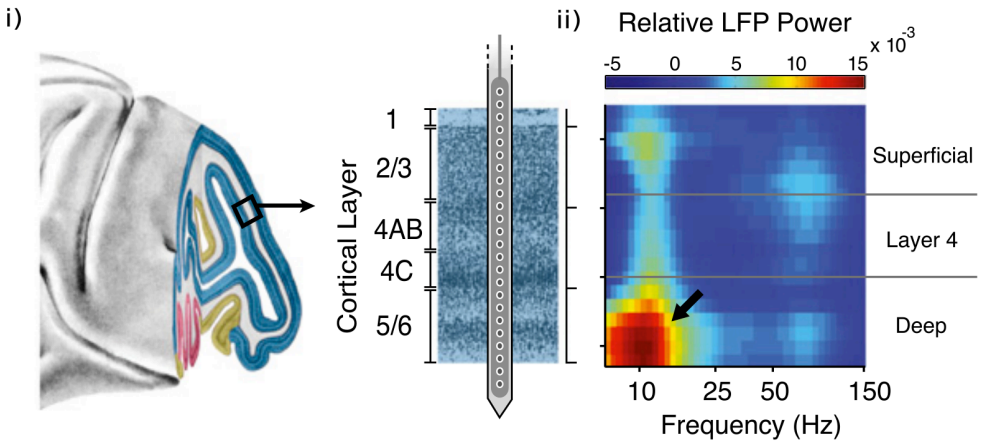


Figure 5 - Alpha is also generated in deep layers of cortex. i) A lateral view of the macaque brain. Regions highlighted in blue correspond to area V1. Multi-depth electrodes implanted into this region enable recording of visual activity across all layers of cortex. ii) A frequency-power spectrogram is show across cortical layers. Relative power in the alpha band is greatest in deep vs. superficial layers (adapted from van Kerkoerle et al., 2014).

THE CHARACTERS OF ALPHA

Alpha the irrelevance

Before discussing the possible contributions of alpha oscillations to visual cognition, it is important to first consider the opposing view that such oscillations may be

an irrelevance. Fourier's theorem states that any periodic signal can be expressed as the sum of many sinusoidal oscillations. However, this does not inevitably mean that the signal was produced by multiple oscillators. For example, known as the Gibbs phenomenon, a single square wave can be described as the product of dozens of sinusoidal oscillations. Furthermore, although microprocessors operate in fixed gigahertz cycles, their averaged electrical activity can be described misleadingly as the product of much slower oscillations (Jonas & Kording, 2017). Consequently, although frequency decompositions of EEG data may estimate power in the alpha band, this does not inevitably mean that alpha oscillations are produced by distinct systems in the brain.

This view is supported by the finding that 3 – 13% of human subjects do not exhibit any EEG alpha power above 1/f noise (Anokhin et al., 1992). Nevertheless, in the frequency spectra of remaining subjects, unique and unmistakable peaks are consistently observed above 1/f noise in the alpha band, with clear maxima over occipitoparietal brain regions (Figure 6; p.50). These oscillations are strongly influenced by genetics (Salmela et al., 2016), and are even preserved across species (Buzsáki, Logothetis, & Singer, 2013). Alpha oscillations are coordinated by dedicated pacemaker cells in the thalamus (Lőrincz et al., 2009), and have been specifically associated with activity in deep layers of cortex (Buffalo et al., 2011; van Kerkoerle et al., 2014). Furthermore, alpha oscillations are strongly associated with propagation of activity through visual regions of the brain (Hindriks et al., 2015), and may even represent an intrinsic rhythm of the human visual system. This latter point is evidenced by the finding that transcranial magnetic stimulation of occipital cortex evokes ringing oscillations mostly in the alpha band, while stimulation of more anterior regions produces only higher frequencies (Rosanova et al., 2009). Consequently, despite concerns about how frequency decompositions of brain activity are interpreted (Jonas & Kording, 2017), current evidence suggests that alpha oscillations represent a distinct feature of brain activity with strong links to visual processing.

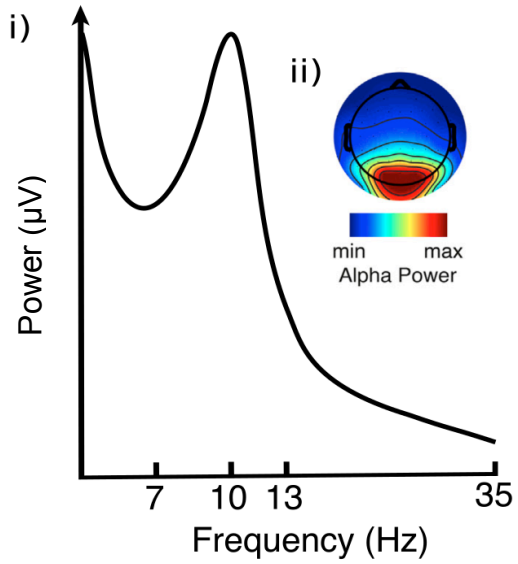


Figure 6 – EEG alpha peak and topography. i) An example of an EEG frequency power spectrum recorded from electrode P3 during a visual attention task. This spectrum follows a negative exponential distribution with the exception of a Gaussian-shaped peak in the alpha band (7 – 13 Hz). ii) When the spatial distribution of this alpha activity is calculated, it is commonly found to be greatest at posterior electrode sites (adapted from Helfrich et al., 2014).

Alpha the inhibitor

Increases in the amplitude of alpha oscillations have generally been associated with impairments in visual processing. Alpha power reduces rapidly in visual regions during periods of increased visual attention, but strengthens when these regions become disengaged (Fries, Womelsdorf, Oostenveld, & Desimone, 2008). This process is observed during shifts of spatial attention, in which reductions in alpha power are observed over the hemisphere processing attended visual space, whereas increases in alpha power are observed over the opposite hemisphere (Figure 7; p.51) (Gould, Rushworth, & Nobre, 2011; Kelly, Lalor, Reilly, & Foxe, 2006; Samaha, Sprague, & Postle, 2016; Worden, Foxe, Wang, & Simpson, 2000). Such differences in alpha power between the two visual hemispheres have been associated with improved detection of lateral stimuli in recordings of both spontaneous (Boncompte, Villena-González, Cosmelli, & López, 2016) and task-related brain activity (Gould et al., 2011). Spontaneous reductions in alpha power have also been associated with increases in the excitability of visual cortex. For example, during spontaneous periods of low alpha power, people are more likely to report seeing visual phosphenes during transcranial magnetic stimulation of visual cortex (Romei, Rihs, Brodbeck, & Thut, 2008), and to perceive visual stimuli when none has been presented (Iemi, Chaumon, Crouzet, &

Busch, 2017). Furthermore, supporting the negative association between alpha power and visual excitability, static magnetic field stimulation of visual cortex, which is thought to inhibit neural activity (Oliviero et al., 2011), induces significant increases in alpha power (Gonzalez-Rosa et al., 2015).

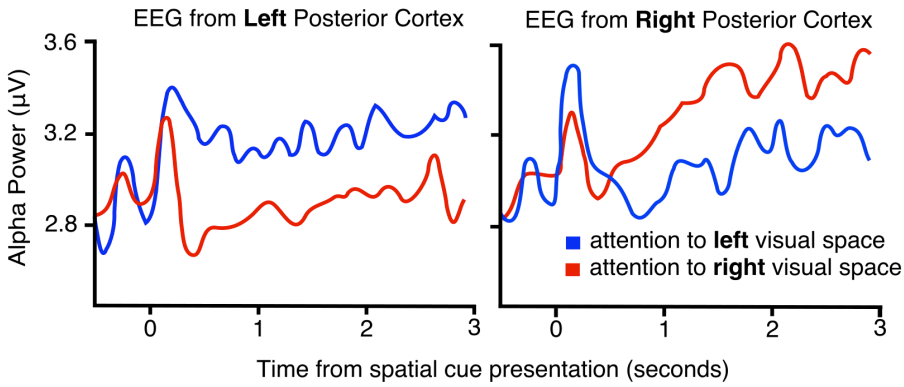


Figure 7 – Lateralised alpha power tracks shifts of attention. Posterior EEG alpha power is shown following presentation of cue stimuli in a visuospatial attention task. These cue stimuli tell participants to shift their attention to either the left or right sides of visual space. This shifting of attention increases alpha power over posterior cortex ipsilateral to the attended hemifield (i.e. over areas of visual cortex that will not process the anticipated visual stimulus) (adapted from Kelly et al., 2006).

Alpha oscillations have therefore been suggested to reflect periods of visual inactivity (Lundqvist et al., 2013; Pfurtscheller et al., 1996). However, in addition to marking disengagement, alpha may also play active roles in suppressing visual activity. Strong evidence in support of this view comes from observations of increased alpha power when visual processing must be actively inhibited. For example, alpha power commonly increases when people are required maintain information in visual working memory, and therefore must prevent memorised information from being corrupted by irrelevant visual inputs (Jensen, Gelfand, Kounios, & Lisman, 2002; Jokisch & Jensen, 2007). When distracting images are presented during these periods of memory retention, increases in alpha power are found to predict reduced processing of task-irrelevant

stimuli (M. Bonnefond & Jensen, 2012, 2013). Furthermore, in contrast to the aforementioned studies linking alpha primarily with visual disengagement (e.g. Iemi et al., 2017), increases in alpha power during periods of memory retention are greatest with increased memory load (Jensen et al., 2002; Tuladhar et al., 2007). Such alpha increases are also associated with improved memory performance (Lozano-Soldevilla, ter Huurne, Cools, & Jensen, 2014).

Alpha oscillations may therefore represent an active mechanism of inhibition in the brain, used to suppress irrelevant visual processing (Clayton et al., 2015; Jensen & Mazaheri, 2010). As mentioned at the end of the previous chapter, alpha oscillations have been suggested to facilitate the maintenance of attention over time by suppress cognitive processes that are irrelevant to the task at hand (Clayton et al., 2015). Causal evidence to support this view of alpha as an inhibitory rhythm is provided by the finding that transcranial magnetic stimulation of lateral visual cortex at 10 Hz, which is known to entrain alpha oscillations (Thut et al., 2011), biases attention away from areas of visual space processed by the stimulated region. This is in contrast to stimulation at 5 and 20 Hz (Figure 8; p.53) (Romei, Gross, & Thut, 2010). Alpha oscillations may suppress visual processing by directly activating inhibitory systems in the brain. This was suggested by van Kerkoerle et al. (2014) who proposed that alpha oscillations are driven in large part by the activity of layer 6 neurons in visual cortex, which are known to inhibit local processing by directly activating local inhibitory neurons (Olsen, Bortone, Adesnik, & Scanziani, 2012). Of relevance to this point is the finding that optogenetic stimulation of layer 6 cortical neurons at 10 Hz inhibits sensory thalamus (Crandall, Cruikshank, & Connors, 2015). Another explanation for the link between alpha and inhibition is that increases in alpha power reflect a transition towards neural hypersynchrony, which is known to impair sensory processing (Rajagovindan & Ding, 2011; Supp et al., 2011). However, despite links between alpha oscillations and suppression, it is important to note that these inhibitory effects of alpha are fundamentally rhythmic rather than tonic in

nature (often referred to as 'pulsed inhibition'; Mathewson et al., 2011). Furthermore, these cycles of inhibition may even play positive roles in visual perception.

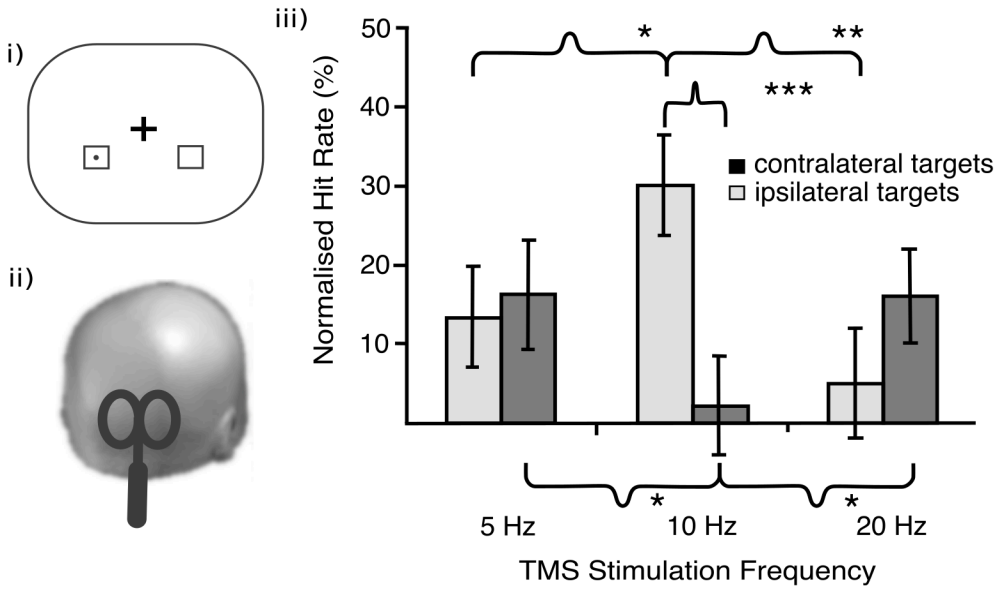


Figure 8 – 10 Hz TMS biases attention towards ipsi-, and away from contra-lateral visual space. i) Participants were required to detect the presentation of faint black dots in either the left or right sides of visual space. ii) TMS was applied at a range of frequencies to lateral visual cortex immediately preceding the presentation of these faint dots. iii) TMS at 10 Hz improved detection performance when delivered to visual cortex ipsilateral to the presented stimuli, but impaired performance when delivered to contralateral visual cortex. *p < 0.05, **p < 0.01, ***p < 0.001 (adapted from Romei et al., 2010).

Alpha the perceiver

A curious visual illusion was recently reported by Sokoliuk and VanRullen (2013) in which a stationary, radial image, composed of black and white spokes, appears to flicker at a rapid pace when viewed in the visual periphery. In a perceptual matching task, in which people were asked to compare this illusion to genuinely flickering stimuli, people reported the closest similarity to flickers at alpha frequencies (Figure 9; p.54). Furthermore, the intensity of this illusion correlated positively with EEG alpha power, with flickers most often reported during periods of high alpha power (Sokoliuk & VanRullen, 2013). This finding suggests that alpha oscillations, rather than universally inhibiting visual processing, may also facilitate periodic sampling of visual information from the

environment. Consistent with this view, many studies have shown that visual stimuli are better processed when presented at the trough of an alpha oscillation compared to its peak (Busch, Dubois, & VanRullen, 2009; Dugué, Marque, & VanRullen, 2011; Mathewson, Gratton, Fabiani, Beck, & Ro, 2009). Furthermore, the amplitude of gamma oscillations (30 – 100 Hz) in visual cortex is known to covary with changes in alpha phase (Bahramisharif et al., 2013; Osipova, Hermes, & Jensen, 2008). As gamma oscillations are strongly associated with stimulus processing (Fries et al., 2008), this again suggests the involvement of alpha oscillations in the cyclical regulation of perception.

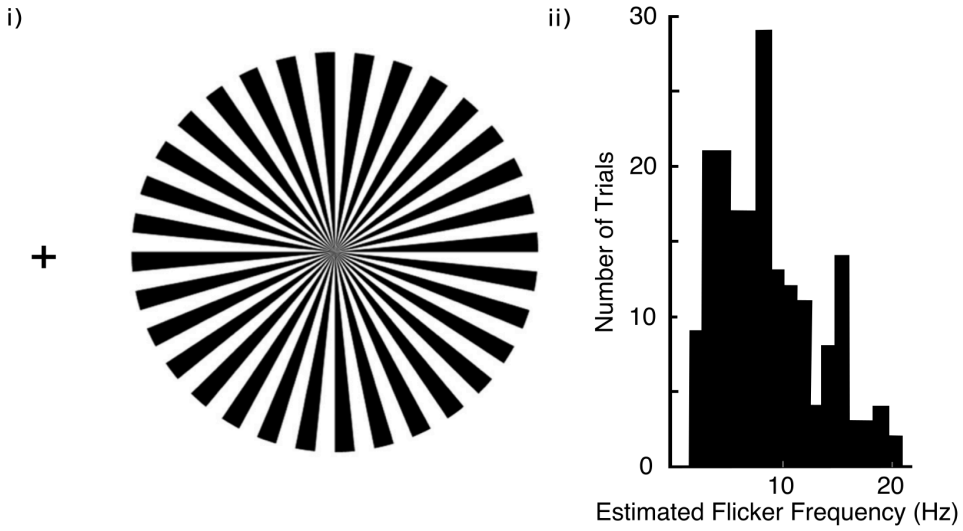


Figure 9 – 'Flickering Wheel' illusion elicits perceptual flickers at alpha frequencies. i) When viewed in the visual periphery (e.g. when focusing on the left-hand fixation cross), these circular spokes are often perceived to flicker. ii) A histogram showing the distribution of estimated frequencies of the perceived illusory flicker over many trials. Participants most commonly matched this illusory flicker to reference flickers in the alpha band. Note that, in the original dataset, the illusion was also matched to a flicker of around 45 Hz on one trial (adapted from Sokoliuk & VanRullen, 2013).

Such cycles may be used as a mechanism to regulate the timing of visual attention. When people are shown images that flicker at alpha frequencies, a process known to entrain alpha oscillations (Notbohm, Kurths, & Herrmann, 2016; Spaak, de Lange, & Jensen, 2014), subsequently presented visual stimuli are better detected when

displayed in-phase with that initial flicker (Mathewson et al., 2012; Spaak et al., 2014). This finding may reflect entrainment of attention at alpha frequencies to predictable, cyclical patterns in the environment (Mathewson, Fabiani, Gratton, Beck, & Lleras, 2010). Similarly, telling someone when an upcoming visual stimulus will be presented facilitates the perception of that stimulus and biases alpha phase towards the optimal position for visual processing (Samaha, Bauer, Cimaroli, & Postle, 2015). Alpha oscillations can also be reset by auditory stimuli, perhaps facilitating multi-sensory interactions to aid perception of external stimuli (Romei, Gross, & Thut, 2012). Nevertheless, it should be noted that expectations of stimulus presentations have been found to modulate alpha power while leaving alpha phase unaffected (van Diepen, Cohen, Denys, & Mazaheri, 2015).

In addition to influencing the timing of visual attention, alpha oscillations in posterior cortex may also regulate the temporal resolution of perception. For example, two visual flashes, presented within one alpha cycle (i.e. ~100 milliseconds) are often perceived as a single event (Kristofferson, 1967). People are better able to correctly classify double flashes as separate events when their peak alpha frequency is high, indicating a positive relationship between the speed of an individual's alpha oscillations and the temporal resolution of their perception (Samaha & Postle, 2015). Furthermore, alpha peak frequencies have been found to increase, compared to periods of rest, when people perform challenging visual tasks that require greater processing of visual information (Haegens, Cousijn, Wallis, Harrison, & Nobre, 2014). It therefore seems that alpha oscillations may play active roles in both segmenting visual inputs into discrete events and regulating the speeds of visual processing. On a related note, it is also interesting to consider that alpha oscillations have been suggested to play an important role the 'triple flash' illusion: a phenomenon where people report seeing three visual stimuli following the presentation of only two stimuli with an stimulus onset asynchrony of ~100 ms. Specifically, it has been theorised that this illusion is caused by the

superposition of two alpha oscillations, evoked by each of the two visual stimuli, that creates a third peak of activation when the delay between these evoked oscillations matches their oscillatory period (e.g. 100 ms; Bowen, 1989). Consistent with this idea, the optimal stimulus onset asynchrony for this illusion has been found to correlate with individual peak alpha frequency in parietal, but not occipital cortex (Gulbinaite, İlhan, & VanRullen, 2017). This finding suggests that alpha oscillations can induce experiences of visual stimuli that have not been presented, further supporting the positive association between alpha in visual perception. The finding also highlights the fact that alpha peak frequencies can differ between regions of posterior cortex (e.g. Haegens et al., 2014), and suggests that alpha activity in parietal cortex may be more important for regulating visual perception than alpha in visual cortex.

In addition to these associations between alpha oscillations and cycles in visual perception, there are also many studies that suggest associations between alpha and perception that go beyond rhythmic fluctuations. For example, although presentation of visual images with low spatial frequency increase gamma power in visual cortex, images with high spatial frequency evoke greater increases in the alpha band (Fründ, Busch, Körner, Schadow, & Herrmann, 2007). Conscious perception of near-threshold visual stimuli has also been associated with increased alpha power in occipital and fronto-parietal regions (Babiloni, Vecchio, Bultrini, Romani, & Rossini, 2006). Furthermore, many event-related components known to be associated with processes of visual perception have been suggested to reflect stimulus-induced modulations of alpha power and phase (W. Klimesch, Fellinger, & Freunberger, 2011). Additionally, in contrast to the view that alpha reflects inhibition of visual processing alone, presentation of flickering lights at alpha frequencies to individuals with their eyes closed has been found to induce a range of visual experiences: rings, squares, and spirals of different colours and intensities (Mauro, Raffone, & VanRullen, 2015; Pearson et al., 2016; Shevelev et al., 2000). These visions are altered by the frequency of the flicker, with individuals most

commonly reporting radial images when stimulated at frequencies of less than 10 Hz, and spiral images when stimulated above 10 Hz (Figure 10; p.57) (Mauro et al., 2015). In general though, such hallucinations are reported with the highest probabilities when flickering stimulation is delivered at an individual's peak alpha frequency (Kamenkovich, Bark, Shevelev, & Sharaev, 1997; Shevelev et al., 2000). Furthermore, these experiences have been reported to vary with the direction in which alpha oscillations propagate through the brain, with ring and spiral hallucinations associated with alpha rhythms travelling from occipital to frontal cortex (Shevelev et al., 2000). Consequently, while an extensive body of research links alpha oscillations to periodic regulation of visual perception, there is also evidence suggesting a positive association between alpha activity and the perception of complex visual images. One reason for this association might be the link between alpha oscillations and feedback signalling in visual cortex.

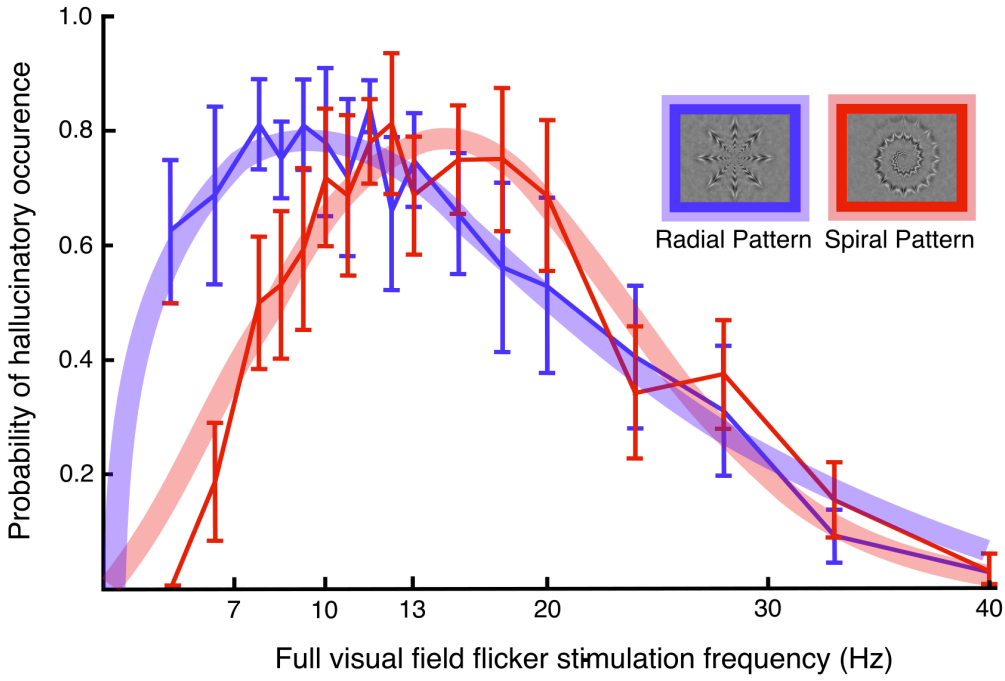


Figure 10 – Flickering visual stimulation at alpha frequencies elicits radial and spiral hallucinations. The probability of the occurrence of spiral and radial hallucinatory patterns is plotted for visual flickers at different frequencies. Radial patterns (blue line) are more commonly reported at flicker frequencies just below 10 Hz, while spiral patterns (red line) are more commonly perceived at flicker frequencies just greater than 10 Hz. In general though, hallucinatory patterns are most commonly perceived at flicker

frequencies in the alpha band (i.e. 7 – 13 Hz). Error bars display SEM across observers. Thick background lines represent the best-fitting Weibull function to the grand-average data (adapted from Mauro et al., 2015).

Alpha the predictor

An interesting feature of alpha oscillations is that they are observed with different levels of synchrony across different cortical layers (although see Haegens et al., 2015). Specifically, alpha oscillations are often recorded with higher amplitudes in deep layers of cortex, while gamma oscillations dominate superficial layers (Buffalo et al., 2011; van Kerkoerle et al., 2014). Pyramidal neurons in superficial layers are thought to project in a bottom-up fashion to higher-level regions, while deep layers exhibit feedback projections in the opposite direction (Felleman & Van Essen, 1991). It has therefore been suggested that these different directions of travel in the brain may be distinguished by different frequencies of neural activity: with gamma oscillations reflecting bottom-up processing, and alpha / low beta oscillations communicating feedback (Bastos et al., 2015; Jensen, Bonnefond, Marshall, & Tiesinga, 2015). This idea was recently supported by Michalareas et al. (2016) who identified areas of visual cortex and classified their interactions as either feedback or feedforward using tractography data collected in macaques. Analysing magnetoencephalography in humans, Michalareas et al. (2016) found that Granger causality from high to low levels of visual cortex (i.e. feedback interactions) was strongest around an alpha peak of 11 Hz, while interactions in the opposite direction dominated in the gamma band (~60 Hz). This view that alpha facilitates feedback processes in the brain is also supported by the finding that electrical stimulation of area V4 in macaques elicits alpha oscillations in the lower area V1, while microstimulation of V1 elicits gamma oscillations in V4 (van Kerkoerle et al., 2014). Interestingly, these electrically evoked alpha rhythms in V4 were suppressed when NMDA receptors were blocked. As NMDA is thought to be involved in feedback processing (Self, Kooijmans, Supèr, Lamme, & Roelfsema, 2012), this suggests a further

interaction between alpha oscillations and the neurochemical mechanisms of top-down control. Of relevance to this point is that finding that a cholinergic agonist strengthens the lateralisation of alpha power in visual cortex when participants shift their attention to one side of visual space (Bauer et al., 2012). Acetylcholine has also been implicated in feedback processing (e.g. Deco & Thiele, 2011).

While the strongest evidence linking alpha / low-beta oscillations to feedback comes from these kinds of physiological investigations, further evidence has also been provided by behavioural studies. For example, when individuals self-generate auditory and visual stimuli (e.g. press a button to display a stimulus), alpha power increases in areas of sensory cortex that process this self-generated information (Cao, Thut, & Gross, 2017; Stenner, Bauer, Haggard, Heinze, & Dolan, 2014). Although such increases in alpha power could reflect suppression of irrelevant sensory processing, these findings also suggest the possible involvement of alpha in communicating predictions to sensory cortex (Cao et al., 2017). This idea has received support from the observation of increased pre-stimulus alpha power in task-relevant brain networks when participants are able to predict the identity of an upcoming stimulus (Mayer, Schwiedrzik, Wibral, Singer, & Melloni, 2016). However, perhaps the strongest evidence to support the involvement of alpha oscillations in top-down prediction comes from a recent study by Sherman, Kanai, Seth, and VanRullen (2016). Here, participants were required to detect the occurrence of rapidly presented Gabor patches. On each task block, participants were told that these patches would be presented on either the minority or majority of trials. As with previous studies, an association was observed between target detection performance and alpha phase at the moment of stimulus presentation. However, participant expectations had a significant effect on this association. Although participants were more likely to respond to a Gabor patch delivered at an intermediate phase position (0°) in blocks with majority target occurrence, this same phase position was conversely associated with a lower propensity to respond in blocks with minority target occurrence

(Figure 11; p.60). In other words, a phase position between the peak and trough of the alpha oscillation was associated with a more liberal response bias when targets were common, but a conservative bias when they were rare. Given that the trough of alpha has, in contrast, been associated with improved processing of external stimuli (e.g. Busch et al., 2009), this suggests that alpha oscillations may reflect periods of alternation between bottom-up processing and top-down predictions in visual cortex.

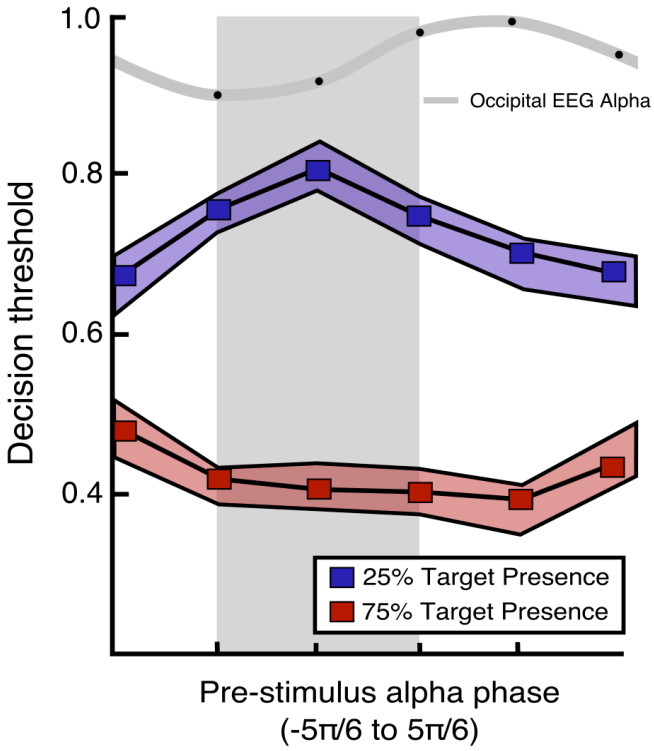


Figure 11 – Expectation alters the association between alpha phase and target detection performance. The relationship between decision threshold and binned occipital 10 Hz EEG phase 119 milliseconds prior to stimulus presentations. Grey shading indicates the phase values that maximally predict the influence of expectation on decision. An intermediate phase position (approximately 0 degrees) was associated with a higher decision threshold in the expect 25% target presence condition, but a lower threshold in the expect 75% target presence condition. In other words, decisions were maximally biased toward reporting “no” when participants did not expect a stimulus to be presented, but toward “yes” when participants did expect a stimulus to be presented. Shaded, coloured outlines represent within-subject SEM (adapted from Sherman et al., 2016).

Alpha the communicator

Similar to this view that alpha facilitates transmission of predictions to visual cortex, alpha oscillations have also been associated with propagation of activity throughout the brain. This is particularly true of communication between occipital, parietal, and frontal regions (Saalmann, Pinsk, Wang, Li, & Kastner, 2012), as well as between thalamus and posterior cortex (Saalmann et al., 2012). A central way in which these oscillations could facilitate propagation of activity is by synchronising cycles of excitability between distant brain areas, and thereby increasing the likelihood that spikes from one area will arrive during the excitable phase of the other (Fries, 2005). Consistent with this idea, when individuals shift their attention to one side of visual space, alpha oscillations in both frontal and parietal cortex have been found to synchronise with alpha oscillations in visual cortex contralateral to the attended hemifield (Doesburg, Green, McDonald, & Ward, 2009; Sauseng et al., 2005). This long-range synchronisation of alpha occurs simultaneously with local alpha synchronisation in ipsilateral visual cortex, suggesting the involvement of alpha in both sensory inhibition and integration of top-down control networks dedicated to the coordination of visual attention (Doesburg et al., 2009). Alpha oscillations have also been reported to synchronise between frontal and parietal areas when individuals recognise visual objects (Freunberger, Klimesch, Griesmayr, Sauseng, & Gruber, 2008), and during retention of information in visual working memory (Daume, Gruber, Engel, & Friese, 2017; Doesburg et al., 2010). However, alpha oscillations may also facilitate long-range transmission of information by propagating across the brain in travelling waves.

Travelling alpha waves were reported in some of the earliest EEG studies (J. R. Hughes, 1995). In contrast to long-range synchronisation, in which phase differences are usually fixed between communicating regions (often with 0° phase-lag; Fries, 2005), travelling waves are defined as periods in which phase differences between brain

regions increase linearly with distance from a target region (Patten et al., 2012). For example, an alpha wave travelling from frontal to posterior cortex would be observed as a gradual increase in the phase lag of alpha activity along a fronto-posterior axis with respect to a frontal lead electrode (Figure 12; p.63). Such travelling waves have been reported in a number of brain regions, and over a range of frequencies (e.g. Lubenov & Siapas, 2009). Nevertheless, alpha and gamma oscillations recorded at occipitoparietal electrode sites have been found to exhibit the most diverse and reliable phase differences with respect to activity recorded at other electrode sites (van Ede, Van Pelt, Fries, & Maris, 2015). Given that alpha waves commonly travel at speeds of 5 – 15 metres per second (J. R. Hughes, 1995), as measured by tracking the progression of alpha phase between electrode sites (e.g. Patten et al., 2012), alpha waves have been argued to most likely reflect intra-cortical propagation of activity (Hindriks, van Putten, & Deco, 2014). However, given the known involvement of the pulvinar in synchronising visual regions at alpha frequencies (Saalmann et al., 2012), travelling alpha waves may also be coordinated by the thalamus (Llinas, Ribary, Contreras, & Pedroarena, 1998).

Travelling waves are thought to play important roles in visual processing (Han, Caporale, & Dan, 2008; Muller, Reynaud, Chavane, & Destexhe, 2014). Consistent with this view, presentation of visual stimuli can generate travelling alpha waves that propagate from occipital to frontal cortex (W. Klimesch, Hanslmayr, Sauseng, Gruber, & Doppelmayr, 2007; Patten et al., 2012). Relatedly, it was previously mentioned that visual hallucinations caused by alpha flickers vary with the direction in which travelling alpha oscillations travel through the brain (Shevelev et al., 2000). Furthermore, in an invasive recording study, Bahramisharif et al. (2013) found that gamma activity in visual cortex, known to play an important role in sensory processing, is coordinated by alpha oscillations that propagated across posterior cortex. Such alpha oscillations have also been found to travel from high- to low-level regions of cortex. For example, alpha oscillations in area V1 lag behind those of V4, with granger causality analysis indicating

a flow of alpha activity between these regions in a top-down manner (van Kerkoerle et al., 2014). Furthermore, reaction times are reportedly faster to visual stimuli that are presented during the occurrence of alpha waves propagating from frontal to occipital cortex, compared to the opposite direction (Patten et al., 2012). This again points to an association between alpha waves travelling along a fronto-posterior axis and the engagement of top-down control. Consequently, it seems that alpha oscillations can facilitate communication of information across the brain through multiple means: both via synchronisation of activity within functional brain networks, and through the direct propagation of activity through the brain.

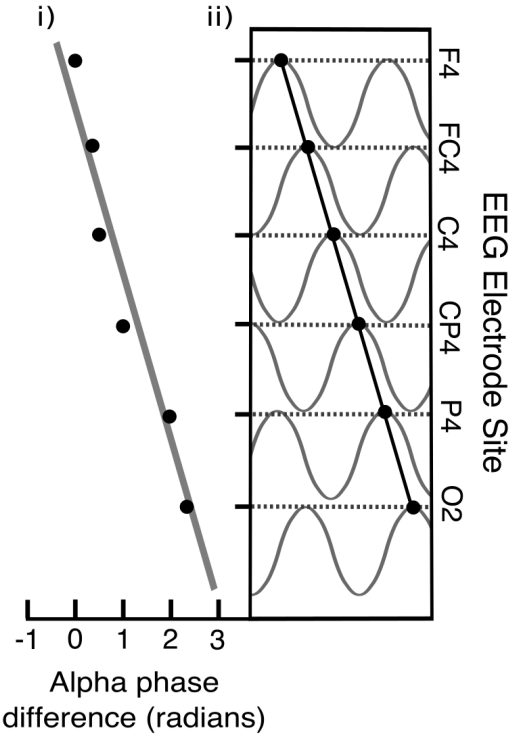


Figure 12 – Alpha wave travelling from frontal to occipital cortex. i) An example of gradual phase shifts along a chain of electrodes from F4 to O2 for one subject. The black dots reflect the different phase difference values. The solid line shows a linear fit to these values (adapted from Patten, Rennie, Robinson, & Gong, 2012). ii) An illustration of how these gradual phase shifts would appear in EEG recordings from F4 to O2.

Alpha the stabiliser

The last point I would like to discuss is the positive association of alpha oscillations with stability in visual processing. This view has been suggested by studies of multistable perception finding that people are more likely to report changes in their perception of ambiguous visual stimuli (e.g. Necker cubes) during periods of reduced alpha power (e.g. Isoglu-Alkaç et al., 2000; Mathes, Pomper, Walla, & Basar-Eroglu,

2010). Such reductions in alpha have been suggested to reflect destabilisation of ongoing perceptual interpretations, facilitating shifts towards alternative interpretations (Piantoni, Romeijn, Gomez-Herrero, Van Der Werf, & Van Someren, 2017; Strüber & Herrmann, 2002). Decreases in alpha power are similarly reported when people switch their attention between different visual tasks (Foxe, Murphy, & De Sanctis, 2014), while increases in alpha power are observed when people maintain information in visual working memory (Jensen et al., 2002; Jokisch & Jensen, 2007). Although this latter finding could reflect suppression of irrelevant visual processing, it may also suggest a positive role for alpha in maintaining on-going processing (Johnson, Sutterer, Acheson, Lewis-Peacock, & Postle, 2011). It is also interesting to note that slow event related potentials, evoked during the retention of information in visual working memory (known as 'contralateral delayed activity'), have been associated with asymmetric modulations in the peaks and troughs of alpha oscillations (Mazaheri & Jensen, 2008; van Dijk, van der Werf, Mazaheri, Medendorp, & Jensen, 2010). This again suggests an involvement of brain activity at alpha frequencies with sustained maintenance of ongoing, visual processing.

One reason why alpha oscillations may promote stability in visual processing is that they are fundamentally bistable in nature. In resting state EEG recordings, alpha rhythms have been found to periodically shift between high- and low-amplitude modes (Freyer, Aquino, Robinson, Ritter, & Breakspear, 2009). This is consistent with computational models in which alpha switches between distinct attractors states, with one representing a default state of reduced stimulus processing, and the other facilitating increased stimulus processing (Lundqvist et al., 2013). Such bistability in alpha oscillations may aid stability in visual attention as switches between two discrete, neural states should require greater changes in neural excitation than gradual changes across a continuum of neural states. In addition, it is also interesting to note that beta oscillations, while also associated with a large number of cognitive processes (e.g.

Bastos et al., 2015; Etchell, Johnson, & Sowman, 2014; Hanslmayr, Matuschek, & Fellner, 2014), have been linked with the maintenance of sensorimotor processing (Engel & Fries, 2010) and are thought to be an intrinsic property of motor cortex (Ferrarelli et al., 2012; Rosanova et al., 2009). As alpha oscillations may be an intrinsic property of visual cortex (Hindriks et al., 2015; Rosanova et al., 2009), this could also suggest a general association between stability of processing in a given brain region and neural activity at the resonant frequency of that region.

CONCLUSION

In this chapter, after describing some of the neural mechanisms that most likely contribute to the generation of alpha oscillations, I reviewed evidence associating these rhythms with five distinct aspects of neurocognitive functioning. To summarise, alpha oscillations are negatively associated with visual attention, as increases in EEG alpha power are strongly associated with reductions in visual processing. This may reflect the involvement of alpha oscillations in suppressing visual activity. Nevertheless, this suppression is fundamentally periodic and may also play important roles in regulating visual perception. This point is supported by evidence linking alpha oscillations to the segregation of visual inputs into discrete events, as well as by the finding that delivery of flickering lights at alpha frequencies during eyes-closed rest can illicit strong visual experiences. One way in which alpha may support perception is by facilitating top-down predictions in visual cortex. Intriguingly, alpha oscillations may periodically regulate the influence of predictions and bottom-up inputs on visual processing. However, alpha oscillations have also been associated with communication across the brain more generally, particularly through long-range phase synchronisation, and through travelling waves that propagate between frontal and posterior brain regions. In addition, alpha oscillations may play important roles in stabilising visual processing.

Alpha oscillations have therefore been associated with a wide variety of cognitive processes. While some of these processes may appear to suppress visual attention (i.e. inhibition), others may be integral to the maintenance of sustained attention (e.g. top-down control, stabilisation). In order to determine the true roles of alpha oscillations in cognition and, more importantly, to better control these rhythms for the purposes of improving sustained attention, it is necessary that we find methods that can facilitate modulation of alpha oscillations in experimental / real-world settings. For this purpose, I focus on *transcranial alternating current stimulation*. I dedicate the following chapter to discussion of this technique.

CHAPTER 3 – TRANSCRANIAL ALTERNATING CURRENT STIMULATION

The idea of using electrical currents to modulate brain activity can be traced back to antiquity (Sarmiento, San-Juan, & Prasath, 2016). Both Plato and Aristotle described how the electrical discharges of torpedo fish could positively influence human health (Althaus, 1873). However, it is only in the last decade or so that transcranial electrical stimulation (tES) at low amplitudes has been applied for basic research purposes. This trend is illustrated in Figure 13 (p.67), which shows consistent growth the number of academic papers on *Web of Science* from 2000 to 2016 that include the term "*transcranial direct current stimulation*" (tDCS). Figure 13 also shows an increase, starting around 2008, in the use of both "*transcranial alternating current stimulation*" (tACS) and "*transcranial random noise stimulation*". This oscillatory form of electrical stimulation (specifically tACS) has been show to modulate oscillatory brain activity, and is a focus of this thesis.

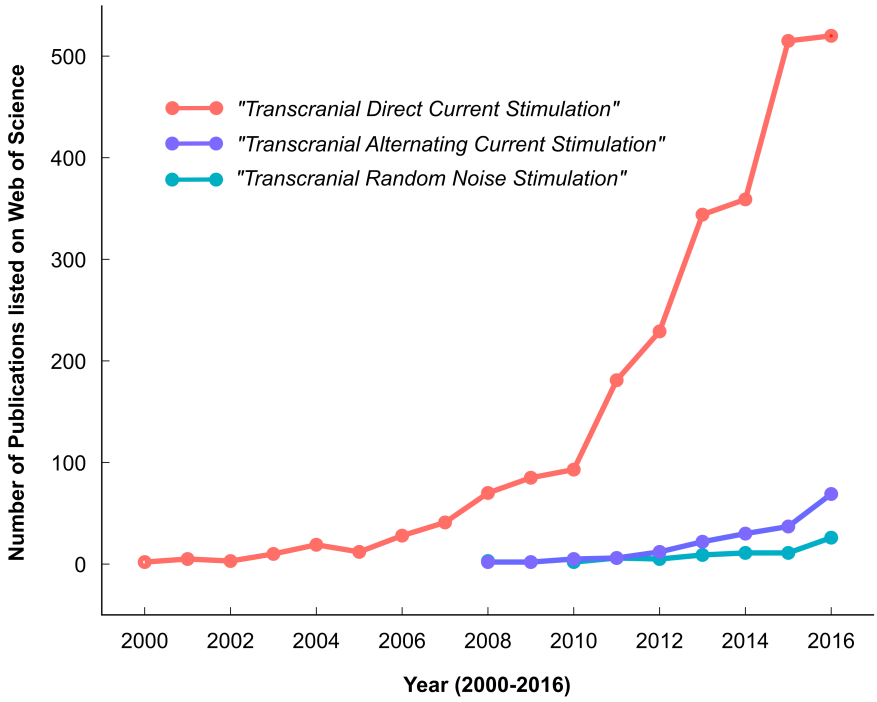


Figure 13 – Growth in studies using tES (2000 – 2016). The number of academic papers on *Web of Science*, from the year 2000 to 2016, including the terms "*transcranial direct current stimulation*", "*transcranial alternating current stimulation*", and "*transcranial random noise stimulation*". A

significant rise in the use of transcranial direct current stimulation is observed from the year 2000. Growth of a similar shape, but reduced size, is also observed in the use of transcranial alternating current and random noise stimulation from around 2008.

In this chapter, I first describe the standard methods by which electrical currents are delivered to the brain. I also discuss reasons why tES is used in cognitive neuroscience (i.e. the strengths of this technique over alternatives). I then review current understanding of the ways in which both direct and alternating electrical fields are thought to influence neural function. I finish by giving an overview of the ways in which tACS has been found to influence brain activity and cognition. These final sections focus predominantly on the effects of ~10 Hz over occipitoparietal cortex.

HOW ELECTRICAL CURRENTS ARE DELIVERED TO THE BRAIN

In all forms of tES, electrical currents are delivered from a battery to the brain via wires connected to electrodes positioned on the head or body. These electrodes generally consist of metal or conductive-rubber electrodes, enclosed in sponge pockets that are saturated in an electrolyte solution (e.g. saline solution). Software is commonly used to control the shape and frequency characteristics of waveforms delivered to the brain. This allows for the delivery of transcranial alternating and random noise stimulation, in addition to direct current stimulation.

In classic implementations of tES, currents are delivered through two large electrodes (usually 20-35 cm^2) on the scalp. Large electrodes have the advantage of increased safety as they reduce the density of currents delivered to the brain (Nitsche et al., 2003). High-density electrical currents are more likely to damage neural tissue (e.g. Bikson, Datta, & Elwassif, 2009). In most studies, it is common to position one electrode over a 'target' brain region (e.g. motor cortex), and to position the other over a 'reference' region (e.g. orbitofrontal cortex) (e.g. Nitsche & Paulus, 2000). To maximise

the extent to which delivered electrical currents penetrate the skull, it is thought that stimulating electrodes should be placed far apart from each other on the scalp (Rush & Driscoll, 1968). Nevertheless, this has the disadvantage of reducing the spatial specificity of electrical currents delivered to the brain. To address this issue, recent modeling studies suggest that specific regions of the brain can be targeted by applying electrical currents through multiple, smaller electrodes (i.e. ~1.5cm^2) arranged in a ring-shape around a target brain region (Datta et al., 2009). However, this increased proximity of electrodes must conversely reduce the depth at which currents can be delivered to the brain.

The extent to which tES influences brain function is difficult to determine. Even with large distances between stimulating electrodes, it has been suggested that around 50% of delivered currents travel only across the scalp, and therefore do not penetrate into cortex (Miranda, Lomarev, & Hallett, 2006; Rush & Driscoll, 1968). In some cases, as much as 90% of delivered currents may bypass the brain in this way (Underwood, 2016). Nevertheless, modelling studies have suggested that, even with these shunting effects, tES should be able to induce intracranial electric fields that are large enough to influence neural function. For example, a modelling study by Miranda et al. (2006) found that tDCS at 2 mA should induce an electric field inside the brain of 0.22 V/m. Similarly, tD/tACS, delivered at 1 mA over visual cortex, should result in a cortical electric field of 0.417 V/m (Neuling, Wagner, Wolters, Zaehle, & Herrmann, 2012). Importantly, electrical fields of comparable strengths have been found to modulate the firing of neural populations exposed to them (e.g. Fröhlich & McCormick, 2010). Consequently, such evidence supports the view that tES has the potential to influence neural activity.

WHY USE tES?

Before addressing the ways in which tES can influence brain activity, it is important to discuss why tES has been chosen as a technique of interest for so many researchers

in cognitive neuroscience. One prominent reason is the idea that tES can allow one to assess the causal roles of different types of brain activity in cognition (e.g. Clayton et al., 2015). Another reason is the view that tES can help facilitate real-world improvements in cognitive functioning (e.g. Cohen Kadosh, 2014). Indeed, both of these aims are listed as central motivations for this PhD project in the prelude to this thesis. For these purposes, tES has a number of limitations. For example, depending on stimulation amplitudes and electrode impedance levels, tES can elicit tickling and itching sensations on the scalp (Poreisz, Boros, Antal, & Paulus, 2007). In extreme cases, tES has even been reported to cause lesions of the skin (Palm et al., 2008). In addition, when applied at moderately low frequencies (i.e. tACS; ~0.1 – 20 Hz), tES can cause perception of visual flickers, generated by direct activation of the retina (Schutter & Hortensius, 2010). Such side effects inevitably limit the usefulness of tES both in assessing the contribution of brain activity to cognition, and in facilitating real-world improvements in cognition (Schutter, 2016). Nevertheless, in comparison to other methods of neuromodulation (e.g. transcranial magnetic stimulation), tES does have a number of distinct advantages.

Transcranial magnetic stimulation (TMS) involves the delivery of rapidly fluxing magnetic fields to the brain. Through electromagnetic induction, these magnetic fields induce electrical currents in neural tissue exposed to them. Such currents can generate action potentials in stimulated neural populations (Wassermann, Epstein, & Ziemann, 2008). TMS is therefore a very effective method of non-invasive brain stimulation. However, TMS can cause uncomfortable contractions of muscles on the head (especially over frontal regions). Furthermore, TMS can only be delivered in pulses, with each pulse generating a loud, clicking noise. Such noises make it difficult to study the roles of neural oscillations in cognition. This is because different frequencies of TMS can easily be distinguished from each other by the different delays periods between clicks. In other words, it is difficult to ensure that both participants and experimenters are blind to stimulation conditions with TMS (Broadbent et al., 2011; Duecker & Sack, 2015). In

contrast, people commonly find it difficult to distinguish between placebo and full-amplitude tES (e.g. Gandiga, Hummel, & Cohen, 2006). Lastly, given its increased intensity, TMS can only be delivered safely for relatively short periods (Rossi, Hallett, Rossini, Pascual-Leone, & Group, 2009). This is in contrast to tES, which can be delivered for longer periods (i.e. ~20 minutes), and over repeated sessions (e.g. Snowball et al., 2013). Furthermore, TMS can usually only be applied through the use of expensive and heavy equipment. This is contrast to tES, which is cheaper, and can be applied wirelessly (as in this project). Consequently, in addition to ensuring good stimulation condition blinding, tES has much greater potential for enhancing cognitive functioning in real-world settings.

THE MECHANISMS OF TRANSCRANIAL ELECTRICAL STIMULATION

The effects of direct electrical currents on neural activity

Short-term effects on stereotypical, pyramidal neurons

Neurons operate in electrically excitable states by maintaining voltage gradients across their membranes. These gradients are created by the combined activity of ion pumps / channels in neural membranes that generate differences in the concentrations of electrically charged ions inside vs. outside the neuron. When the neuron is inactive, it operates a resting voltage of around -70 mV. However, if this voltage moves towards 0 mV (e.g. following depolarising inputs from a pre-synaptic neuron), and if it passes around -55 mV, channels in the neural membranes will open, allowing positively charged, extracellular sodium ions to rush in, pushing the voltage of the neuron to around +30 mV. This depolarisation moves along the axon of the neuron, creating an 'action potential' that in turn influences the voltage of post-synaptic neurons that receive input from the active, presynaptic neuron. This is the basis of all neural activity and communication.

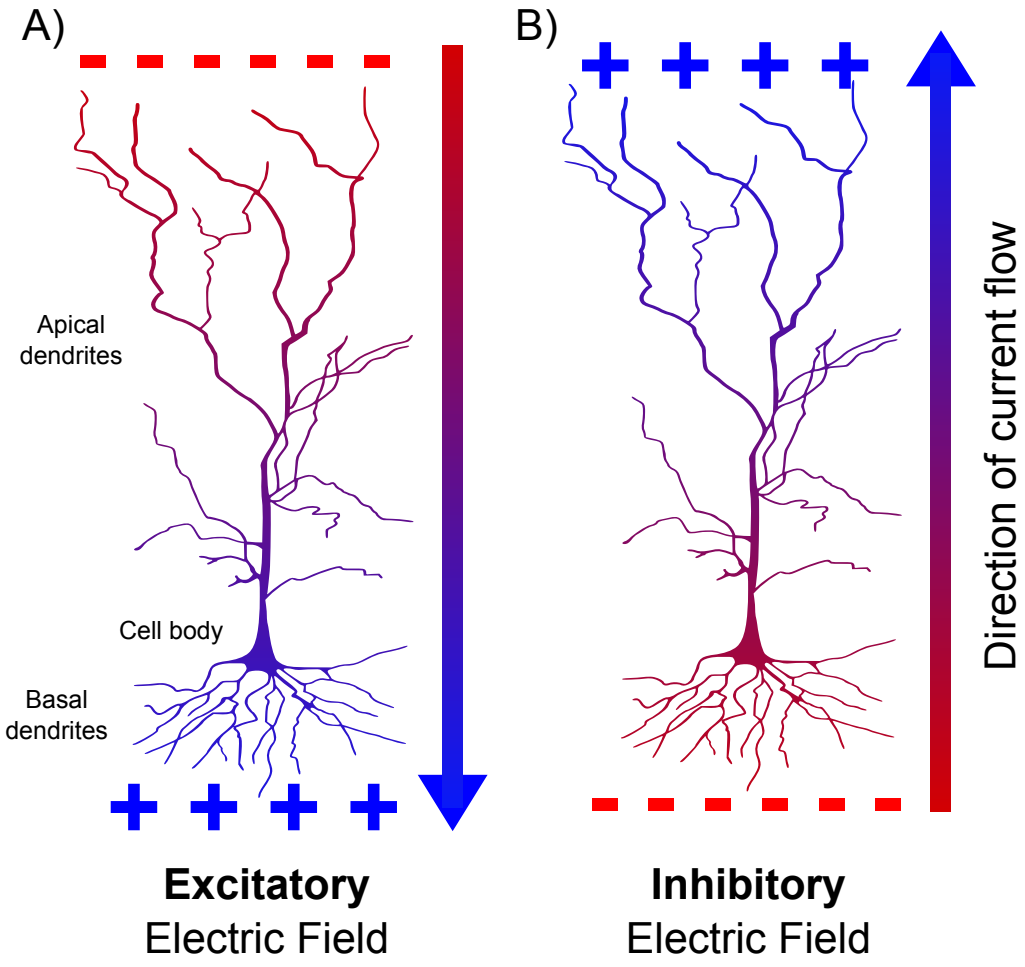


Figure 14 – Effects of electrical currents on pyramidal neuron excitability. A) An electrical current flows from the apical dendrites of a pyramidal neuron towards its cell body. This causes hyperpolarisation of the apical dendrites and depolarisation of the cell body. This increases the likelihood that the neuron will fire, and is therefore considered to have an 'excitatory' effect on neural activity. B) An electrical current flows in the opposite direction, from the cell body to the apical dendrites. This causes hyperpolarisation of the cell body, and decreases the likelihood that the neuron will fire. This direction of current flow is therefore considered to have an 'inhibitory' effect on neural activity (adapted from a slide of a talk given by Giulio Ruffini in Oxford in 2017).

When a neuron is placed inside an electrical field, the field causes ions of different charges to move in opposite directions inside the neuron. Positively charged ions to move towards the cathode, while negatively charged ions move towards the anode. This modifies the distribution of charge inside the neuron and therefore affects its resting potential difference. If a homogenous, direct current is applied to a stereotypical

pyramidal neuron, pointing from its apical dendrites to its cell body, this will cause hyperpolarisation of the dendrites and depolarisation of the cell body (Figure 14A; p.72). Such changes will in turn increase the likelihood that the neuron will generate an action potential (i.e. increased excitability). However, if a direct current is applied in the opposite direction, from the cell body to its apical dendrites, this will cause hyperpolarisation of the cell body, and will therefore reduce the likelihood that the neuron will generate an action potential (i.e. reduced excitability) (Figure 14B; p.72). It is via these opposing mechanisms that anodal vs. cathodal direct current stimulation is thought to exert excitatory vs. inhibitory effects on neural activity (e.g. Ruffini et al., 2013).

Differences between neuronal cells types and orientations

The previous section described the stereotyped effects of static electrical fields on a stereotypical, pyramidal neuron. It is thought that such fields are more likely to influence the activity of pyramidal neurons, in contrast to other neuronal cells types, due to the structure of these neurons. With their axons and dendrites separated along a unidirectional axis, voltage differences between these two ends of a pyramidal neuron are likely to be large when exposed to an electric field (Radman, Ramos, Brumberg, & Bikson, 2009). This is in contrast to, for example, a stellate cell, which has dendritic trees radiating in all directions from its cell body. For this reason, inhibitory neurons in cortex have been suggested to be less sensitive to electrical fields (i.e. due to their symmetrical geometry; Radman et al., 2009).

In addition to the structure of neurons, the orientation of neurons is also thought to have a significant influence on the effects of electrical fields on neural voltage differences (Kabakov, Muller, Pascual-Leone, Jensen, & Rotenberg, 2012). As described before, electrical currents can increase the likelihood that a neuron will fire depending on whether it flows from the axon to the dendrites, or vice-versa. In addition though, if an electrical current flows in a direction that is orthogonal to this axis (i.e. not

between the axon and dendrites), the voltage difference between the two ends of the neuron will be unaffected. This is important given that human cortex exhibits significantly folding, with neurons in cortical gyri and sulci oriented orthogonally to neurons positioned in-between these folds. Consequently, while electrical currents may be delivered to a specific brain region in experimental settings, different subpopulations of neurons in this region will most likely respond differently to these electrical currents depending on their relative orientations to the direction of current flow.

In addition to neural structure and orientation, many additional factors have also been found to influence the effects of electrical fields of neural activity. For example, the extent to which electrical currents influence the excitability of neural populations appears to depend on electric field strength. Moliadze, Atalay, Antal, and Paulus (2012) used motor-evoked potentials, which are observed following the delivery of single-pulse transcranial magnetic stimulation, to measure the effects of high-frequency alternating current stimulation on excitability in motor cortex. They found that, although stimulation at high-intensities (>1 mA) increased motor excitability, low-intensities decreased motor excitability. Furthermore, intermediate intensities were found to have no effect. This suggests that inhibitory neurons in motor cortex may be more susceptible to weak electric stimulation than excitatory neurons. In addition, it has also been found that the responsiveness of neurons to electrical stimulation changes depending of the frequency of alternating current stimulation (e.g. Bikson et al., 2004).

Long-term effects on neural activity

Early studies on the effects of electrical fields on neural activity revealed that they were not restricted to short-term modulations of firing rates. Instead, direct current stimulation of neural populations was found to induce changes in neural excitability that outlasted the cessation of stimulation (Bindman, Lippold, & Redfearn, 1964; Purpura & McMurtry, 1965). Such effects were replicated in later studies of direct current

stimulation in humans, in which researchers observed sustained (e.g. 20 minute) increases in the excitability of motor cortex following short periods of anodal stimulation of this region (e.g. Nitsche & Paulus, 2000, 2001). Such long-term changes in neural excitability were suggested to reflect the consequences of long-term potentiation and depression (Nitsche & Paulus, 2000). In addition though, anodal direct current stimulation has been found to decrease GABA concentrations in cortex, while cathodal stimulation decreases Glx and GABA concentrations (Stagg et al., 2009). tES may therefore influence neural functioning by affecting the relative concentrations of inhibitory and excitatory neurotransmitters in the brain. tES may also affect communication between neurons by influencing intracellular calcium levels (Monai et al., 2016).

The effects of alternating electrical currents on neural activity

Short-term entrainment of neural firing

The previous sections described the ways in which neural populations are influenced by the delivery of direct (i.e. static) electrical fields. As this thesis focuses exclusively on tACS, I now discuss on the ways in which neurons respond to oscillating electrical fields. In general, sinusoidally alternating electrical fields sinusoidally modulate the voltage potential of neurons exposed to them. For example, when neurons are exposed to alternating electrical fields, their firing aligns to the phase these alternating fields (Figure 15; p.76) (Francis, Gluckman, & Schiff, 2003). As with direct current, the extent to which such neurons will be (de)polarized depends on the intensity of the delivered stimulation (Chan & Nicholson, 1986). However, it has been found that the firing rates of neurons can be coordinated by electrical fields that are very weak (<0.5 mV/mm; Fröhlich & McCormick, 2010). Of relevance to this point, it has even been suggested that weak electrical fields produced by neural populations in the brain may serve as a natural mechanism for coordinating activity in neighbouring neural populations (known as 'ephaptic coupling'; Anastassiou, Perin, Markram, & Koch, 2011).

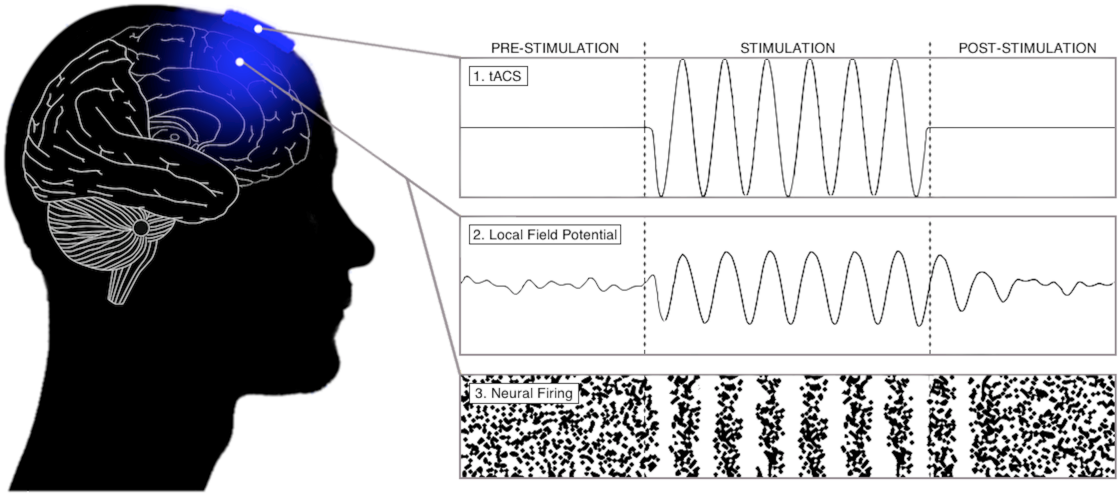


Figure 15 – Theorised effects of tACS on neural activity. In this example, tACS is delivered to frontal cortex (note that, while no reference electrode is shown, it would be required). Before tACS delivery, local field potential data, recorded from medial frontal cortex, shows no clear oscillation. Similarly, there is no rhythmicity in neural firing data recorded from the same neural region during this period. However, when stimulation is delivered, neural firing becomes entrainment to the alternating, electrical current, generating a noticeable oscillation in the local field potential data. This entrainment continues for a short period following the cessation of stimulation. However, with enough time, neural activity desynchronises again, and neural firing returns to its pre-stimulation levels of rhythmicity (taken from Battleday, Muller, Clayton, & Cohen Kadosh, 2014).

Correspondence between endogenous and exogenous frequencies

Although neural activity can be modulated by alternating electrical fields, the strength of this modulation appears to depend on the correspondence between the frequency of the electrical stimulation and the dominant frequency of the neural population being stimulated. For example, Reato, Rahman, Bikson, and Parra (2010) reported that low-amplitude stimulation entrained neural firing only when electrical fields matched the frequency of ongoing neural oscillations in the stimulated area. Similar effects have also been observed in modeling studies (Ali, Sellers, & Frohlich, 2013). This phenomenon is known as ‘resonance’. However, when delivered electrical currents are sufficiently strong, oscillations in neural activity can be induced regardless of the fundamental frequency of the neural population. This is known as the *Arnold tongue* principle, as illustrated in Figure 16 (p.77) (Pikovsky, Rosenblum, & Kurths, 2003).

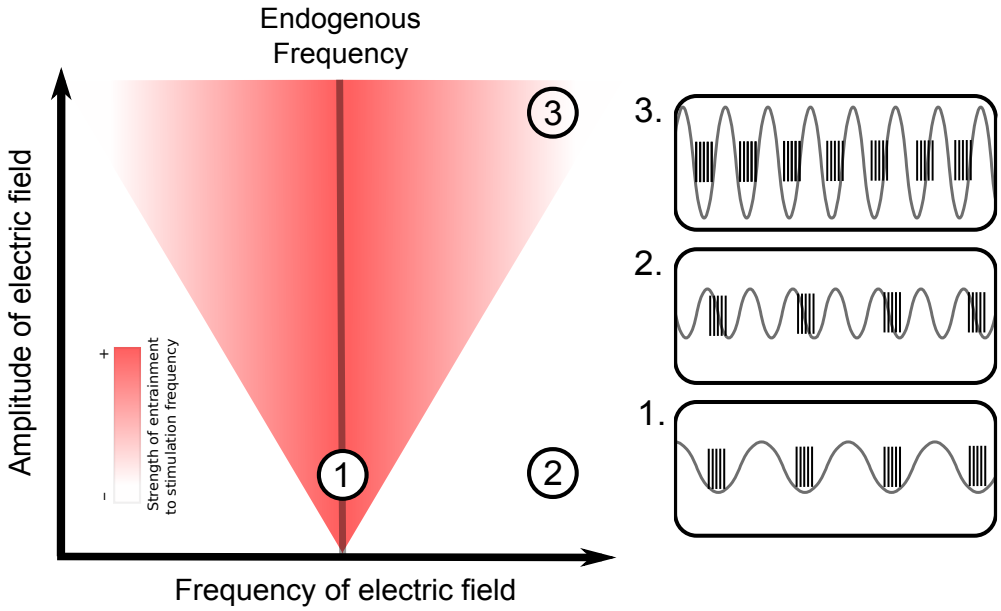


Figure 16 – Oscillatory entrainment and the Arnold tongue. Entrainment of neural oscillations with tACS is maximal when the frequency of stimulation matches that of ongoing oscillations (the 'endogenous frequency'). However, this effect depends on the amplitude of stimulation. The larger the stimulation amplitude, the larger the range of frequencies at which tACS can entrain neural activity (*shaded in red*). This is known as the *Arnold tongue* principle. In example ①, stimulation is delivered at low amplitude, but matching the endogenous frequency of the stimulated region. Successful entrainment is therefore observed. In example ②, stimulation is delivered at low amplitude, but discordant with the endogenous frequency. Therefore, no neural entrainment occurs. However, in example ③, stimulation frequency is discordant with the endogenous frequency, but delivered at high amplitude. Moderately successful entrainment of neural activity is therefore observed (taken from Fröhlich, 2016).

Long-term modulations of oscillatory power

As described later in this chapter, tACS can induce sustained changes in EEG power in specific frequency bands. Most notably, tACS over occipitoparietal regions at ~10 Hz can induce long-term (i.e. 20-40 minute) increases in EEG alpha power (7 – 13 Hz; Helfrich et al., 2014; Zaehle, Rach, & Herrmann, 2010). These results suggest that tACS, in addition to exerting rhythmic influences on neural firing rates during stimulation, can induce long-term effects on neural activity following the cessation of stimulation. Although the precise mechanisms behind such sustained effects are unclear, it was

suggested by Zaehle et al. (2010) that long-term potentiation and depression may again play important roles. These researchers modeled the activity of a single, 'target' neuron, connected to 2,500 'input' neurons. Each of these connections had variable delays, meaning that the time it took for impulses to travel from an input neuron to the target neuron and back again varied substantially between input neurons (Figure 17A; p.79). The researchers referred to this length of time as the '*total synaptic delay*'. An artificial, 10 Hz current was then delivered to the modeled, target neuron, and equations of spike-timing-dependent plasticity were used to modulate synaptic weights between input neurons and the target neuron. According to these equations, if a target neuron is activated by an input neuron before the target neuron fires, synapses between these neurons will be strengthened. However, if a target neuron is activated by an input neuron *after* the target neuron fires, synapses between these neurons will be weakened (Figure 17B) (Markram, Lübke, Frotscher, & Sakmann, 1997). Using this computational model, Zaehle et al. (2010) found that, following 10 Hz stimulation of the target neuron, synaptic weights within neural circuits with a total synaptic delay of 100 ms or below (i.e. a single 10 Hz cycle) were significantly strengthened compared to circuits with a total synaptic delay greater than 100 ms (Figure 17C). This finding therefore suggests that increases in the relative power of ~100 ms (i.e. 10 Hz) oscillations following 10 Hz tACS may reflect the differential strengthening of synapses with resonant frequencies of around 10 Hz. This simulation therefore also suggests that processes of neuroplasticity may be central to the enhancing effects of ~10 tACS on EEG alpha power. Consistent with this interpretation, delivery of tACS for only short periods of time (e.g. ~8 seconds) has been found to exert no changes in brain activity (Strüber, Rach, Neuling, & Herrmann, 2015; Vossen, Gross, & Thut, 2014).

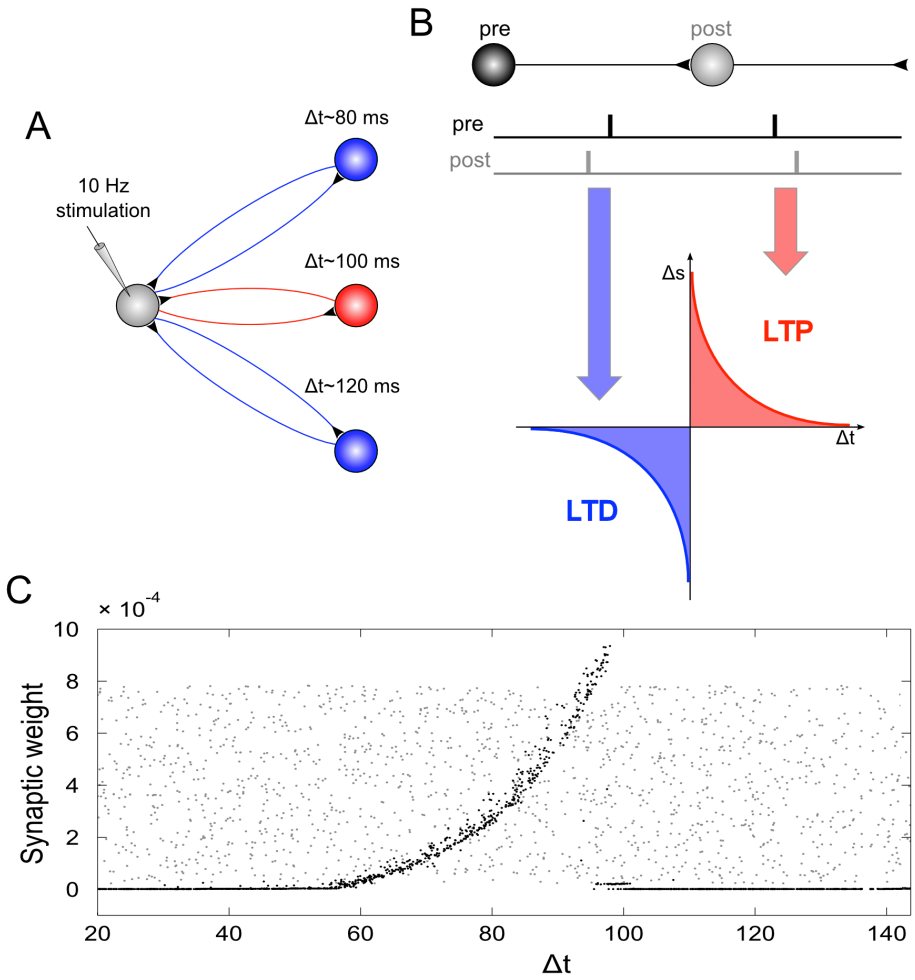


Figure 17 – Zaehle et al. (2010) model of the EEG effects of alpha-tACS. A) *Schematic illustration of the network*. A driving neuron establishes a recurrent loop with each neuron of a hidden layer. The total synaptic delay (Δt; i.e. the sum of both delays of the loop) varied between 20 and 160 ms. The driving neuron was stimulated with a spike train of 10 Hz repetition rate. B) *Spike timing dependent plasticity*. Synaptic weights are increased if a post-synaptic potential follows a pre-synaptic spike (long-term potentiation, LTP). Weights are decreased if a post-synaptic potential occurs prior to a pre-synaptic spike (long-term depression, LTD). C) *Synaptic weights of the back-projection as a function of the total synaptic delay of the recurrent loops*. Grey dots display synaptic weights at the start of the simulation. Black dots represent synaptic weights after the end of simulation. External stimulation of the driving neuron at 10 Hz resulted in increased weights for recurrent loops with a total delay between 60 and 100 ms, and dramatically reduced synaptic weights for loops with total delays outside this interval. Note that the highest synaptic weights are observed at 100 ms, i.e., for loops with a resonance frequency near the stimulation frequency (taken from Zaehle et al., 2010).

EFFECTS OF tACS ON BRAIN ACTIVITY

The previous section focused on the mechanisms by which electrical fields (both direct and alternating) are thought to influence neural activity. This discussion was based on results from computational modeling studies, and *in vitro* electrophysiology. In the following section, I focus on the *in vivo* effects of alternating currents on brain activity. Given the focus of this thesis on alpha oscillations, I give priority to discussion of studies applying tACS at alpha frequencies over posterior cortex (7 – 13 Hz). I refer to this type of stimulation from here on as '*alpha-tACS*'.

Effects on oscillatory power

One of strongest and best-replicated effects of tACS on brain activity is on oscillatory EEG/MEG power. Most consistently, alpha-tACS has been found to increase the power of posterior alpha oscillations (Dowsett & Herrmann, 2016; Helfrich et al., 2014; Kasten, Dowsett, & Herrmann, 2016; Kasten & Herrmann, 2017; Neuling et al., 2013; Ruhnau, Neuling, et al., 2016; Vossen et al., 2014; Zaehle et al., 2010). Similarly, tACS at theta frequencies (4 – 7 Hz) increases theta power in EEG recordings (Pahor & Jaušovec, 2014; Vosskuhl, Huster, & Herrmann, 2015). Nevertheless, such power enhancements are not always reported. For example, alpha-tACS has no effect on EEG alpha power when delivered during periods of eyes-closed rest (Neuling et al., 2013; Ruhnau, Neuling, et al., 2016). Given that eyes-closed rest is associated with high levels of EEG alpha power (Berger, 1929), such findings suggest that alpha-tACS may only increase alpha power when it alpha power naturally low. On a separate note, when delivered over somatosensory cortex, alpha-tACS has contrastingly been reported to *reduce* centromedial alpha power (Gundlach, Muller, Nierhaus, Villringer, & Sehm, 2017). Furthermore, tACS can often modulate power in frequency bands that do not include the stimulation frequency. For example, alpha-tACS over bilateral temporal regions has been found to increase delta power (0.1 – 4 Hz) in addition to alpha power

(Neuling, Rach, Wagner, Wolters, & Herrmann, 2012). Similarly, tACS at both theta (Pahor & Jaušovec, 2014) and gamma frequencies (Boyle & Frohlich, 2013) has been found to reduce alpha power. Such multi-frequency effects of tACS may reflect the fact that electrical fields that alternate at fixed frequencies contain power at their harmonic frequencies (e.g. Ruhnau, Keitel, Lithari, Weisz, & Neuling, 2016). In addition, it is well established that oscillations in different frequency bands can modulate each other through cross-frequency interactions. For example, power in the gamma band has been reported to covary with alpha phase (Osipova et al., 2008; Spaak, Bonnefond, Maier, Leopold, & Jensen, 2012).

Effects on oscillatory phase

In addition to its effects on power, tACS has been reported to modulate the phase of ongoing neural oscillations. For example, alpha-tACS has ben found to entrain the phase of ongoing alpha oscillations in visual cortex. In other words, the phase of endogenous alpha oscillations has been found to synchronize with the phase of delivered, alternating currents (Ruhnau, Neuling, et al., 2016). Similar effects have also been reported with frontomedial theta oscillations following the delivery of tACS at theta frequencies over frontal cortex (Chander et al., 2016). Such *in vivo* results replicate those of previously described *in vitro* studies reporting entrainment of neural firing to the phase of alternating, electrical currents (e.g. Francis et al., 2003). In addition, tACS delivered simultaneously at alpha frequencies to frontal and parietal regions (van Schouwenburg, Zanto, & Gazzaley, 2016), as well as to parietal and occipital regions (Stonkus, Braun, Kerlin, Volberg, & Hanslmayr, 2016), has been found to modulate the phase relationships of alpha oscillations in this distant, cortical areas. However, as with modulations of oscillatory power, phase effects following tACS are also not observed consistently across studies. For example, Ruhnau, Neuling, et al. (2016) found again that alpha-tACS only modulated alpha oscillations when ongoing alpha power was low.

Furthermore, when applying alpha-tACS over posterior cortex for periods of 3 and 8 seconds, Vossen et al. (2014) found no entrainment of alpha phase to delivered stimulation.

Effects on wider brain activity

In addition to influencing neural oscillations, tACS has also been found to exert broad effects on brain activity generally. Such findings have come from studies that record neuroimaging data at the same time as the delivery of tACS. I focus here on studies applying tACS at alpha frequencies. In general, such studies have reported diverse effects of alpha-tACS on brain activity. For example, using functional magnetic resonance imaging (fMRI), Vosskuhl, Huster, and Herrmann (2016) found that alpha-tACS (i.e. Oz-Cz montage) significantly reduced haemodynamic activation in visual cortex during presentation of visual stimuli. This is consistent with the results of previous modelling studies suggesting that tACS directs electrical current through occipitoparietal cortex (e.g. Neuling, Wagner, et al., 2012). Furthermore, given that alpha-tACS has been found to increase posterior alpha power (e.g. Helfrich et al., 2014), this finding is also consistent with the view that posterior alpha oscillations reflect reduced processing in visual cortex (e.g. Foxe & Snyder, 2011). However, in contrast to such findings, a very similar fMRI study by Cabral-Calderin et al. (2016) found that alpha-tACS, during presentation of visual images, influenced activation mainly in frontal, temporal, and parietal areas. Furthermore, in contrast to both of these studies, Alekseichuk, Diers, Paulus, and Antal (2016) observed no changes in fMRI activation during a visual perception task while alpha-tACS was being applied, but did observe widespread reductions in activation across the brain following cessation of stimulation. As these studies did not use identical methods (e.g. varying in stimulation intensities and control conditions), they suggest that the effect of tACS may be very sensitive to the precise parameters of stimulation. More generally though, as the studies of Cabral-Calderin et al.

(2016) and Alekseichuk et al. (2016) reported effects of posterior alpha-tACS on widespread cortical areas, such studies also suggest that tACS does not only influence neural activity immediately beneath stimulating electrodes.

EFFECTS OF tACS ON COGNITION

As well as effects on brain activity, tACS has been found to influence performance on a range of cognitive tasks. A comprehensive review of these behavioural findings is beyond the scope of this chapter. Therefore, given the focus of this thesis on posterior alpha oscillations, I give an overview of reported, behavioural effects of alpha-tACS specifically.

As described in Chapter 2, alpha oscillations have perhaps been most strongly associated with both rhythmic fluctuations in visual attention (e.g Mathewson et al., 2011), and attentional inhibition (e.g. Foxe & Snyder, 2011). Consistent with this first association, Helfrich et al. (2014) reported that, when people received alpha-tACS, their ability to detect faint visual stimuli varied with the phase of the delivered current. Similar results were also reported by Neuling, Rach, et al. (2012). The second association of alpha oscillations (i.e. with attentional inhibition) also received some support from Veniero, Benwell, Ahrens, and Thut (2017). Here, researchers studied the effects of alpha-tACS, delivered to right posterior cortex, on performance of a line bisection task. In their first experiment, alpha-tACS was found to induce a small, rightward shift in the average, estimated midpoint of presented lines. This suggested that alpha-tACS to right-posterior cortex suppressed processing of left visual space. Consequently, the result appeared to provide causal support for the previously mentioned idea that increased posterior alpha power reflects reduced visual attention. However, when these researchers attempted to replicate this result in a second experiment, they were unable to do so. Furthermore, in many similar experiments, researchers have not found

evidence of the kinds of impairments in visual task performance that would be predicted from the view that alpha oscillations primarily reflect disengagement of visual attention.

For example, despite observing sustained increases in posterior alpha power following alpha-tACS, Kasten et al. (2016) found no effects of this stimulation on visual vigilance task performance. Although Helfrich et al. (2014) observed phasic modulation of visual target detection performance during identical stimulation, they reported only a weak, positive effect of alpha-tACS on overall target detection performance. Similarly, despite negative associations between posterior alpha power and performance of visual conjunction search tasks (Gonzalez-Rosa et al., 2015), alpha-tACS was reported by Müller et al. (2015) to *improve* visual conjunction search task performance. In addition to such findings, many studies have also reported effects of alpha-tACS on cognition that go well beyond basic effects on visual attention. For example, Kasten and Herrmann (2017) found that alpha-tACS improved accuracy on a mental rotation task, which required participants to manipulate shapes in visual working memory. Furthermore, alpha-tACS has been found to increase the precision with which people are able to track the location of external objects following body movement ('spatial updating'; Gutteling, Schutter, & Medendorp, 2017). In addition, alpha-tACS has been suggested by Kar and Krekelberg (2014) to influence processes of neural adaptation, defined as the changed responsiveness of sensory systems to constant stimuli over time. In this study, researchers displayed upward moving dots in either left or right visual space, while delivering alpha-tACS over either left or right visual cortex. Short exposure to upward moving dots is known to cause illusory perception of downward motion in subsequently presented, static dots (Van Wezel & Britten, 2002). This illusion can be measured by the impairment it causes in discrimination of motion direction in subsequently presented, moving dots (Van Wezel & Britten, 2002). However, Kar and Krekelberg (2014) found that, when alpha-tACS was delivered contralateral to the initial motion stimulus, and specifically when alpha-tACS was delivered during the presentation of this stimulus,

discrimination of motion direction in subsequent dots was significantly improved. The researchers therefore concluded that alpha-tACS seemed to have attenuated motion adaptation in visual cortex. Consequently, while alpha oscillations have been consistently associated with processes of visual attention, alpha-tACS appears to exert a broad range of effects on neural processing.

SUMMARY

In this chapter, I reviewed the ways in which tES is applied to the brain, as well as the reasons why tES is used in research settings. I then described current understanding of how electrical currents influence neural functioning. I then finished by with an overview of the ways in which tACS has been found to influence brain activity and cognition. In the next section, I will go over the information reviewed in all three of the introductory chapter. Specifically, I will describe the central decisions I made when planning my experiments, and the reasons why I made those decisions.

CHAPTER 4 – VISUAL CONTINUOUS TEMPORAL EXPECTANCY TASK

In the previous, introductory chapters, I reviewed current literature on sustained attention, alpha oscillations, and tACS. I now describe the methods and results of my experiments. Note that the main purpose of this first experiment was to study the effects of tACS, delivered at an alpha frequency over posterior cortex, on the performance of a sustained visual attention task. As the techniques used in this study are replicated across the many experiments of this thesis, I begin this chapter with a relatively detailed description and justification of my methods. I then finish by discussing the results of the experiment, as well as their possible interpretations.

EXPERIMENTAL DESIGN AND RATIONALE

Participant numbers, safety, and ethics

Fifty-two healthy adults took part in this first experiment. One participant was excluded due to excessive EEG noise. Three participants were also excluded because their accuracy on at least one task block was more than 2 standard deviations below mean accuracy on that block across all participants. This exclusion criterion was used to reject participants from analysis that disengaged their attention to an abnormal extent during task performance. The final sample therefore consisted of 48 participants (31 females, 6 left-handed, mean age = 22.7, SD = 2.9). Each of these participants gave their informed consent before participating in the experiment. Participants also completed a health questionnaire to ensure that they were well hydrated, well slept (> 6 hours sleep), and had not consumed recreational drugs less than 24 hours before participating in the experiment. All procedures were approved by both the Clinical Trials and Research Governance at Oxford and the UK Ministry of Defence Research Ethics Committee (550/MODREC/14).

Task choice

Why the visual Continuous Temporal Expectancy Task?

A central decision to be made about this first experiment was which cognitive task to use. As detailed in Chapter 1 (see p.14), many different tasks can be used to study sustained attention, each of which has their own strengths and weaknesses. One of the main purposes of this project was to improve performance of real-world tasks where responding is rare. For example, a soldier on patrol must generally remain vigilant only to the presence of rare threats. Consequently, it seemed that that the most appropriate kind of task for this first experiment was a 'rare-responding' task. Specifically, I decided to use the visual Continuous Temporal Expectancy Task (vCTET).

In the vCTET, participants are required to monitor a stream of visual stimuli and detect when a stimulus has been presented for longer than usual. The task used in the current experiment was adapted from one previously used by O'Connell et al. (2009) and Berry, Li, Lin, and Lustig (2014). I chose the vCTET partially because of its prior application in sustained attention research (Berry et al., 2014; Wilson, Gray, Van Klinken, Kaczmarczyk, & Foxe, 2017). Importantly, previous studies had also reported that errors on this task are preceded by significant increases in EEG alpha power (Dockree et al., 2017; O'Connell et al., 2009). This strengthened my assumption that performance of this task would be affected by the delivery of alpha-tACS. In addition, it also makes intuitive sense that a task requiring people to monitor the temporal durations of stimuli would test sustained attention more optimally than a task requiring participants to classify stimuli based only on their semantic identity. For example, if a task required participants to identify the letter 'X' in a continuous stream of letters (e.g. as in the CPT; Rosvold et al., 1956), one could argue that, once participants had processed a letter stimulus and confirmed that it was not a target, their attentional systems could partially rest until the next stimulus is presented. In contrast, when a task requires participants to

judge the length of time each stimulus is presented for, it is arguable that participants must direct their attention to that stimulus for the full duration of its presentation. Consequently, they will have no opportunities for partial rests during task performance, increasingly the likelihood of deteriorations in task performance over time.

Description of the vCTET

All stimuli were presented on a Dell® 23-inch LCD monitor (60 Hz refresh rate) using the Psychophysics Toolbox in MATLAB (Brainard, 1997). The task was performed in a well-lit room. On every trial, an 8-cm^2 square was presented centrally on a grey background. This square consisted of 10 x 10 grid of identical square tiles. Each tile was diagonally split into black and white halves. These tiles shifted their orientation by 90° in a random direction on every trial. The stimulus was presented for 800 ms on ~91% of trials ('standard trials'; 300 per block). On the other ~9% of trials (30 per block), the stimulus was presented for 1070 ms ('target trials') (Figure 18; p.89). The order of trials was pseudo-randomised such that between 7 and 15 (mean = 10) standard trials were presented between targets. All trials were preceded by a 20 ms grey-screen interval. Participants were instructed to monitor the length of time each stimulus was presented for and to press the space bar whenever they detected a target trial. Responses were classified as correct if made less than 2.46 seconds (3 trials) after a target trial (Berry et al., 2014). However, while subjects were told to maximise their accuracy, they were not asked to prioritise response speed.

Practice task design

Participants practiced this task before starting the main experiment. Specifically, participants were required to identify 6 target trials consecutively without missing any, and without incorrectly classifying any standard trials as targets. Following misses, "**Target Missed**" was presented in red lettering below the next image in the stimulus

stream. Following incorrect classifications, "**Not a Target**" was presented in blue lettering at the same location. When a target was correctly classified, "**Correct [n]/6**" was presented in green lettering above the next image in the stream ('n' indicating how many targets had been consecutively detected so far). Feedback was not given during the main task.

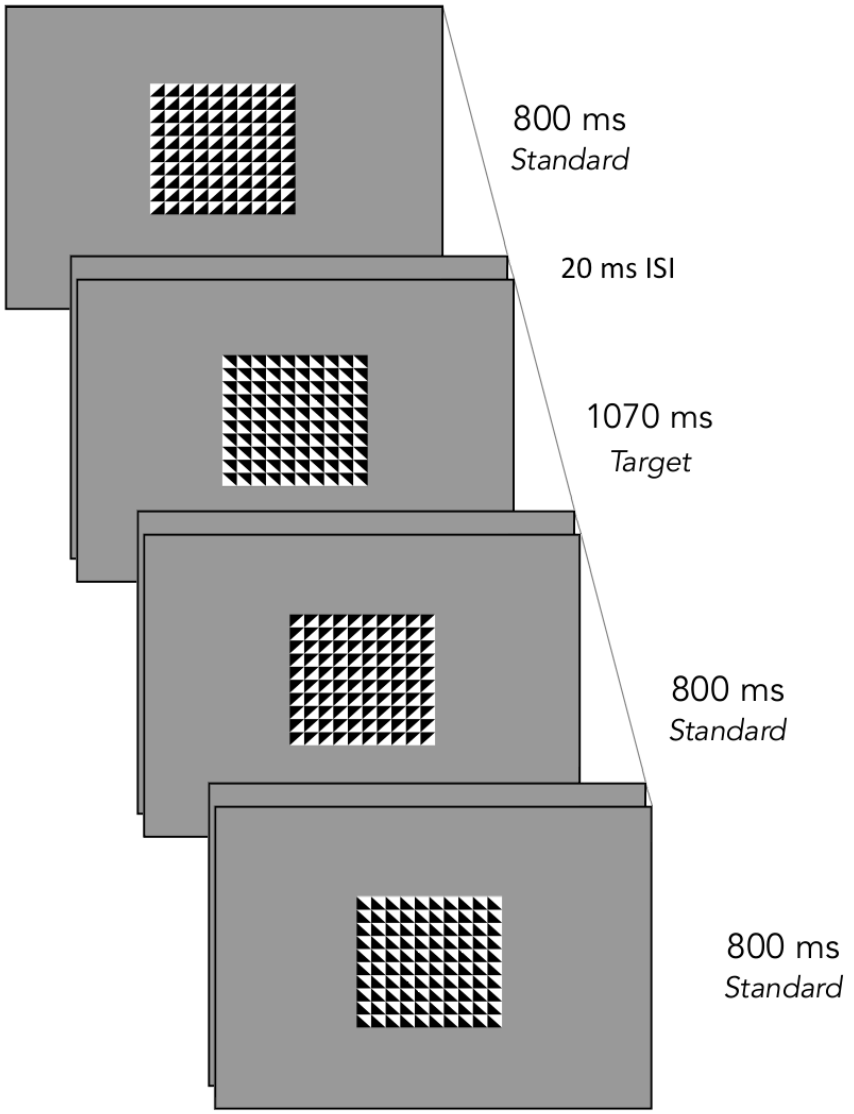


Figure 18 – Visual Continuous Temporal Expectancy Task. Participants monitored a continuous stream of centrally presented, patterned stimuli. Standard stimuli were presented for 800 ms. Target stimuli were presented for a longer duration of 1070 ms. All stimuli were preceded by a 20 ms grey-screen interval. Participants were required to press the space bar following all target trials (O'Connell et al., 2009).

Lengths of task performance and breaks

In the main experiment, all participants performed two 'task sessions' on a single day. A task session consisted of four tasks blocks, each of which lasted 4 minutes and 50 seconds. Between blocks, participants were given a fixed-duration break of 40 seconds. These breaks were included to increase participant comfort. However, they were of a short, fixed duration to increase the likelihood of deteriorations of task performance over time. Each session therefore lasted 21 minutes and 20 seconds. This duration was also chosen to maximise participant comfort, but to ensure that each experimental session lasted no more than 2 hours. I thought that an experimental session of longer than 2 hours would be too tiring for participants.

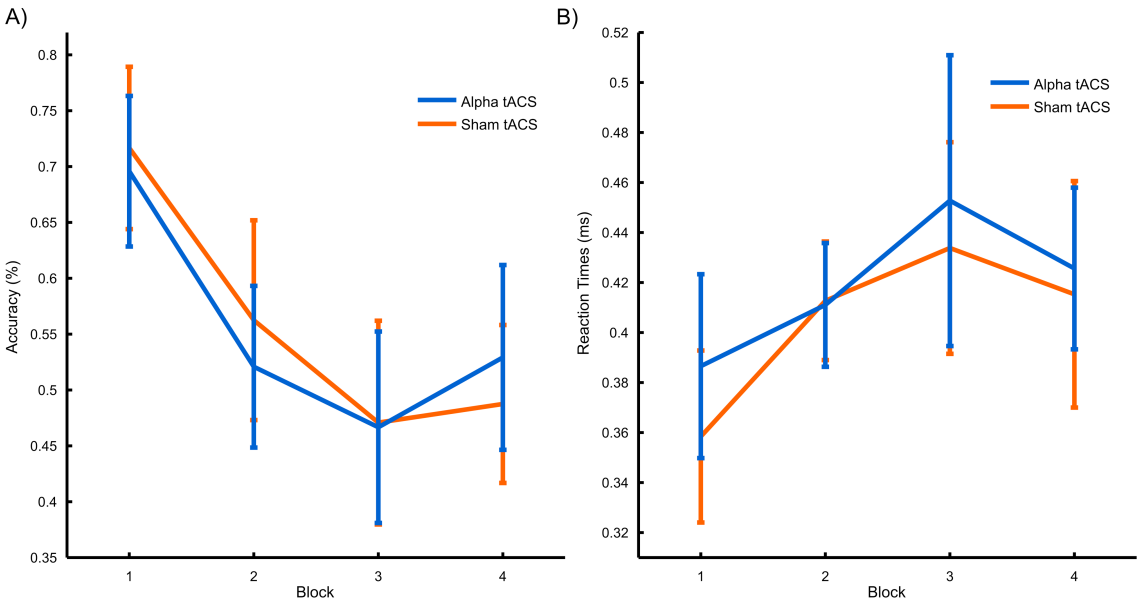


Figure 19 – Behavioural results of the pilot study. A) Percentage accuracy on the vCTET across all 4 tasks blocks. Reliable declines in accuracy were observed over this period during both alpha- and sham-tACS sessions. B) Reaction times on the vCTET across all 4 tasks blocks. Trend level increases in reaction times were observed over this period.

To test whether this task design elicited deteriorations in performance over time, I applied it in a pilot study with 8 participants. Performance accuracy and RTs in this pilot were then submitted to a repeated measures ANOVA. For task accuracy, I observed a

strong, main effect of task block ($F_{(3,21)}$=11.52, p<.001, η^2_p=.622, ANOVA). This confirmed that vCTET accuracy deteriorated reliably over the course of each ~20-minute task session. For reaction times, I observed a marginal effect of task block ($F_{(3,21)}$=3.03, p=.057, η^2_p=.302, ε=.923, ANOVA), suggesting a trend-level increase over this same period (Figure 19; p.90). My pilot study therefore confirmed that the previously mentioned task design induced reliable deteriorations in task performance across participants.

Breaks between task sessions

Between each task session, participants were given a break of 25 minutes. This break was given to help participants recover from any mental fatigue they experienced during the first task session. One possibility was to have participants do nothing during this period. However, I was concerned this approach could simply have increased participant boredom and further accentuated their mental fatigue. Instead, I showed participants an episode of the BBC's *Planet Earth* during this period. Viewing images of natural scenes has been found to help people recover from mental fatigue (Kaplan, 1995). Furthermore, given that *Planet Earth* is designed for a wide audience, and does not depend heavily on language comprehension (making it suitable for non-native English speakers), it seemed like an ideal program to show people during the break.

To test the suitably of this design, I again analysed task performance from my pilot study. Specifically, I found that mean task accuracy on the first block of the first task session (73.3%) did not differ reliably from mean accuracy on the first block of the second task session (67.9%) (M=5.4%, SD=13.7%, $t_{(7)}$=1.12, p=.30, paired-samples t-test). I therefore concluded task performance recovered reliably during the break period, supporting the use of this break duration and design in my further experiments.

Transcranial alternating current stimulation

tACS electrode positioning

In addition to these questions about cognitive tasks and experimental procedures, I also had to decide how best to deliver alpha-tACS to the brain. For example, where was the best place to position stimulating electrodes on the scalp? One possibility was to place them bilaterally over posterior cortex (i.e. one over left posterior cortex, one over right posterior cortex)**.** This electrode montage was used in one of the first studies showing increased EEG alpha power following alpha-tACS (Zaehle et al., 2010). However, a larger number of studies then since have reported increased EEG alpha power using alpha-tACS with a different montage: with one electrode positioned centrally over occipital cortex (Oz) and the other positioned centrally over motor cortex (Cz) (Helfrich et al., 2014; Kasten et al., 2016; Neuling et al., 2013; Neuling et al., 2015; Ruhnau, Neuling, et al., 2016). Given this weight of evidence in favour of a occipitocentral montage, as well as evidence from modelling studies that it directs current flow through occipitoparietal cortex (Neuling, Wagner, et al., 2012), I therefore decided to use this montage in all of my experiments. Specifically, I applied tACS through two, 25-cm^2 circular sponge electrodes (Figure 20A; p.93), positioned at Oz and Cz. Stimulation was delivered using a *Starstim*® device (Neuroelectrics, Barcelona), and electrodes were positioned using a *Neuroelectrics*® cap, according to the 10-20 system (Figure 20D)

tACS timing, duration, and amplitude

Another important parameter to decide was the precise timing and duration of tACS. One possibility was to deliver stimulation in 'early' and 'late' phases of task performance. This approach was used in a recent study in which participants received tDCS for 10 minutes at either the start or end of a 40-minute vigilance task (Nelson et al., 2014).

However, dividing participants into subgroups would inevitability have reduced my statistical power, and increase the number of participants needed to study the effects of stimulation in each group. To avoid this issue, I chose to deliver tACS at the same point for each participant: for a period of 11 minutes from the start of the second block to the start of the fourth block (Figure 20E; p.93). I chose this design to allow me to record EEG and behavioural data both before and after the delivery of tACS. I was therefore able to study effects of tACS on both EEG and behaviour with respect to pre-stimulation baselines. Given that each task session was designed to last ~20 minutes (see p.90), I chose a tACS duration of 10 minutes to allow sufficient recording of EEG data (i.e. ~5 minutes) before and after tACS. The timing of stimulation was controlled using *MatNIC*, which is a MATLAB® toolbox designed by *Neuroelectrics*®.

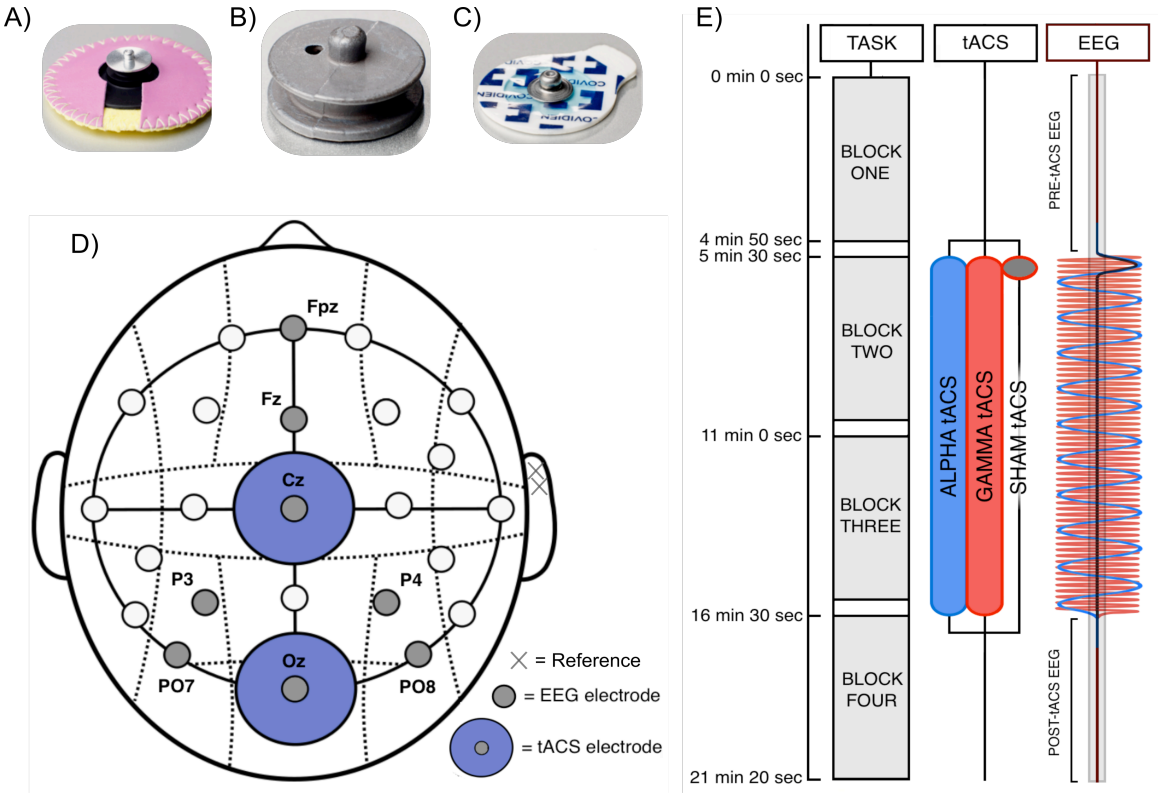


Figure 20 – Electrode placement and experimental timing. A) tACS electrodes (*Sponstim 25; NE026a*). Rubber electrode placed inside 25 cm^2 circular sponges, soaked in saline solution). B) EEG electrodes (*Geltrode; NE022*). Ag/AgCl coated electrodes (diameter = 12mm, contact area = 1cm2). C) Reference electrodes (*Covidien*, *H124SG*). D) Reference electrodes were positioned on and just below the right mastoid bone. tACS electrodes were positioned at Oz and Cz. EEG electrodes were positioned at PO7, PO8, P3, P4, Fz, and Fpz. E) Participants

performed four task blocks, each lasting 4 minutes and 50 seconds. A fixed-duration break of 40 seconds was allowed between blocks. EEG was recorded before and after the delivery of stimulation. During alpha- and gamma-tACS, stimulation was applied for 9 minutes and 30 seconds from the start of the second block to the start of the fourth block. During sham-tACS, stimulation was applied at 10 Hz during only the first 50 seconds of this period (including ramp-up and down times). In all experiments, participants performed two task sessions, separated by a break of 25 minutes.

10 minutes is a relatively short period of time to deliver stimulation. Other studies of alpha-tACS have generally delivered stimulation for ~20 minutes (e.g. Helfrich et al., 2014; Kasten et al., 2016; Neuling et al., 2013). To compensate for this, tACS was delivered with a relatively high amplitude of 2 mA peak-to-peak. This amplitude was chosen to make it more likely that the total charge delivered to the brain (current density x total stimulation duration) would be equivalent to that of previous tACS studies. Computational modeling has also suggested that 2 mA tES can generate intracranial electric fields of 0.22 V/m (Miranda et al., 2006), which are known to be of sufficient strength to modulate neural activity (e.g. Fröhlich & McCormick, 2010). In addition though, my decision to deliver tACS at 2 mA was motivated by the consideration that tACS is more likely to influence ongoing neural oscillations when delivered at high amplitudes (Pikovsky et al., 2003). This is known as the *Arnold tongue* principle (Chapter 3; p.76).

tACS frequency

In addition to this point about stimulation amplitude, the Arnold tongue principle also states that neural oscillations will be influenced most significantly when stimulation is delivered at the natural frequency of those oscillations. Consequently, another important parameter to determine for this experiment was the frequency of tACS. In many alpha-tACS studies, the stimulation has been delivered to each participant at their 'individual alpha frequency' (Neuling et al., 2013; Ruhnau, Neuling, et al., 2016; Zaehle et al., 2010). Given the assertions of the Arnold tongue principle, it would make sense

theoretically that such individualisation of tACS would maximize its effects on brain activity. However, there are a number of issues with this approach. For example, 3 – 13% of human subjects do not exhibit any EEG alpha power above 1/f noise (Anokhin et al., 1992). It is therefore not possible to determine peak alpha frequencies for these subjects. Furthermore, in contrast, many people exhibit two distinct alpha peaks (Haegens et al., 2014). Consequently, one must create a rule for deciding how best to determine individual alpha frequencies for these subjects (e.g. the mean of the two peak frequencies). However, one of the biggest issues with individualising alpha frequencies is that, while it makes theoretical sense to do so, there is little evidence that it enhances the effects of tACS. For example, Helfrich et al. (2014) delivered tACS over posterior cortex at 10 Hz and found no influence of individual alpha frequency on the effects of stimulation on EEG alpha power. Given such findings, as well as the previously mentioned technical challenges involved in estimating individual peak frequencies, I therefore decided to deliver alpha-tACS with a fixed frequency of 10 Hz. This is consistent with many other studies showing effects of alpha-tACS on EEG and behaviour (Helfrich et al., 2014; Hopfinger, Parsons, & Fröhlich, 2017; Kar & Krekelberg, 2014).

Another parameter that had to be decided regarding tACS frequencies was the appropriate frequency of control-tACS. It was important that this control stimulation was sufficiently different to alpha-tACS that it did not exert comparable effects on EEG and behaviour. I was therefore wary of delivering control stimulation in either the theta (4 – 7 Hz) or beta frequency bands (13 – 30 Hz), as these are close the alpha band in frequency space. Instead, I delivered control-tACS at a much higher frequency of 50 Hz. As this frequency is the ‘gamma’ band, I refer to it from here on as ‘gamma-tACS’. Interestingly, in contrast to alpha-tACS, gamma-tACS has been reported to cause reductions in EEG alpha power (Boyle & Frohlich, 2013). I was therefore intrigued by the

possibility of using gamma-tACS to study the effects of both increased and decreased EEG alpha power on vCTET performance.

Sham stimulation and condition blinding

In all my experiments, 50% of participants received gamma-tACS, while the others received sham-tACS (in addition to alpha-tACS). I refer to sham- and gamma-tACS from here on collectively as 'control-tACS'. Participants were randomly assigned to these subgroups, and the order of alpha- and control-tACS was counterbalanced across participants. During sham-tACS, stimulation was applied at 10 Hz during the first 50 seconds of the second task block (including ramp-up and down times). In all cases, tACS was ramped up over 30 seconds and ramped down over 20 seconds. The purpose of this sham-tACS was to induce the subjective sensations of stimulation (e.g. scalp sensations), while not exerting significant effects on brain activity. The idea is that this should, in turn, reduce the likelihood that participants know the task session in which alpha-tACS was delivered, and therefore should limit the influence of placebo effects on recorded data. However, a number of additional steps were also taken to reduce these kinds of effects.

Firstly, both the experimenter and participants were blinded to stimulation condition. Secondly, impedance levels of tACS electrodes were measured before the main experiment and, if greater than 5 kΩ, additional conductive gel was injected onto the surface of each electrode. Low levels of impedance reduce the subjective sensations caused by tES and, therefore, should reduce awareness of differences between stimulation conditions. Thirdly, to ensure that stimulation was comfortable for all participants, 20 seconds of tACS was delivered at 10 Hz with a ramp-up time of 30 seconds, first at an amplitude of 1 mA and then, if well-tolerated, at 2 mA peak-to-peak. In this experiment, only participants that tolerated this higher amplitude of stimulation

performed the full experiment. Lastly, at the end of each experimental session, participants were told about the common side effects of tACS, and were asked to state in which of the two tasks sessions they thought these effects were most intense. I then calculated the percentage of participants that reported most intense experiences during alpha-tACS and compared this to chance (i.e. 50%) using a binomial test. My assumption was that, if participants were able to reliably notice the difference between alpha- and control-tACS in this experiment, they should be more likely to state that subjective experiences of alpha-tACS were more intense (e.g. visual phosphenes and flickering).

Electroencephalography

In addition to these questions about task performance and tACS delivery, EEG data was also recorded during this experiment. This data was collecting using a *Starstim*® device (Neuroelectrics, Barcelona) with Ag/AgCl coated electrodes (diameter = 12mm, contact area = 1cm^2) (Figure 20B; p.93). Data collection was controlled using *MatNIC* (a MATLAB® toolbox). EEG electrodes were filled with electrolyte gel (*Signagel*®, Parker Laboratories) to ensure good conductivity with the scalp. They were placed at PO7, PO8, P3, P4, Fz, and FPz, using a *Neuroelectrics*® cap according to the 10-20 system (Figure 20D). Two reference electrodes (*Covidien*, H124SG) were positioned on and just below the right mastoid bone (Figure 20C). It is important to note that 8 electrodes is a relatively small number of electrodes to use, compared to other studies observing EEG effects following alpha-tACS (which have often used >50 electrodes; e.g. Helfrich et al., 2014; Neuling et al., 2015). This small number of electrodes was the maximum allowed by *Starstim*® device. However, similarly sparse placement of EEG electrodes was used by both Zaehle et al. (2010) and Kasten et al. (2016) in their studies finding enhancements of EEG alpha power following alpha-tACS. Furthermore, in my pilot study data, I also observed large alpha peaks in average EEG

frequency spectra taken from posterior electrode sites (Figure 21; p.98). I was therefore confident that this EEG setup, while suboptimal, allowed decent measurement of EEG alpha oscillations over posterior cortex.

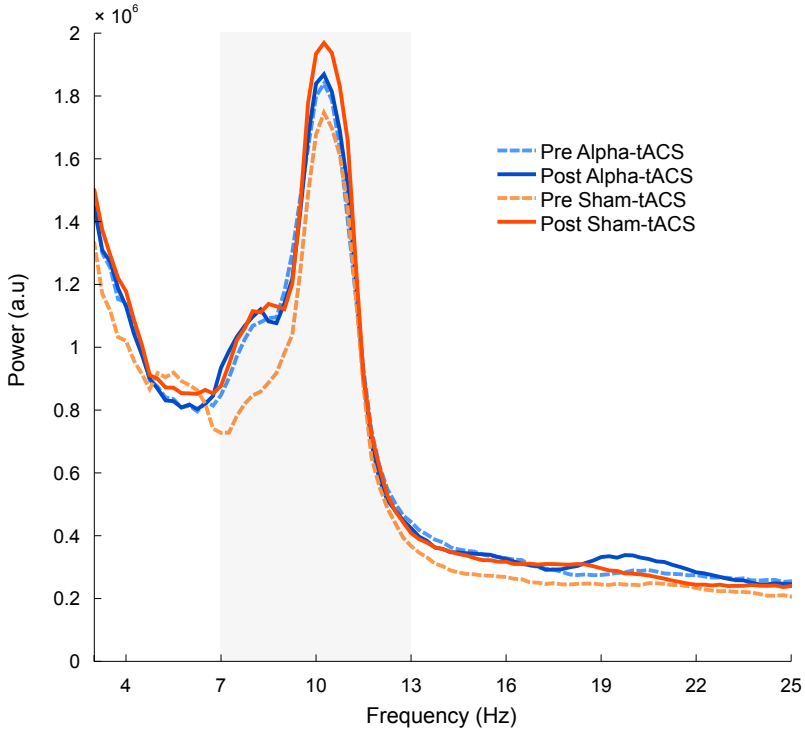


Figure 21 – Pilot EEG spectra before vs. after stimulation. Raw EEG spectra (taken from PO7, PO8, P3, P4) are plotted for data collected before and after the delivery of alpha- vs. sham-tACS. No enhancing effects of alpha-tACS were observed on EEG alpha power. However, a clear peak in the alpha band (grey shading) was observed in all frequency spectra. This supports the use of my EEG electrode positioning for recording of EEG alpha power.

STATISTICAL ANALYSIS

Power analyses

EEG power estimation

I now describe the ways in which this data was analysed. I focus first on EEG power estimation. Firstly, EEG data were band-pass filtered between 1 and 100 Hz using the *pop_basicfilter()* function, which is part of the EEGLAB package in MATLAB. This

function applied a finite impulse response filter with a filter order of 1156. This function also removed the mean value (DC offset) before filtering. Segments of filtered EEG data were then epoched, depending on the analysis I was performing. For example, in my analysis of EEG alpha power before correct vs. error trials, I extracted EEG data recorded before the presentation of detected vs. undetected target trials (see p.101). Bad channels and epochs with excessive noise were identified manually and excluded. Power spectra were then calculated for these cleaned epochs using the *ft_freqanalysis()* function of the Fieldtrip toolbox (Oostenveld, Fries, Maris, & Schoffelen, 2010). Power was estimated between 1 and 30 Hz, with a frequency resolution of 0.25 Hz. Multi-tapering, using discrete prolate spheroidal sequences, was applied with 1 Hz spectral smoothing.

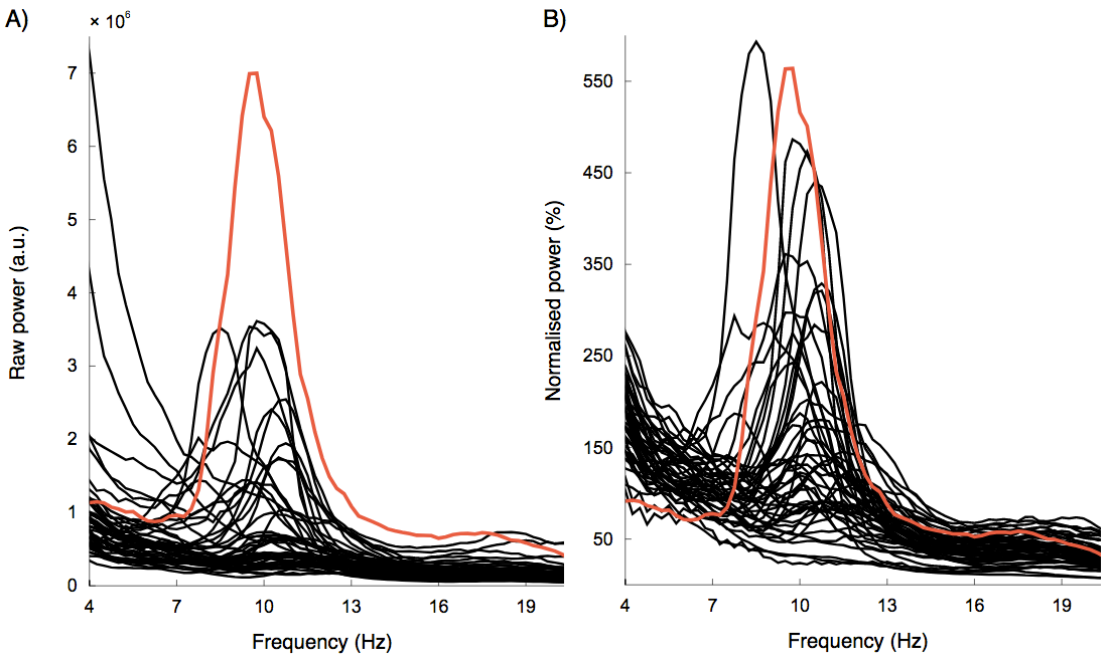


Figure 22 – Illustration of the need for EEG normalisation. A) Raw EEG spectra from a single task block (averaged over all posterior electrodes) are plotted for all subjects in the current experiment. These spectra are dominated by the alpha peak of a single subject (highlighted in red), which would dominate any group-wide estimate of EEG alpha power. B) When each of these individual spectra are normalised (e.g. divided by mean power between 1 and 30 Hz), this single subject no longer dominates the spectra.

The question of normalisation

These raw power estimates exhibited substantial variability across subjects. This variability is illustrated in Figure 22A (p.99), in which raw EEG spectra, collected during a single task block, are plotted for all subjects. In this example, raw spectra are dominated by the alpha peak of a single subject (highlighted in red). This means that any estimate of mean alpha power for this group would be biased towards that subject. Such variation in EEG power can reflect differences across subjects that are not fundamentally of interest. For example, power can vary due to differences in tissue conductivity (Wen & Li, 2006), or muscle tension (Goncharova, McFarland, Vaughan, & Wolpaw). Arguably, it is therefore preferable to normalise EEG power spectra to limit the influence of such subjects on group-wide averages of power.

One method of doing this is to divide each EEG spectrum (i.e. for each electrode, block, and subject) by the mean power in that spectrum within a given frequency range (Cohen, 2014a). For example, in Figure 22B, all spectra are divided by mean power between 1 and 30 Hz. The subject that exhibited significantly elevated raw alpha power is again highlighted in red in this figure. However, in these normalised spectra, this subject would longer exert a disproportionate influence on group-wide measures of mean alpha power. This method of normalisation is therefore appealing. However, it does suffer from a disadvantage that one must make a relatively arbitrary decision about which frequency band to using when normalising. As previously stated, Figure 22B shows EEG spectra normalised to mean power between 1 and 30 Hz. However, a different choice of frequency band (e.g. 4 – 25 Hz) could significantly influence the final estimates of power. To avoid this issue, I chose instead to normalise each EEG spectrum (i.e. for each electrode, block, and subject) to its equivalent, reference spectrum. For example, in my correct vs. error trial analysis, EEG power spectra for error trials were divided by EEG power spectra for correct trials. This yielded a normalised measure of differences in power before error vs. correct trials. Values greater than 100%

indicated that EEG power was greater before errors. Importantly though, this normalisation procedure did not require me to choose an arbitrary frequency band within which to normalise.

Canonical vs. individualised alpha power

In my EEG analyses, one possibility was to analyse alpha power within a canonical alpha band (e.g. 7 – 13 Hz). However, given that individual alpha frequencies (IAFs) vary substantially across participants (Haegens et al., 2014), it seemed more appropriate to use individualised alpha bands. To determine these bands, average power spectra for each participant were calculated from EEG data collected during both task sessions from all posterior electrodes (i.e. PO7, PO8, P3, P4). This was achieved by applying the *ft_freqanalysis()* function in the same way as described on page 99. IAFs were then identified by picking the highest peak in the spectrum within an extended alpha band of 6 – 14 Hz (Haegens et al., 2014). For participants with identifiable alpha peaks, the alpha band was defined as IAF ± 3 Hz (Franciotti, Brancucci, Della Penna, Onofrj, & Tommasi, 2011; W Klimesch, Doppelmayr, Schimke, & Pachinger, 1996). For participants displaying no identifiable alpha peaks (11.4%), the canonical alpha band of 7 – 13 Hz was used. EEG power spectra were then centred on each participant's IAF. Individualised theta bands were defined as IAF-6 – IAF-3 Hz. Individualised low beta bands were defined as IAF+3 – IAF+6 Hz. I observed no significant interactions when the detectability of alpha peaks was included as a between-subject factor (identifiable vs. unidentifiable). Furthermore, the significance of all results and effect sizes were unaffected when these participants were excluded from analyses.

Error vs. correct trial EEG power analyses

I now provide a detailed description of how these EEG power estimates were analysed with respect to my experimental hypotheses. I start with my efforts to

replicate previous findings of increased EEG alpha power before error vs. correct vCTET trials (Dockree et al., 2017; O'Connell et al., 2009). In their original study, O'Connell et al. (2009) found that EEG alpha power was increased up to 20 seconds before the commission of vCTET errors. However, they also performed a shorter-range analysis focused on EEG data collected 3200 ms before to 800 ms after the presentation of target stimuli. I used these exact parameters in my analysis, extracting EEG epochs (-3200:+800 ms) before error vs. correct vCTET trials. This data was taken from EEG recorded before and after the delivery of tACS (i.e. from blocks 1 and 4 only). These EEG epochs were then analysed using the previous described methods, and individualised alpha power measures (averaged over posterior electrodes) were submitted to a one-way repeated-measures ANOVA with the within-subjects factor of 'frequency band' (i.e. individualised theta, alpha, and low beta). Where there were violations of the assumption of sphericity, the Huynh-Feldt correction was applied. In these cases, the corresponding epsilon value (ε) is stated alongside the ANOVA results.

Pre- vs. post-tACS power analyses

I also assessed whether EEG alpha power was increased following alpha- vs. control-tACS. To perform this analysis, I extracted EEG data recorded before and after the delivery of stimulation for each participant. This EEG data was then divided into multiple, two-second segments, and analysed using the previous described methods. This process extracted frequency power spectra for EEG data recorded before vs. after the delivery of alpha- vs. control-tACS for each subject. Using the same approach as Neuling et al. (2013), post-tACS EEG spectra were then divided by pre-tACS EEG spectra to produce a normalised measure of percentage power change for each participant in each session. These percentage power change values (averaged over posterior electrodes) were then submitted to a two-way repeated-measures ANOVA

with the within-subjects factors of 'stimulation' (alpha- vs. control-tACS) and 'frequency band' (individualised theta, alpha, and low beta). In all analyses, stimulation order and control group (sham- vs. gamma-tACS) were included as between-subjects factors. Where there were violations of the assumption of sphericity, the Huynh-Feldt correction was again applied.

Behavioural analyses

I now discuss the analysis of behavioural data. Percentage accuracy and RTs were averaged for each block in each session. These data were then submitted to a two-way, repeated measures ANOVA with within-subjects factors of 'stimulation' (alpha- vs. control-tACS) and 'task block' (1-4). As with my EEG analysis, stimulation order and control group (sham- vs. gamma-tACS) were included as between-subjects factors. Again, where there were violations of the assumption of sphericity, the Huynh-Feldt correction was again applied.

Behavioural-EEG regression analyses

I also assessed the association between the behavioural and electrophysiological effects of alpha-tACS. To do this, I first calculated the difference in performance slopes between alpha- and control-tACS (alpha-tACS performance slope minus control-tACS performance slope). This gave me a single measure of the effect of tACS on performance changes over time for each participant. I next calculated the difference in percentage power change in the alpha band following alpha- vs. control-tACS. This gave me a single measure of the effect of alpha-tACS on alpha power. I then submitted these values to a linear regression analysis, with my single behavioural measure as the dependent variable and my alpha power measure as the predictor variable.

Event-related potential analysis

Lastly, in addition to these analyses of EEG power and task performance, I also studied the effects of tACS on event-related potentials (ERPs). I did this by calculating average responses to stimulus presentations over posterior electrode sites (i.e. PO7, PO8, P3, P4). EEG data was first band-pass filtered between 1 and 100 Hz. I then extracted ERPs by epoching this data from 200 ms before to 800 ms after the presentation of vCTET trials. Each ERP was baseline corrected by subtracting from itself its mean amplitude 200-0 ms before stimulus presentation. ERPs were then categorised according the task block (i.e. block 1 vs. 4) and stimulation condition in which they were recorded (i.e. alpha- vs. control-tACS). In their original study, O'Connell et al. (2009) focused on P1 responses to vCTET stimuli, recorded around Oz. They identified the P1 as having a peak amplitude 95-135 ms after stimulus presentations. Following this example, I therefore calculated mean ERP amplitudes to all stimuli within this interval. To determine if P1 amplitudes were influenced by tACS, I then submitted these mean amplitudes to a two way, repeated measures ANOVA with within-subjects factors of 'stimulation' (alpha- vs. control-tACS) and 'task block' (1-4). Stimulation order and control group were again included as between-subjects factors.

STATEMENT OF PREDICTIONS

To summarise, in this experiment, participants performed two ~21-minute sessions of a sustained attention task. These task sessions were separated by a break of 25 minutes. tACS was delivered over occipitoparietal cortex for ~11 minutes in the middle of each session. EEG was recorded throughout task performance. Using a counterbalanced design, each participant received 10 Hz-tACS (alpha-tACS) or sham-/50 Hz-tACS (control-tACS). This allowed me to compare the effects of alpha- vs. control-tACS using a within-subjects design.

Following the results of previous tACS studies (Neuling et al., 2013; Ruhnau, Neuling, et al., 2016; Zaehle et al., 2010), I expected to observe consistent increases in EEG alpha power at posterior electrode sites following alpha-tACS. As errors on the vCTET have been found to be preceded by increases in EEG alpha power (Dockree et al., 2017; O'Connell et al., 2009), I also expected to replicate this effect, in addition to observing consistently impairing effects of alpha-tACS on vCTET performance, starting from the onset of stimulation. In addition, given negative associations between EEG alpha power and early, visual event-related potentials (e.g. Gruber, Klimesch, Sauseng, & Doppelmayr, 2004; Villena-González, López, & Rodríguez, 2016), I expected that these impairing effects of alpha-tACS on vCTET performance would be accompanied by reductions in P1 amplitudes.

RESULTS

EEG alpha power was increased before error vs. correct trials

I focused first on the question of whether EEG alpha power was increased before error vs. correct vCTET trials. Specifically, I compared normalised EEG power within individualised theta, alpha, and low beta bands 3200 ms before to 800 after the presentation of target trials. Note that values greater than 100% reflect greater EEG power before error vs. correct trials. I observed a significant effect of frequency band ($F_{(2,94)}$=3.38, p=.044, ε=.893, η^2_p=.067, ANOVA). Decomposition of this effect revealed that normalised power in the alpha band (error / correct) was greater than theta power (M=8.1%, SD=17.3%, $t_{(47)}$=3.27, p=.002, d=0.47, paired-samples t-test), but did not differ reliably from beta power (M=2.8%, SD=23.2%, $t_{(47)}$<1, paired-samples t-test) (Figure 23; p.106). It was also surprising to note that broadband power (i.e. theta to low beta) was higher than 100% (M=111.5%, SD=15.4%, $t_{(47)}$=5.19, p<.001, d=0.75, one-sample t-test). This indicates, unexpectedly, that EEG power was generally elevated before error vs. correct trials.

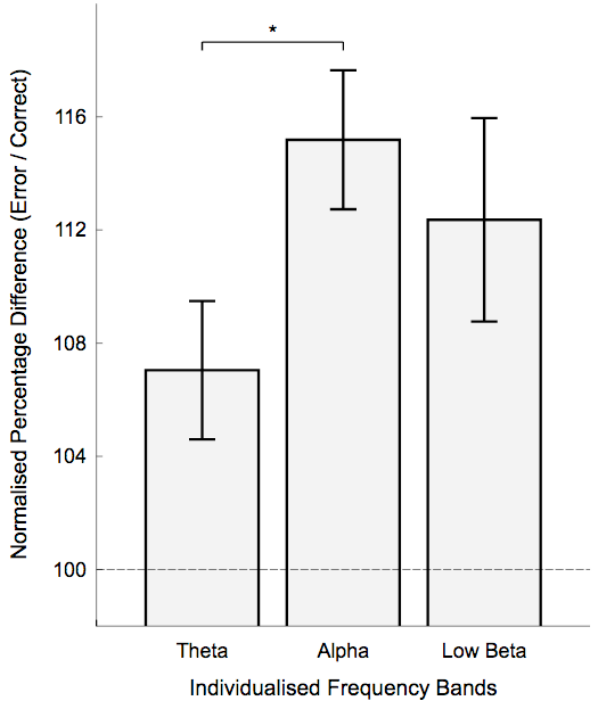


Figure 23 – Normalised EEG power is shown for individualised theta, alpha, and beta bands (error / correct). Alpha power was greater before error vs. correct trials with respect to theta power, but not with respect to beta power. Surprisingly, broadband power (i.e. theta–beta) was significantly elevated before error vs. correct trials. Error bars show ±1 standard error of the mean.

EEG alpha power was also increased following alpha-tACS

I focused next on the effects of tACS on EEG power (averaged over electrodes PO7, PO8, P3, and P4) in individualised theta, alpha, and low beta bands. Figure 24 (p.107) shows frequency power spectra before and after the delivery of alpha- vs. control-tACS. However, in my main analysis, I compared normalised percentage change in EEG power between stimulation conditions.

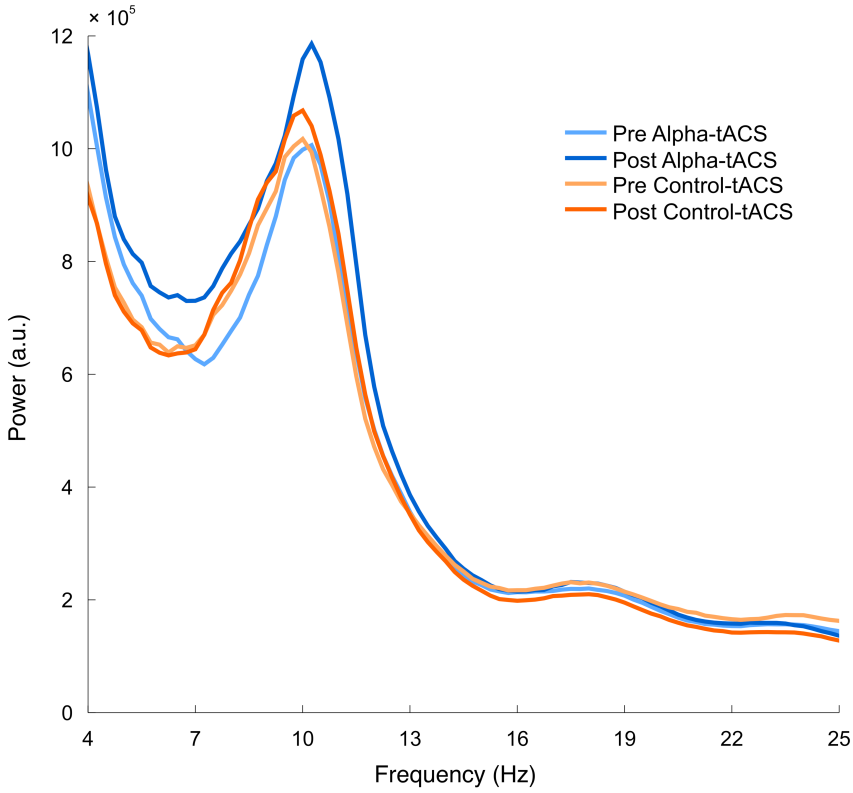


Figure 24 – Raw EEG spectra (averaged over PO7, PO8, P3, P4), before and after the delivery of alpha- vs. control-tACS.

In this analysis, I observed significant main effects of stimulation ($F_{(1,44)}$=9.00, p=.004, η^2_p=.170, ANOVA), and frequency band ($F_{(2,88)}$=7.99, p=.001, η^2_p=.154, ANOVA) that were qualified by a significant interaction between stimulation and frequency band ($F_{(2,88)}$=3.17, p=.047, η^2_p=.067, ANOVA). The main effect of frequency band indicated that, regardless of whether participants received alpha- or control-tACS, EEG alpha power increased reliably from the start to the end of each task session (M=114.0%,

SD=21.3%, $t_{(47)}$=4.55, p<.001, d=0.66, one-sample t-test [test value = 100%]). This replicates typical findings in sustained attention research (Craig, Tran, Wijesuriya, & Nguyen, 2012; Gharagozlou et al., 2015; Lim, Quevenco, & Kwok, 2013; E. A. Schmidt et al., 2009; Wascher et al., 2014). No corresponding increases were consistently observed in the theta band (M=103.1%, SD=16.0%, $t_{(47)}$=1.33, p=.190, d=0.19, one-sample t-test [test value = 100%]) or low beta band (M=103.8%, SD=21.0%, $t_{(47)}$=1.27, p=.211, d=0.18, one-sample t-test [test value = 100%]). The main effect of stimulation, and the interaction with frequency band, indicated that this increase in alpha power was accentuated following alpha-tACS. In line with my predictions, planned comparisons revealed that percentage change in EEG power was indeed greater following alpha- vs. control-tACS in the alpha band (M=15.0%, SD=44.3%, $t_{(47)}$=2.35, p=.023, d=0.34, paired-samples t-test). However, no reliable differences were observed in the theta (M=5.1%, SD=29.5%, $t_{(47)}$=1.19, p=.240, d=0.17, paired-samples t-test) or low beta bands (M=5.2%, SD=28.2%, $t_{(47)}$=1.27, p=.209, d=0.18, paired-samples t-test). Thus, alpha-tACS exerted a specific, enhancing effect on EEG alpha power (Figure 25; p.109). There were no main effects or interactions with control group (i.e. sham- vs. gamma-tACS; Figure 26II-III; p.109). However, a significant three-way interaction was observed between stimulation, frequency band, and stimulation order ($F_{(2,88)}$=7.64, p=.001, η^2_p=.148, ANOVA), indicating that enhancements in EEG alpha power were greater when alpha-tACS was delivered in the first vs. second task session. Decomposition of this effect revealed a significant interaction between stimulation and frequency band for participants who received alpha-tACS in the first task session ($F_{(2,40)}$=5.93, p=.006, η^2_p=.229, ANOVA) but not for participants receiving alpha-tACS in the second task session ($F_{(2,48)}$=1.07, p=.353, η^2_p=.043, ANOVA) (Figure 26IV-V).

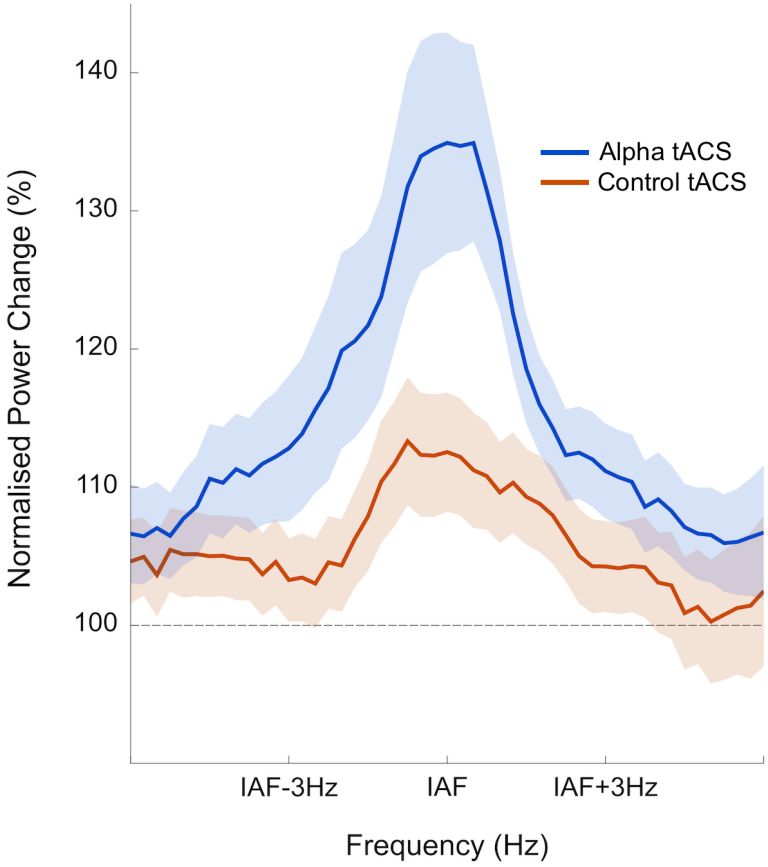


Figure 25 – Normalised percentage change in EEG power (centred around individual alpha frequency [IAF]) during alpha- vs. control-tACS sessions. Significantly greater percentage change in alpha power was observed following alpha- vs. control-tACS. Coloured shading shows ±1 standard error of the mean.

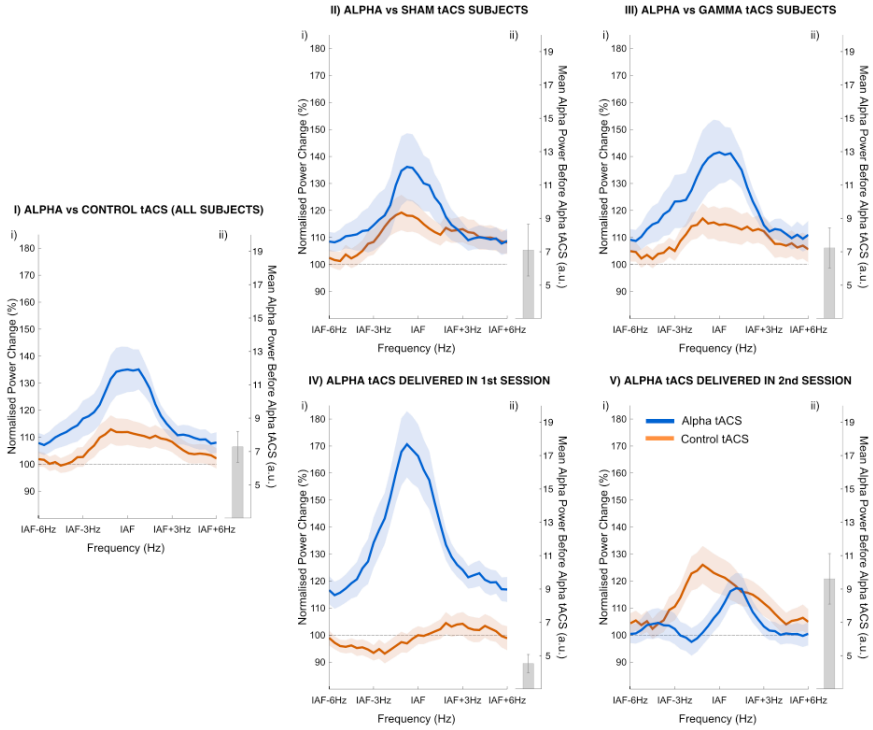


Figure 26 – Normalised change in EEG power, divided by experimental subgroup. Data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Coloured shading shows ±1 standard error of the mean.

The effects of tACS on vCTET accuracy

After confirming that alpha-tACS exerted its predicted influence on brain activity, I next focused on the behavioural effects of stimulation on vCTET performance. As I instructed participants to prioritise performance accuracy over reaction times, I focused first on accuracy data (Figure 27; p.110). I observed a significant main effect of task block ($F_{(3,132)}$=37.54, p<.001, η^2_p=.460, ε=.819, ANOVA) with a strong linear trend ($F_{(1,44)}$=59.44, p<.001, η^2_p=.575, ANOVA). This confirms that vCTET accuracy deteriorated steadily over time. I also observed a significant interaction between stimulation and task block ($F_{(3,132)}$=3.20, p=.026, η^2_p=.068, ANOVA), suggesting an effect of alpha-tACS on the slope of deteriorations in task accuracy over time. There were no main effects or interactions with stimulation order or control group (i.e. sham- vs. gamma-tACS) (Figure 28; p.111).

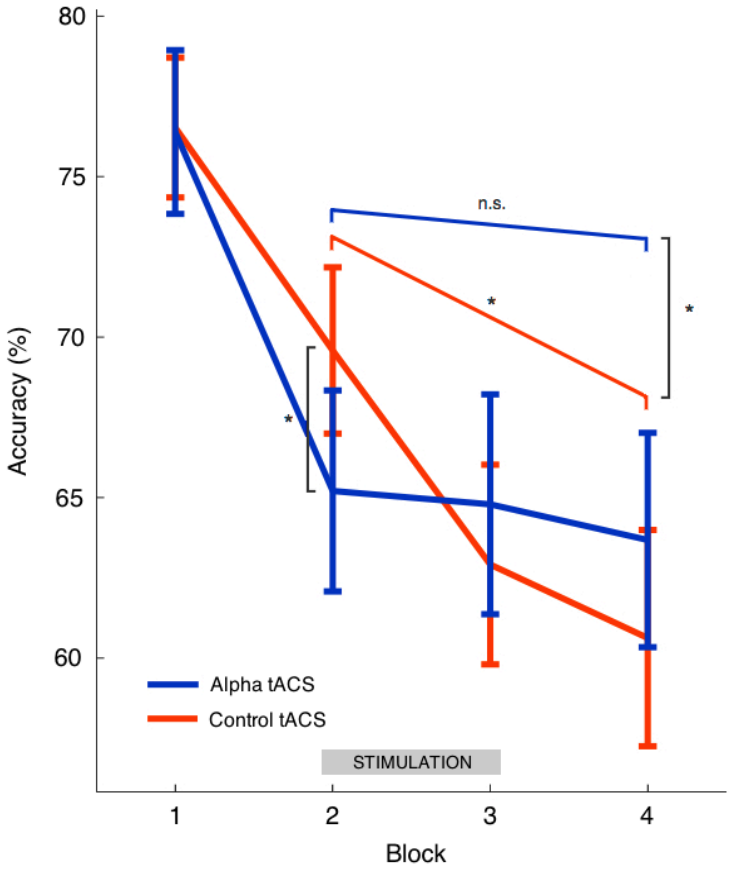


Figure 27 – Effects of tACS on vCTET accuracy. vCTET accuracy is displayed for blocks 1-4 during alpha- vs. control-tACS. Error bars show ±1 standard error of the mean. * = p < .05.

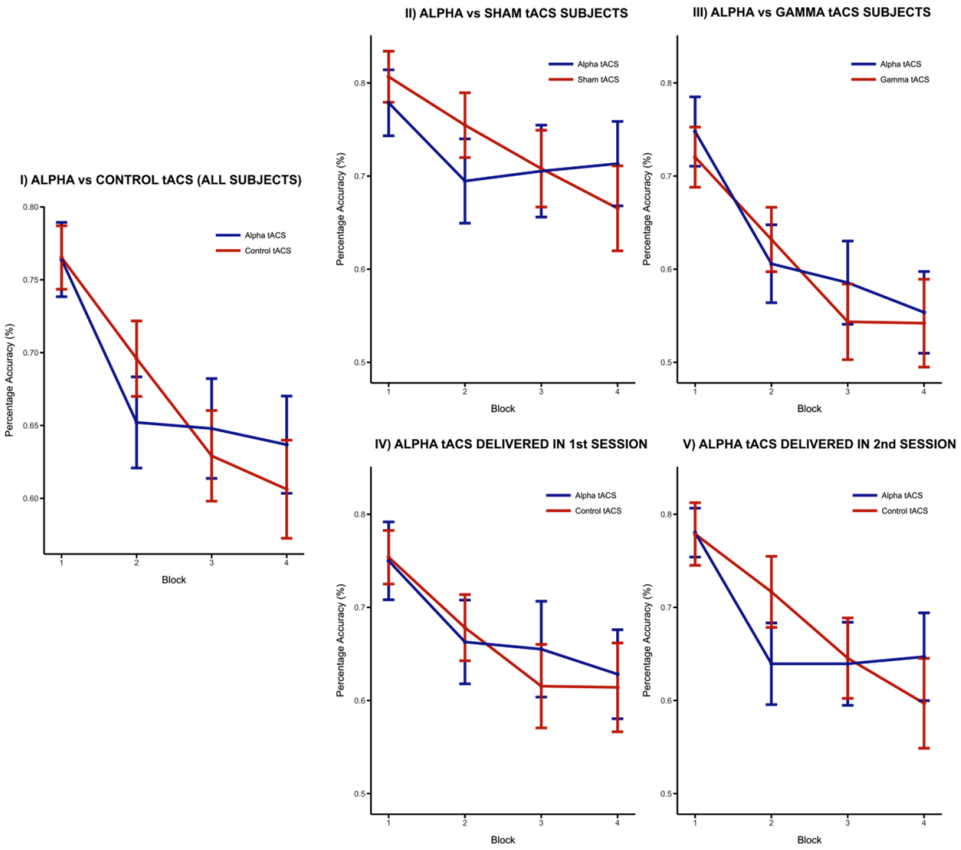


Figure 28 – tACS effects on accuracy, divided by experimental subgroup. vCTET accuracy data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Error bars show ±1 standard error of the mean.

To investigate further this interaction between stimulation and task block, I used linear regression to find the line of best fit through performance from the start of stimulation to the end of the task (i.e., from block 2 to 4) for each participant in each session (alpha- and control-tACS). This slopes-based analysis was applied as an exploratory analysis. I looked at changes in performance from the start of block 2 in order to examine the effects of stimulation (given that stimulation was delivered from the start of block 2). I refer to these from here on as '*performance slopes*'. A significant, negative performance slope was observed for control-tACS (M=-0.093, SD=0.140, $t_{(47)}$=-4.59, p<.001, d=-0.66, one-sample t-test [test value = 0]), indicating a significant deterioration in task accuracy from block 2 to 4. In contrast, the mean accuracy

performance slope for alpha-tACS did not differ significantly from zero (M=-0.024, SD=0.138, $t_{(47)}$=-1.20, p=.235, d=0.17, one-sample t-test [test value = 0]) and, importantly, was less negative than that observed for control-tACS (M=0.069, SD=0.196, $t_{(47)}$ = 2.43, p=.019, d=0.35, paired-samples t-test). These results therefore indicate that, while significant declines in task accuracy were observed during control-tACS from the start of stimulation onwards, alpha-tACS alleviated such declines. However, when I assessed the individual difference correlation between this behavioural effect and EEG alpha power enhancement following alpha-tACS, I found no consistent association (β=.100, F<1, linear regression).

Possible influence of a floor effect

It is noteworthy that task accuracy was significantly lower during alpha- vs. control-tACS in block 2 (M=-4.4%, SD=13.6%, $t_{(47)}$=-2.22, p=.031, d=-0.32, paired-samples t-test). This finding raises the question of whether reduced deteriorations in task accuracy during alpha-tACS could have been caused by a floor effect. In other words, deteriorations in performance could have been less pronounced during alpha-tACS simply because task accuracy reached its lowest point during the first five minutes of stimulation, making any further deteriorations in accuracy less likely. However, this was not the case as accuracy in block 2 during alpha-tACS was significantly higher than in block 4 during control-tACS (M=4.5%, SD=13.6%, $t_{(47)}$=2.33, p=.024, d=0.34, paired-samples t-test). This suggests that performance in block 2 did not reach its lowest level and, therefore, that the observed effects of alpha-tACS on behaviour were not the result of a floor effect.

Effect of tACS on vCTET RTs

All aforementioned analyses were repeated for median reaction times (Figure 29; p.113). A significant main effect of block was again observed ($F_{(3,132)}$=9.57, p<.001,

η^2_p=.179, ε=.898, ANOVA), with a significant linear trend ($F_{(1,44)}$=10.61, p=.002, η^2_p=.194, ANOVA). This indicates that reaction times increased reliably over time. However, no interaction was observed between stimulation and task block (F<1, ANOVA). Performance slopes analysis also revealed that reaction times did not change reliably from block 2 to 4 (p>.1), and that these slopes did not differ between alpha- and control-tACS (p>.5). I therefore conclude that the effects of alpha-tACS on vCTET performance were restricted to task accuracy. As before, there were also no significant effects of either stimulation order or control group.

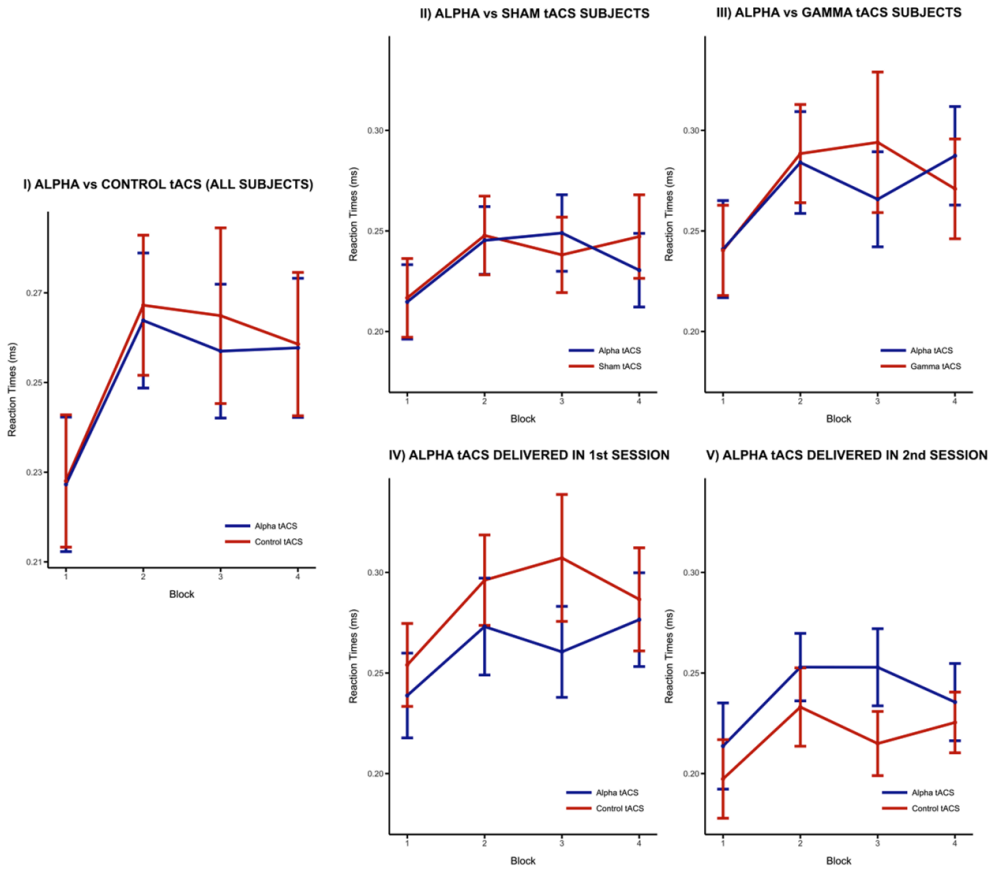


Figure 29 – tACS effects on RTs, divided by experimental subgroup. vCTET RT data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Coloured shading shows ±1 standard error of the mean.

Event-related potential data

In addition to these analyses of EEG power and task performance, I also assessed the effects of tACS on ERP amplitudes. Specifically, I compared P1 amplitudes (defined as occurring 95 – 135 ms after stimulus presentations) before vs. after the delivery of alpha- vs. control-tACS. I observed no effect of task block, indicating that ERP amplitudes did not change reliably from the start to the end of each task session ($F_{(1,44)}$<1). However, I did observe a main effect of stimulation condition ($F_{(1,44)}$=4.52, p=.039, η^2_p=.093, ε=1.0, ANOVA), which was driven by generally higher P1 amplitudes during alpha- vs. control-tACS sessions (M=0.86μV vs. 0.58μV; SD=0.89μV). The important interaction between stimulation condition and task block approached marginal significance ($F_{(1,44)}$=2.77, p=.103, η^2_p=.059, ε=1.0, ANOVA). However, closer inspection of this trend revealed that ERP amplitudes were significantly greater during alpha- vs. control-tACS in the first task block (M=0.94μV vs. 0.43μV, SD=1.27μV, $t_{(47)}$=2.759, p=.008, d=.40), but the last task block (M=0.77μV vs. 0.73μV, SD=1.21μV, $t_{(47)}$<1) (Figure 30; p.115). Consequently, while ERP amplitudes were generally higher during alpha- vs. control-tACS, this effect appeared to have been driven by higher amplitudes before vs. after tACS. I therefore conclude that alpha-tACS had no reliably effect on P1 amplitudes.

Stimulation condition blinding

Lastly, I also sought to confirm that my results could not be explained by side effects of tACS differing reliably between my stimulation conditions. At the end of the experiment, participants were told about the most common side effects of stimulation (i.e. scalp sessions and phosphenes), and were asked in which task session they thought these subjective effects were most intense. An administrative error meant that responses were lost for 5 participants. However, among the remaining participants (n=43), 46.5% said that the subjective effects of stimulation were more intense during

the alpha-tACS session. A binomial test indicated that this proportion was not significantly greater than chance (i.e. 50%; p=.729). I therefore conclude that the subjective effects of stimulation did not differ reliably between alpha- and control-tACS sessions.

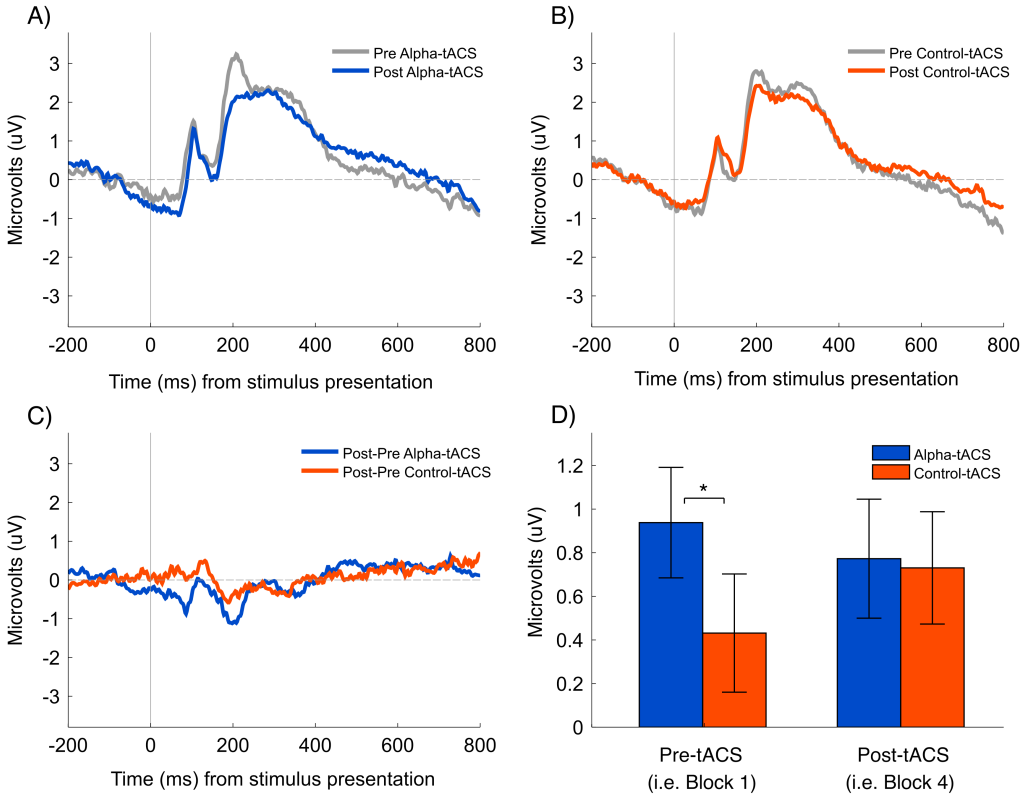


Figure 30 – Event-related potentials (ERPs) are show before and after the delivery of A) alpha-tACS and B) control-tACS. C) The change in ERP amplitudes (i.e. Post-Pre) did not differ reliably between stimulation conditions. D) P1 amplitude (95-135 ms), were significantly higher in the first task block before alpha- vs. control-tACS. However, as no difference was observed in the last task block, I conclude that tACS had no reliable effect on P1 amplitudes. Error bars show ±1 standard error of the mean.

DISCUSSION

In this first experiment, participants performed the vCTET in two task session of ~20 minutes each. Participants received either alpha- or control-tACS (sham- / gamma-tACS) during the middle ten minutes of these sessions. Poor performance on the vCTET has previously been associated with increased EEG alpha power (Chaumon & Busch, 2014; Gonzalez-Rosa et al., 2015; O'Connell et al., 2009). This association was replicated in the current experiment, with alpha power increased before the error vs. correct vCTET trials. Furthermore, alpha power also increased reliably from the start to the end of each task session, alongside deteriorations in task performance, and regardless of stimulation condition. Given such negative links between alpha and vCTET performance, I therefore expected to observe only impairing effects of alpha-tACS on vCTET performance. Consistent with my expectations, EEG alpha power was increased following alpha-tACS. Furthermore, the behavioural and EEG effects were not found to be different between sham- and gamma-tACS. However, the effects of alpha-tACS on vCTET performance did not follow my predictions. I also observed no effects of alpha-tACS on P1 amplitudes.

Alpha-tACS initially inhibits vCTET performance

Alpha-tACS significantly impaired vCTET performance during the first five minutes of stimulation. This suggests that, while alpha-tACS has not previously been found to suppress visual attention, it can induce such suppression – albeit for limited periods of time. It is interesting to note that this finding is difficult to reconcile with the view that EEG alpha oscillations reflect idling, or are simply an epiphenomenon of large-scale brain activity (Chapter 2; p.48). If this was the case, tACS should not have exerted alpha-specific effects on vCTET performance. Instead, my results suggest an active association between alpha oscillations and visual attention. However, these cognitive effects of alpha-tACS exhibited significant time-dependency and bidirectionality.

Attentional support followed this initial suppression

In addition to enhancing EEG alpha power, alpha-tACS caused both impairment and facilitation of CTET performance over different timescales. Although alpha-tACS did impair CTET performance in the first five minutes of stimulation, these impairments were followed by significant protection of performance from deteriorations over time. Specifically, although task accuracy decreased from the start of stimulation onwards during control-tACS (i.e. block 2-4), the slope of this deterioration was significantly less negative during alpha- vs. control-tACS. Importantly, such apparent protection of vCTET accuracy during alpha-tACS could not be explained by task accuracy reaching its lowest limit during the first five minutes of alpha-tACS. Task accuracy during this early period was significantly greater than at the end of control-tACS. The important question posed by this finding is therefore: if alpha oscillations are so robustly associated with impaired vCTET performance (Dockree et al., 2017; O'Connell et al., 2009), why did alpha-tACS affect vCTET performance in two opposite directions?

General enhancing effects of tES

One possible answer is that alpha-tACS improved visual attention through secondary effects of stimulation. For example, tES has been found to block adenosine A1 receptors in rabbits (Márquez-Ruiz et al., 2013). Such blocking of adenosine receptors is thought to be responsible for the enhancing effects of caffeine on sleepiness and fatigue (Davis et al., 2003). Furthermore, a recent study found that tDCS over prefrontal regions could protect sustained attention from deteriorations more significantly than caffeine (McIntire, McKinley, Goodyear, & Nelson, 2014). These findings suggest that tES may have effects on behaviour that are independent of its intended effects on brain activity (e.g. increases in neural excitability or oscillatory power). It may be therefore that, while alpha-tACS initially impaired vCTET performance by strengthening inhibitory processes associated with alpha oscillations, alpha-tACS also supported

sustained attention by exerting parallel effects on adenosinergic, or other related systems. This would explain the bidirectional effects of alpha-tACS on vCTET performance. However, it does not explain why these effects were not observed during gamma-tACS (i.e. and therefore appear to be frequency specific). Furthermore, this perspective does not explain why the impairing effects of alpha-tACS on task performance were so short-lived.

The possible role of overreaction to initial impairment

Another possible answer is that subjects detected and reacted to the early, inhibitory effects of alpha-tACS on attention. While post-experiment interviews confirmed that subjects did not notice any differences between the subjective effects of alpha- and control-tACS (see p.114), EEG alpha power has been found to correlate negatively with subjective ratings of attentional focus (J. S. Macdonald et al., 2011). Consequently, subjects may have identified deteriorations in their attention during the first 5 minutes of alpha-tACS and, in response, increased their attentional control for the remainder of the task. However, this hypothesis cannot explain why EEG alpha oscillations were significantly enhanced following alpha-tACS. Given the negative association between visual attention and EEG alpha power, any increases in attentional control should have been accompanied by comparable suppressions of EEG alpha power.

The possible role of neural fatigue in processes of inhibition

Another possibility is that these behavioural effects were caused by time-varying activation of inhibitory attentional systems. As posterior alpha oscillations have been strongly associated with perceptual inhibition, it is assumed that enhancements of these oscillations should increase the activity of inhibitory systems. Such increases would explain why alpha-tACS impaired CTET performance during the first 5 minutes of stimulation. However, it is known that prolonged, high-amplitude transcranial stimulation

can induce opposite effects to lower amplitude stimulation, perhaps due to neural fatigue or regulatory responses to excessive excitation/inhibition (Batsikadze, Moliadze, Paulus, Kuo, & Nitsche, 2013). Therefore, it is conceivable that, following a prolonged period of stimulation, inhibitory systems activated by alpha-tACS will have become fatigued, or switched into a facilitatory mode, in response to increasing stimulation. Such changes will have resulted in the significant release of visual processing from inhibition, and therefore will have supported CTET performance as stimulation continued.

Possible mechanisms behind this inhibitory fatigue

Such an account explains the unexpectedly enhancing effect of alpha-tACS on vCTET performance while still maintaining the fundamental link between EEG alpha oscillations and inhibitory processes. However, if alpha-tACS induces activation of inhibitory processes, what might these processes actually be? One possible answer can be found by focusing on recent research into corticothalamic feedback. As mentioned in the Chapter 2 (see p.58), EEG alpha oscillations have been suggested to reflect the activity of L6CT neurons (Womelsdorf et al., 2014). Alternating electrical fields have been found to exert disproportionate effects on neural populations firing at the frequency of stimulation (Fröhlich & McCormick, 2010). As a result, it is possible that the effects of alpha-tACS are not distributed uniformly across occipitoparietal cortex, but rather are exerted most significantly on L6CT networks that oscillate readily at alpha frequencies. This is important as, consistent with the negative association between alpha oscillations and visual perception, optogenetic activation of L6CT neurons has been found to induce robust inhibition of visual processing (Bortone, Olsen, & Scanziani, 2014; Olsen et al., 2012). Furthermore, intriguingly, a recent study found that 10 Hz stimulation of L6CT neurons induced time-dependent, bidirectional effects on sensory thalamic activity that were comparable to the temporal pattern of my behavioural results. Specifically, while 10 Hz stimulation of L6CT neurons initially suppressed thalamic activity, this suppression

was reversed after a short period of time and, eventually, activity in sensory thalamus was increased by L6CT stimulation. This reversal was caused by synaptic depression in the thalamic reticular nucleus, which projects inhibitory connections to sensory thalamus and is monosynaptically activated by L6CT neurons (Crandall et al., 2015). Consequently, it may be that the time-dependent, bidirectional effects of alpha-tACS on vCTET performance were mediated by initial activation, followed by fatigue, within occipitoparietal L6CT networks.

No association between EEG and behavioural effects of tACS

Lastly, it is important to state that, although alpha-tACS had significant effects on both EEG and task performance, I found no evidence of associations between these two effects. In other words, participants who exhibited the greatest increases in EEG alpha power following alpha-tACS did not also exhibit the greatest changes in task performance. It is difficult to draw conclusions from such null results. For example, it is arguably unsurprising that I observed only weak correlations between two noisy measures. However, it should also be stated that this absence of an association between the EEG and behavioural effects of tACS could suggest that alpha-tACS does not influence task performance via changes in EEG alpha power. In other words, the EEG and behavioural effects of tACS may have been largely independent. This would suggest against some of the previously mentioned ideas that, for example, alpha-tACS exerted bidirectional effects on task performance through excessive stimulation of alpha-related, inhibitory networks.

CHAPTER 5 – VISUAL THRESHOLD DETECTION TASK

The last experiment studied the effects of alpha-tACS on vCTET performance. Previous studies have found that errors on this task are preceded by increases in EEG alpha power (Dockree et al., 2017; O'Connell et al., 2009). I replicated this effect in my own data. Consequently, given that alpha-tACS is known to increase EEG alpha power (e.g. Helfrich et al., 2014), I strongly predicted that alpha-tACS would consistently impair vCTET performance. However, although alpha-tACS did initially impair vCTET accuracy (i.e. in the first block of stimulation), it also protected accuracy from additional deteriorations over time. It was clear that such results needed further investigation.

Given that my findings contrasted so significantly with my initial predictions, and that they were observed in just one experiment, it was important that I replicated them in a second experiment. Such a replication would suggest that the results did not occur simply by chance. Furthermore, while the vCTET appears to be a good task of sustained attention, inducing significant deteriorations in task performance over time, it is arguable that the vCTET does not provide a pure measure of visual attention. This is because the vCTET requires participants to judge the length of time each stimulus is presented for and, consequently, relies to a significant extent on time perception abilities. Therefore, given that time perception has previously been associated with changes in EEG alpha power (e.g. Babiloni et al., 2004), it is possible that alpha-tACS exerted its surprising effects on vCTET performance via modulation of time perception abilities, rather than visual attention per se. It was therefore important to run a second experiment using a task that did not depend on time perception. Lastly, I suggested at the end of the previous chapter that the bidirectional effects of alpha-tACS on vCTET accuracy could reflect activation, followed by fatigue within inhibitory, sensory systems. For example, I suggested that such fatigue could occur within corticothalamic networks, dedicated to the transmission of information from visual thalamus to visual cortex. From

the perspective of this account, I would assume that changes within such inhibitory systems would exert their clearest effects on low-level, visual processing. However, target classification in the vCTET depends on relatively high-level visual processing (i.e. due to reliance on time perception). Therefore, it was also important that this second experiment used a task that was sufficiently simple that it tested only low-level visual processing.

For these purposes, I chose a visual threshold detection task. Specifically, I used the task of Chaumon and Busch (2014). Here, participants must respond to faint stimuli that are presented for a brief period in their visual periphery. This task has the advantage that it tests low-level visual perception, while not testing time perception abilities. My prediction was that, if my previous results reflected the true influence of alpha-tACS on visual attention, I should observe very similar behavioural effects in this experiment (i.e. initial suppression, followed by protection of task performance). However, if I observed substantially different effects, this would suggest that the results of my previous experiment were either gained by chance, or that they reflect the influence of alpha-tACS on vCTET performance specifically (i.e. and therefore not on visual attention more generally). In addition, it should be noted that, because this threshold detection task includes the presentation of brief stimuli, it also facilitated study of the influence of alpha-tACS phase on task performance. In their previous experiment, Helfrich et al. (2014) found that the accuracy with which participants could detect briefly presented, visual stimuli varied with alpha-tACS phase. Specifically, they found that detection accuracy was increased around peak phase positions. Consequently, in addition to the previously mentioned predictions, I also analysed the association between alpha-tACS phase and task performance (both task accuracy and RTs), predicting that visual targets would be detected most optimally when presented during the peak vs. trough of alpha-tACS.

METHODS

Experimental design

This experiment used near identical methods to the previous experiment. The following sections detail the small areas of difference between these experiments.

Participants

Thirty-nine healthy adults took part in this experiment. Two participants were excluded because their accuracy on at least one task block was more than 2 standard deviations below mean accuracy on that block across all participants. The final sample therefore consisted of 37 participants (20 females, 2 left-handed, mean age = 23.7, SD = 3.5).

Visual Threshold Detection Task

In this experiment, participants performed a visual threshold detection task (Chaumon & Busch, 2014), in which they had to detect an unpredictable and briefly presented dot stimulus. A small, white fixation cross (6 mm^2) was continuously displayed in the centre of a black screen. Target stimuli consisted of small grey dots (diameter = 1 mm) that appeared with equal frequency for 16.7 ms on either the left or right side of the screen. These dots were presented between two white, vertical lines continuously displayed 8.5 cm either side of the central fixation cross (Figure 31; p.124). Participants were instructed to focus on the central cross and respond to the presentation of dot targets as quickly and as accurately as possible by pressing the space bar. Inter-stimulus intervals varied randomly between 2500 and 3500 ms (mean = 3000 ms). Stimulus perceptibility was varied by adjusting stimulus luminance. At the beginning of the experiment, participants completed a single task block in which an

adaptive staircase procedure was used to determine 50% detection thresholds for each participant (Watson & Pelli, 1983). During the main experiment, stimuli were presented with equal frequency at three different luminance levels: 0, 1, and 3 decibels from 50% threshold. Each block consisted of 96 trials, again lasting 4 minutes and 50 seconds. It is important to note that, as in Chaumon and Busch (2014), participants performed all sessions of this task in dark conditions.

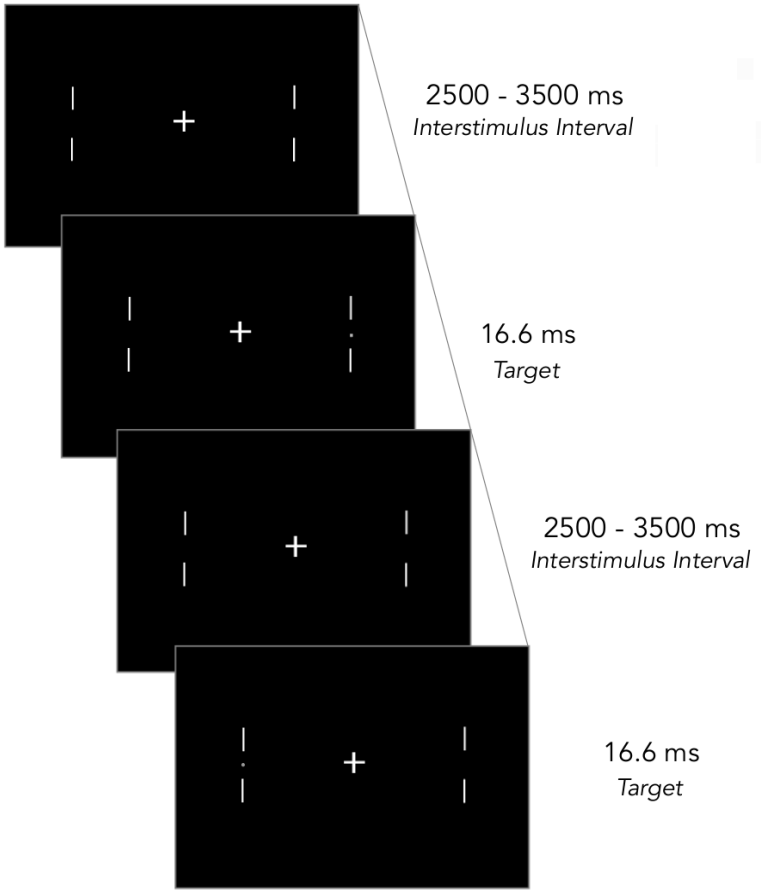


Figure 31 – Visual Threshold Detection Task. A fixation cross, surrounded by two pairs of placeholders, was constantly present in the centre of the screen. With a variable inter-stimulus interval (2500-3500 ms), a grey dot was presented in the middle of either the left- or right-hand placeholders. These white dots varied in their intensities. Participants were required to respond to the presentation of each white dot by pressing the space bar as quickly as possible (adapted from Chaumon & Busch, 2014).

Statistical analyses

As with the experimental methods, the statistical analyses for this experiment were near identical to those of the previous experiment. The following sections detail the small areas of difference.

Alpha power before errors vs. correct trials

Similar to the previous experiment, I assessed whether EEG alpha power was increased before error vs. correct trials. In their original study, Chaumon and Busch (2014) found that alpha power was greater before the presentation of visual targets that were subsequently missed vs. detected. In an attempt to replicate this finding, I extracted EEG data from -4000 to 0 ms before the presentation of visual targets. Normalised power for individualised frequency bands (error / correct spectra) was then calculated and analysed in the same way as in the previous experiment.

Phase based analysis of task accuracy and RTs

I also assessed the influence of alpha-tACS phase on target detection performance. To conduct this analysis, I first extracted phase information from EEG data recorded during the delivery of alpha-tACS. I focused on data collected from Fpz as the tACS artifact led to saturation of EEG signal at posterior electrode sites. This frontal data was then submitted to a Hilbert transform using the *hilbert()* function in MATLAB. Phase angles in radians were extracted from the Hilbert transformed data using the *angle()* function, and converted into degrees using the *rad2deg()* function (Figure 32; p.126). This process gave me a continuous measure of alpha-tACS phase during the delivery of stimulation. To determine the association between alpha-tACS phase and target detection performance, I then extracted for each trial the alpha-tACS phase position at the point of stimulus presentation. Phase positions were divided into

4 bins: 45 to 135°, 135 to -135°, -135 to -45°, and -45 to 45°. Mean detection accuracy and RTs were then calculated for targets presented in each of these phase bins. This performance data, divided by phase bins, were then submitted separately to one-way repeated-measures ANOVAs, with the within-subjects factor of 'phase bin'. This analysis was based on the previous analysis by Helfrich et al. (2014).

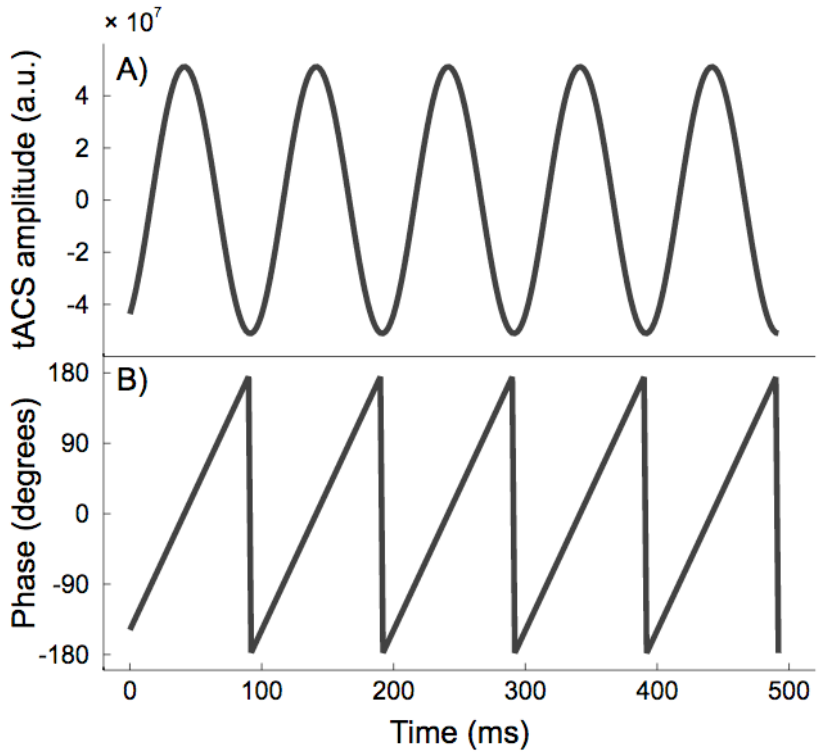


Figure 32 - Extraction of phase information from EEG signal. A) Sample EEG data recorded from electrode Fpz during the delivery of alpha-tACS. Approximately five cycles of a 10 Hz oscillation can be seen. B) This frontal data was submitted to a Hilbert transform using the *hilbert()* function in MATLAB. Phase angles in radians were then extracted from the Hilbert transformed data using the *angle()* function, and converted into degrees using the *rad2deg()* function

RESULTS

Alpha power was not increased before error trials

As in Experiment 1, I focused first on the question of whether EEG alpha power was increased before error vs. correct vCTET trials. Specifically, I compared normalised EEG power (error / correct) 4000 to 0 ms before the presentation of targets. However, in contrast to Experiment 1, I observed no effect of frequency band ($F_{(2,72)}$<1, ANOVA) (Figure 33; p.127). I therefore concluded that, although EEG alpha power was increased before error vs. correct trials in the original study by Chaumon and Busch (2014), this effect was not replicated in the current experiment.

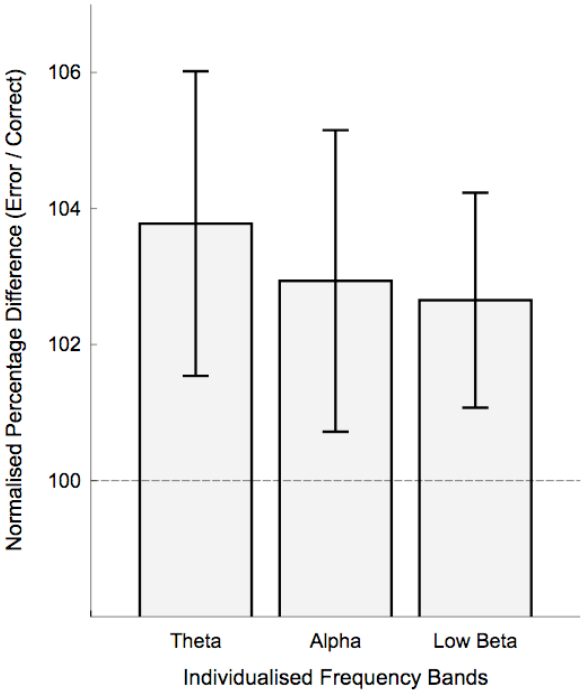


Figure 33 – Normalised EEG power is shown for individualised theta, alpha, and low beta bands (error / correct). EEG power was not significantly greater before error vs. correct trials in any frequency band. Normalised alpha power did not differ from theta or low beta power. Error bars show ±1 standard error of the mean.

No effects of alpha-tACS on EEG alpha power

I next examined the effects of stimulation on EEG power in individualised theta, alpha, and low beta bands. Figure 34 (p.128) shows raw frequency power spectra before and after the delivery of alpha- vs. control-tACS.

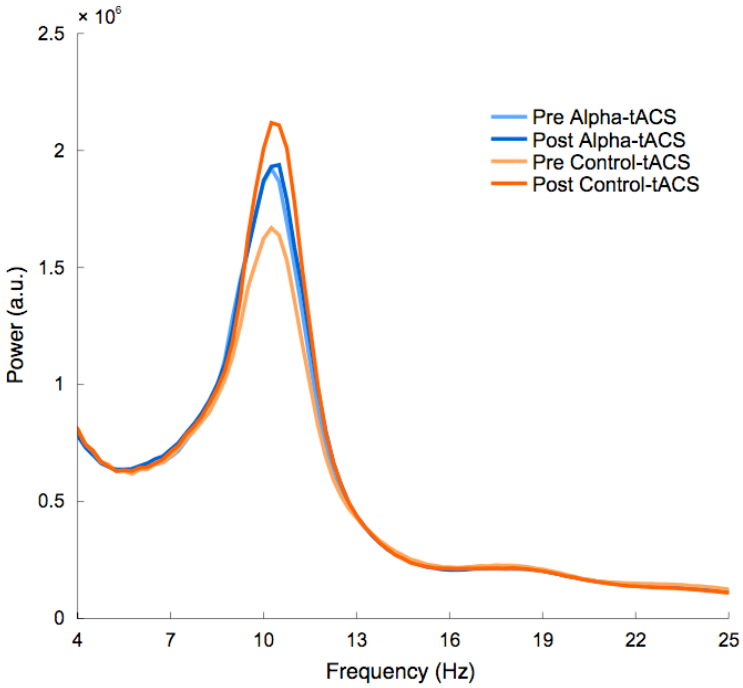


Figure 34 – Raw EEG spectra (averaged over PO7, PO8, P3, P4) are plotted before and after the delivery of alpha- vs. control-tACS.

In my main analysis, I compared normalised percentage change in EEG power between stimulation conditions. As in Experiment 2, I observed a main effect of frequency band ($F_{(2,66)}$=4.65, p=.018, η^2_p=.124, ε=.843, ANOVA). This effect was driven by significantly increased percentage change in EEG power, independent of stimulation condition, in the alpha band (M=108.8%, SD=23.0%, $t_{(36)}$=2.33, p=.026, d=0.38, one-sample t-test [test value = 100%]), but not in the theta (M=102.6%, SD=10.8%, $t_{(36)}$=1.46, p=.154, d=0.24, one-sample t-test) or low beta bands (M=97.9%, SD=12.2%, $t_{(36)}$=-1.03, p=.310, d=-0.17, one-sample t-test). This result indicates again that, regardless of whether participants received alpha- or control-tACS, EEG alpha power increased reliably from the start to the end of each task session, replicating previous studies of sustained attention (Craig et al., 2012; Gharagozlou et al., 2015; Lim et al., 2013; E. A. Schmidt et al., 2009; Wascher et al., 2014). However, the important interaction between stimulation and frequency band was not found to be significant ($F_{(2,66)}$=1.57, p=.216, η^2_p=.045, ANOVA). Planned comparisons, motivated by my initial predictions and the results of Experiment 1, revealed that percentage change in EEG power did not differ reliably following alpha- vs. control-tACS in either the theta (M=1.9%, SD=23.9%, $t_{(36)}$<1, paired-samples t-test), alpha (M=-7.0%, SD=41.0%, $t_{(36)=}$-1.03, p=.309, d=0.17, paired-

samples t-test) or low beta bands (M=0.1%, SD=20.9%, $t_{(36)}$<1, paired-samples t-test) (Figure 35; p.129). I observed no higher order interactions with stimulation order or control group (Figure 36; p.129). I therefore concluded that alpha-tACS had no reliable effect on EEG alpha power in the current experiment.

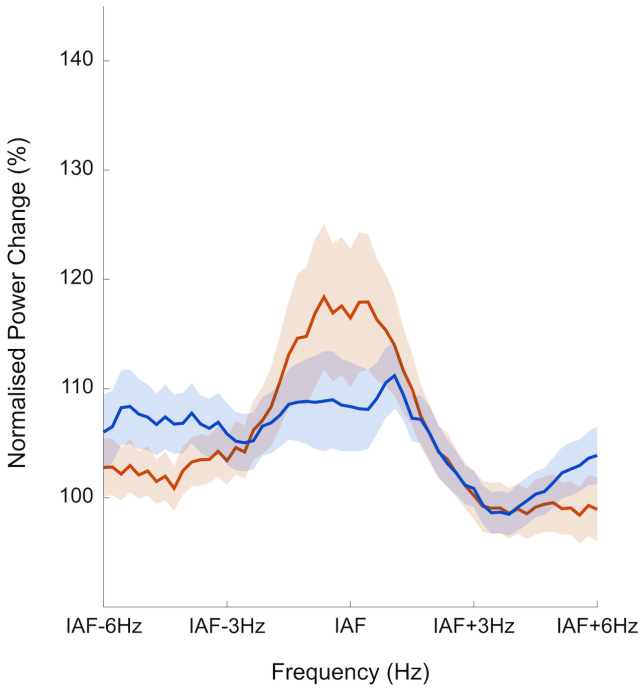


Figure 35 – Normalised percentage change in EEG power (centred around individual alpha frequency [IAF]) did not differ between alpha- and control-tACS sessions. Coloured shading shows ±1 standard error of the mean.

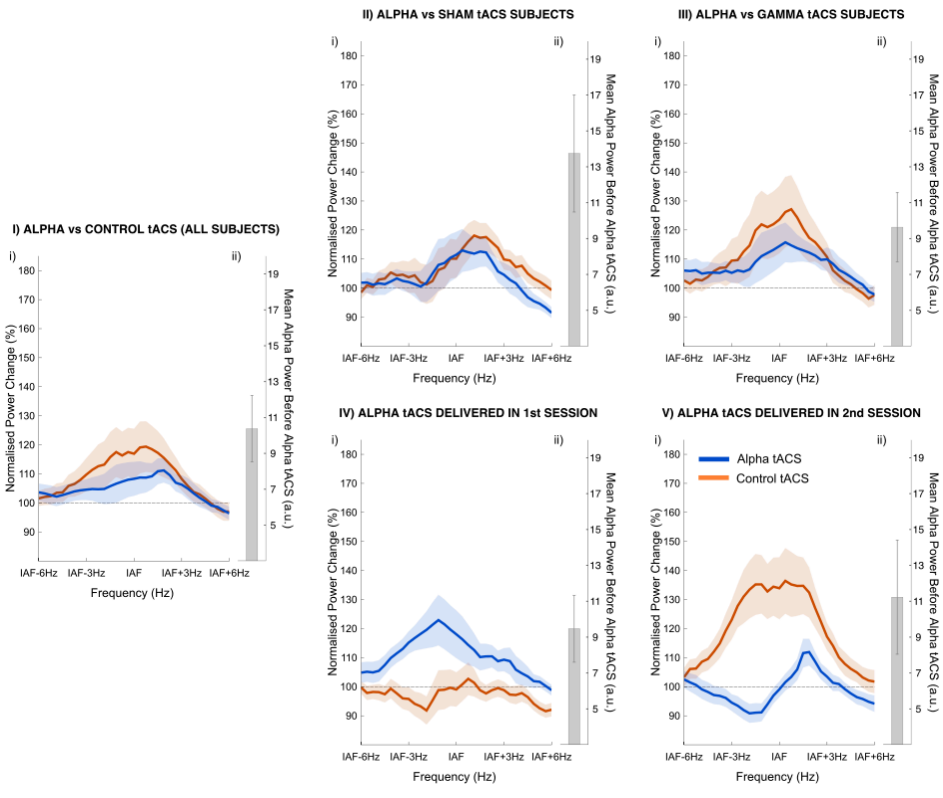


Figure 36 – Normalised change in EEG power, divided by experimental subgroup. Percentage change in EEG power for all participants is shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Coloured shading shows ±1 standard error of the mean.

No effects of alpha-tACS on detection task accuracy

I focused next on task performance, looking first at task accuracy (Figure 37; p.130). A significant main effect of block was again observed ($F_{(3,99)}$=30.58, p<.001, η^2_p=.481, ε=.920, ANOVA) with a strong linear trend ($F_{(1,33)}$=52.18, p<.001, η^2_p=.613, ANOVA). This indicates that task accuracy decreased reliably over time. However, no significant interaction was observed between task block and stimulation ($F_{(3,99)}$=1.15, p=.332, η^2_p=.034, ANOVA). Using the slopes analysis applied in the previous experiment, I also found that performance slopes did not change significantly from block 2 to 4 during either alpha- (M=0.039, SD=0.12, $t_{(36)}$=-1.93, p=.062, d=0.32, one-sample t-test [test value = 0]) or control-tACS (M=0.026, SD=0.14, $t_{(36)}$=-1.11, p=.275, d=-0.18, one-sample t-test), and that these slopes did not differ between stimulation conditions (M=-0.014, SD=0.128, $|t_{(36)}|$=<1, paired-samples t-test). I therefore conclude that there was no effect of alpha-tACS on task accuracy in the current experiment.

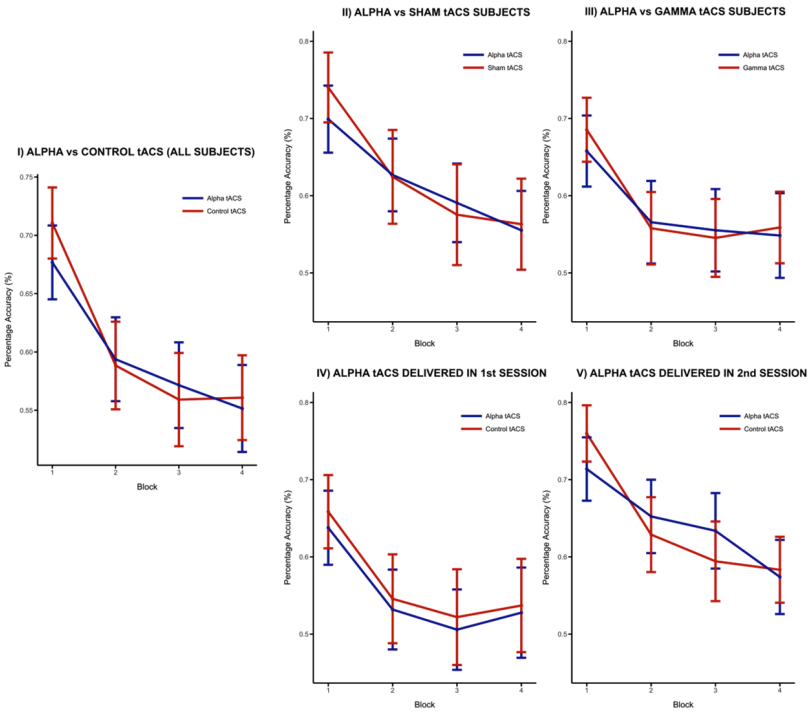


Figure 37 – tACS effects on accuracy, divided by experimental subgroup. Target detection accuracy data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Error bars show ±1 standard error of the mean.

Trend-level protection of RTs from further deteriorations

I next focused on median reaction times (Figure 38; p.132). This analysis again revealed a significant main effect of task block ($F_{(3,99)}$=13.03, p<.001, η^2_p=.283, ε=.644, ANOVA), with a strong linear trend ($F_{(1,33)}$=20.49, p<.001, η^2_p=.383, ANOVA). This indicates consistently worsening performance over the course of each task session. Importantly though, similar to Experiment 1, I observed a marginally significant interaction between stimulation and task block ($F_{(3,99)}$=2.36, p=.084, η^2_p=.067, ε=.884, ANOVA). This suggested an effect of alpha-tACS on block-wise increases in reaction times. Again, using my previously described slopes analysis to investigate this effect, I observed a significant, positive slope for control-tACS (M=0.022, SD=0.042, $t_{(36)}$=3.15, p=.003, d=0.52, one-sample t-test [test value = 0]), indicating a reliable slowing of responses over time. The mean slope for alpha-tACS did not differ reliably from zero (M=-0.004, SD=0.045, $|t_{(36)}|$=<1, one-sample t-test [test value = 0]) and, importantly, was significantly less positive than that of control-tACS (M=0.026, SD=0.067, $t_{(36)}$=2.36, p=.024, d=0.39, paired-samples t-test). Consequently, in a comparable manner to Experiment 1, while reaction times slowed during control-tACS from the start of stimulation to the end of the task, such deteriorations in performance were not observed during alpha-tACS. This finding therefore suggests that alpha-tACS again exerted a supportive effect on task performance. Consistent with this interpretation, post-hoc t-tests revealed that reaction times were marginally faster in block 4 during alpha- vs. control-tACS (M=-18.9 ms, SD=65.3ms, $t_{(36)}$=-1.76, p=.086, η^2_p=.076, paired t-test). No interactions were observed with stimulation order or control group (Figure 39; p.132). I also observed no association across participants between this stabilising effect of alpha-tACS on reaction times and changes in EEG alpha power following alpha-tACS (β=.110, F<1, linear regression).

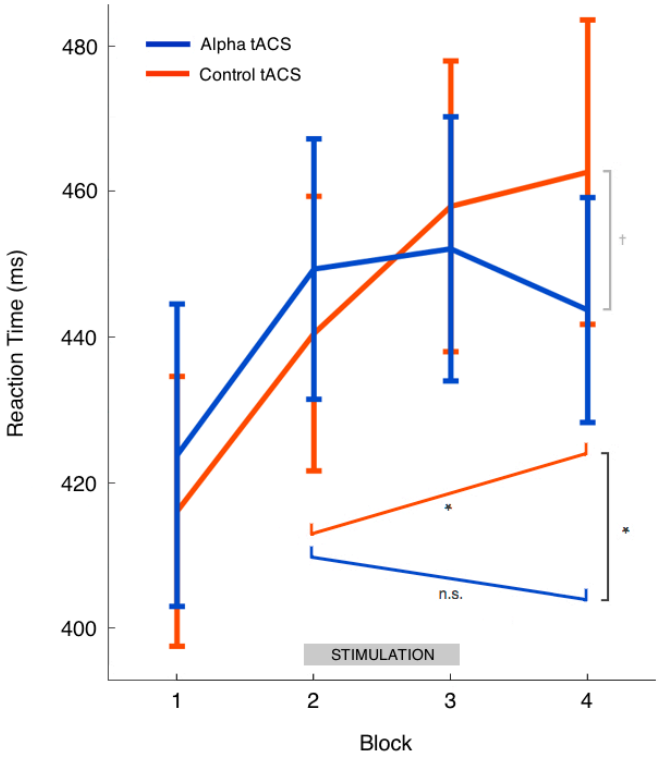


Figure 38 – Effects of tACS on target detection RTs. Target detection RTs are displayed for blocks 1-4 during alpha- vs. control- tACS. Significant, positive slopes in performance were observed (block 2-4) during control-tACS. However, the same slopes during alpha-tACS did not differ reliably from zero. In fact, they were significantly less negative than those observed during control-tACS. Error bars show ±1 standard error of the mean. * = p < .05.

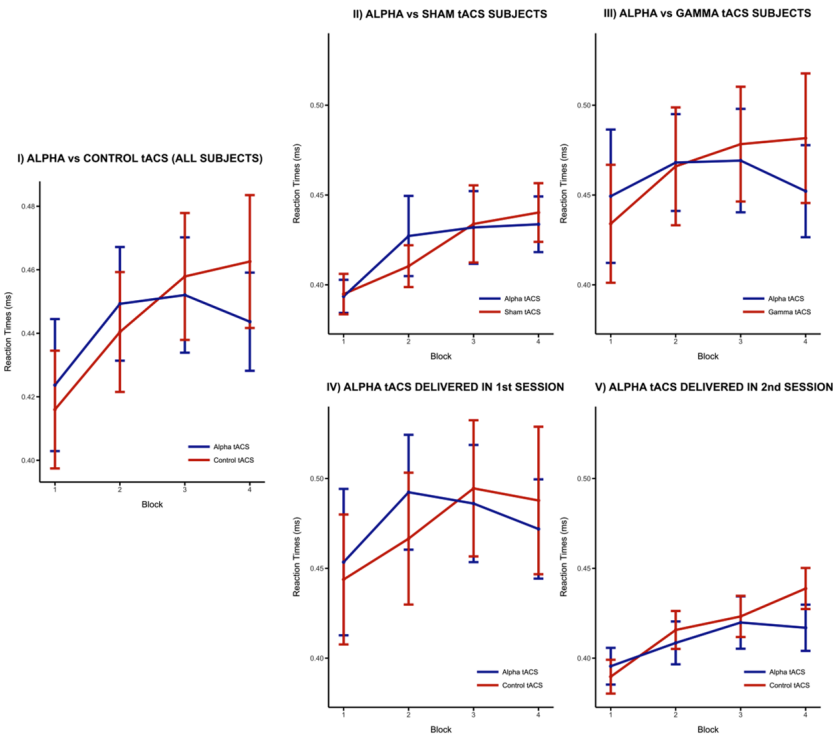


Figure 39 – tACS effects on RTs (by experiment subgroup). Target detection RT data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Error bars show ±1 standard error of the mean.

Stimulation condition blinding

I again sought to confirm that my results could not be explained by side effects of tACS differing reliably between stimulation conditions. Using the same method as in

Experiment 1, 59.5% of participants said that the subjective effects of stimulation were more intense in the alpha-tACS session. A binomial test indicated that this proportion was not significantly greater than chance (i.e. 50%; p=.162). I therefore conclude that, as in Experiment 1, the subjective effects of stimulation did not differ reliably between alpha- and control-tACS sessions.

No effects of alpha-tACS phase on target detection

Lastly, I sought to determine whether the ability of participants to detect target presentations varied with alpha-tACS. To do this, I compared mean accuracy and RTs for trials presented within four different phase bins. However, I observed no effect of phase bin on either task accuracy (Figure 40A (p.133); $F_{(3,108)}$=1.92, p=.131, η^2_p=.051, ANOVA) or RTs (Figure 40B; $F_{(3,108)}$<1, ANOVA). I therefore concluded that, in contrast to previous studies (e.g. Helfrich et al., 2014), task performance did not vary with alpha-tACS phase in the current experiment.

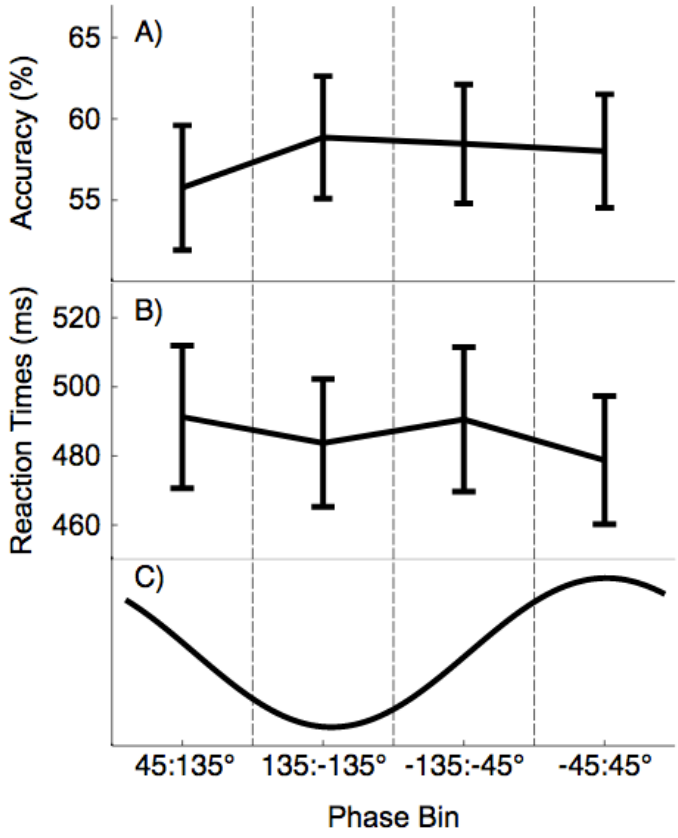


Figure 40 – Effects of alpha-tACS phase on task performance. I observed no effects of alpha-tACS phase on either A) task accuracy or B) RTs. Subplot C) shows the phase positions included in each phase bin. Error bars show ±1 standard error of the mean.

DISCUSSION

In this second experiment, I attempted to replicate the results of my first experiment. The results were mixed. For example, although I previously replicated the finding that EEG alpha power is increased before error vs. correct vCTET trials, I was not able to replicate this effect in the current experiment. Furthermore, although EEG alpha power was significantly increased following alpha vs. control-tACS in my first experiment, I observed no such enhancements in the current experiment. Looking at my behavioural data, task accuracy also showed no correspondence with the results of my first study. However, importantly, when assessing median RTs, I did find evidence to suggest that task performance was protected from deteriorations during the delivery of alpha-tACS. Specifically, my slopes analyses revealed that, although RTs increased reliably from the start of stimulation onwards during control-tACS (i.e. block 2-4), no such increases were observed during alpha-tACS. Furthermore, as with my first study, the difference between the mean slopes during alpha- and control-tACS slopes was found to be reliable. Consequently, I believe this experiment provides a partial replication of the behavioural results of my first experiment. I dedicate the following sections to the discussion of these results.

No replication of EEG effects

EEG alpha power was not increased before errors

As described above, I found that errors in this second experiment were not preceded by increases in EEG alpha power. This contrasts with the previous findings of Chaumon and Busch (2014). Nevertheless, this failed replication is perhaps unsurprising given that the experiment was not designed with this specific analysis in mind. For example, given the electrical artifacts caused by tACS (Noury, Hipp, & Siegel, 2016), my analysis focused only on EEG data recorded before and after the delivery of stimulation.

This limited my analysis to data recorded in just four task blocks (i.e. block 1 & 4, before & after tACS). With each block including 96 trials, this meant that a maximum of 384 trials could be analysed per participant. However, the original analysis by Chaumon and Busch (2014) used 1120 trials per participants (i.e. nearly 3 times more). Consequently, it may be that I simply did not have a sufficient number of trials, and therefore signal-to-noise ratio, to detect small increases in EEG alpha power before errors.

EEG alpha power was not increased following alpha-tACS

Another finding was that EEG alpha power did not increase significantly following alpha- vs. control-tACS. This result is surprising given the large number of studies that have reported increases in EEG alpha power following alpha-tACS (Helfrich et al., 2014; Kasten et al., 2016; Neuling et al., 2013; Neuling et al., 2015; Ruhnau, Neuling, et al., 2016). The result is also surprising because alpha power was increased following alpha-tACS in my first study, which used near-identical methods to the current experiment. Given that alpha-tACS was found to have an effect on visual detection task performance (discussed below), the fact that I observed no accompanying increases in EEG alpha power in the current experiment suggests that the effects of alpha-tACS on EEG and visual attention task performance may be independent. This view is consistent with the finding of my previous experiment that the behavioural and EEG effects of alpha-tACS were unrelated. However, in addition, it is also possible that no increases in alpha power were observed in the current experiment because alpha power was substantially higher in this experiment, compared to my first experiment (Figure 41; p.136).

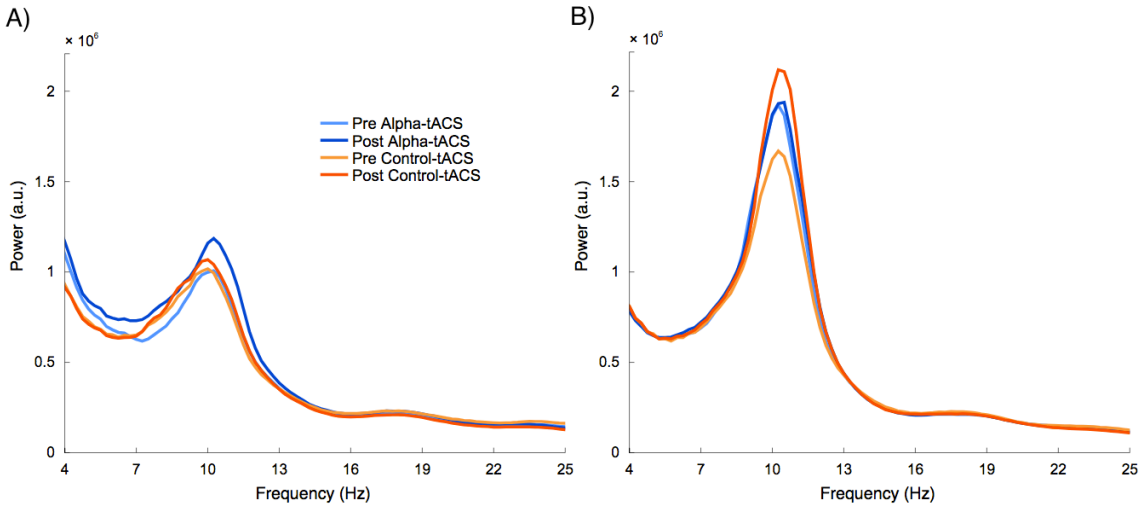


Figure 41 – EEG power in 1st and 2nd experiments. Power spectra are plotted before vs. after the delivery of alpha vs. control-tACS in A) Experiment 1, and B) Experiment 2 (i.e. the current experiment)

To assess this difference statistically, I calculated mean alpha power in all task sessions (7 – 13 Hz) during my first and second experiments, and submitted these mean power estimates to a one-way ANOVA with a between-subjects factor of 'experiment' (i.e. Experiment 1 vs. 2). I observed a significant, main effect of experiment ($F_{(1,83)}$=4.363, p=.040, η^2_p=.050, ANOVA), confirming that mean alpha power was indeed lower during my first vs. second study. This difference could reflect the fact that the vCTET includes presentation of large, high-contrast images, while the current experiment included presentation of only faint targets. Furthermore, the current experiment was performed in dark conditions, while my first experiment was performed in a well-lit room. Consequently, visual cortex may have been generally less activated during the current experiment, compared to the previous experiment, generating higher levels of disengagement and, therefore, EEG alpha power. Importantly, higher levels of EEG alpha power may, in turn, have reduced the likelihood of further increases in alpha power following alpha-tACS. This idea is suggested by previous findings that alpha-tACS increases EEG alpha power only when alpha power is naturally low. For example, alpha-tACS has been found to increase EEG alpha power during eyes-open, but not eyes-closed rest (Alagapan et al., 2016; Neuling et al., 2013). Eyes-closed rest is classically

associated with large increases in EEG alpha power (Berger, 1929). Consequently, although alpha-tACS may have been delivered to the brain in an identical manner to the previous experiment, this stimulation may not have influenced EEG alpha power due to a ceiling effect.

Partial replication of behavioural results across experiments

Although I did not observe an effect of alpha-tACS on task accuracy, this second experiment nevertheless replicated the behavioural results of my first in median reaction times: Although reaction times increased naturally during control-tACS, and although poor performance on this task had previously been associated with increased alpha power (Chaumon & Busch, 2014), delivery of alpha-tACS prevented such deteriorations in reaction times from the start of stimulation onwards. In other words, alpha-tACS was again found to exert a supportive influence on task performance. This view is supported by the additional finding that RTs exhibited a trend level reduction during fourth block of alpha- vs. control-tACS sessions. Overall then, these results appear to provide a partial replication of my previous findings. Furthermore, given the substantial differences between the tasks used in my first two experiments, these results suggest that the supportive effects of alpha-tACS on visual attention are not task specific. I dedicate the following section to discussion of these behavioural results.

Task accuracy vs. RTs

It is interesting to note that the supportive effect of alpha-tACS on task performance in the current experiment was expressed in median RTs, while supportive effects were expressed in task accuracy in the first experiment. Why would such similar behavioural effects be expressed in different task measures? This issue of cognitive effects appearing differently in different performance measures is a long-standing issue in psychology (Pachella, 1973). One reason for this difference may simply be that

vCTET and threshold detection tasks are very different in nature. For example, while the threshold detection task required participants to respond as quickly as possible while maximising accuracy, participants were not told to prioritise RTs during the vCTET. Consequently, it may be unsurprising that similar cognitive effects expressed themselves differently in each of these tasks. However, another possibility refers to the fact that performance slopes for task accuracy (i.e. block 2 to 4) did not differ reliably from zero across stimulation conditions in the current experiment. Therefore, as task accuracy did not deteriorate naturally from block 2 to 4 in this experiment, it is perhaps unsurprising that alpha-tACS exerted no additionally supportive effects on accuracy performance slopes. Of relevance to this point is the finding that RT performance slopes were unaffected by alpha-tACS in my first experiment, and also did not differ significantly from zero.

No evidence of initial inhibition

Another important difference between the behavioural effects of my two studies so far is the absence of impairing effects of alpha-tACS in the current experiment. In my first experiment, alpha-tACS was found to impair vCTET accuracy during the first five minutes of stimulation (i.e. block 2), but then prevented further deteriorations in performance over time. In the current experiment, I observed similar protection of RT from deteriorations over time, but no evidence that these protections were preceded by impairment of task performance.

This result has a number of important implications for the way these two experiments are interpreted. For example, this pattern of results appears fundamentally inconsistent with my prediction that alpha-tACS would consistently impair visual task performance. I have so far observed little evidence that alpha-tACS suppresses visual attention. Furthermore, this absence of an initially impairing effect of alpha-tACS on task performance reduces my confidence in some of the suggestions I made at the end

of the previous chapter. In these sections, I speculated that the protective effects of alpha-tACS on vCTET accuracy could have been caused either by participants overcompensating to initially impairing effects of alpha-tACS on their performance (see p.118), or by neural fatigue within inhibitory systems (see p.118 & 119). However, these suggested explanations cannot explain why alpha-tACS only exerted a *supportive* effect on task performance in the current experiment. Instead, my results appear most consistent with the view that alpha-tACS exerts a generally enhancing effect on visual attention. This idea will be the focus of the following, two chapters.

No effect of alpha-tACS phase on task performance

The last result I would like to discuss is the observation that task performance (both accuracy and RTs) was unaffected by alpha-tACS phase. Although Helfrich et al. (2014) found that the ability of participants to detect briefly presented, visual stimuli was greatest when stimuli were presented around peak phase positions, I was not able to replicate this finding. It is clearly difficult to make theoretical conclusions from such null results. This is especially true as my analysis focused only on data recorded during the two blocks of alpha-tACS, and therefore used a maximum of just 192 trials per participant. However, it is interesting to note that, consistent with these results, previous authors have suggested that alpha-tACS does not influence alpha phase. For example, when applying alpha-tACS over posterior cortex for periods of 3 and 8 seconds, Vossen et al. (2014) found no entrainment of alpha phase to the delivered stimulation. Consequently, the alpha-tACS phase results of the current experiment may be interpreted as broadly consistent with this line of research, and may have been driven by a failure of alpha-tACS to entrain ongoing, alpha oscillations.

CHAPTER 6 – AUDITORY CONTINUOUS TEMPORAL EXPECTANCY TASK

Although I did not observe an effect of alpha-tACS on task accuracy, my second experiment replicated the behavioural results of my first in terms of median RTs: Whereas RTs increased naturally during control-tACS, and while poor performance on this task had previously been associated with increased alpha power (Chaumon & Busch, 2014), delivery of alpha-tACS prevented such deteriorations in RTs from the start of stimulation onwards. This experiment had a number of issues. For example, it was unclear why the supportive effect of alpha-tACS on task performance was expressed in accuracy in the first experiment, but in reaction times in this second experiment. Furthermore, in contrast to my first experiment, this supportive effect of alpha-tACS on task performance was not accompanied by increases in EEG alpha power. Nevertheless, given the significant differences between the tasks used in these two experiments, the replication of my first experiment at the behavioural level appears to suggest that the effects of alpha-tACS may be generalisable across different domains of visual attention. A remaining question was therefore why alpha-tACS would exert such generalisable effects on visual attention task performance.

One possibility is that alpha-tACS influences processes in the brain that are dedicated to visual processing and attention. However, alternatively, alpha-tACS could exert generalised, modality-independent effects on cognitive processing. For example, it has been suggested that tDCS may improve sustained attention performance by blocking the activity of adenosine A1 receptors, leading to increased levels of wakefulness (McIntire et al., 2014). To answer this question of whether the effects of alpha-tACS are modality-specific, I delivered the same stimulation as in my two previous experiments while participants performed an auditory version of the Continuous Temporal Expectancy Task (aCTET). In other words, participants performed an auditory version of the task used in Experiment 1. If the effects of alpha-

tACS were specific to the visual domain, I would not expect to replicate my previous behavioural results in this experiment. However, if modality-independent mechanisms mediated the behavioural effects of alpha-tACS, I would expect to observe similar protections of auditory task performance.

METHODS

Experimental design

As with the previous experiment, this experiment used near identical methods to the first experiment. In the following sections, the small differences between these experiments are detailed.

Participants

Forty-four healthy adults took part in the third experiment. Three participants were excluded because their accuracy on at least one task block was more than 2 standard deviations below mean accuracy on that block across all participants. The final sample therefore consisted of 41 participants (26 females, 7 left-handed, mean age = 23.2, SD = 2.7).

Auditory Continuous Temporal Expectancy Task

Participants performed an auditory version of the Continuous Temporal Expectancy Task (aCTET), in which participants had to detect when an auditory stimulus had been played for longer than usual. This task was adapted from one previously used by Berry et al. (2014) and was chosen to enable both the study of auditory attention and comparability with the results of the vCTET task in Experiment 1. On each trial, an auditory stimulus was played through in-ear headphones. Each stimulus consisted of two, simultaneously played square wave tones, one at 220 Hz and the other at 329.63 Hz. This stimulus was presented for 800 ms on ~91% of trials ('standard trials'; 300 per block) and 1000 ms on the other ~9% of trials ('target trials'; 30 per block) (Figure 42; p.143). As in the vCTET, the order of trials was pseudo-randomised such that between 7 and 15 (mean = 10) standard trials were presented between targets. All trials were preceded by a 20 ms period of silence. The aim of the

task was to assess the length of time each tone was played for and to press the space bar whenever a longer, 'target' trial was heard. Responses were classified as correct if made less than 2.46 seconds (3 trials) after a target presentation (Berry et al., 2014). However, participants were again not asked to prioritise response speed, but were told to maximise their accuracy. As in Experiment 1, participants completed a practice session of this aCTET in which they had to identify 6 target trials consecutively without missing any, and without incorrectly classifying any standard trials as targets. Feedback was given during this practice as in Experiment 1, but was not given during the main task.

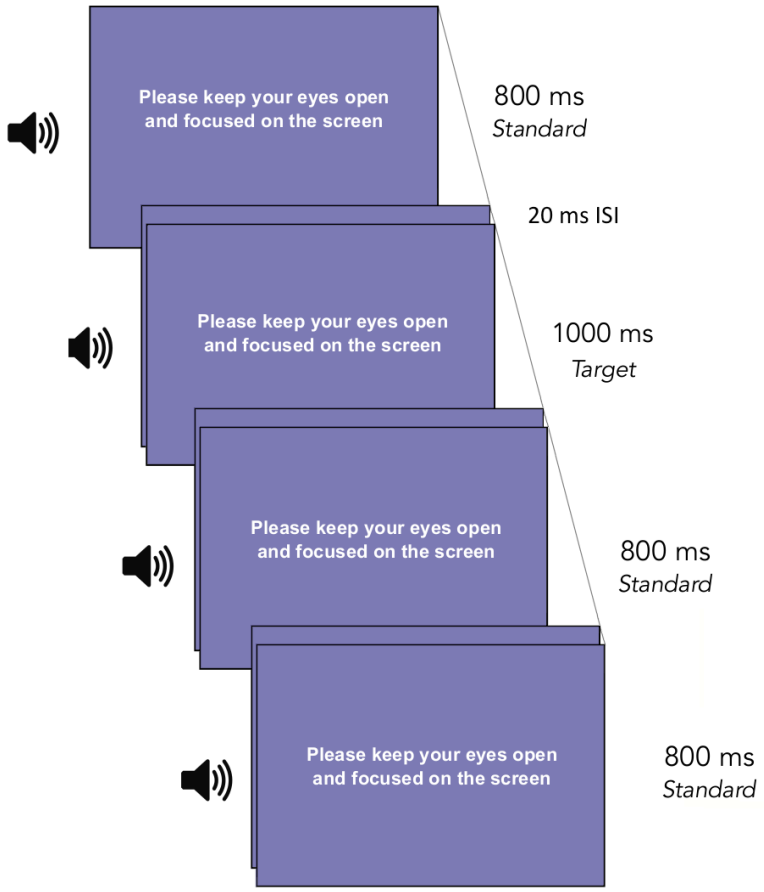


Figure 42 – Auditory Continuous Temporal Expectancy Task. Auditory Continuous Temporal Expectancy Task (Experiment 3). Participants were repeatedly played an auditory stimulus. On standard trials, this stimulus lasted 800 ms. On target trials, this stimulus lasted 1000 ms. All stimuli were preceded by a 20 ms period of silence. As in the vCTET, participants were required to press the space bar following all target trials (Berry et al., 2014).

Statistical analyses

The effects of alpha-tACS on vCTET vs. aCTET accuracy

This experiment applied identical analyses to those of Experiment 1. However, an additional analysis was performed in this experiment to compare the effects of alpha-tACS on vCTET vs. aCTET accuracy. To enable comparison between experiments, I divided task accuracy performance slopes (from block 2 to 4) during alpha-tACS for each participant by their mean task accuracy performance slope during control-tACS in each experiment. A value of less than one on this measure indicates that the slope of decline during alpha-tACS was less steep than the slope during control-tACS. In other words, a value of less than one indicates reduced deterioration (or stabilisation) in task accuracy during alpha-tACS. I then submitted these normalised slope values to a three-way ANOVA with between-subjects factors of 'sensory modality' (i.e., vCTET vs. aCTET), 'stimulation order', and 'control group'. I predicted that, if alpha-tACS influences only visual attention, these normalised slopes would be reliably lower for my first experiment, compared to the current experiment. I therefore used a one-tailed test of significance in my assessment of this prediction.

RESULTS

No effects of alpha-tACS on EEG alpha power

As my previous experiments, I focused first on the effects of alpha-tACS on EEG power. Figure 43 (p.145) shows raw frequency power spectra before and after the delivery of alpha- vs. control-tACS.

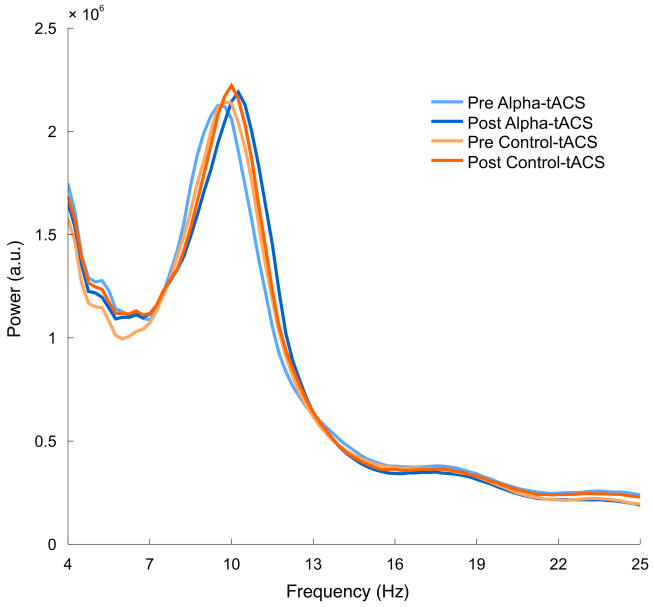


Figure 43 – Raw EEG spectra (averaged over PO7, PO8, P3, P4) are plotted before and after the delivery of alpha- vs. control-tACS.

In my main analysis of normalised percentage change in EEG power, I observed no significant main effects, and no interaction between stimulation and frequency band (F<1, ANOVA). Planned comparisons, motivated by my initial predictions and the results of Experiment 1, revealed that percentage change in EEG power did not differ reliably following alpha- vs. control-tACS in either the theta (M=-3.2%, SD=41.7%, $|t_{(40)}|$=<1, paired-samples t-test), alpha (M=0.1%, SD=68.9%, $t_{(40)}$<1, paired-samples t-test) or low beta bands (M=-3.2%, SD=46.4%, $|t_{(40)}|$=<1, paired-samples t-test). Thus, alpha-tACS had no reliable effects on EEG power in the current experiment (Figure 44; p.146). I also observed no higher order interactions with stimulation order or control group (Figure 45; p.146).

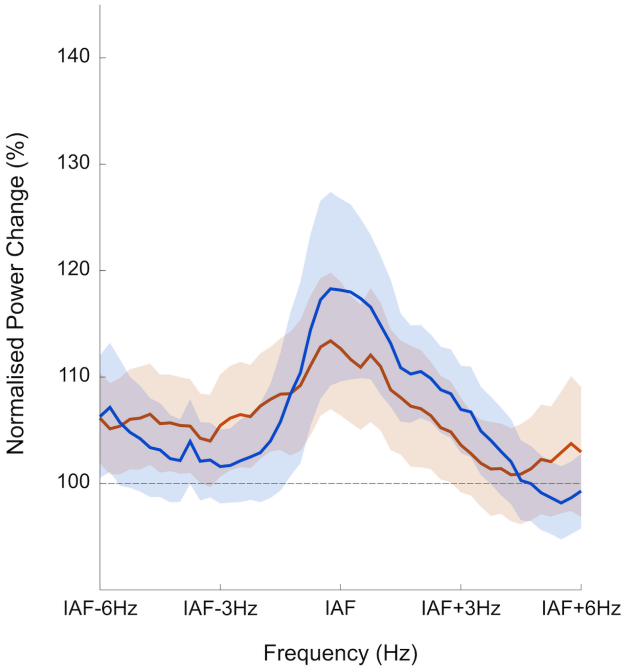


Figure 44 – Normalised percentage change in EEG power (centred around individual alpha frequency [IAF]) did not differ between alpha- and control tACS sessions. Coloured shading shows ±1 standard error of the mean.

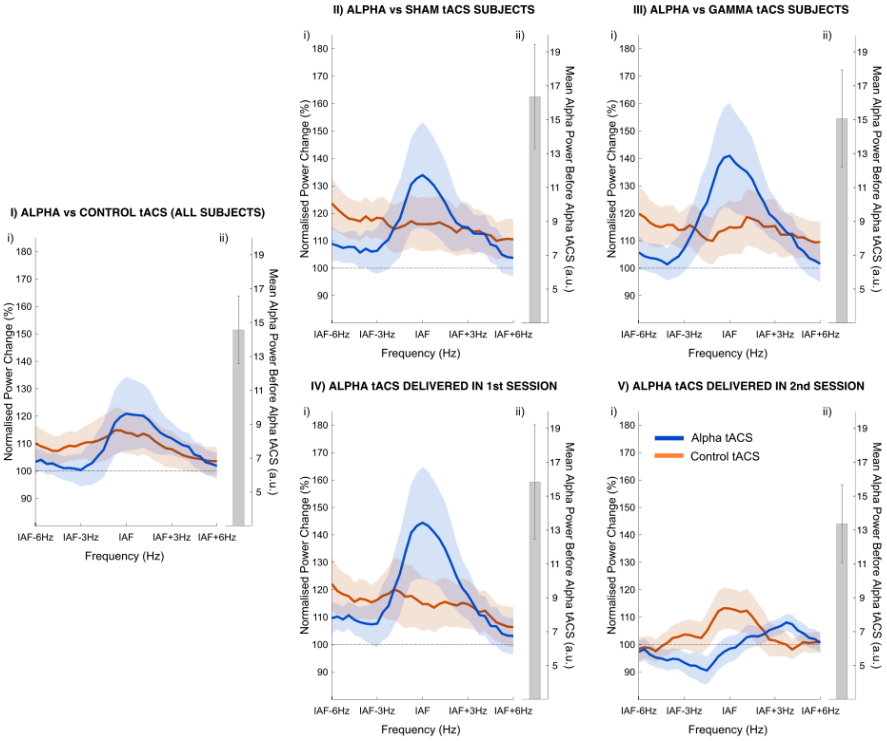


Figure 45 – Normalised change in EEG power, divided by experimental subgroup. Data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Coloured shading shows ±1 standard error of the mean.

No effects of alpha-tACS on aCTET accuracy or RTs

I next focused on task performance, and the effect of alpha-tACS on aCTET accuracy (Figure 46; p.147). As expected, I observed a significant main effect of task block ($F_{(3,111)}$=22.44, p<.001, η^2_p=.377, ε=.806, ANOVA) with a strong linear trend ($F_{(1,37)}$=33.99, p<.001, η^2_p=.479, ANOVA). Slopes analysis revealed that task accuracy

declined significantly from block 2 to 4 during both alpha- (M=-0.042, SD=0.117, $t_{(40)}$=-2.32, *p*=.026, *d*=-0.36, one-sample t-test [test value = 0]) and control-tACS (M=-0.036, SD=0.110, $t_{(40)}$=-2.11, *p*=.041, *d*=-0.33, one-sample t-test). However, in contrast to Experiment 1, I did not observe a significant interaction between stimulation and task block (*F*<1, ANOVA). I observed no higher order interactions with stimulation order or control group (Figure 47; p.148). I also observed no difference in accuracy performance slopes between alpha- and control-tACS (t>1). Overall then, these results suggested that alpha-tACS had no influence on aCTET accuracy in the current experiment. However, given the theoretical importance of this null result, I decided to run a Bayesian paired-samples t-test of accuracy performance slopes during alpha- vs. control-tACS using JASP (2017). The estimated Bayes factor for this comparison (null/alternative) suggested that the observed slopes data were 5.77 times more likely to occur under a model in which alpha- vs. control-tACS slopes did not differ from each other, compared to a model in which these slopes did differ. This Bayesian comparison therefore indicated the presence of moderate evidence in favour of the hypothesis that alpha-tACS had no effect on deteriorations in aCTET accuracy over time.

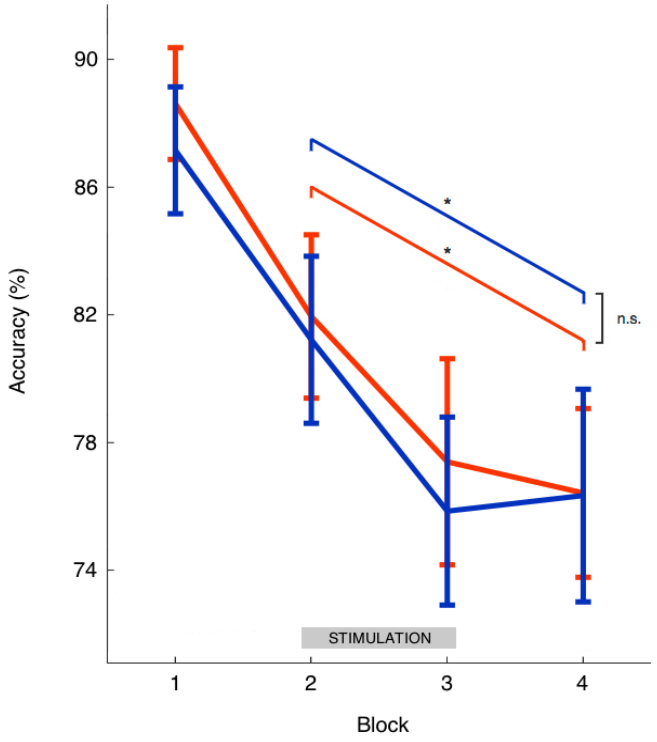


Figure 46 – Effects of tACS on aCTET accuracy. aCTET accuracy is displayed for blocks 1-4 during alpha- vs. control- tACS. Significant, positive slopes in performance were observed (block 2-4) during both alpha- and control-tACS. These performance slopes did not differ significantly from each other. Error bars show ±1 standard error of the mean. * = p < .05.

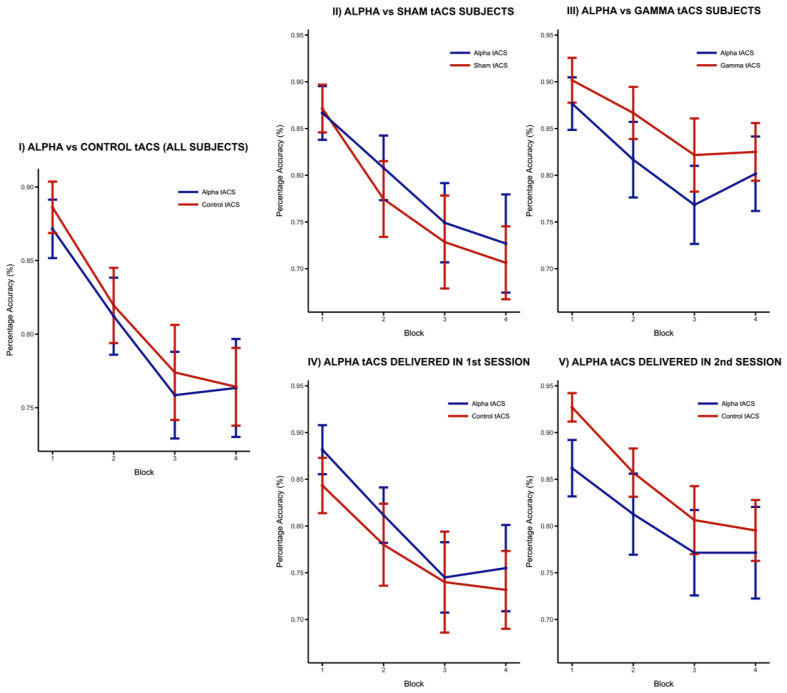


Figure 47 – tACS effects on accuracy, divided by experimental subgroup. aCTET accuracy data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Error bars show ±1 standard error of the mean.

I then applied the same analyses to median reaction times (Figure 48; p.149). I again observed a significant main effect of task block ($F_{(3,111)}$=8.95, p<.001, η^2_p=.195, ε=.868, ANOVA) with a strong linear trend ($F_{(1,37)}$=17.38, p<.001, η^2_p=.320, ANOVA). This indicates that reaction times increased reliably from the start to the end of each task session. However, slopes analysis showed that reaction times did not increase from block 2 to 4 during either alpha- (M=0.006, SD=0.029, $t_{(40)}$=1.29, p=.205, d=0.20, one-sample t-test [test value = 0]) or control-tACS (M=0.006, SD=0.027, $t_{(40)}$=1.38, p=.175, d=0.22, one-sample t-test). I also observed no significant interaction between stimulation and task block (F<1, ANOVA), and no higher order interactions with stimulation order or control group. Similarly, I observed no significant differences between the reaction time performance slopes of alpha- vs. control-tACS (p>.5). Using the same analysis applied to task accuracy, I again decided to run a Bayesian paired-samples t-test of this slope comparison using JASP. The estimated Bayes factor for this comparison (null/alternative) suggested that the observed slopes data were 5.93 times more likely to occur under a model in which alpha- vs. control-tACS slopes did not differ from each

other, compared to a model in which these slopes did differ. This Bayesian comparison therefore indicated the presence of moderate evidence in favour of the hypothesis that alpha-tACS had no effect on increases in aCTET RTs over time.

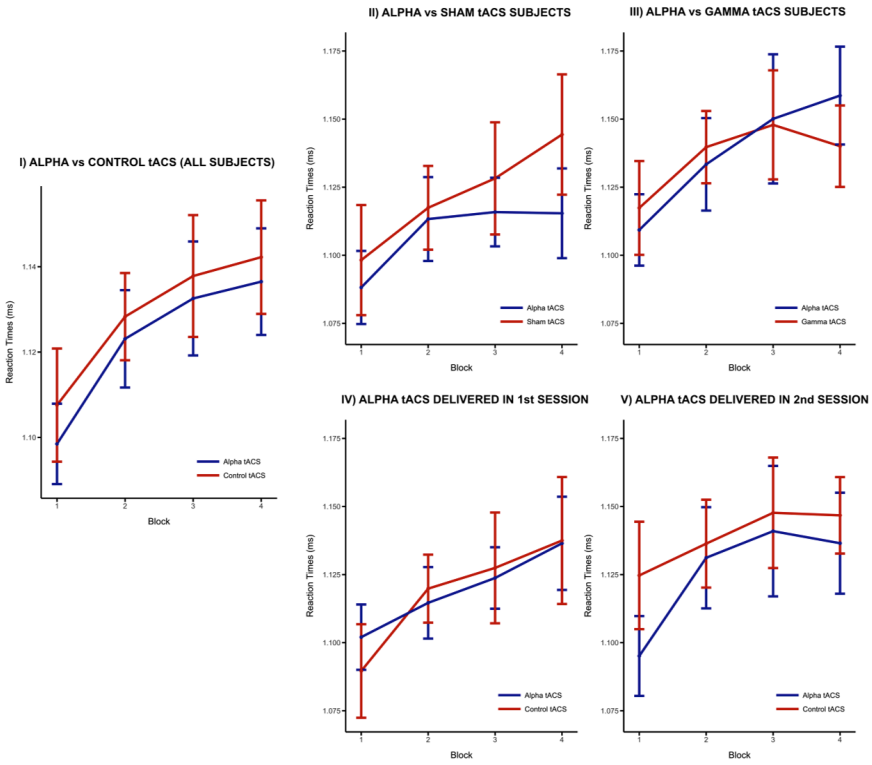


Figure 48 – tACS effects on RTs, divided by experimental subgroup. aCTET RT data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Error bars show ±1 standard error of the mean.

Stimulation condition blinding

I again sought to determine whether the subjective effects of stimulation differed between my stimulation conditions. 60.1% of participants said that these subjective effects of stimulation were more intense during alpha-tACS. A binomial test indicated that this proportion was not significantly greater than chance (i.e. 50%; p=.106). I therefore concluded, again, that the subjective effects of stimulation did not differ reliably between alpha- and control-tACS sessions.

Comparison of alpha-tACS effects of vCTET and aCTET accuracy

An important, remaining question was whether the behavioural effects of alpha-tACS were significantly different between visual and auditory versions of the CTET (i.e. Experiment 1 vs. 3). To perform this analysis, I divided task accuracy performance slopes (from block 2 to 4) during alpha-tACS for each participant by their task accuracy performance slope during control-tACS in each experiment (see p.144). One sample t-tests revealed that normalised slopes were significantly lower than one in Experiment 1 (vCTET; M=0.259, SD=1.493, $t_{(47)}$=-3.44, p=.001, d=-0.50, one-sample t-test [test value = 1]), but not in Experiment 3 (aCTET; M=1.16, SD=3.207, $t_{(40)}$<1, one-sample t-test [test value = 1]). Comparing these normalised slopes between experiments, I observed a main effect of sensory modality ($F_{(1,88)}$=2.96, p=.045 [one-tailed], η^2_p=.035, ANOVA), indicating a difference in the effects of alpha-tACS on performance deteriorations in the vCTET vs. aCTET. No higher order interactions reached statistical significance. This suggests that alpha-tACS exerted a greater, protective effect of vCTET accuracy, compared to its effect on aCTET accuracy.

DISCUSSION

In this experiment, I aimed to determine whether the effects of alpha-tACS are specific to the visual domain. I did this by replicating my first experiment using an auditory version of the Continuous Temporal Expectancy Task (aCTET). Consistent with the view that alpha-tACS influences visual attention specifically, I found no effects of alpha-tACS on aCTET accuracy or RTs. Furthermore, I observed that alpha-tACS reduced the slope of performance deteriorations more significantly during vCTET vs. aCTET performance. However, similar to my previous experiments, I again observed no effects of alpha-tACS on EEG power. I dedicate the following sections to discussion of these results.

No effects of alpha-tACS on EEG power

I observed no evidence that EEG alpha power was increased following alpha- vs. control-tACS. As with my previous experiment, one possible explanation for this null result is that EEG alpha power was elevated throughout aCTET performance. To assess this statistically, I calculated mean alpha power in all task sessions (7 – 13 Hz) in the current experiment, as well as for my first experiment, and submitted these power estimates to a one-way ANOVA with a between-subjects factor of 'experiment' (i.e. Experiment 1 vs. 3). I again observed a significant, main effect of experiment ($F_{(1,87)}$=11.18, p=.001, η^2_p=.114, ANOVA), confirming that mean alpha power was indeed higher during the current experiment, compared to my first experiment (Figure 49; p.152). I assume that this difference reflects the fact that aCTET performance does not require visual attention, allowing people to disengage visual processing, leading to relative increases in EEG alpha power. Importantly though, as alpha-tACS has previously been found to increase the power of EEG alpha oscillations only when they are naturally weak (e.g. Alagapan et al., 2016; Neuling et al., 2013), such elevated alpha

power during aCTET performance could again explain why I again observed no EEG effects of alpha-tACS in the current experiment.

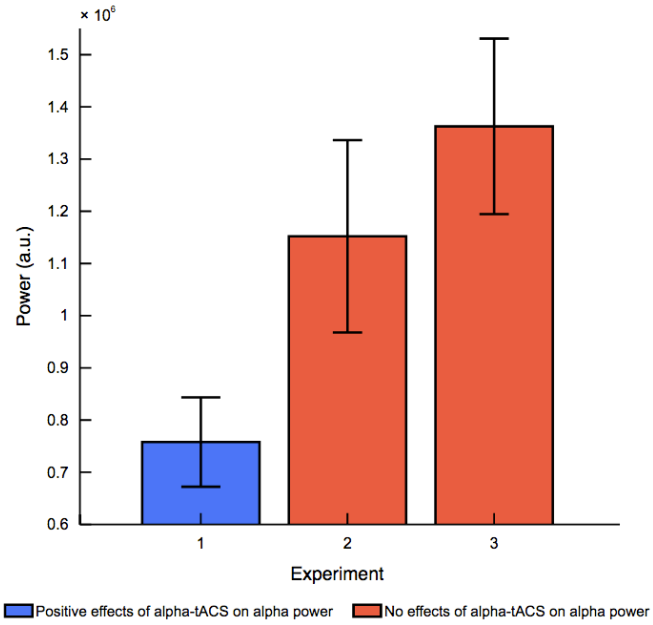


Figure 49 – Raw alpha power before the delivery of alpha-tACS across Experiments 1 – 3. Raw alpha power in Experiments 2 and 3 was significantly higher than alpha power in Experiment 1. Blue shading indicates that alpha power was increased following alpha- vs. control-tACS in that experiment. Red shading indicates that alpha power was not increased following alpha- vs. control-tACS in that experiment. Error bars show ±1 standard error of the mean.

No effects of alpha-tACS on aCTET performance

In addition to these null, EEG results, I also observed no effects of alpha-tACS on aCTET performance (i.e. neither accuracy or RTs). Given that alpha-tACS did not modulate EEG alpha power, it is possible that this null behavioural result simply reflects a failure of alpha-tACS to influence brain activity in the current experiment. Nevertheless, behavioural effects of alpha-tACS were observed in Experiment 2 in the absence of accompanying electrophysiological effects, suggesting that alpha-tACS can influence task performance while leaving EEG unaffected. Consequently, it is arguably more likely that alpha-tACS did not influence aCTET performance because alpha-tACS does not affect auditory attention. This idea was an original assumption of the current

experiment, and is supported by the important finding that alpha-tACS reduced the slope of performance deteriorations more significantly during the vCTET vs. aCTET experiments. I therefore concluded from the results of this experiment that alpha-tACS most likely exerts its effects on visual task performance via changes in visual processing specifically (as hypothesised), and not via generalised effects on cognition (e.g., changes in arousal). Nevertheless, if this were the case, the mechanisms by which alpha-tACS influences visual task performance still remained unclear. This question is the primary focus of the following chapter.

CHAPTER 7 – VISUAL CONJUNCTION SEARCH TASK

The results of my previous experiments indicated that alpha-tACS protects visual attention from deteriorations over time, but exerts no influence on auditory task performance. Given that alpha-tACS had no effect on EEG in the previous experiment, this null result could simply reflect a failure of alpha-tACS to modulate brain activity during aCTET performance. However, alpha-tACS protected visual task performance in my second experiment while leaving EEG unaffected. Consequently, I favoured an alternative interpretation that alpha-tACS modulated brain activity during aCTET performance in the same way as in all previous experiments, but that this modulation had no effect on auditory attention. This suggests that alpha-tACS does not influence task performance through generalised effects on cognition (e.g. changes in arousal, or wakefulness) but, instead, exerts an enhancing effect on visual processing specifically. It was this idea of visual enhancement that was the primary focus of this fourth experiment.

The view that alpha-tACS supports visual attention came primarily from the combined results of Experiments 1 and 2. Here, alpha-tACS was found to protect task performance from natural deteriorations over time. However, how robust are such enhancing effects of alpha-tACS across different experimental conditions? For example, if alpha-tACS promotes general improvements in visual attention, how might alpha-tACS influence performance on a visual task in which performance naturally *improved*, rather than deteriorated over time? If alpha-tACS enhances visual attention, one would expect to observe further improvements in the performance of such a task during alpha-tACS. However, if alpha-tACS did not exert such effects, or if alpha-tACS even prevented such improvements, this would be incompatible with the view that alpha-tACS enhances visual attention. Instead, alternative explanations for the effects of alpha-tACS on task performance would be required.

To address this question, I delivered alpha- and control-tACS, as in my previous experiments, but while participants performed a visual conjunction search task. I chose a visual search task as learning on this task has been reported widely (Lobley & Walsh, 1998; Sireteanu & Rettenbach, 2000). Given the results of my previous, visual experiments, I expected that alpha-tACS would again be found to support task performance. This view was strengthened by the recent results of Müller et al. (2015), who reported that alpha-tACS *improves* performance on a visual conjunction search task (with respect to sensitivity; d'). However, it should be noted that, as with my previous experiments, poor performance on this task had been associated with increases in EEG alpha power (Gonzalez-Rosa et al., 2015). Furthermore, Gonzalez-Rosa et al. (2015) found that task performance was impaired by the application of static magnetic field stimulation over visual cortex, which induces significant increases in posterior alpha power (most likely through inhibition of neural activity; Oliviero et al., 2011). Such findings therefore lead me to assume that, if alpha-tACS does increase posterior alpha power, this stimulation could also be found to impair visual search task performance in this experiment.

METHODS

Visual Conjunction Search Task

43 healthy adults took part in this experiment (27 females, 6 left-handed, mean age = 23.1, SD=3.1). All participants performed a visual conjunction search task in which they searched for a target object (an orange square) among distractor items that shared common features with the target (blue squares and orange triangles) (Gonzalez-Rosa et al., 2015). On each trial, a 7x7 object array was presented. The orange square target was present in the array on 50% of trials. Each shape had a height and width of 1.5 cm. A black fixation cross was presented for 500 ms before every trial. All stimuli were presented on a white background. Each grid was presented for 3000 ms (Figure 50; p.157). Participants were instructed to press 'M' on the keyboard when they detected an orange square, or 'Z' if they believed that no orange square was present in the grid. Participants were asked to perform this task as quickly and as accurately as possible. The number of orange triangles ('same-colour distractors') in each grid varied on every trial between 24, 33, or 42. Each distractor ratio was presented with equal frequency. Each block consisted of 84 trials.

During the practice task, participants performed 60 trials of this task. During the first 30 trials, the number of same-colour distractors increased by one with every trial (i.e. one distractor on trial 1, two distractors on trial 2, etc.). From the 31st trial to the end of the practice task, the number of same-colour distractors in each grid varied randomly between 24, 33, and 42 (as in the main experiment). Feedback was given after every trial of this practice period, but was not given during the main task. Reaction times were calculated from hit and correct rejection trials (i.e. correct trials only).

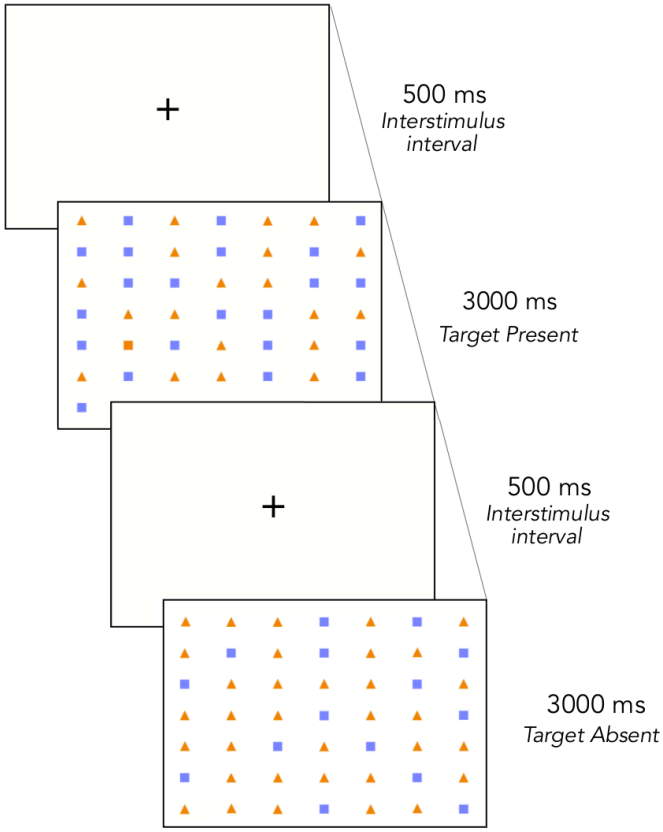


Figure 50 – Visual Conjunction Search Task. Participants were repeatedly presented with a 7 x 7 grid of coloured shapes (blue squares, orange triangles, and orange squares). Each grid was presented for 3000 ms, with a fixed inter-stimulus interval of 500 ms. If an orange square was present in a grid, participants were required to press 'M' as quickly as possible. If an orange square was not present, participants were required to press 'Z' (Gonzalez-Rosa et al., 2015).

Signal detection analysis

In addition to reaction times, task performance was measured using the signal detection theoretic measures of sensitivity (d') and response criterion (c) (as in Müller et al., 2015). To perform this analysis, 'hit rates' were calculated for each block, defined as the percentage of trials in each block correctly classified as containing a target. 'False alarm rates' were also calculated, defined as the percentage of trials in each block that were incorrectly classified as containing a target. Both hit and false alarm rates were then submitted to the *dprime_simple()* function in MATLAB (Cox, 2014). This function uses the following equation to calculate d',

$$d' = \Phi^{-1}(H) - \Phi^{-1}(F).$$

Where d′ is determined by subtracting the z score corresponding to the false-alarm rate from the z score corresponding to the hit rate. Positive d' values indicate increased sensitivity to presented stimuli. The *dprime_simple()* function also uses the following equation to calculate c,

$$c = -\frac{\Phi^{-1}(H) + \Phi^{-1}(F)}{2}.$$

Where c is determined by averaging the z score corresponding to the hit rate and the z score corresponding to the false- alarm rate, then multiplying the result by negative one. Negative c values indicate a bias towards responding, while positive values indicate a bias against responding (i.e. more liberal vs. conservative response bias) (Stanislaw & Todorov, 1999). These measures were analysed in the same way as percentage accuracy and RTs in previous experiments.

RESULTS

EEG alpha power increased following alpha- vs. control-tACS

I focused first on the effects of alpha-tACS on EEG power. Figure 51 (p.159) shows raw frequency power spectra before and after the delivery of alpha- vs. control-tACS.

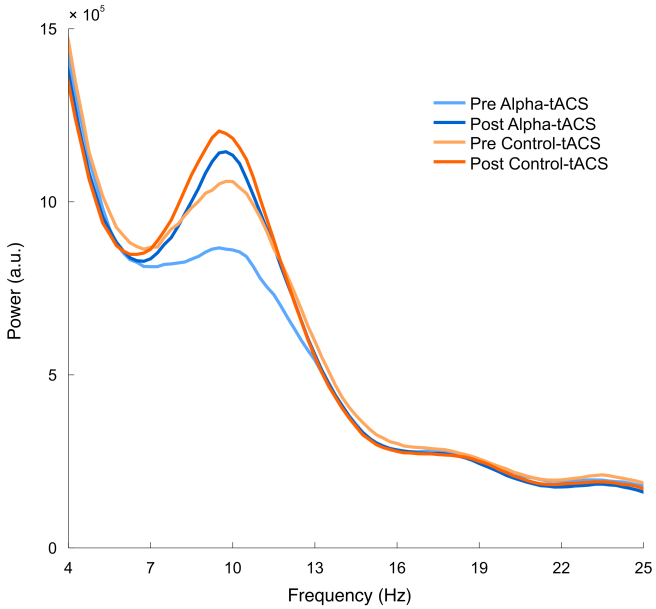


Figure 51 – Raw EEG spectra (averaged over PO7, PO8, P3, P4) are plotted before and after the delivery of alpha- vs. control-tACS.

My main analysis of normalised percentage change in EEG power revealed a significant main effect of stimulation ($F_{(1,39)}$=4.109, p=.050, η^2_p=.095, ANOVA), with greater percentage change in broadband EEG power (theta-low beta) following alpha- vs. control-tACS (105.7% vs. 99.8%, respectively). I also observed a significant main effect of frequency band ($F_{(2,78)}$=17.04, p<.001, η^2_p=.304, ANOVA). This effect was driven by a significantly increased percentage change in EEG power, independent of stimulation condition, in the alpha band (M=111.7%, SD=18.9%, $t_{(42)}$=4.06, p<.001, d=0.62, one-sample t-test [test value = 100%]), that was not observed in the theta (M=97.2%, SD=9.6%, $t_{(42)}$=-1.92, p=.062, d=-0.29, one-sample t-test) or low beta bands

(M=99.3%, SD=10.2%, $|t_{(42)}|$=<1, one-sample t-test). This again indicates that, regardless of whether participants received alpha- or control-tACS, EEG alpha power increased reliably from the start to the end of each task session. Although the interaction between stimulation and frequency band did not reach significance ($F_{(2,78)}$=1.97, p=.146, η^2_p=.048, ANOVA), planned comparisons motivated by my initial predictions and the results of Experiment 1 revealed that percentage change in EEG power was significantly greater following alpha- vs. control-tACS in the alpha band (M=9.9%, SD=30.4%, $t_{(42)}$=2.14, p=.038, d=0.33 paired-samples t-test) (Figure 52; p.161). However, no reliable differences were observed in the theta (M=4.2%, SD=17.5%, $t_{(42)}$=1.61, p=.115, d=0.25, paired-samples t-test) or low beta bands (M=4.0%, SD=21.3%, $t_{(42)}$=1.22, p=.229, d=0.02, paired-samples t-test). Collectively, these analyses indicate that EEG alpha power was significantly increased following alpha- vs. control-tACS, but that these increases were not significantly greater than those observed in the theta or low beta bands. A significant three-way interaction was also observed between stimulation, frequency band, and stimulation order ($F_{(2,78)}$=17.06, p<.001, η^2_p=.304, ANOVA), indicating that alpha enhancement was greater when alpha-tACS was delivered in the first vs. second task session. Nevertheless, decomposition of this interaction revealed significant interactions between stimulation and frequency band for subjects who received alpha-tACS in both the first ($F_{(2,40)}$=10.16, p<.001, η^2_p=.337, ANOVA) and second sessions ($F_{(2,38)}$=8.65, p=.001, η^2_p=.313, ANOVA) (Figure 53; p.161).

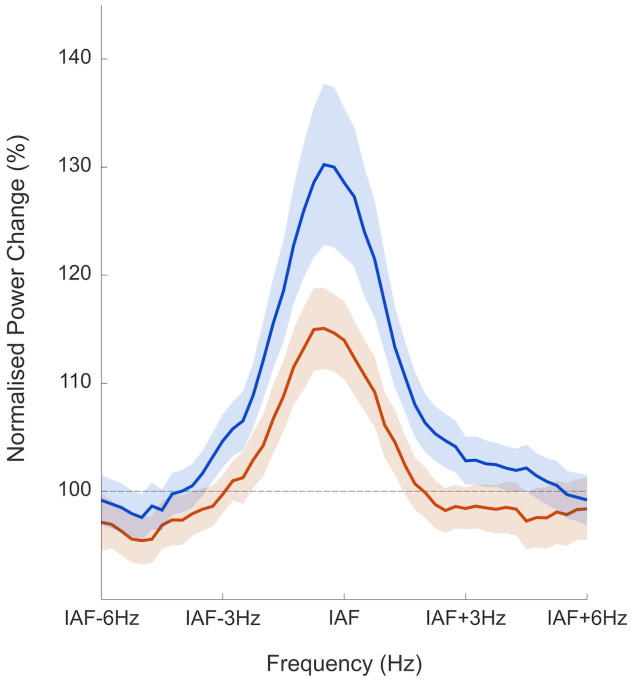


Figure 52 – Normalised percentage change in EEG power (centred around individual alpha frequency [IAF]). Significantly greater percentage change in alpha power was observed following alpha- vs. control-tACS. Coloured shading shows ±1 standard error of the mean.

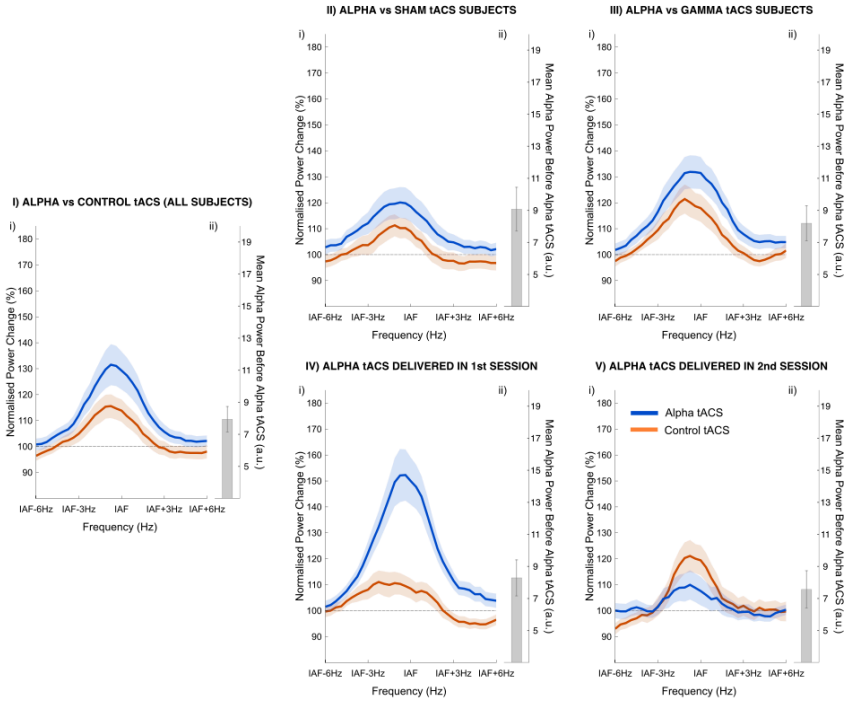


Figure 53 – Normalised change in EEG power, divided by experimental subgroup. Data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Coloured shading shows ±1 standard error of the mean.

Effects of alpha-tACS on sensitivity (d')

Following these electrophysiological analyses, I next focused on the effects of alpha-tACS on task performance. I quantified task accuracy using the signal-detection theoretic measure d', as in previous visual search experiments (Muggleton, Kalla,

Juan, & Walsh, 2011). The d' measure is a composite of both target identification rate and correct rejection rate. I observed a significant main effect of task block ($F_{(3,117)}$=12.73, p<.001, η^2_p=.246, ε=.923, ANOVA) with a strong linear trend ($F_{(1,39)}$=21.60, p<.001, η^2_p=.356, ANOVA). This indicates that d' improved steadily and reliably over time. Importantly, as in Experiments 1 and 2, I also observed a significant interaction between stimulation and task block ($F_{(3,117)}$=2.71, p=.048, η^2_p=.065, ANOVA), confirming an effect of alpha-tACS on changes in d' over time (Figure 54; p.163). To investigate this effect further, I again used the linear regression analysis from Experiment 1 to find the line of best fit through d' values from the start of stimulation to the end of the task (i.e. from block 2 to 4). A significant positive slope was observed for control-tACS (M=0.042, SD=0.063, $t_{(42)}$=4.36, p<.001, d=0.67, one-sample t-test [test value = 0]), indicating an improvement in task performance over time. In contrast, however, the mean slope for alpha-tACS did not differ significantly from zero (M=0.01, SD=0.098, t<1, one-sample t-test [test value = 0]) and, importantly, was significantly less positive than that observed for control-tACS (M=-0.041, SD=0.118, $t_{(42)}$=-2.29, p=.027, d=0.35, paired-samples t-test). These results therefore indicate that the significant improvements in task performance during control-tACS from the start of stimulation to the end of the task were reduced by alpha-tACS. Supporting this conclusion, post-hoc t-tests revealed that d' was significantly lower in block 4 during alpha- vs. control-tACS (M=-.154, SD=.49, $t_{(42)}$=-2.05, p=.046, η^2_p=.091, paired t-test). I again found no association across participants between the magnitude of the effect of alpha-tACS on task performance and the magnitude of change in EEG alpha power (β=-.041, F<1, linear regression).

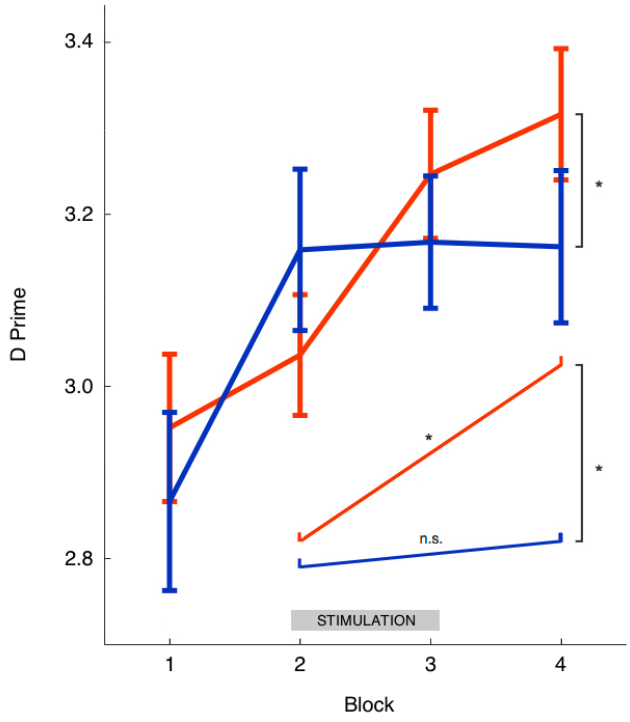


Figure 54 – Effects of tACS on d'. Sensitivity (d') is displayed for blocks 1-4 during alpha- vs. control- tACS. Error bars show ±1 standard error of the mean. * = p < .05.

Higher order interaction with stimulation order

I observed no higher order interactions with control group, suggesting that the effects of sham- and gamma-tACS on d' were approximately equivalent. However, I did observe a significant, three-way interaction between stimulation type, block, and stimulation order ($F_{(3,117)}$=9.30, p<.001, η^2_p=.193, ANOVA). Decomposition of this effect revealed significant interactions between stimulation and block when alpha-tACS was delivered in both the first ($F_{(3,60)}$=4.17, p=.009, η^2_p=.173, ANOVA) and second task sessions ($F_{(3,57)}$=7.76, p<.001, η^2_p=.290, ANOVA). For participants receiving alpha-tACS in the first session, this interaction was driven by reduced d' values during alpha- vs. control-tACS in block 1 (M=-0.553, SD=0.572, $t_{(21)}$=-4.54, *p*<.001, *d*=-0.97, paired-samples t-test). For participants receiving alpha-tACS in the second session, this interaction was driven by *increased* d' values during alpha- vs. control-tACS in blocks 1 (M=0.404, SD=0.604, $t_{(20)}$=3.06, *p*=.006, *d*=0.69, paired-samples t-test) and 2 (M=0.413, SD=0.561, $t_{(20)}$=3.375, *p*=.006, *d*=0.74, paired-samples t-test). Put simply, these interactions were driven in both cases by reduced d' in the first blocks of the first task

session (Figure 55; p.164). This suggests that d' increased steadily during the first task session, but remained at high levels during the second task session. To assess this statistically, I calculated mean d' values for first vs. second task session performance, and submitted these values to a two-way, repeated measures ANOVA, with a within-subjects factors of 'task session' and 'task block', and a between subjects factor of 'control group' (i.e. sham- vs. gamma-tACS). I observed a significant interaction between task session and task block ($F_{(3,123)}$=8.10, p<.001, η^2_p=.165, ANOVA), driven by reduced d' values during the first task session in blocks 1 (M=-0.480, SD=0.801, $t_{(42)}$=-3.93, p<.001, d=0.60, paired-samples t-test) and 2 (M=-0.281, SD=0.855, $t_{(42)}$=-2.16, p=.037, d=0.33, paired-samples t-test). This suggests that performance was not appropriately matched in the first vs. second task sessions, with learning observed predominately during the first task session (Figure 56; p.165).

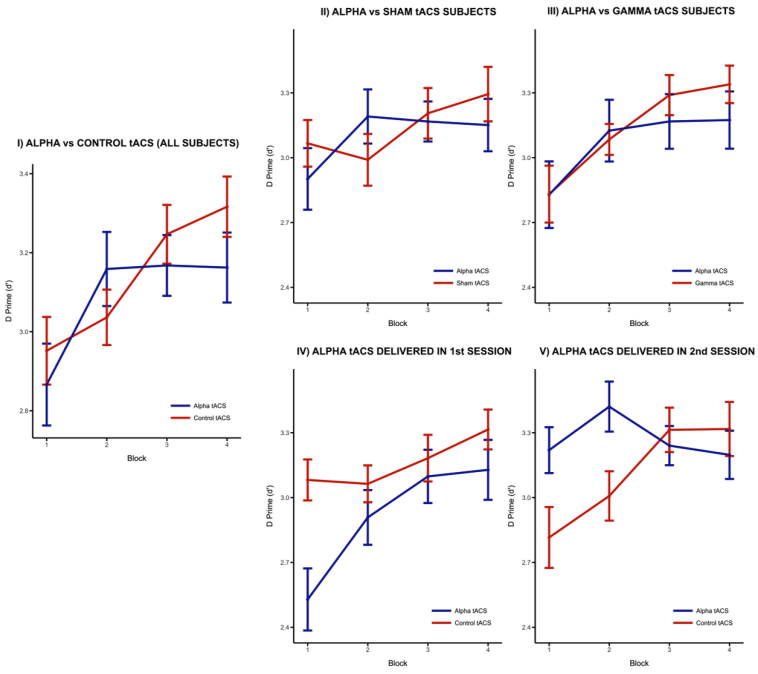


Figure 55 – Effects of tACS on d', divided by experimental subgroup. Sensitivity (d') data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Error bars show ±1 standard error of the mean.

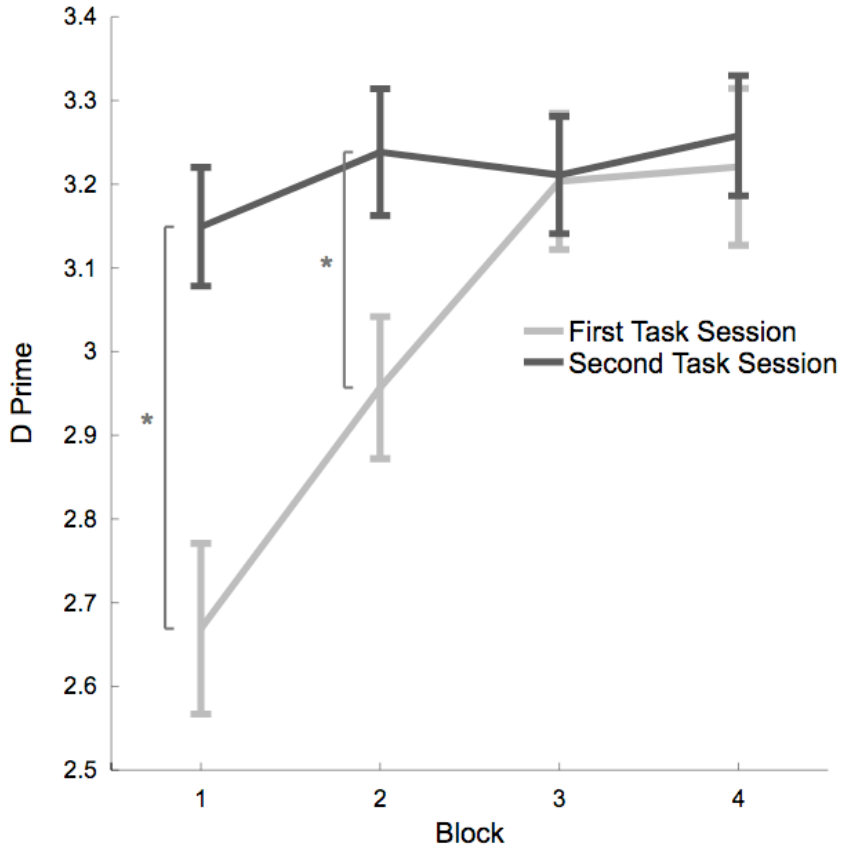


Figure 56 – Sensitivity (d') plotted for first and second task sessions. Target detection sensitivity was significantly reduced in the first two blocks of first vs. second task session performance. This effect suggests that, although participants exhibited learning during their first task session, their performance remained at peak levels throughout the second task session. Error bars show ±1 standard error of the mean.

Effect of alpha-tACS on response criterion (c)

In addition to d' values, I also assessed the effect of alpha-tACS on response criterion (c). I performed this analysis by submitted c values to the same analyses as all previous, behavioural measures. In doing so, I again observed a significant interaction between stimulation and block ($F_{(3,117)}$=5.86, p=.001, η^2_p=.131, ANOVA). Slopes analysis revealed that c values exhibited a trend level reduction from block 2 to 4 during control-tACS (M=-0.767, SD=2.70, $t_{(42)}$=-1.86, *p*=.070, *d*=-0.28, one-sample t-test [test value = 0]), but not during alpha-tACS (M=0.42, SD=4.93, $t_{(42)}$<1, one-sample t-test). However,

these slopes did not differ reliably from each other (M=1.194, SD=5.457, $t_{(42)}$=1.43, *p*=.159, *d*=0.22, paired-samples t-test). When decomposing this interaction with paired comparisons, I found that c values were significantly increase during the second block of control-tACS sessions (M=0.67, SD=1.39, $t_{(42)}$=3.15, *p*=.003, *d*=0.48, paired-samples t-test). There were no higher order interactions with either stimulation order or control group, suggesting that this increase in c was observed in all experimental subgroups (Figure 57; p.166). I was surprised by this observation as it suggested that response thresholds became more conservative during the first five minutes of control-tACS, but then returned to average levels in subsequent blocks. This was surprising as, in all my previous experiments, both sham- and gamma-tACS were found to exert no influence on task performance or brain activity.

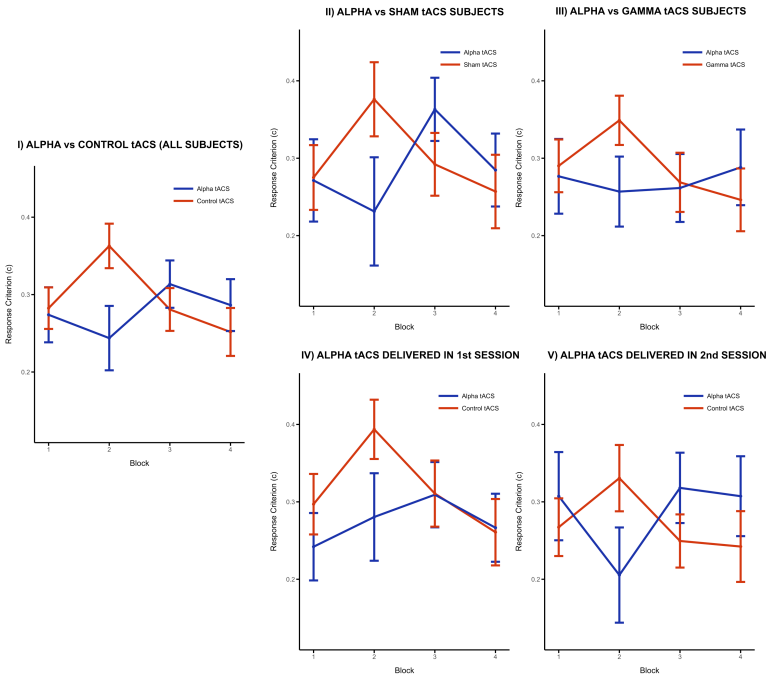


Figure 57 – Effects of tACS on response criterion (c), divided by experimental subgroup. Data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Error bars show ±1 standard error of the mean.

No effect of alpha-tACS on RTs

All aforementioned analyses were also conducted on median reaction times (Figure 58; p.167). A significant main effect of block was again observed ($F_{(3,117)}$=88.29, *p*<.001, η^2_p=.694, ε=.908, ANOVA) with a strong linear trend ($F_{(1,39)}$=221.01, *p*<.001, η^2_p=.850, ANOVA). Slopes analysis revealed that reaction times decreased significantly

from block 2 to 4 during both alpha- (M=-0.052, SD=0.052, $t_{(42)}$=-6.53, p<.001, d=-0.99, one-sample t-test [test value = 0]) and control-tACS (M=-0.034, SD=0.052, $t_{(42)}$=-4.31, p<.001, d=-0.66, one-sample t-test). However, no interaction was observed between stimulation and task block ($F_{(3,117)}$=1.33, p=.270, η^2_p=.033, ε=.876, ANOVA). I also observed no difference in reaction time performance slopes between alpha- and control-tACS (M=-0.018, SD=0.082, $t_{(42)}$=-1.42, p=.163, d=-0.216, one-sample t-test [test value = 0]). The effects of alpha-tACS on visual conjunction search task performance were therefore limited to d' and response criterion.

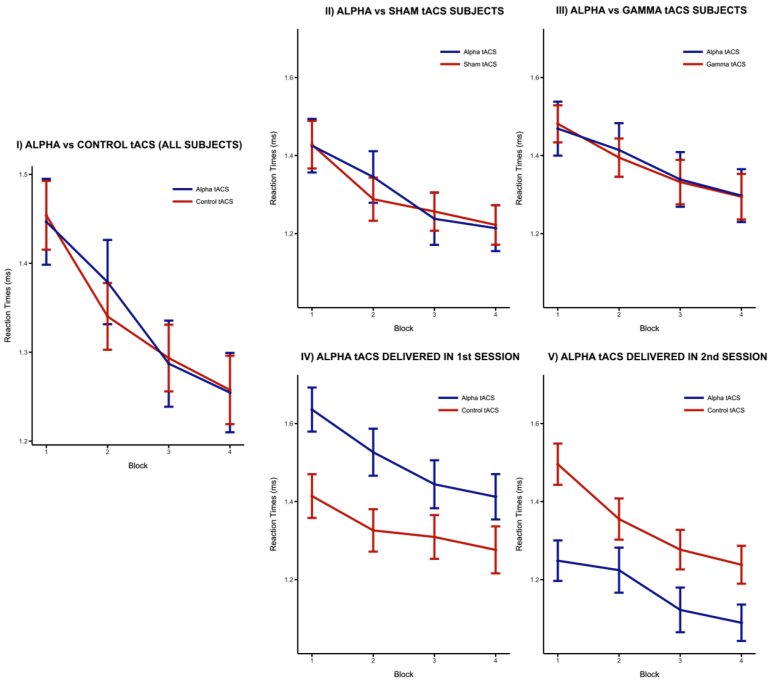


Figure 58 – Effects of tACS on RTs, divided by experimental subgroup. RT data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Error bars show ±1 standard error of the mean.

Stimulation condition blinding

Lastly, I again asked whether the subjective effects of stimulation differed between my stimulation conditions. 46.5% said that these subjective effects were more intense in the alpha-tACS session. A binomial test indicated that this proportion was not significantly greater than chance (i.e. 50%; p=.729). I therefore conclude again that the subjective effects of stimulation did not differ reliably between alpha- and control-tACS sessions.

DISCUSSION

In this experiment, I tested the hypothesis that alpha-tACS causes general improvements in visual attention. If this hypothesis was correct, I assumed that alpha-tACS would consistently improve rates of learning on a visual conjunction search task. Alpha-tACS was found to increase EEG alpha power, confirming the intended effect of this stimulation on brain activity. However, in contrast to my predictions, I found no evidence to suggest that alpha-tACS improved visual search task performance. Instead, alpha-tACS was found to limit the slope of improvements in visual search task sensitivity from the start of stimulation onwards. This was in addition to a confusing effect of control-tACS on search task response criterion, and a null effect on reaction times. I dedicate the following section to the discussion of these results.

Alpha-tACS enhanced EEG alpha power

One of the primary results of this experiment was that, in line with previous studies (e.g. Helfrich et al., 2014; Kasten et al., 2016; Neuling et al., 2013), as well as the results of my first experiment, alpha-tACS caused significant increases in EEG alpha power. This was a welcome finding given failures to replicate this effect in my previous two experiments. In contrast to these experiments, it seems likely that these increases in EEG alpha power were facilitated by low levels of alpha power during visual search task performance. To assess this statistically, I calculated mean alpha power in all task sessions (7 – 13 Hz) in the current experiment, as well as for my second and third experiments, and submitted these power estimates to a one-way ANOVA with a between-subjects factor of 'Experiment' (i.e. Experiment 2 & 3 vs. 4). I again observed a significant, main effect of Experiment ($F_{(1,119)}$=4.215, p=.042, η^2_p=.034, ANOVA). However, when I repeated this analysis to compare mean alpha power in the current experiment to that of my first experiment, I observed no effect of Experiment ($F_{(1,89)}$=1.171, p=.282, η^2_p=.013, ANOVA) (Figure 59; p.169). This confirms that alpha

power was lower during the current experiment, compared to my second and third experiments, but was not different to mean alpha power in my first experiment. Consequently, these results are consistent with the view that alpha-tACS increases alpha power only when alpha power is naturally low. Nevertheless, it is interesting to note from the raw frequency spectra that EEG alpha power was increased following alpha-tACS only with respect to a low, baseline level of alpha power before stimulation (light blue line in Figure 51; p.159). This observation reduces my confidence to some extent in the view that stimulation was the primary cause of increased normalised percentage change in alpha power following alpha-tACS.

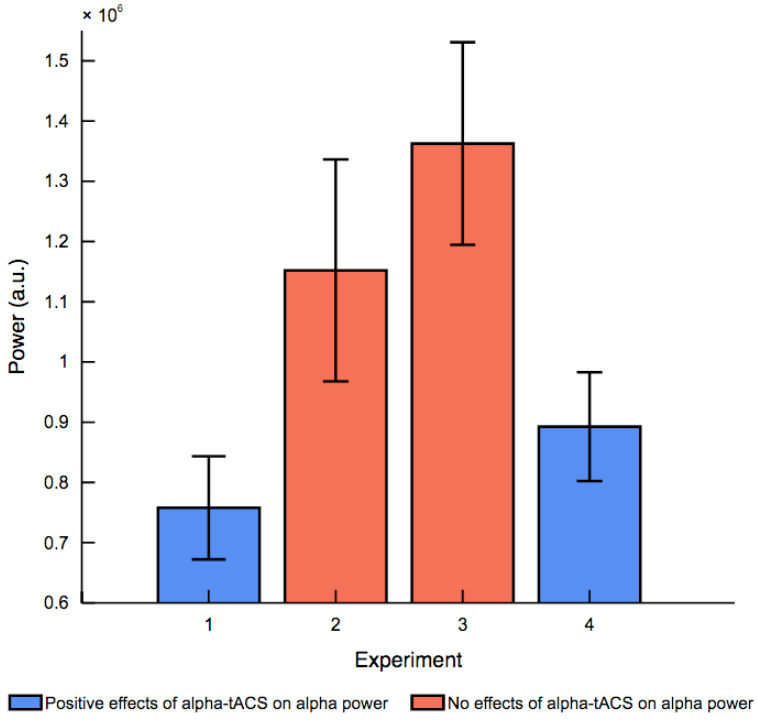


Figure 59 – Raw alpha power before alpha-tACS across Experiments 1 – 4. Mean frequency power spectra for Experiments 1 – 4. Raw alpha power in the current experiment was significantly lower than in Experiment 2 and 3, but was not different to Experiment 1. Blue shading indicates that alpha power was increased following alpha- vs. control-tACS in that experiment. Red shading indicates that alpha power was not increased following alpha- vs. control-tACS in that experiment. Error bars show ±1 standard error of the mean.

Alpha-tACS impaired d'

The other primary result of this experiment was the effect of alpha-tACS on d'. In contrast to my previous experiments, in which alpha-tACS protected task performance from deteriorations over time, alpha-tACS was instead found to limit the slope of improvements in d' from the start of stimulation onwards. This observation is important as it represents a rare case in which alpha-tACS has been found to impair visual attention task performance, as would be predicted from previous evidence showing that poor visual search task performance is preceded by increased alpha power (Gonzalez-Rosa et al., 2015). This observation is also striking as it appears to represent an almost mirror image of the results of Experiments 1 and 2. Importantly though, this finding is also significant as it suggests against the view, described at the start of this chapter, that alpha-tACS exerts a generally enhancing effect on visual attention. An important question posed by these results is therefore: why would alpha-tACS reduce the slope of performance deteriorations in Experiments 1 and 2, but limit the slope of performance *improvements* in the current experiment?

Alpha-tACS stabilises visual attention?

As described in Chapter 2, despite the consistent association between alpha oscillations and reduced visual attention, recent studies have also suggested that alpha may play important roles in visual processing. For example, alpha oscillations have been suggested to facilitate communication of feedback signals in the brain (Michalareas et al., 2016; van Kerkoerle et al., 2014). It is therefore possible that alpha-tACS influenced task performance in my experiments by affecting top-down processes in visual cortex. Such processes are known to be highly dynamic. Patterns of neural activity thought to reflect the engagement of top-down control have complex spatiotemporal profiles (Oehrn et al., 2014). Similarly, while neural oscillations are often modelled as regular sinusoids, they are commonly observed only as short bursts in raw

recordings (Jones, 2016; Simon et al., 2011). This contrasts with alpha-tACS, which is delivered with a highly regular structure, for a sustained period of time, and often with no correspondence to the events of cognitive tasks being performed (e.g. alpha-tACS is rarely phase-locked to task cues). Consequently, it is possible that alpha-tACS would exert a disruptive influence on top-down signalling. I would like to suggest that, in theory, such disruption could play a role in the behavioural effects observed in this study. Nevertheless, it must be stated that this suggested explanation is only a speculative hypothesis.

Specifically, I suggest that my results could be explained by alpha-tACS reducing the changeability of visual attention by interfering with top-down signals that aim to adjust visual attention over time. In order to protect task performance from deteriorations, it is important that attention does not shift away from on-going, task-relevant processes (Clayton et al., 2015). However, contrastingly, in order to improve visual task performance over time, it is important that visual attention is continuously adjusted in response to task demands (Law & Gold, 2009). Put simply, to maintain one's task performance, it is necessary to maintain one's cognitive state. However, to *improve* one's task performance, it is necessary to *change* one's cognitive state. If internal commands to switch visual attention away from the current task were disrupted by alpha-tACS due to disruption of top-down signals in posterior cortex, this could have made it more likely for attention, and therefore task performance, to remain unchanged over time. This could explain why alpha-tACS reduced the slope of task performance deteriorations in Experiments 1 and 2. Conversely, if internal commands to focus and reorient visual attention were disrupted by alpha-tACS, it is likely that learning, and therefore improvements in task performance, would be equally restricted. This would therefore also account for why alpha-tACS prevented improvements in task performance in Experiment 4.

Issues with the stabilisation account

This stabilisation account appears to provide a simple view of how alpha-tACS could exert both supportive and impairing effects on visual task performance. However, this account does have a number of issues. For example, although this stabilisation account focuses on the idea that alpha-tACS prevented learning in the current experiment, it should be noted that, although significant learning was observed across participants in the first task session of this experiment, performance remained at higher levels during the second task session (Figure 56; p.165). This observation arguably limits the extent to which the current experiment can be said to assess learning effects, given that learning only really occurred during the first 3 blocks of this 8-block experiment. In addition, it should be noted that control-tACS had a strange effect on response criteria in the current experiment, with response thresholds becoming more conservative during the first five minutes of control-tACS, but then returning to average levels in subsequent blocks. This effect was surprising because control-tACS should have little effect on brain activity. However, it may partially explain why target detection sensitivity was descriptively lower during control- vs. alpha-tACS in the second task block. This reduced sensitivity during the second block of control-tACS may have contributed to the increase performance slope from block 2 to 4 during control-tACS, and therefore to the find that performance slopes were significantly different between alpha- and control-tACS.

Comparisons with previous studies

Lastly, I would also like to note some interesting differences between the results of the current experiment and previous studies assessing the effects of brain stimulation on alpha oscillations and visual conjunction search task performance. As described in the introduction, Gonzalez-Rosa et al. (2015) found that performance of this visual search task was impaired by static magnetic field stimulation of visual cortex, which in

turn increased posterior alpha power. Given that visual search task was also impaired by alpha-tACS in the current experiment, and that EEG alpha power was again increased by alpha-tACS in the current experiment, my results appear to represent an approximate replication of Gonzalez-Rosa et al. (2015). This is despite the fact that tACS and static magnetic field stimulation should have very different effects on brain activity (Oliviero et al., 2011). In contrast, however, Müller et al. (2015) found that alpha-tACS exerted an *enhancing* effect on visual conjunction search task performance, increasing the sensitivity (d') of participants to target presentations. This is despite the fact that they used a near-identical stimulation montage to this experiment (Oz-Cz; 1517 ± 379 μA), which should, therefore, have had very similar effects on brain activity. It is difficult to determine the fundamental causes for the differences in results across studies. However, they would appear to suggest that the effects of brain stimulation on behaviour can vary quite significantly, even when using near-identical tasks and stimulation montages.

CHAPTER 8 – AUDIOVISUAL TASK SWITCHING

At the beginning of this project, I assumed that alpha-tACS would cause only impairments in visual task performance. However, in Experiments 1 and 2, alpha-tACS was instead found to limit the slope of performance deteriorations that otherwise occurred during sham and 50 Hz tACS. Importantly though, in my last experiment, in which rapid learning was observed during control-tACS, alpha-tACS was found to limit the slope of such improvements over time. These results contrasted with those of Experiment 3, in which alpha-tACS was found to have no effect on auditory attention task performance (Figure 60; p.174).

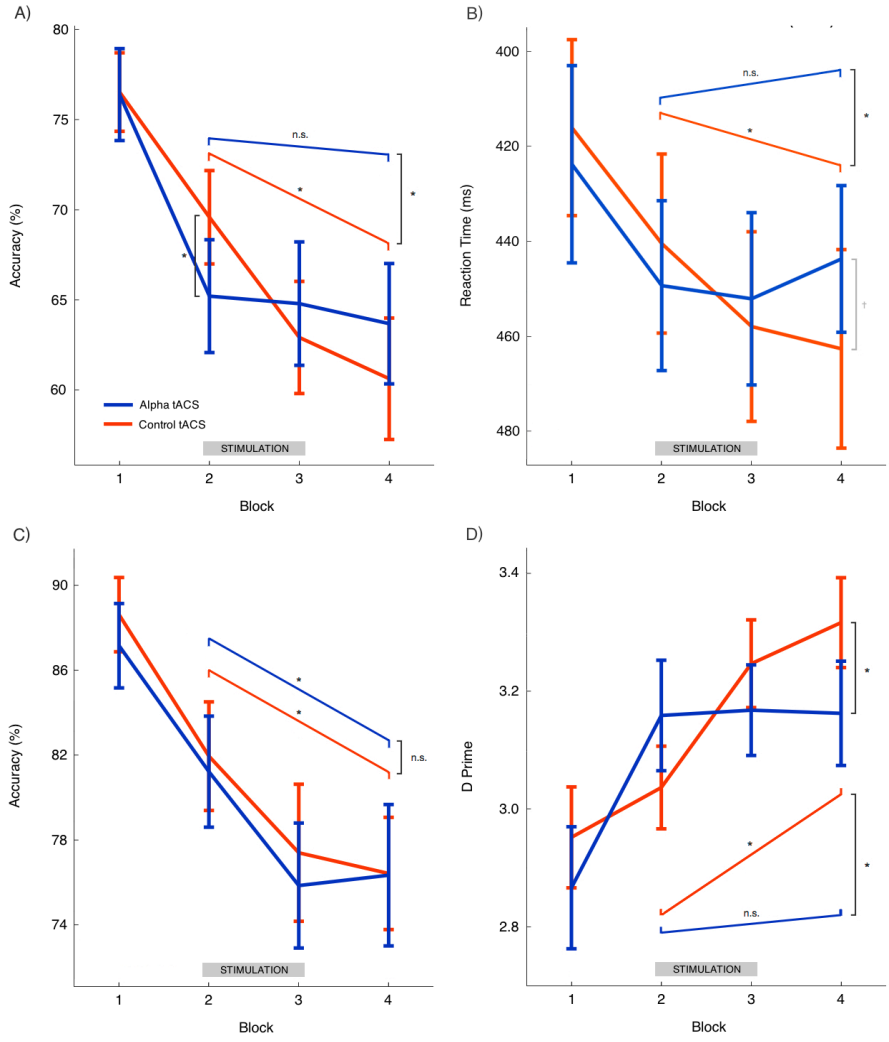


Figure 60 – Summary of behavioural results (Experiments 1 - 4). A) In Experiment 1, alpha-tACS was found to reduce the slope of deteriorations in vCTET accuracy that otherwise occurred during control-tACS. B) Experiment 2 revealed a similar effect on threshold detection RTs (note the inverted y-axis for easier comparability between experiments). C) No effects were observed on auditory attention in Experiment 3. D) However, in Experiment 4, alpha-tACS was conversely found to limit the slope of performance improvements over time.

It was unclear why I obtained this surprising pattern of results. However, given that alpha-tACS seemed to prevent both deteriorations and improvements in visual task performance, one interesting possibility was that alpha-tACS exerted a stabilising effect on visual attention (see p.170). This idea was consistent with evidence that EEG alpha power associates positively with the stability of ongoing, perceptual interpretations (Piantoni et al., 2017; Strüber & Herrmann, 2002) (see p.63). I therefore dedicated the current experiment to investigating this view. I did this by delivering alpha-tACS while participants performed a task that required rapid switches of attention between motion, colour, and auditory subtasks. As in my previous experiments, the effects of alpha-tACS were compared to those of sham and 50 Hz tACS (i.e. control-tACS). My central hypothesis was that, if alpha-tACS prevents changes in visual attention (i.e. stabilises visual processing), it should make it harder for participants to switch their attention between visual tasks. This view was suggested by evidence that effective switching between visual tasks is negatively associated with EEG alpha power (e.g. Poljac & Yeung, 2012). Importantly though, as I previously found in Experiment 3 that alpha-tACS influenced visual task performance alone, I assumed that alpha-tACS would have little effect of switches between auditory and visual subtasks. Electroencephalography (EEG) data was collected throughout the experiment. I predicted that alpha-tACS would have an enhancing effect on EEG alpha power and that these alpha enhancements would be associated with increased visuovisual vs. audiovisual switch costs.

METHODS

Pre-registration

The hypotheses, method, and planned analyses for this experiment were pre-registered with the Open Science Framework before the data were collected (*The effects of 10 Hz tACS on visual task switching*; https://osf.io/f6b3s/).

Participants

A total of 40 subjects participated in this study. One subject was excluded because their overall task accuracy was more than 3 standard deviations below the sample mean. Another participant was excluded because they failed to press any response button on the final block of one session. The final sample therefore consisted of 37 subjects (17 females, 8 left-handed, mean age = 23.64, SD = 4.35).

Transcranial Alternating Current Stimulation

Stimulation was delivered in a near-identical manner to all previous experiments. tACS was delivered at a maximum intensity of 2 mA (peak-to-peak). However, for subjects who found this intensity too unpleasant or distracting (n=10), stimulation amplitudes were lowered in this experiment to ensure that subjects were comfortable throughout. This approach of using variable stimulation intensities is well established in the field (e.g. Kasten et al., 2016; Neuling et al., 2013; Neuling et al., 2015). Mean stimulation intensity was therefore 1.81 mA (SD=.35). Participants who could not tolerate <1 mA stimulation did not participate in the experiment and were replaced (n = 2).

Audiovisual switching task

All stimuli were presented on a Dell® 23-inch LCD monitor (60 Hz refresh rate) using the Psychophysics Toolbox in MATLAB (Brainard, 1997). The timing of stimulation

and EEG recording was controlled using *MatNIC* – a toolbox designed by *Neuroelectrics*® to enable control of tACS and EEG using MATLAB. Throughout the task, a central box with a black outline was presented in the centre of a grey screen ('cue box'; [height = 15 cm; width = 1.8 cm]). Two larger boxes were presented behind this cue box, the smaller of which would contain moving dots ('motion box'; [height = 12.5 cm; width = 10 cm]), and the larger of which would fill with colour during stimulus presentation ('colour box'; [height = 15cm; width = 13.5cm]). At the start of each trial, a single word (RGB = [0, 0, 0]) was displayed in the centre of the cue box for 250 ms (known as the 'cue presentation period'; Figure 61A; p.178). These cues told participants which task they would need to perform in the upcoming trial (either 'MOTION', 'COLOUR', or 'SOUND'). Following this cue presentation, participants were simultaneously presented with motion, colour, and auditory stimuli for a period of 300 ms ('stimulus presentation period'; Figure 61B). During this time, the colour box turned either red (RGB = [255, 100, 100]) or blue (RGB = [100, 100, 255]). During the same period, a grid of black dots (diameter = 0.5 cm) was presented inside the motion box, which moved with 100% coherence in either an upward or downward direction (at a rate of 50 pixels per second). No dots were presented outside of the motion box. In addition, participants were also played audio, through earphones, of the vocalization of the letters 'E' or 'O'. These audio files were downloaded from the sound archive of the Psychology Experiment Building Language (http://prdownloads.sourceforge. net/pebl/pebl-sounds-0.1.zip?download). If participants had been cued to perform the motion task, they needed to determine whether the central dots moved in an upward or downward direction. If participants had been cued to perform the colour task, they were required to classify the shade of the outer box as either red or blue. Lastly, if participants had been cued to perform the auditory task, they had to classify the auditory vocalization as either 'E' or 'O'. Response keys were always 'M' and 'Z' on the keyboard. Stickers were placed on these keys to aid performance.

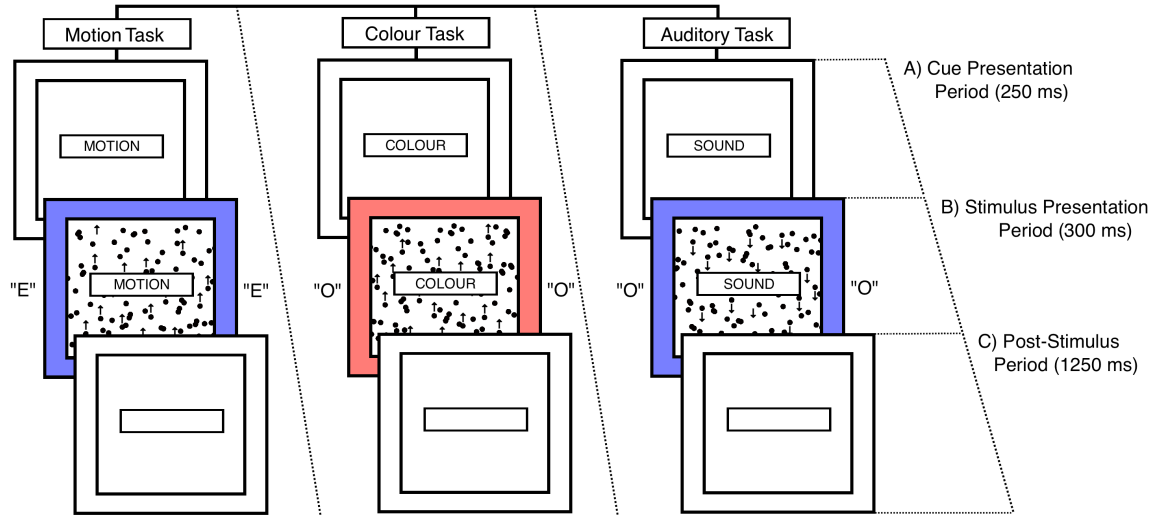


Figure 61 – Illustration of a single, audio-visual switch trial. A) During the cue presentation period, which lasted for 250 ms, a word was presented in the central box telling participants which task to perform ('MOTION', 'COLOUR', or 'SOUND). B) This was followed by the stimulation presentation period, during which the outer box filled with either red or blue, the inner box filled with black dots that moved in either an upward or downwards direction, and the letter 'E' or 'O' was played through earphones. This period lasted for 300 ms. C) Participants could respond until the end of the post-stimulus period, which lasted for 1250 ms.

Following the stimulus presentation period ('post-stimulus period'; Figure 61C; p.178), the cue, motion, and colour boxes filled with blank, white space. This post-stimulus period lasted for 1250 ms. Responses were recorded and timed from the beginning of the stimulus presentation period. However, the majority of responses occurred during the post-stimulus period. If a response was not recorded during this period, the trial was classified as a missed trial. The response profiles of all tasks was pseudo-randomised such that uncued tasks signaled the same response as the cued task on 50% of trials, and signaled the opposite response on the other 50% of trials. For example, if participants were cued to perform the motion task, and the correct response for this task was a left button press, the simultaneously presented auditory and colour

stimuli would signal the same response of 50% of trials. This was done to control for effects of inter-task response congruency.

General Experimental Design

Subjects completed a first practice session, which lasted for approximately 6 minutes. This allowed them to familiarise themselves with the rules of the task. During this period, participants performed each task individually (motion, colour, auditory) in separate blocks of 60 trials. Participants then completed a full block of the main task (162 trials), in which they were required to switch between tasks when cued. Following this first practice, EEG and tACS electrodes were positioned on the head. Once the set up was complete, participants then performed a second practice session in which they again completed a full block of the main task. Feedback was given after every trial in all practice sessions, with words “CORRECT” (Green; RGB = [100, 255, 100]) and “ERROR” (Red; RGB = [255, 100, 100]) presented below the colour box following correct vs. error trials, respectively.

In the main experiment, subjects completed 2 sessions of 5 task blocks, with each block consisting of 162 trials and lasting 4 minutes and 50 seconds. Participants were given a fixed-duration break of 100 seconds between blocks. During this rest period, participants were shown images of pleasant, natural scenes, which changed every 20 seconds. These images were chosen to facilitate recovery from mental fatigue (e.g. Kaplan, 1995). In total, each session lasted 30 minutes and 50 seconds. During alpha and gamma tACS, stimulation was applied for 19 minutes and 30 seconds from the start of the second block to the start of the fifth block. Sham tACS was applied at 10 Hz during only the first 50 seconds of this period. This sham stimulation was ramped up over 30 seconds and ramped down over 20 seconds (Figure 62; p.180). As with my previous experiments, alpha- and control-tACS sessions were separated by a break of

25 minutes in which participants watched a nature documentary. Participants were told to relax during this period.

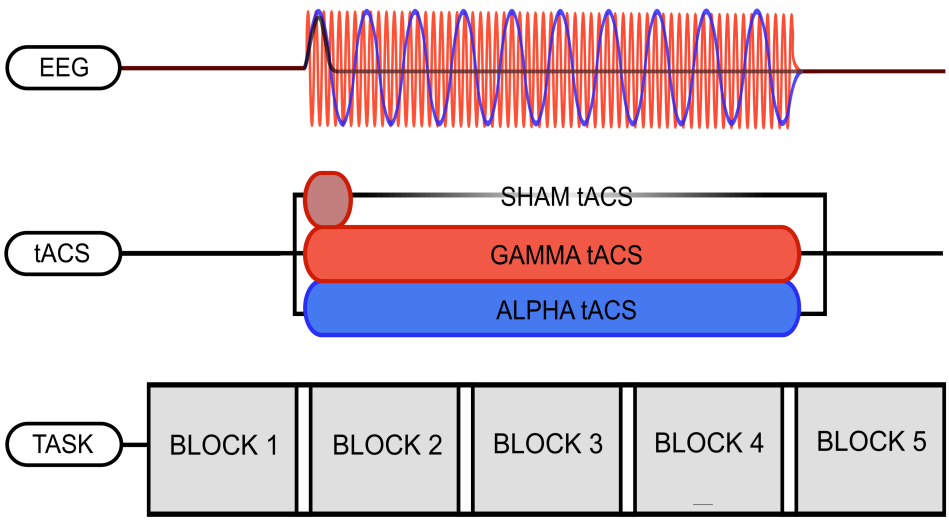


Figure 62 – Task and stimulation timing. Participants performed five task blocks in a single task session, with each block lasting 4 minutes and 50 seconds. A fixed-duration break of 100 seconds was allowed between blocks. EEG was recorded before and after the delivery of stimulation. During alpha- and gamma-tACS, stimulation was applied for 19 minutes and 30 seconds from the start of the second block to the start of the fifth block. During sham-tACS, stimulation was applied at 10 Hz during only the first 50 seconds of this period (including ramp-up and down times). Participants each performed two task sessions (i.e. 8 blocks in total), separated by a break of 25 minutes.

On one third of trials (i.e. ~33%), participants performed the same task as in the previous trial (i.e. repeat trials). On the other two thirds of trials (i.e. ~66%), participants performed a different task to the previous trial (i.e. switch trials). Each switch type (e.g. motion-colour, colour-motion, auditory-colour, etc.) occurred with equal frequency. Participants therefore switched task on 108 trials, and each switch type was performed 18 times per block. Tasks were also performed with equal frequency (54 trials in each block).

PLANNED ANALYSES

Behavioural analyses

All data analyses were performed using MATLAB. Mean percentage accuracy and median reaction times (RTs) were calculated for all trial types. Analyses were focused on visuovisual (within-modality) and audiovisual (cross-modality) switch trials. Visuovisual switch trials were defined as visual trials performed following a different visual task (i.e. colour-motion, motion-colour). Audiovisual switch trials were defined as visual trials performed following the auditory task (i.e. auditory-motion, auditory-colour). These data were then submitted, separately for accuracy and RTs, to a mixed, repeated measures ANOVA with within-subjects factors of 'stimulation type' (alpha- vs. control-tACS), 'previous task modality' (visual vs. auditory), 'current task type' (motion vs. colour), and 'task block' (2-5). Performance data from block 1 was excluded from analysis to allow me to focus on the effects of tACS (which was delivered in blocks 2-4). However, my results did not change significantly when all tasks blocks were included. I also assessed the effects of alpha-tACS on visuoauditory switching as a secondary analysis (i.e. motion-auditory and colour-auditory trials). I performed this analysis by taking visuoauditory switch performance during alpha -vs. control-tACS sessions (both accuracy and RTs), and comparing it to mean performance on visuovisual and audiovisual switch trials in each of these sessions. In all analyses, stimulation order and control group were included as between-subjects factors. Where there were violations of the assumption of sphericity, the Huynh-Feldt correction was applied. In these cases, the corresponding epsilon value (ε) is stated alongside the ANOVA results.

Behavioural-EEG regression analyses

I also assessed the association between the behavioural and electrophysiological effects of alpha-tACS. Electrophysiological effects were analysed using the same

methods as all previous experiments. To do analyse such associations, I first subtracted RTs and percentage accuracy for visuovisual switches from those of audiovisual switches performed during and after the delivery of alpha- vs. control-tACS. This gave us a single measure of the effect of alpha-tACS on visuovisual vs. audiovisual switching for each subject. I then generated a single measure of the effect of alpha-tACS on EEG by subtracting normalised percentage change in alpha power following alpha- vs. control-tACS. I ran a linear regression analysis using these measures (separately for RT and percentage accuracy data).

RESULTS OF PLANNED ANALYSES

EEG analyses

I focused first on tACS-related changes in EEG power. Figure 63A (p.183) shows raw frequency power spectra before vs. after the delivery of alpha- vs. control-tACS. However, my main analysis compared normalised percentage change in EEG power between stimulation conditions. I observed a significant main effect of frequency band ($F_{(2,66)}$=8.647, p<.001, η^2_p=.208, ANOVA), indicating that power increased from the start to the end of each task session more consistently in the alpha band than in both the theta and beta bands (M=119.3 vs. 106.4%, SD=26.6%, $t_{(36)}$=2.955, p=.005, d=0.49, paired-samples t-test). However, the important interaction between stimulation type and frequency band was not significant ($F_{(2,66)}$=1.695, p=.191, η^2_p=.049, ANOVA). This indicates that alpha-tACS had no specific effect on EEG alpha power (Figure 63B; p.183).

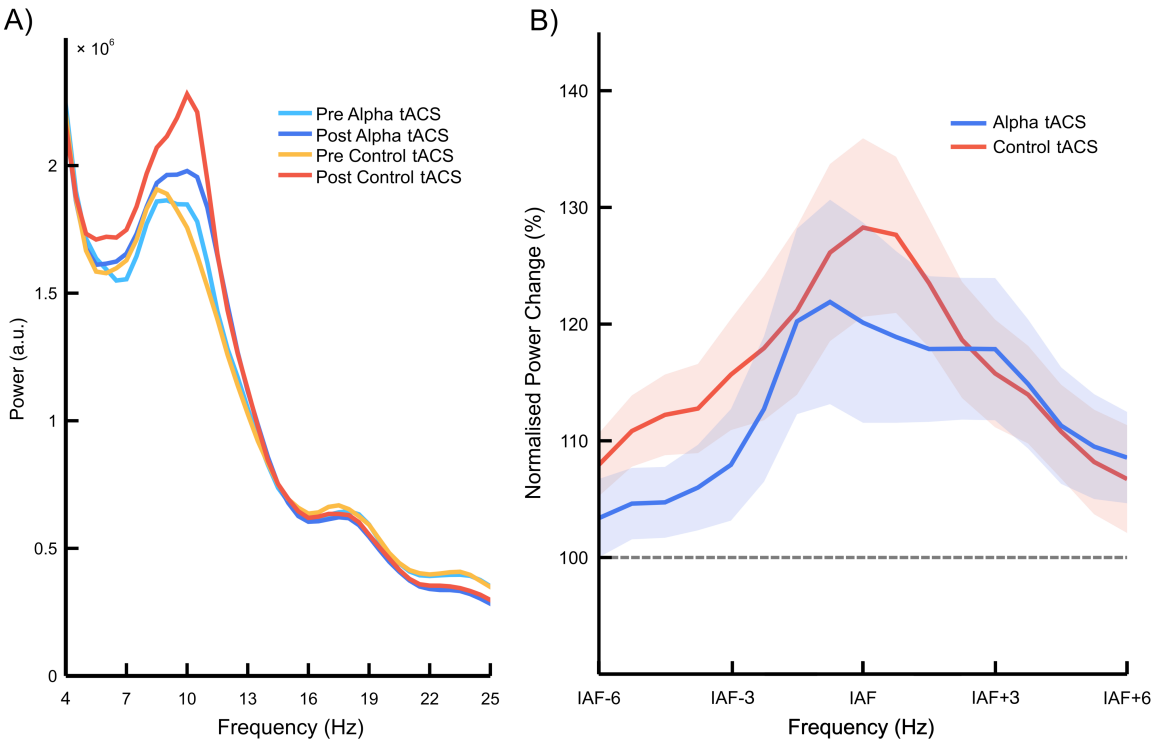


Figure 63 – Effects of alpha- vs. control-tACS on overall alpha power. A) Raw EEG power spectra. Mean power is plotted between 4 and 25 Hz, averaged over posterior electrodes

(i.e. PO7, PO8, P3, P4) before vs. after the delivery of alpha- vs. control-tACS. B) Normalised percentage change in EEG power. Relative changes in posterior EEG power (i.e. post-tACS / pre-tACS) are plotted for alpha- vs. control-tACS. Alpha-tACS was not found to exert an influence on EEG alpha power beyond that of control-tACS. Shading shows ±1 standard error of the mean.

I did observe a significant interaction between stimulation type, frequency band, and stimulation order ($F_{(2,66)}$=10.737, p<.001, η^2_p=.245, ANOVA). Decomposition of this effect revealed significant interactions between stimulation and frequency band for participants receiving alpha-tACS in both the first ($F_{(2,34)}$=4.173, p=.024, η^2_p=.197, ANOVA) and second task sessions ($F_{(2,32)}$=7.716, p=.002, η^2_p=.325, ANOVA). However, although this effect was driven in the former case by increased alpha vs. non-alpha power (i.e. theta + beta) following alpha-tACS (M=12.6%, SD=24.0%, $t_{(18)}$=2.294, p=.034, d=0.53, paired-samples t-test), the effect was driven in the latter case by greater increases in alpha power following control-tACS (M=22.2%, SD=20.9%, $t_{(17)}$=4.489, p<.001, d=1.06, paired-samples t-test). Consequently, the three-way interaction appeared to reflect a general tendency for alpha power to increase more significantly in the first vs. second task session, regardless of stimulation condition (135.1 vs. 103.6%, $t_{(36)}$=4.029, p<.001, d=0.66, paired-samples t-test) (Figure 64; p.185). I observed no such higher order interactions with control group (p>.2), suggesting that effects of sham and gamma tACS were approximately equivalent (Figure 64; p.185). I therefore concluded that, despite previous results showing enhancements of EEG alpha power following alpha-tACS, I did not observe reliable enhancement of this kind in the current experiment.

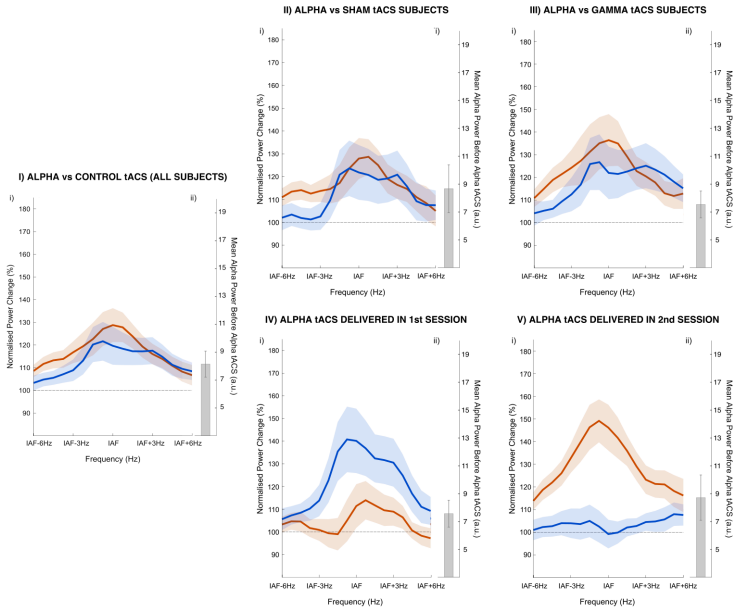


Figure 64 – Normalised change in EEG power, divided by experimental subgroup. Data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving alpha-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Coloured shading shows ±1 standard error of the mean.

Task accuracy

Following these EEG analyses, I looked at tACS-related effects on task accuracy. I observed no main effects of stimulation type or previous task modality ($F_{(1,33)}$<1, ANOVA). Although I predicted that alpha-tACS would impair visuovisual switching specifically, I also observed no interaction between stimulation type and previous task modality ($F_{(1,33)}$=1.687, p=.203, η^2_p=.049, ANOVA). This suggests that alpha-tACS had no reliable effect on visuovisual vs. audiovisual switching accuracy. Nevertheless, supplementary analysis did show a trend for task accuracy to be lower during alpha- vs. control-tACS sessions on visuoauditory switch trials (i.e. vs. visuovisual and audiovisual switches; $F_{(1,33)}$=3.501, p=.070, η^2_p=.096, ANOVA). This suggests that alpha-tACS exerted a mildly impairing effect on switches away from visual tasks, towards the auditory task. I observed no higher-order interactions with stimulation order, suggesting that the effects of stimulation did not depend on whether alpha-tACS was delivered in the first or second task session ($F_{(1,33)}$<1, ANOVA). I also observed no significant interactions with control type ($F_{(1,33)}$<1, ANOVA), suggesting that the effects of sham and gamma tACS did not differ reliably from each other. I therefore concluded that, although

alpha-tACS exerted a trend-level effect on visuoauditory switching accuracy, this stimulation did not impair visuovisual vs. audiovisual switching accuracy in the way I anticipated. Mean percentage accuracy values for visuovisual, audiovisual, and visuoauditory switch trials during alpha- vs. control-tACS are displayed in Figure 65A (p.187). Mean accuracy values for all trial types during alpha- vs. control-tACS are displayed in Figure 65B.

Reaction times

I looked next at RTs. Here, I observed a marginal, main effect of stimulation type ($F_{(1,33)}$=2.974, p=.094, η^2_p=.083, ANOVA). This effect was driven by faster RTs during alpha- vs. control-tACS sessions (663 vs. 682 ms). I also observed a marginal, main effect of previous task modality ($F_{(1,33)}$=3.350, p=.076, η^2_p=.092, ANOVA). This effect was driven by faster RTs on visuovisual vs. audiovisual switch trials (669 vs. 676 ms). However, the important interaction between stimulation type and previous task modality was not found to be significant ($F_{(1,33)}$<1, ANOVA). This suggests that alpha-tACS exerted no reliable effect on visuovisual vs. audiovisual switch trial RTs. Secondary analysis also revealed no effect of alpha-tACS on visuoauditory switching (i.e. vs. visuovisual and audiovisual switches; $F_{(1,33)}$<1, ANOVA). I again observed no higher order interactions with either stimulation order or control type ($F_{(1,33)}$<1, ANOVA). The former result suggests that the effects of stimulation on RTs did not differ depending on whether alpha-tACS was delivered in the first or second task session ($F_{(1,33)}$<1, ANOVA). The latter result suggests that the effects of sham and gamma tACS were approximately equivalent. I therefore concluded that, although alpha-tACS seemed to exert an overall, enhancing effect on RTs, it did not influence visuovisual vs. audiovisual switch RTs in the manner I expected. Mean RT values for visuovisual, audiovisual, and visuoauditory switches during alpha- vs. control-tACS are displayed in Figure 65C (p.187). Mean RT values for all trial types during alpha- vs. control-tACS are displayed in Figure 65D.

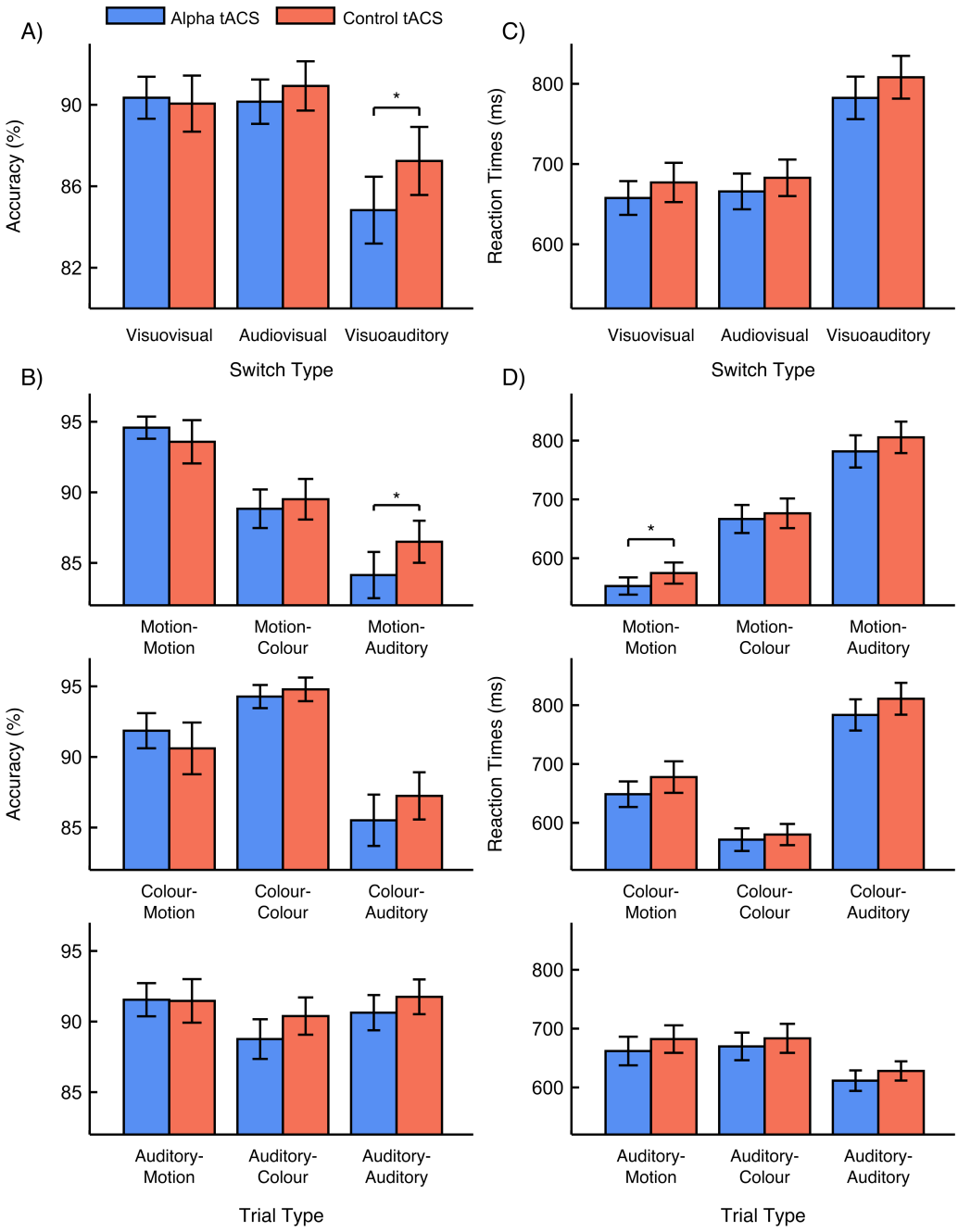


Figure 65 – Effects of alpha- vs. control-tACS on task performance. A) Mean performance accuracy for visuovisual, audiovisual, and visuoauditory switch trials. In contrast to predictions, alpha-tACS had no effect on visuovisual vs. audiovisual switching, but did impair accuracy on visuoauditory switch trials. B) Mean performance accuracy is displayed for all trial types. C) Median RTs for visuovisual, audiovisual, and visuoauditory switch trials. D) Median RTs are displayed for all trial types. Error bars show ±1 standard error of the mean. * = $p < .05$.

Behavioural-EEG correlations

In the last of my planned analyses, I looked at associations between the behavioural and electrophysiological effects of alpha-tACS. To do this, I compared a single measure of percentage change in alpha power following alpha- vs. control-tACS with a single measure of the effect of alpha-tACS on visuovisual vs. audiovisual switching accuracy and RTs. However, this individual difference correlation revealed no significant association between changes in EEG alpha power and either task accuracy (β = -.147, $F_{(1,36)}<1$, linear regression) or RTs (β = -.105, $F_{(1,36)}<1$, linear regression). I therefore concluded that there were no associations across participants between alpha-tACS related changes in EEG alpha power and visuovisual vs. audiovisual task switching.

RESULTS OF EXPLORATORY ANALYSES

As described above, the results of my planned analysis did not support my initial predictions. In fact, these analyses suggested that alpha-tACS had little effect on either EEG or task performance. In response to these results, I next sought to perform exploratory, post-hoc analyses to investigate the presence of unanticipated patterns in my data.

RT variability

I first assessed whether alpha-tACS had any effect on RT variability. RT variability has previously been identified as a measure of task performance that can provide unique insights into attentional processes beyond those of accuracy and RT central tendencies (e.g. Esterman et al., 2013) (see p.21). To conduct this analysis, RT variability measures were submitted to the same repeated measures ANOVA as median RTs. However, these results were not significantly different to those of median RTs

(Figure 66A; p.190). There were no main effects of stimulation type or previous task modality (p>.3). There were also no interactions between stimulation type and either previous task modality or current task type (p>.3). This suggests that alpha-tACS exerted no influence on visuovisual vs. audiovisual switching with respect to RT variability.

EZ-diffusion model parameters

I then analysed my behavioural data using a diffusion model. I did this to allow measurement of task performance, while considering task accuracy and RTs simultaneously. This enabled us to assess task performance using measures that are less sensitive to speed-accuracy trade-offs. This was important given that alpha-tACS was found to reduce overall RTs, indicating a possible trend towards impulsive responding. To perform this analysis, I used the EZ-diffusion model proposed by Wagenmakers, Van Der Maas, and Grasman (2007). Using this model, the following measures were calculated from mean RTs, RT variability, and task accuracy: 1) *drift rate*, which estimates the quality (or signal-to-noise ratio) of information processing, 2) *boundary separation*, which estimates participant bias towards responding and 3) *non-decision time*, which estimates the time taken for participants to process stimuli and respond. I did observe a marginal, main effect of stimulation type on non-decision times ($F_{(1,33)}$=4.092, p=.051, η^2_p=.110, ANOVA), driven by reduced non-decision times on visuovisual vs. audiovisual switch trials (433 vs. 450 ms). However, for all other measures, I observed no significant main effects or higher-level interactions. Consequently, using diffusion model parameters that are less sensitive to speed-accuracy trade-offs, I concluded that, with the exception of a possible influence of alpha-tACS on stimulus processing times, this stimulation had no effect on visuovisual vs. audiovisual task switching (Figure 66B-D; p.190).

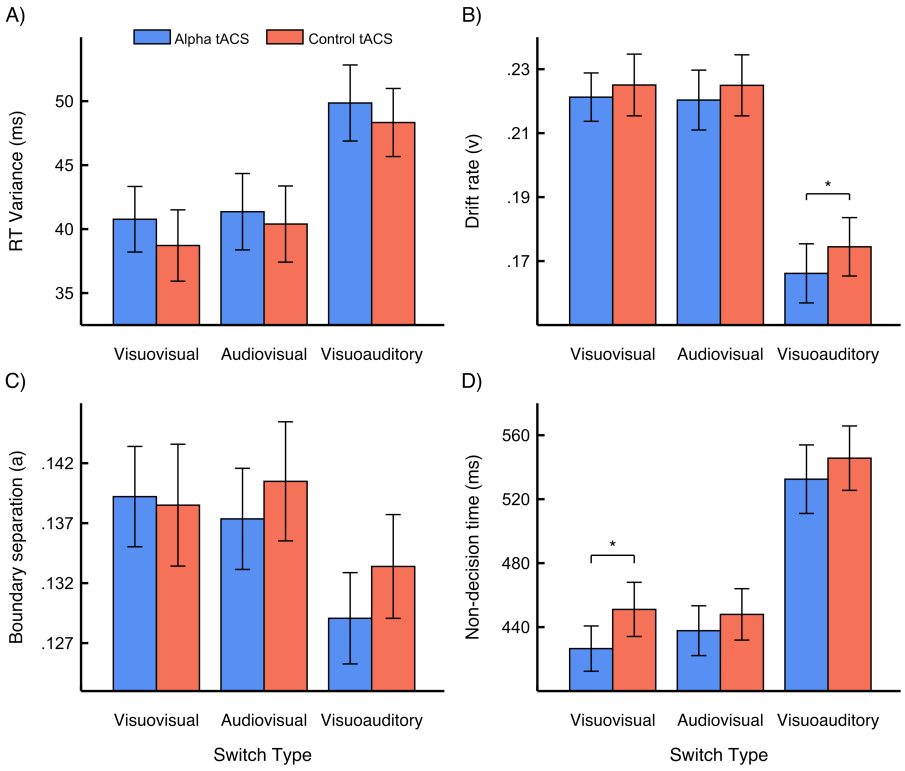


Figure 66 – Effects of alpha- vs. control-tACS on A) RT variance, B) drift rate, C) boundary separation, and D) non-decision time. Error bars show ±1 standard error. * = p < .05.

Repeat and easy-hard vs. hard-easy trial performance

I also assessed whether alpha-tACS had an effect on trials where participants performed the same task twice ('repeat trials'). I did this by calculating mean accuracy and RTs for repeat trials in the four blocks that followed the beginning of alpha- vs. control-tACS (i.e. blocks 2-5). I then submitted this data to a 3-way repeated measure ANOVA, with within-subjects factors of stimulation type, task type (motion, colour, auditory), and task block. However, I again observed no effects in either accuracy or RTs beyond those of my switch analyses (p>.3) (Figure 67A-B; p.191). Lastly, I assessed whether the effects on alpha-tACS on visuovisual switching were affected by individual differences in task difficulty. This question was partly inspired by recent reports that differences between individuals in their aptitudes for given tasks can affect the direction with which transcranial electrical stimulation influences their task performance (Looi et al., 2016; Popescu et al., 2016; Sarkar, Dowker, & Cohen Kadosh, 2014). Specifically, I

asked whether alpha-tACS might have exerted different effects on switching between visual tasks that participants found easier vs. more difficult, compared to switching from the difficult to easy task. To conduct this analysis, I looked at median RTs for each subject on motion vs. colour trials. The task with faster RTs was defined as the 'easier' task for that subject, while the other task was defined as 'harder'. I then calculated mean accuracy and RTs for 'Easy-Hard' and 'Hard-Easy' switch trials for alpha- vs. control-tACS sessions. This reformatted data was then submitted to a two-way repeated-measures ANOVA, with within-subjects factors of 'trial type' and 'stimulation type'. I observed significant main effects of trial type in both accuracy ($F_{(1,33)}$=5.154, p=.030, η^2_p=.135, ANOVA) and RTs ($F_{(1,33)}$=15.865, p<.001, η^2_p=.325, ANOVA). This reflects the unsurprising fact that performance was slower and less accurate when participants switched to the harder task. However, I observed no other effects beyond those previously reported (p>.2) (Figure 67C-D; p.191). I therefore found no evidence in either accuracy or RTs to support the idea that individual differences in task difficulty influenced the effects of alpha-tACS on visual task switching

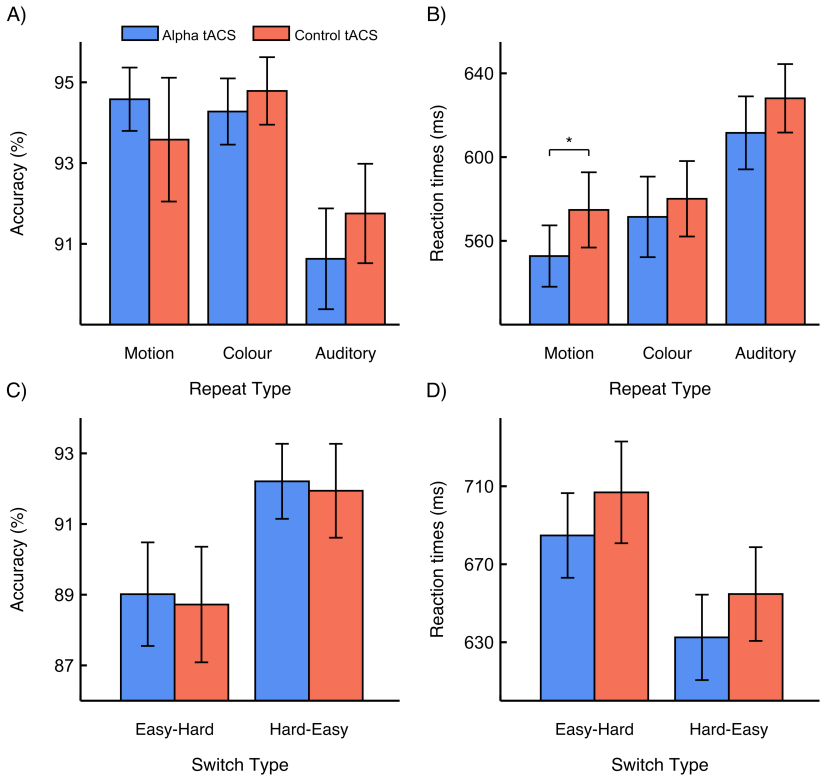


Figure 67 – Effects of alpha- vs. control-tACS on repeat trial performance (accuracy and RTs, A-B), and switching between easy vs. difficult visual tasks (accuracy and RTs, C-D). Error bars show ±1 standard error of the mean. * = p < .05.

DISCUSSION

In this pre-registered experiment, I sought to determine the effects of alpha-tACS on visuovisual vs. audiovisual task switching. EEG and task performance were measured before, during, and after the delivery of alpha- vs. control-tACS. Given the results of my previous experiments, in which alpha-tACS was found to stabilise visual attention task performance, I predicted that alpha-tACS would make it harder for participants to switch between visual tasks, but would have little effect on audiovisual switching. However, my data did not support this prediction.

My primary analyses revealed no effect of alpha-tACS on visuovisual vs. audiovisual switching accuracy. While analysis of RT data showed that overall response times were faster during alpha- vs. control-tACS, the important interaction between stimulation type and previous task modality was again not found to be significant. This indicates that alpha-tACS did not influence visuovisual vs. audiovisual task switching performance. However, supplementary analysis of task accuracy did indicate a mildly impairing effect of alpha-tACS on visuoauditory switching. Consequently, while alpha-tACS did not impair switching between visual tasks as I anticipated, this stimulation did seem to make it harder for people to switch away from visual tasks. As in a number of my previous experiments (i.e. Experiments 2 and 3), alpha-tACS did not induce greater increases in EEG alpha power than control-tACS. Furthermore, there were no associations across participants between alpha-tACS related changes in EEG alpha power and visuovisual vs. audiovisual task switching. Following these planned comparisons, I performed a number of exploratory analyses to investigate the presence of unanticipated patterns in my behavioural data. These post-hoc analyses showed that alpha-tACS similarly had no influence on RT variability, diffusion model parameters, or on the performance of repeat trials. The effects alpha-tACS on visuovisual switching were not affected by variation across participants in the difficulty of visual tasks. I

dedicate the following sections of this chapter to the discussion of the possible reasons why alpha-tACS did not influence task performance or EEG in the ways I predicted.

Too high switch frequency?

I predicted that alpha-tACS would impair switching between different states of visual attention (i.e. task sets). However, it is possible that the high frequency of task switching in this experiment (66.6%) encouraged participants to engage all tasks sets concurrently (i.e. motion, colour, and audition). Some participants may therefore have been near-continuously prepared to perform each task, meaning that task performance depended less on switching between task sets, and depended more on activating multiple task sets simultaneously. Evidence that high switch frequencies promote continuous engagement of multiple task sets comes from findings that switch costs reduce (i.e. suggesting more effective performance of multiple tasks) both with increased switch frequency (Duthoo, De Baene, Wühr, & Notebaert, 2012; Monsell & Mizon, 2006), and when people are uncertain about which tasks they will need to perform moment-to-moment (Lange, Seer, Müller, & Kopp, 2015). Nevertheless, despite these concerns about high switch frequency, I did observe quite robust switch costs in the current experiment. Consequently, if alpha-tACS does influence switching between attentional states, it is arguable that I should have observed reliable effects of stimulation on behaviour.

Short stimulation duration, and ceiling effects in task accuracy

Another potential reason why my results did not match my predictions is the short duration of stimulation. Given that tACS was delivered for less than 20 minutes in this experiment, it is possible that a longer period of stimulation would have produced clearer effects on task performance. However, my previous experiments used near-identical methods to the current study and observed replicable effects of alpha-tACS on visual

task performance. Consequently, it seems unlikely that short stimulation duration can explain the pattern of results observed in this experiment. Alternatively, it is also possible that behavioural effects of alpha-tACS in this experiment were obscured by generally high task accuracy (M = 90.3%, SD = 6.4%). Although such levels of accuracy do not indicate a ceiling effect, one might argue that the influence of alpha-tACS on task accuracy could have been obscured by participants making very few errors overall. However, this argument cannot be made for RTs, in which I observed no evidence of tACS-related effects on visuovisual vs. audiovisual switching. Consequently, again, such arguments do not seem to explain why the results of this experiment did not match my predictions.

Does alpha-tACS stabilise visual attention?

It is clearly difficult to make conclusions from null results. Nevertheless, if I assume that alpha-tACS was delivered to the brain as I intended, and that no aspect of my task design contributed to my null results, I am left with a few remaining interpretations. One possibility is that alpha-tACS simply does not impair visuovisual task switching, and therefore may not influence the stability of visual processing. This idea is consistent with the recent finding that, while gamma tACS to posterior cortex (60 Hz) increases the rate at which people's perception of multistable images changes over time, alpha-tACS exerts no such effects on the stability of ongoing, perceptual interpretations (Cabral-Calderin, Schmidt-Samoa, & Wilke, 2015). However, if alpha-tACS does not promote stability in visual processing, it remains unclear why alpha-tACS exerted stabilising effects on behaviour in my previous experiments. One possibility is that alpha-tACS does not exert immediate effects on brain activity, but rather a slow influence through processes of neuroplasticity (e.g. Neuling et al., 2013; Vossen et al., 2014). The importance of neuroplasticity to the effects of tACS is suggested by the finding that alpha-tACS increases alpha power only when delivered in long trains (Strüber et al.,

2015; Vossen et al., 2014), and that alpha oscillations induced by alpha-tACS need not be phase-locked to delivered stimulation (i.e. suggesting against direct entrainment; Vossen et al., 2014). Consequently, it is possible that key effects of alpha-tACS on brain activity occur gradually over relatively long periods (i.e. ~30 minutes), as has previously been observed with other forms of tES (Santarnecchi et al., 2014; Terney, Chaieb, Moliadze, Antal, & Paulus, 2008). This could make it less likely that one would observe effects of alpha-tACS on mean performance across a small number of blocks, as was a focus in this experiment. However, in addition to this possibility, it should also be noted that I did observe a trend-level, impairing effect of alpha-tACS on visuoauditory task switching accuracy. Consequently, an alternative, post-hoc explanation for my results could be that alpha-tACS does not influence switching between visual tasks, but instead exerts an impairing effect on transitions in attention away from the visual domain. Such impairments in visuoauditory switching could be important as they might explain why alpha-tACS was found to support performance on sustained visual tasks in my previous experiments. Specifically, if alpha-tACS impairs switching of attention away from visual tasks, this could suggest that alpha-tACS helps to focus attention on ongoing, visual tasks by preventing unwanted transitions of attention away from those tasks, and towards irrelevant, non-visual processes (e.g. mind-wandering). Nevertheless, as I did not predict such effects at the start of this study, further experiments will be required to investigate the replicability of these tACS-induced impairments in visuoauditory switching.

Null effects of alpha-tACS on EEG

The last aspect of these results I would like to discuss is that fact that alpha-tACS did not exert any effects on EEG alpha power in the current experiment. Similar results were observed in Experiment 2 and 3, in which EEG alpha power was not influenced by the delivery of alpha- vs. control-tACS. In these previous experiments, an appealing

explanation for this null effect was the presence of significantly elevated EEG alpha power during Experiments 2 and 3. It has been suggested that alpha-tACS increases EEG alpha power only when alpha power is naturally low (Alagapan et al., 2016; Neuling et al., 2013). However, a striking feature of the current experiment is that, while I again observed no increases in EEG alpha power following alpha-tACS, mean alpha power was not especially high (Figure 68; p.196). In fact, statistical analysis revealed that mean alpha power in the current experiment was significantly lower than mean alpha power in Experiments 2 and 3 ($F_{(1,114)}$=5.271, p=.024, η^2_p=.044, ANOVA), but no different to alpha power in Experiment 1 and 4 ($F_{(1,127)}$<1, ANOVA). These results are therefore inconsistent with the view that alpha-tACS increases alpha power only when it is naturally low. The results therefore generate new doubts about the reasons why the effects of alpha-tACS are so variable across experiments. This question is addressed in further detail in the final chapter of this thesis (Chapter 10; p.217).

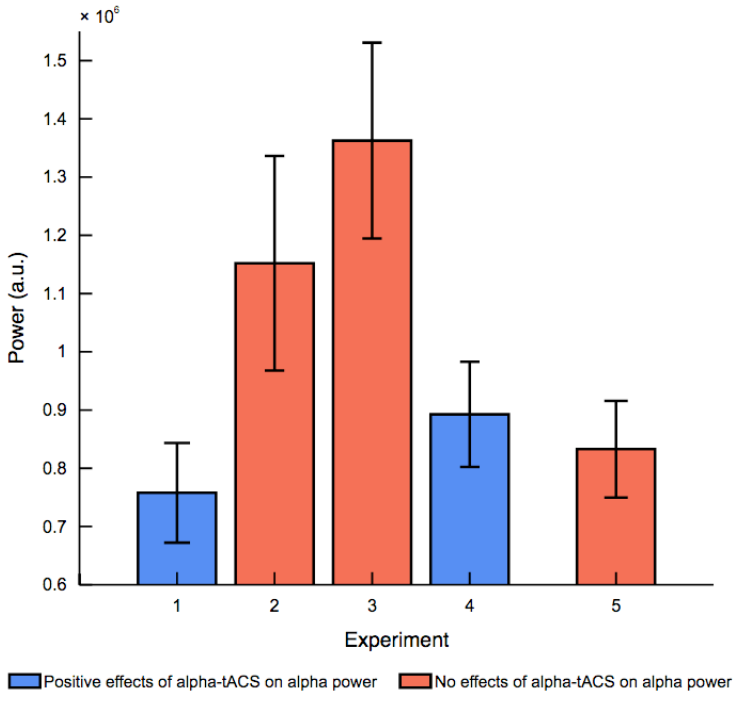


Figure 68 – Raw alpha power across Experiments 1 – 5. Raw alpha power in the current experiment was significantly lower than mean alpha power in Experiments 2 and 3, but no different to alpha power in Experiment 1 and 4. Blue shading indicates that alpha power was increased following alpha- vs. control-tACS in that experiment. Red shading indicates that alpha power was not increased following alpha- vs. control-tACS in that experiment.

CHAPTER 9 – THETA-tACS

The results of Experiments 1 – 4 indicated that, instead of impairing visual attention as expected, alpha-tACS seems to exert a stabilising effect on visual task performance. The results of Experiment 5 showed that alpha-tACS does not influence switching between visual tasks. This could suggest that alpha-tACS does not stabilise visual attention over short periods, but may instead exert a more specific effect on changes in visual attention that occur over longer periods of time (i.e. 15 minutes). Alternatively though, given that alpha-tACS was found to exert a mildly impairing effect on visuoauditory switching accuracy, this stimulation may instead prevent switching of attention away from the visual domain.

These results are discussed in further detail in the following chapter, which focuses on the primary conclusions of this project (see p.216). However, before finishing this series of experiments, there was a final study that I thought was necessary to run. Due to practical constraints, I had so far delivered tACS at just two frequencies: 10 Hz and 50 Hz. Although I would ideally have tested the effects of tACS across a broad range of frequencies (e.g. 4, 10, 20, and 30 Hz), this would have involved the recruitment of potentially hundreds of additional subjects per experiment, divided into multiple subgroups that would have each received stimulation at different frequencies. This would have drastically reduced the number of full experiments I could have run, perhaps giving me have a better appreciation of the frequency-specificity of tACS effects, but little understanding of how those effects are expressed across multiple task types (which was a focus of this project). Furthermore, the inclusion of multiple stimulation frequencies would have complicated my statistical analyses due to issues of multiple comparisons. Nevertheless, without such multi-frequency experiments, it is arguably very difficult to determine the theoretical implications of my results.

I have so far assumed that, if 10 Hz tACS has effects on task performance that are not observed during sham or 50 Hz tACS, this must reflect the specific consequences of 10 Hz stimulation. However, this assumption is arguably nothing more than a hope. It is perfectly possible, in theory, that the previously described effects of 10 Hz tACS on task performance would be observed just as clearly during 5 or 15 Hz tACS. If correct, this would significantly limit the extent to which the results of my experiments could be said to describe the specific contributions of alpha oscillations to visual attention. Furthermore, a different frequency of stimulation could theoretically have stronger, and more reliable effects on visual task performance than 10 Hz tACS. Given that a primary goal of this project was to discover new ways of improving sustained attention with tACS, it was therefore necessary that I investigate such alternative possibilities. However, contrariwise, if such additional experiments showed that only 10 Hz tACS stabilised visual task performance, this would focus the theoretical implications of my results on alpha oscillations specifically. Furthermore, such findings would highlight the potential importance of selecting the correct frequency of stimulation (e.g. 10 Hz) when using tACS for the purpose of improving sustained attention in real-world settings.

The central parameter to decide for this experiment was therefore the frequency of stimulation. Given that my previous experiments had focused on alpha-tACS, it was important that the frequency of stimulation was well outside of the alpha band (i.e. 7 – 13 Hz). This left two options: stimulation in the upper beta band (i.e. 15 – 30 Hz), or the theta band (i.e. 1 – 6 Hz). Beta stimulation had the advantage that, as with alpha rhythms, beta oscillations have been associated with communication of feedback signals to visual cortex (e.g. Bastos et al., 2015; Jensen et al., 2015). Consequently, assuming the accuracy of my speculative hypothesis that alpha-tACS prevents long-term changes in visual attention due to disruption of top-down signalling (see Chapter 7, p.170), I would expect to observe similar effects of beta-tACS on visual task performance.

However, beta-tACS also had the *disadvantage* that it involves high frequency stimulation. I had previously found that gamma-tACS (i.e. 50 Hz) has no influence on visual task performance. Consequently, if I found that beta-tACS also had no influence on task performance, this would strength my view that the effects of alpha-tACS differ from those of high-frequency tACS, but would leave me with unanswered questions about the effects of low-frequency tACS. I therefore decided to stimulate at a theta frequency of 4 Hz. This frequency had the advantage that theta rhythms have also been positively associated with the transmission of top-down control signals from prefrontal to visual cortex (Oehrn et al., 2014) (see p.39). It therefore seemed plausible that theta-tACS would also exert protective effects on visual task performance. It should be stated, in addition, that tACS has been shown to affect neural activity at both sub- and super-harmonics of the stimulation frequency (e.g. Ali et al., 2013). I therefore chose to stimulate at 4 Hz, which is not a subharmonic of 10 Hz.

The last aspect of this experiment to be decided was the visual attention task. I chose to run an approximate replication of my first experiment, and therefore used the vCTET (Figure 18; p.89). This task elicited the most reliable deterioration in performance across tasks, reflected in the greater size of the main effect of task block for accuracy in Experiment 1, compared to RTs in Experiment 2 and d' in Experiment 4 (η^2_p = .460 vs. .283 & .246). In addition, the effect size of the main interaction between stimulation and task block was marginally greater in Experiment 1 vs. 2 and 4 (η^2_p = .068 vs. .067 & .065). This suggested that alpha-tACS had the strongest influence on vCTET deteriorations. Therefore, if theta-tACS were to influence visual attention in a similar way to alpha-tACS, I believed that the vCTET would best facilitate the observation of this effect.

METHODS

This experiment was an approximate replication Experiment 1. In other words, participants performed the vCTET in two task sessions, each consisting of 4 blocks of 4 minutes and 50 seconds each. A fixed-duration break of 40 seconds was allowed between blocks and participants received tACS from the start of the second block to the start of the fourth block. The central difference between these experiments was that, instead of 10 Hz (i.e. alpha-tACS), tACS was delivered at 4 Hz (theta-tACS). The following sections detail the remaining areas of difference.

Participants

Forty healthy adults took part in this experiment. This sample size was chosen based on the sample sizes of my previous experiments. Four participants were excluded because their accuracy on at least one task block was more than 2 standard deviations below mean accuracy on that block across all participants. The final sample therefore consisted of 36 participants (19 females, 4 left-handed, mean age = 24.1, SD = 5.4).

Variable stimulation intensities

Stimulation was delivered in a near-identical manner to all previous experiments. tACS was delivered at a maximum intensity of 2 mA (peak-to-peak). However, as with my last experiment, for subjects who found this intensity too unpleasant or distracting (n = 9), stimulation amplitudes were lowered to ensure that subjects were comfortable throughout the task. Mean stimulation intensity was therefore 1.77 mA (SD = .41). A single participant who could not tolerate <1 mA stimulation did not participate in the experiment and was replaced.

Analysis of theta-tACS effects on 4 Hz power

In addition to performing the same EEG analyses as in all previous experiments (i.e. looking at tACS effects on percentage change in individualised theta, alpha, and low beta bands), I also assessed whether theta-tACS had an effect on EEG activity at the frequency of stimulation. To do this, I calculated mean power between 1 and 7 Hz (i.e. 4 ±3 Hz) before and after the delivery of tACS. As with my previous analyses, I then divided post-tACS theta power by pre-tACS theta power to generate a measure of percentage change in theta power from the start to the end of each task session. I then submitted these power estimates to a one-way repeated measures ANOVA, with a within subjects factors of 'stimulation' (i.e. theta- vs. control-tACS). 'Stimulation order' and 'control group' were also included as between-subjects factors.

RESULTS

EEG alpha power was increased before error vs. correct trials

I focused first on the question of whether EEG alpha power was increased before error vs. correct vCTET trials. As in Experiment 1, I compared normalised EEG power within individualised theta, alpha, and low beta bands 3200 ms before to 800 after the presentation of target trials. However, in contrast to Experiment 1, I observed no significant effect of frequency band ($F_{(2,70)}$=2.34, p=.144, η^2_p=.060, ANOVA). Planned comparisons revealed that normalised power in the alpha band (error / correct) was greater than theta power (M=4.4%, SD=11.2%, $t_{(35)}$=2.37, p=.024, d=0.39, paired-samples t-test), but did not differ reliably from beta power (M=2.9%, SD=12.2%, $t_{(35)}$=1.47, p=.150, d=0.12, paired-samples t-test). This suggests that, as in Experiment 1, alpha power was greater than theta, but no different to beta power, before error vs. correct trials (Figure 69; p.202). Furthermore, broadband power (i.e. theta to low beta) was again found to be higher than 100% (M=111.6%, SD=11.1%, $t_{(35)}$=6.25, p<.001, d=1.04, one-sample t-test). This indicates that EEG power was generally elevated before error vs. correct vCTET trials.

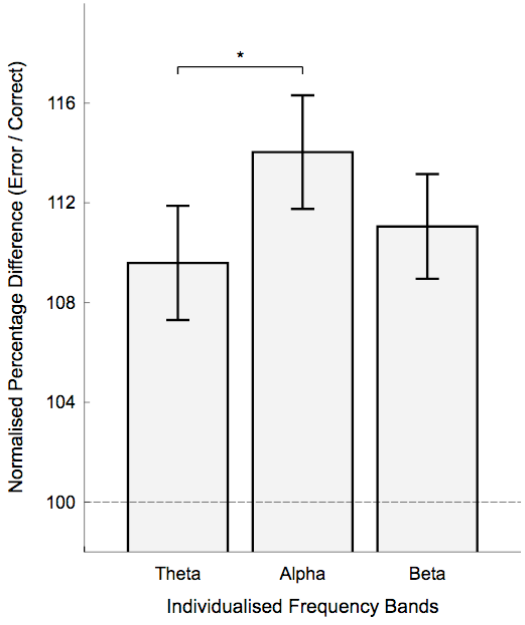


Figure 69 – Normalised EEG power is shown for individualised theta, alpha, and beta bands (error / correct). Alpha power was greater before error vs. correct trials with respect to theta power, but not with respect to beta power. As in Experiment 1, broadband power (i.e. theta–beta) was significantly elevated before error vs. correct trials. Error bars show ±1 standard error of the mean. * = p < .05.

EEG alpha power did not change following theta-tACS

I focused next on the effects of theta-tACS on EEG power. Figure 70 (p.203) shows raw frequency power spectra before and after the delivery of theta- vs. control-tACS.

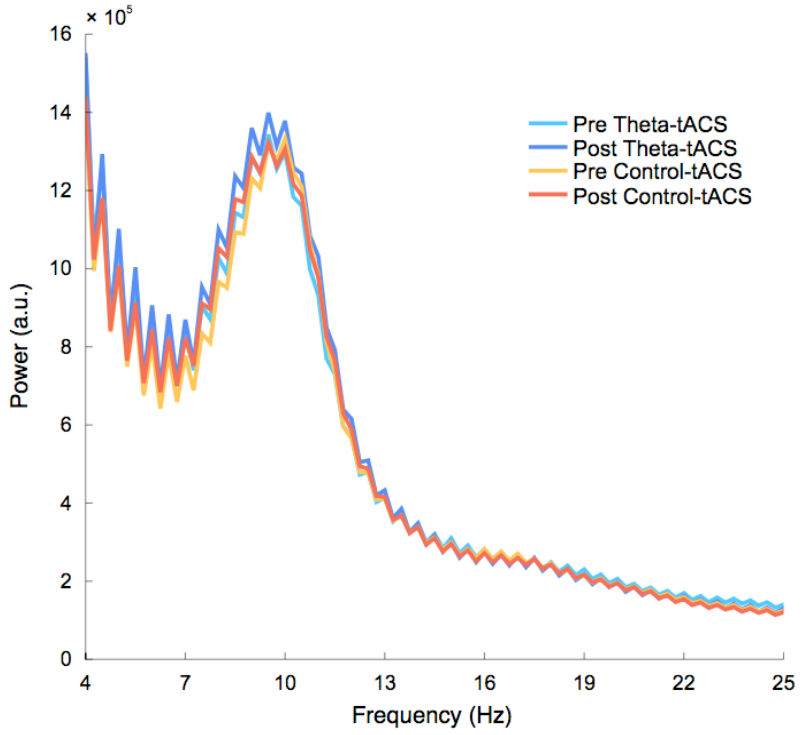


Figure 70 – Raw EEG frequency spectra (averaged over PO7, PO8, P3, P4) are plotted before and after the delivery of theta- vs. control-tACS.

In my main analysis of normalised percentage change in EEG power, I observed a significant effect of frequency band ($F_{(2,64)}$=5.220, p=.009, ε=.948, η^2_p=.140, ANOVA). This effect indicated that, regardless of whether participants received theta- or control-tACS, EEG power increased reliably from the start to the end of each task session in the alpha band (M=106.2%, SD = 15.4%, $t_{(35)}$=2.40, p=.022, d=0.40), but not in the theta (M=101.0%, SD = 10.9%, $t_{(35)}$<1) or beta bands (M=100.1%, SD = 10.5%, $t_{(35)}$<1). However, I observed no significant interaction between stimulation and frequency band ($F_{(2,64)}$<1, ANOVA). This suggests that theta-tACS had no specific influence on changes

in EEG power in individualised theta, alpha, or low beta band (Figure 71; p.204). I also observed no higher order interactions with stimulation order or control group (Figure 72; p.204).

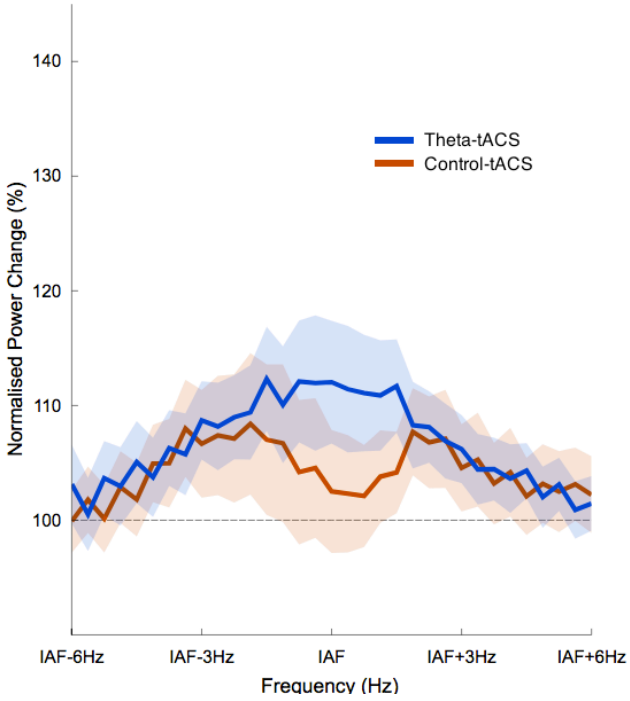
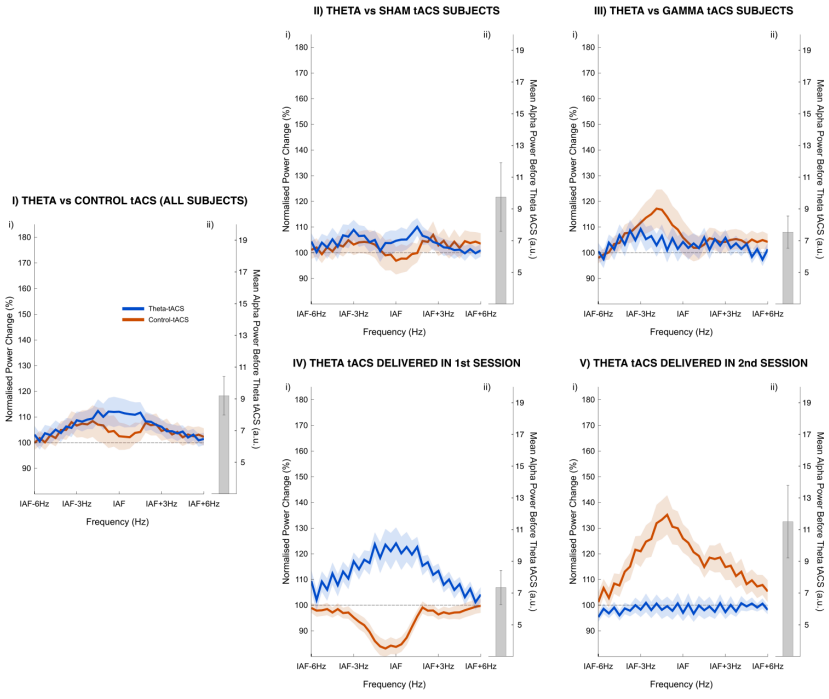


Figure 71 – Percentage change in EEG power. Normalised percentage change in EEG power (centred around individual alpha frequency [IAF]) did not differ between theta- and control tACS sessions. Coloured shading shows ±1 standard error of the mean.

Figure 72 – Normalised change in EEG power, divided by experimental subgroup. Percentage change in EEG power for all participants is shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving theta-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Coloured shading shows ±1 standard error of the mean.



No effects of theta-tACS on 4 (±3) Hz power

In addition to these standard analyses, I also assessed whether theta-tACS had an effect on 4 Hz (±3) Hz power. However, when conducting this analysis, I found no significant difference in percentage change values in 4 Hz power following theta- vs. control-tACS ($F_{(1,32)}$=2.206, p=.147, η^2_p=.064, ANOVA) (Figure 73; p.205). There were also no main effects of, or interactions with, stimulation order or control group. I therefore concluded that theta-tACS also had no effect on neural activity around the frequency of stimulation.

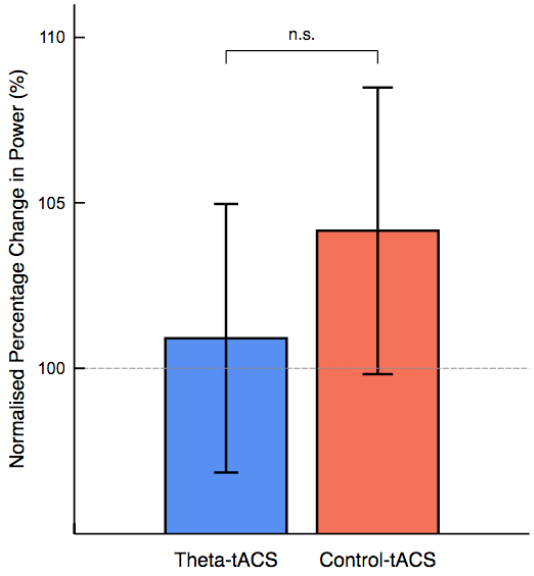


Figure 73 – Mean, normalised percentage change in theta power (1 – 7 Hz) is shown for theta- vs. control-tACS sessions (i.e. post- / pre-tACS). I observed no effects of theta-tACS on changes in theta power from the start to the end of each task session. Error bars show ±1 standard error of the mean.

The effects of theta-tACS on vCTET accuracy

I looked next at the effect of theta-tACS on vCTET accuracy. As in my previous experiments, I observed a main effect of task block ($F_{(3,96)}$=41.14, p<.001, η^2_p=.562, ANOVA), with a strong linear trend ($F_{(1,32)}$=73.12, p<.001, η^2_p=.696, ANOVA). This confirms that vCTET accuracy deteriorated from the start to the end of each task session. However, slopes analysis revealed that task accuracy showed only trend-level deteriorations from block 2 to 4 during control- (M=-0.032, SD=0.104, $t_{(35)}$=-1.83, p=.076, d=-0.30, one-sample t-test [test value = 0]) and theta-tACS (M=-0.035, SD=0.129, $t_{(35)}$=-1.63, p=.112, d=-0.27, one-sample t-test). Furthermore, the important interaction

between stimulation and task block was not found to be significant ($F_{(3,96)}$<1, ANOVA). This suggests that there was no effect of theta-tACS on vCTET accuracy (Figure 74; p.206). I again observed no higher order interactions with stimulation order or control group (Figure 75; p.207).

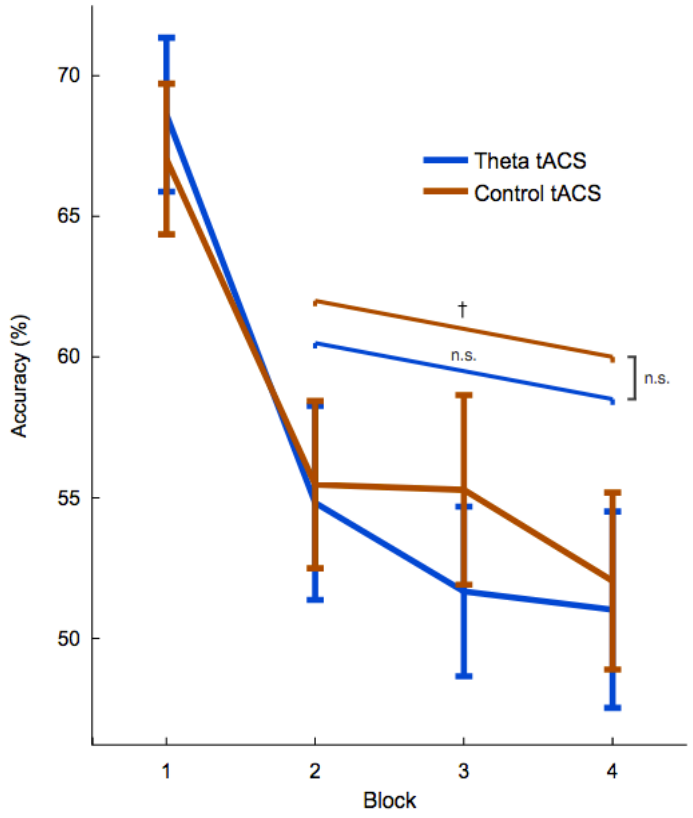


Figure 74 – vCTET accuracy is displayed for blocks 1-4 during theta- vs. control- tACS. A marginally significant, negative slope was observed during control-tACS between blocks 2 and 4, while the equivalent slope during theta-tACS sessions did not differ reliably from zero. However, these slopes did not different between theta- and control-tACS sessions. This suggests that theta-tACS exerted no influence on deteriorations in vCTET accuracy from the start of stimulation onwards. Error bars show ±1 standard error of the mean. † = p < .10.

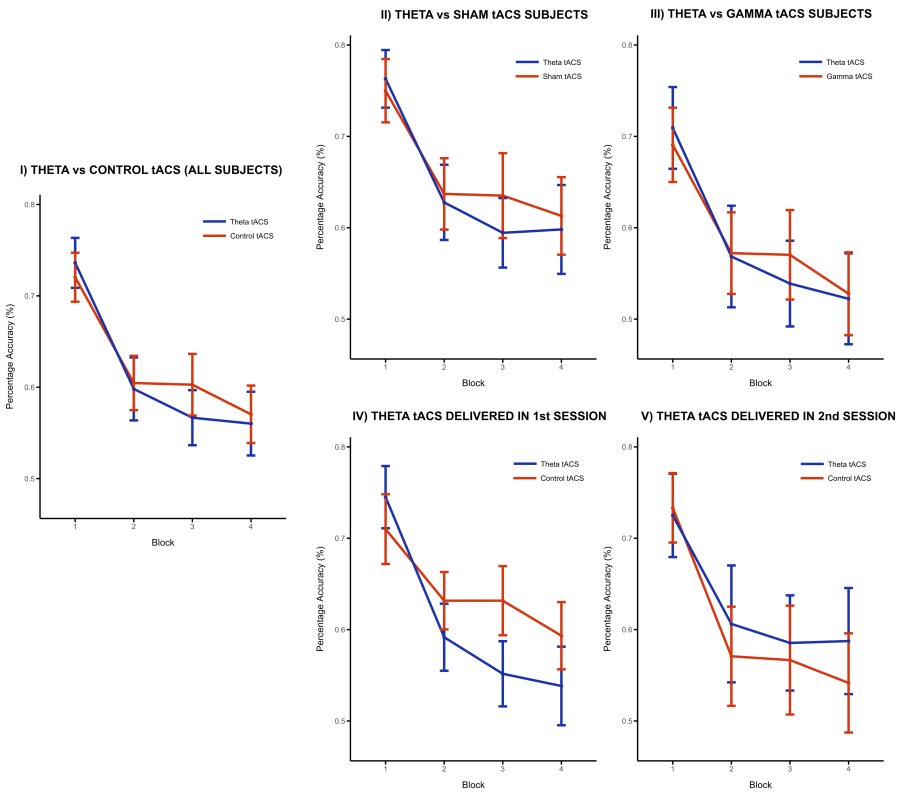


Figure 75 – Effects of tACS on accuracy, divided by experimental subgroup. vCTET acc-uracy data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving theta-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Error bars show ±1 standard error of the mean.

Effect of theta-tACS on vCTET RTs

I then focused on vCTET RTs. Again, I observed a main effect of task block ($F_{(3,96)}$=11.65, p<.001, η^2_p=.267, ANOVA), with a linear trend ($F_{(1,32)}$=20.01, p<.001, η^2_p=.385, ANOVA). This confirms that, as with task accuracy, vCTET RTs deteriorated (i.e., increased) from the start to the end of each task session. However, in addition to this standard observation, I also observed a number of weak, but interesting effects of stimulation. For example, I observed a trend-level, main effect of stimulation ($F_{(1,32)}$=3.68, p=.064, η^2_p=.103, ANOVA), with RTs lower during theta- vs. control-tACS sessions (M=260 vs. 293ms, SD=34ms). I also observed a trend-level interaction between stimulation and task block ($F_{(1,32)}$=2.50, p=.064, η^2_p=.072, ANOVA). Slopes analysis revealed that RTs showed a trend-level increase from block 2 to 4 during control-tACS (M=0.090, SD=0.28, $t_{(35)}$=1.93, p=.062, d=0.32, one-sample t-test [test value = 0]), but not during theta-tACS (M=0.001, SD=0.21, $t_{(35)}$<1, one-sample t-test). However, the difference between these slopes was not reliable (M=-0.09, SD=0.39, $t_{(35)}$=-1.36, p=.182,

d=0.23, paired-samples t-test). Applying the same analysis as in Experiment 3 using JASP (2017), I ran a Bayesian paired-samples t-test to assess the strength of this null result. The estimated Bayes factor for this comparison (null/alternative) suggested that the observed slopes data were 2.40 times more likely to occur under a model in which theta- vs. control-tACS slopes did not differ from each other, compared to a model in which these slopes did differ. This Bayesian comparison therefore indicated the presence of anecdotal, but positive evidence in favour of the hypothesis that theta-tACS had no effect on increases in vCTET RTs from the start of stimulation onwards. Nevertheless, it is interesting that a paired-samples t-test did reveal that RTs were significantly lower in block 4 of theta- vs. control-tACS sessions (M=-62ms, SD=162ms, $t_{(35)}$=-2.284, *p*=.029, *d*=-0.38, paired-samples t-test). This suggests that theta-tACS may have increased the speed of RTs towards the end of the task, after stimulation had ceased (Figure 76; p.208). I observed no higher order interactions with stimulation order or control group (p>.2) (Figure 77; p.209).

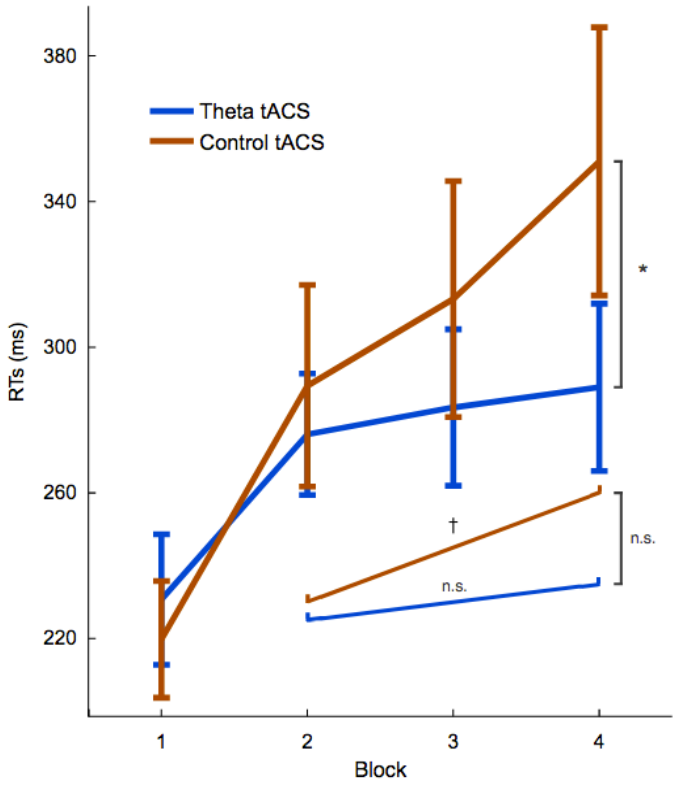


Figure 76 – Effects of tACS on vCTET RTs. vCTET RTs are displayed for blocks 1-4 during theta- vs. control-tACS. Similar to task accuracy, a marginally significant, positive slope was observed during control-tACS between blocks 2 and 4, while the equivalent slope during theta-tACS sessions did not differ reliably from zero. However, these slopes did not differ between theta- and control-tACS sessions. This suggests that theta-tACS exerted no influence on increases in vCTET RTs from the start of stimulation onwards. However, RTs were significantly faster in the fourth block of theta- vs. control-tACS session. Error bars show ±1 standard error of the mean. † = p < .10.

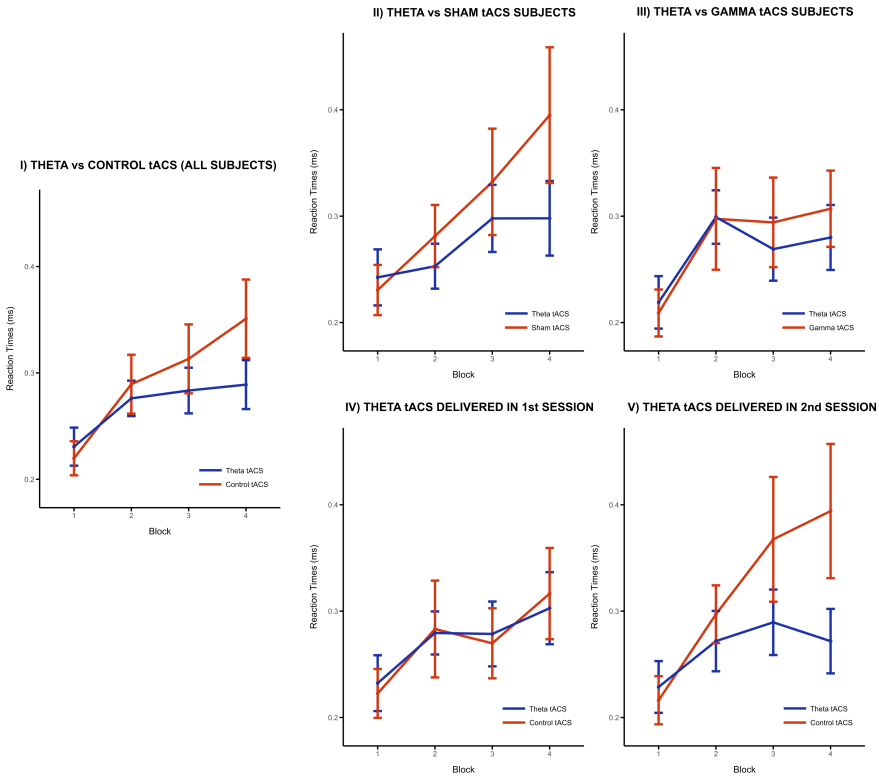


Figure 77 – Effects of tACS on RTs, divided by experimental subgroup. vCTET RT data from all participants are shown in the far left figure (I). To the right of this figure, data for subjects receiving sham- (II) and gamma-tACS (III) are shown in the upper row (left vs. right), while data for subjects receiving theta-tACS in the first (IV) and second task sessions (V) are shown in the lower row (left vs. right). Error bars show ±1 standard error of the mean.

Stimulation condition blinding

Lastly, I sought to confirm that the side effects of tACS did not differ reliably between stimulation conditions. At the end of the experiment, participants were told about the most common side effects of stimulation (i.e. scalp sessions and phosphenes), and were asked in which task session they thought these subjective effects were most intense. 41.7% said that the subjective effects of stimulation were more intense during the theta-tACS session. A binomial test indicated that this proportion did not differ significantly from chance (i.e. 50%; p=.405). I therefore conclude that the subjective effects of stimulation did not differ between theta- and control-tACS sessions.

DISCUSSION

The aim of this final experiment was to test the frequency-specificity of the effects of tACS on vCTET performance. The experiment was an approximate replication of Experiment 1, with stimulation being delivered at 4 Hz, instead of 10 Hz. My prediction was that, if the behavioural results of my previous experiments reflected the specific consequences of alpha-tACS, I should observe null, or very different effects of theta-tACS on vCTET performance in the current experiment. In contrast though, if the previously observed effects of alpha-tACS reflected more general effects of, for example, low-frequency tACS, I expected to observe an approximate replication of the results of Experiment 1 in the current experiment.

Supporting the view that my previous results reflected the specific consequences of alpha-tACS, I observed no effects of theta-tACS on vCTET accuracy. Although deteriorations in vCTET accuracy occurred with equivalent reliability in the current experiment with respect to Experiment 1 (main effect of block, η^2_p=.562 vs. .460), theta-tACS exerted no effects on such deteriorations over time. However, a different pattern of results was observed in RTs. Here, a trend-level interaction was observed between stimulation and task block. Although this interaction was only marginally significant, the effect size was similar to the equivalent effect in Experiment 1 (i.e. stimulation * task block; η^2_p= .072 vs. .068). Performance slopes for RTs (block 2-4) did not differ between theta- and control-tACS. Nevertheless, at least at a descriptive level, the effects of theta-tACS on performance slopes were very similar to those of alpha-tACS in Experiment 1. Furthermore, providing additional support for the view that theta-tACS protected vCTET RTs from increases over time, RTs were significantly faster in the final block of theta- vs. control-tACS sessions. I dedicate the following sections to possible issues with these results. I then go on to discuss their possible interpretations.

Possible issues

Possible role of stimulation order

Closer examination of these trend-level effects of theta-tACS on RTs revealed a number of aspects that needed further investigation. For example, when viewing the RTs results divided by experimental subgroup, it seemed that the apparently supportive effects of theta-tACS on vCTET RTs were not expressed equally across all participants. Instead, increases in RTs over time during control- vs. theta-tACS appeared more prevalent among subjects receiving theta-tACS in the second task session. Furthermore, it seemed that the differences between stimulation conditions were driven more by a large increase in RTs during control-tACS among subjects receiving theta-tACS in the second task session, rather than by any noticeable reductions in RTs during theta-tACS generally (Figure 77V; p.209). This pattern of results arguably casts doubt on the extent to which differences in RTs between stimulation conditions could be said to reflect enhancing effects of theta-tACS on task performance. Nevertheless, I observed no significant interaction between stimulation, task block, and stimulation order. Therefore, despite these descriptive differences between experimental subgroups, it seems that they cannot be interpreted as reliable effects.

Possible influence of an outlier

Another aspect of these RTs results that needed further investigation was the possible influence of one subject that exhibited a RT performance slope during control-tACS that was more than 4 standard deviations above the sample mean (Figure 78; p.212). It was therefore possible that the apparently protective effects of theta-tACS on RTs could have been driven to a significant extent by the unusually large deterioration in RTs observed during control-tACS for this subject. Supporting this view, removal of this participant from the RTs ANOVA eliminated the trend-level interaction between

stimulation and task block ($F_{(3,93)}$=1.85, p=.144, η^2_p=.056, ANOVA). However, given that I did not plan to exclude participants based on their performance slopes, it is difficult to draw conclusions from such post-hoc exclusions. It is arguably unsurprising that the effects of theta-tACS on vCTET RTs are reduced by the removal of a subject showing the greatest difference in RTs between stimulation conditions. Furthermore, it is interesting to note that the exclusion of this participant had only a small effect on the difference in RTs between theta- vs. control-tACS in the fourth task block (M=-50ms, SD=149ms, $t_{(34)}$=-1.996, p=.054, d=-0.34, paired-samples t-test). Although this reduction in RTs during theta-tACS became less reliable (p= .054 vs. =.029), the effect size was only slightly reduced (d=-0.34 vs. -0.38). Such findings suggest that the inclusion of the extreme subject cannot totally explain the observation of apparently supportive effects of theta-tACS on vCTET RTs.

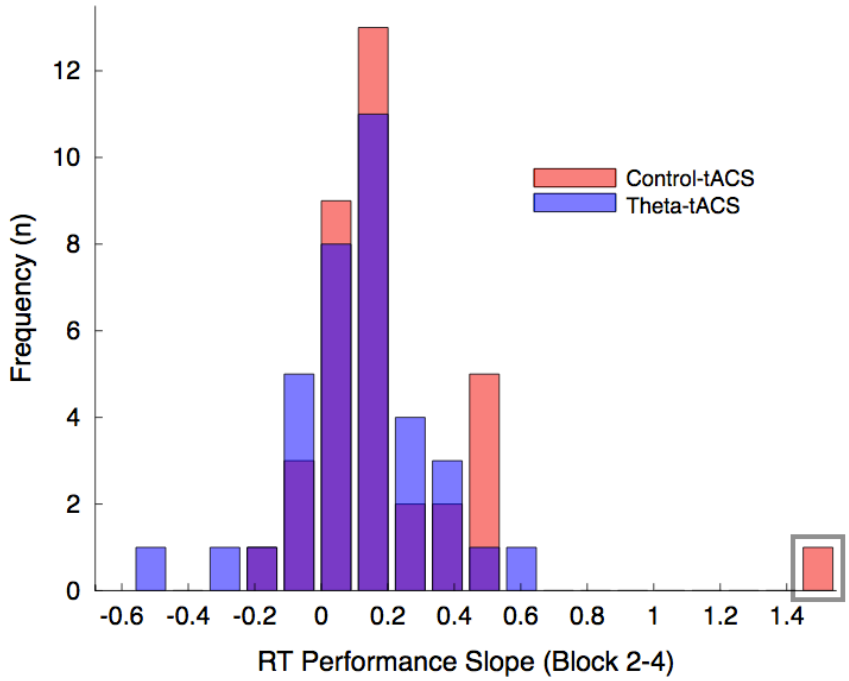


Figure 78 – A histogram showing RT performance slopes (block 2 – 4) during theta- and control-tACS sessions. Although most subjects exhibited RT performance slopes of around 0.2, a single subject exhibited a performance slope during control-tACS of 1.4. This was more than 4 standard deviations above the sample mean.

Possible interpretations

Why RTs?

For the purposes of argument, I will assume in the following paragraphs that these previously mentioned concerns did not play a crucial role in the observed effects of theta-tACS on RTs. I will also assume, despite the limited the strength and reliability of these effects, that theta-tACS did exert a supportive effect on vCTET RTs (similar to that observed in previous experiments). This assumption is based primarily on the strikingly similarity, if only at the descriptive level, between the effects of alpha- and theta-tACS on vCTET performance (i.e. limiting the slope of deteriorations that were otherwise observed during control-tACS). Upon accepting these assumptions, one of the first questions provoked is, why would alpha-tACS influence vCTET accuracy in Experiment 1, but theta-tACS influence vCTET RTs in the current experiment? The observation that tACS exerts similar behavioural effects in different measures of task performance is a common theme of this project. For example, alpha-tACS was found to influence task accuracy in Experiment 1, but RTs in Experiment 2. Given that these experiments used different cognitive tasks, I suggested that this heterogeneity in results could stem from methodological differences between experiments (see p.137). However, given that the current experiment used the same task as Experiment 1 (i.e. the vCTET), such explanations cannot be used here to explain these differences between vCTET experiments. A potential alternative could be that some aspect of theta-tACS influence neurocognitive processes related to response speed, while alpha-tACS modulates processes related to the accuracy of target detection. However, given that this explanation is a post-hoc rationalisation of the observed data, no significant consideration can be given to such speculative hypotheses without further experimentation.

Alpha vs. low-frequency tACS

In addition to this issue of heterogeneity between task measures, the previously mentioned assumptions also provoke a wider question about the specificity of the behavioural effects of alpha-tACS; If theta-tACS also prevents deteriorations in vCTET performance, perhaps any form of low-frequency tACS (e.g. 1 – 15 Hz) could be used to achieve similar results? As suggested before, the limited strength and reliability of the effects of theta-tACS on vCTET performance make it very difficult to draw strong conclusions from the current results. Unfortunately, their ambiguity means that the hypothesis that theta-tACS supports visual attention in a similar way to alpha-tACS can be neither strongly confirmed nor rejected. However, it is interesting to note that, at least at a descriptive level, theta-tACS did prevent deteriorations in RTs over time. It is also interesting to consider that, although the interaction between stimulation and task block did not reach significance in this experiment, the effect size of the interaction in this experiment was comparable to that observed in Experiment 1 (η^2_p= .072 vs. .068). Consequently, it seems that there is some reason to believe that theta-tACS may exert similar effects on visual task performance as alpha-tACS.

No effect of theta-tACS on EEG power

The last aspect of these results that I would like to discuss is the fact that theta-tACS exerted no influence on EEG power. It is perhaps unsurprising that theta-tACS had no enhancing effect on EEG alpha power as the frequency of stimulation (i.e. 4 Hz) was designed to have no influence on alpha oscillations. However, the more interesting result is that theta-tACS also had no effect on neural activity around 4 Hz. This observation might be predicted given the difficulty I have had in this project in increasing EEG alpha power using alpha-tACS. Nevertheless, taken together, these results strengthen the view that modulation of oscillatory brain activity with tACS is not an easy task. Furthermore, as I am aware of no previous studies showing enhancements of posterior theta power

following theta-tACS, such results also suggest that, in addition to exerting variable effects on EEG power, tACS might only be able to modulate oscillations within specific frequency bands (e.g. alpha oscillations). Due to differences in the physiology of their generation, for example, some frequencies of neural oscillations may be less sensitive to modulation with transcranial currents.

CHAPTER 10 – CONCLUSIONS

I begin this chapter with a brief summary of the main results of this thesis. My experiments focused of the effects of alpha-tACS on sustained attention. Poor performance on all visual tasks used in this project had previously been associated with increased EEG alpha power. I therefore assumed, at the beginning of the project, that alpha-tACS would reliably impair visual task performance. However, this was not what I observed. Instead, in my first two experiments, alpha-tACS was found to reduce the slope of deteriorations in task performance that otherwise occurred during control-tACS (i.e. sham- and 50-Hz-tACS). In other words, alpha-tACS appeared to protect task performance. My third experiment suggested that these effects are specific to the visual domain. Furthermore, in a fourth experiment, I observed near-opposite results to those of my first two experiments. Although performance on the conjunction search task used in this experiment naturally improved over time, alpha-tACS was found to limit the slope of such improvements. Overall, I interpreted these results as suggesting that alpha-tACS exerts a stabilising effect on visual attention. This hypothesis was tested in my fifth experiment, in which alpha-tACS was delivered during an audiovisual switching task. Here, alpha-tACS was not found to impair visuovisual task switching as I predicted. However, alpha-tACS was found to reduce accuracy on visuoauditory switch trials, suggesting that this stimulation may prevent transitions of attention away from the visual domain. A final study indicated that 4-Hz-tACS exerts weak, but descriptively similarly effects on visual task performance as those observed during alpha-tACS in my first two experiments. Throughout my experiments, tACS was found to exert highly variable and inconsistent effects on EEG power.

This final chapter provides a broad discussion of these results. I focus first on the theoretical implications of the results. I then finish by discussing possible directions for future research, as well as the potentials strengths and weaknesses of using tACS for the purpose of improving sustained attention in real-world settings.

KEY QUESTIONS AND INTERPRETATIONS OF RESULTS

The EEG effects of alpha-tACS are weak and high variable

One consistent observation of the current project is that, despite a number of previous studies reporting increases in EEG alpha power following alpha-tACS (Helfrich et al., 2014; Neuling et al., 2013; Neuling et al., 2015), such effects appeared to be only moderate in strength and highly variable across subjects and experiments. This point is reflected in the observation that alpha-tACS led to post-stimulation increases in EEG alpha power in just 2 of my 5 experiments. The point is further illustrated by the observation that, when my EEG results were combined across all alpha-tACS experiments (i.e. Experiments 1-5), although alpha power was descriptively greater following alpha- vs. control-tACS (Figure 79; p.217), this difference was not reliable (M=3.5%, SD=46.2%, $t_{(206)}$=1.091, *p*=.277, *d*=.076, paired-samples t-test). Furthermore, a Bayesian paired samples t-test (implemented using JASP) suggested that the observed data was 7.17 times more likely to occur under a model in which alpha power did not differ following alpha- vs. control-tACS, compared to a model in which it did.

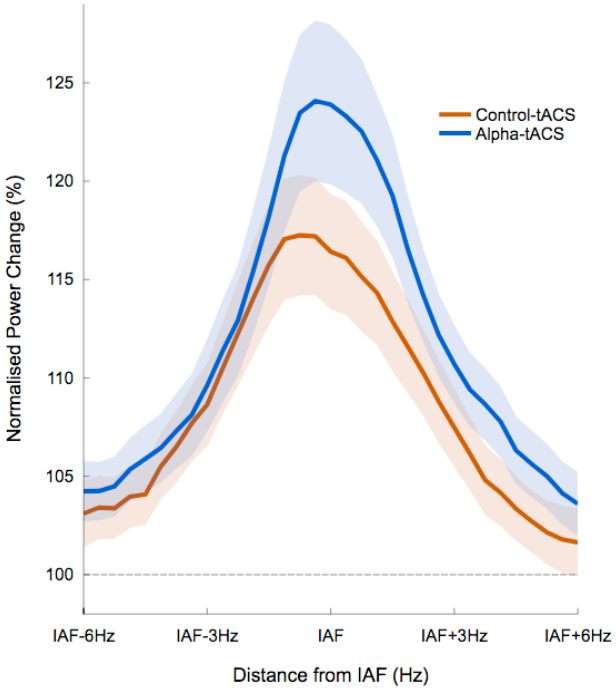


Figure 79 – The effects of alpha- vs. control-tACS on normalised EEG power (combined across Experiments 1 – 5)

Following the results of my first four experiments, I suggested that alpha-tACS might influence EEG alpha power only when baseline alpha power is low. This hypothesis was supported by the finding that overall alpha power was higher in experiments were alpha-tACS had no influence on EEG alpha power, compared to those experiments where alpha power was increased following alpha-tACS (i.e. Experiments 2 & 3 vs. 1 & 4). However, this explanation was contradicted by the results of Experiment 5 in which, although baseline alpha power was consistently low, no enhancement in alpha power was observed following alpha-tACS. It is interesting to note that theta-tACS was also found to have no influence on EEG power. Consequently, the answer to the question of why tACS exerted such variable effects on EEG power remained unclear.

The difficulties of transcranial electrical stimulation

In contrast to the view that the effects of alpha-tACS might depend on baseline conditions, it is important to state the potential relevance of an alternative hypothesis: that alpha-tACS did not exert its predicted effects on EEG activity due to fundamental limitations in the extent to which tACS can be delivered consistently across subjects. A central problem with any method of tES is that it is extremely difficult to know exactly where and at what intensities stimulation has been delivered to the brain. For example, it has recently been estimated that as much as 90% of the electrical current delivered during tES travels across the skin and therefore bypasses the brain altogether (Lafon et al., 2017; Underwood, 2016). Furthermore, despite the best efforts of researchers to position electrodes at fixed locations on the scalp, electrodes can easily shift during long stimulation sessions, significantly changing the spatial distribution of delivered electrical currents in a manner that is difficult to determine or control (Woods, Bryant, Sacchetti, Gervits, & Hamilton, 2015). This problem of uncertainty around the delivery of electrical stimulation is compounded by the fact that, even if one could be certain about the paths of delivered electrical currents, one cannot be sure about how these electrical currents

will influence brain activity. For example, due to variability in brain morphology across individuals, electrical stimulation delivered from the same scalp positions can have significantly different effects on underlying cortex across participants (Laakso, Tanaka, Koyama, De Santis, & Hirata, 2015; Opitz, Paulus, Will, Antunes, & Thielscher, 2015). Furthermore, the influence of tES on neural activity is not linearly associated with the intensity of stimulation, as increased excitability is often observed at intermediate intensities, but increased inhibition has been reported at higher intensities (Batsikadze et al., 2013). Lastly, even if one could know exactly where and how delivered electrical currents influenced brain activity, it would still be difficult to predict the precise, neural effects of stimulation due to the immense interconnectivity of the brain. For example, even if a given tES procedure influenced neural activity only in occipitoparietal cortex, it is highly likely that this modulation would travel across the brain, reverberating through it in an indeterminate and subject-specific manner. In simple terms, although we commonly worry about issues of "measurement error" in scientific research (i.e. differences between a measured value of a quantity and its true value), studies of neuromodulation techniques (e.g. tES, TMS, drug interventions) can be said to suffer from additional issues of "manipulation error" (i.e. differences between the intended nature of an experimental manipulation and its true consequences).

This uncertainty around the influence of electrical stimulation on brain function can be seen in the varying results of recent neuroimaging studies of alpha-tACS (i.e. the same stimulation procedure used across the experiments of this project). Using functional magnetic resonance imaging (fMRI), Vosskuhl et al. (2016) found that alpha-tACS (i.e. 10Hz; Oz-Cz) significantly reduced haemodynamic activation in visual cortex during presentation of visual stimuli. This finding is consistent with the results of previous modelling studies suggesting that alpha-tACS directs electrical current through occipitoparietal cortex (e.g. Neuling, Wagner, et al., 2012). However, in contrast, a very similar fMRI study by Cabral-Calderin et al. (2016) found that alpha-tACS (Oz-Cz again),

during presentation of visual images, influenced activation mainly in frontal, temporal, and parietal areas. Furthermore, in contrast to both of these studies, Alekseichuk et al. (2016) observed no changes in fMRI activation during a visual perception task while alpha-tACS was being applied, but did observe widespread reductions in activation across the brain following cessation of stimulation. Although these studies did not use identical methods (e.g. differing in stimulation intensities and control conditions), such findings demonstrate the difficulty in determining exactly how alpha-tACS might have influenced brain activity in the current project. It is therefore possible that alpha-tACS did not exert consistent effects on EEG power in my experiments because the effects of this stimulation on brain activity were more variable across participants, or substantially different in nature, to what I intended.

Associations between EEG and behavioural effects of tACS

Such considerations provide a somewhat pessimistic view of the consistency and interpretability of alpha-tACS effects on brain activity. However, in contrast to this view, it must be noted that alpha-tACS was found to exert quite reliable effects on visual attention task performance. Across a range if visual tasks, alpha-tACS was found to limit the slope of changes in performance (e.g. deteriorations) that otherwise occurred during control-tACS. This suggests that the effects of alpha-tACS on brain activity were not as weak and variable as suggested in the previous section. However, if this was the case, why did alpha-tACS exert such different effects on EEG and task performance?

This mismatch between the behavioural and electrophysiological effects of alpha-tACS is perhaps best illustrated by the observation that, in experiments where alpha-tACS did influence visual task performance, these influences were found to be unrelated to changes in EEG alpha power at the individual level. Such findings are not uncommon in the tACS literature. For example, in a recent review, the neural and behavioural

effects of tACS were found to correlate only in a minority of studies (Veniero, Vossen, Gross, & Thut, 2015). The reasons for this might be mundane, such as the simple statistical observation that correlations between two noisy indices are likely to be weak. There may have been issues with the quality of my EEG data given the small number of EEG electrodes used in my experiments (see p.226). Furthermore, tACS-induced artifacts in EEG make it difficult to record online effects of stimulation (Noury, Hipp, & Siegel, 2016) (although see Neuling, Ruhnau, Weisz, Herrmann, & Demarchi, 2016), meaning that researchers must focus on after-effects of stimulation that may be substantially weaker than, or different from, online effects. However, in addition, the observation that behavioural and EEG effects of tACS are often unrelated could also suggest that tACS can exert significant, frequency-specific effects on cognition that are independent of its ability to modulate EEG in a lasting, measurable way. This arguably raises an important challenge to the idea that tACS can be used to assess the causal roles of oscillations in cognition. Specifically, if tACS at a given frequency is found to influence behaviour, but this behavioural effect occurs independently of lasting changes in brain activity at the frequency of stimulation (i.e. as in the current project), it is arguable that such findings cannot be used to infer causal associations between the two (Thut, Schyns, & Gross, 2011).

Implications of behavioural effects on theories of alpha

This last point about causal associations is important given that one of the central aims of this project was to assess the contributions of alpha oscillations to visual attention (see Rationale and Primary Aims; p.3). Because the electrophysiological and behavioural effects of alpha-tACS were unrelated in my experiments, it is perhaps arguable that my results cannot provide conclusive evidence to select between competing theories of the mechanistic roles of alpha oscillations in visual attention. Nevertheless, if one does assume, for the purposes of argument, that the behavioural

effects of alpha-tACS observed this project do reflect the broad associations between alpha oscillations and cognition, my results can be seen to have a number of interesting implications.

No evidence of tACS-related impairments in visual attention

As described in Chapter 2 (see p.50), posterior alpha oscillations have been strongly associated with reductions in visual attention. Supporting this view, sustained attention studies have commonly found that deteriorations in visual attention over time are accompanied by increases in EEG alpha power (Craig et al., 2012; Lim et al., 2013; Wascher et al., 2014). This finding was replicated in a number of my experiments. However, despite this consistent negative association between alpha power and visual attention, I observed no reliable evidence that alpha-tACS impaired visual task performance. Although alpha-tACS limited task accuracy in the second block of Experiment 1, and reduced the slope of improvements in visual search task performance in Experiment 3, these impairments contrasted with the wider protections in task performance that were observed during alpha-tACS in Experiments 1 and 2. Such findings are interesting given that, to the best of my knowledge, no existing alpha-tACS studies have reported impairments in visual task performance. In fact, Kar and Krekelberg (2014) and Müller et al. (2015) found that alpha-tACS improved visual detection and conjunction search task performance. As suggested before, it is difficult to draw strong conclusions from such results about the mechanistic roles played by alpha oscillations in cognition. However, if nothing else, such results are certainly inconsistent with the idea that alpha rhythms primarily reflect processes of attentional disengagement. Arguably, these results instead are more consistent with emerging theories linking alpha oscillations with processes of top-down control and perceptual stability (Chapter 2, p.58 & 63).

Alpha-tACS stabilises visual attention?

This association between alpha and perceptual stability is suggested primarily by the observation that, across the experiments of this project, alpha-tACS appeared to limit changes in visual attention task performance that were otherwise observed during control-tACS. Such effects were observed across a range of tasks, suggesting that the effects are highly replicable and are not restricted to specific, cognitive contexts (e.g. time perception tasks). Possible mechanisms for such effects were described in Chapter 7 (see p.170). Here, I suggested that alpha-tACS might stabilise performance on visual attention tasks by scrambling communication of top-down signals to visual areas that would otherwise bring about reorientation of visual attention (e.g. away from the current task, causing deteriorations in task performance). This speculative hypothesis predicted that the delivery of alpha-tACS during an audiovisual switching task should impair switching between visual tasks, as this stimulation should interfere with processes dedicated to reorientation of visual attention. The results of this experiment did not support this original prediction, with visuovisual vs. audiovisual task switching being unaffected by the delivery of alpha- vs. control-tACS. Consequently, it is possible that alpha-tACS does not exert its effects through stabilisation, or that alpha-tACS only influences changes in attention that occur over long periods of time (e.g. 15 minutes) (Chapter 8; p.194). This latter idea is consistent with the model of Zaehle et al. (2010), which suggests that alpha-tACS influences neural activity through slow processes of long-term potentiation that increase connectivity within neural circuits with a resonant frequency of ~10 Hz (Chapter 3; p.77). However, in contrast to this perspective, it is important to note that I did observe an impairing effect of alpha-tACS on visuoauditory switching accuracy in Experiment 5. Consequently, it is also possible that alpha-tACS does not affect transitions of attention between visual tasks, but instead prevents switching of attention away from the visual domain. As described in Chapter 8 (see p.194), such effects are potentially significant as they could explain why alpha-tACS

supported task performance in Experiments 1 and 2. Specifically, if alpha-tACS impairs switching of attention away from visual tasks, this might suggest that alpha-tACS helps to focus visual concentration by preventing unwanted transitions of attention away from the visual domain. However, given that this finding was not originally predicted, it is difficult to determine the extent to which it can be interpreted. Future studies are clearly needed to assess whether such impairing effects of alpha-tACS on visuoauditory switching replicate across experiments. Nevertheless, given the broad consistency with which alpha/theta-tACS was found, at least to some extent, to stabilise performance on a range of visual tasks (i.e. in Experiments 1, 2, 3, 5, and 6), it seems likely that such replication studies would be successful. If so, I believe the hypothesis that alpha-tACS stabilises visual attention would provide the most parsimonious explanation for the many behavioural effects reported in this thesis.

Effective induction of short-term deteriorations in attention

Following this discussion of the possible implications of this project for theories of alpha, as well as the potential mechanisms that could explain my behavioural effects, I now focus on the broader implications of this project for sustained attention research more generally. Throughout my experiments, I observed consistent changes in task performance from the start to the end of each task session. These changes were expressed most notably in performance deteriorations in Experiments 1, 2, 3, and 6. Such deteriorations were crucial to the operation of this project. Without them, I could not have studied the effects of alpha-tACS on changes in visual attention over time. However, it was by no means certain at the beginning of this project that such deteriorations in visual attention could be reliably observed. Indeed, the fact that such consistent deteriorations in attention were observed in my experiments could be considered one of the central successes of this project.

As described in Chapter 1 (see p.14), a common weakness of many sustained attention tasks is that they do not always induce reliable impairments in performance over time, or must be performed for long periods to induce such impairments. For example, ceiling effects are often observed in performance accuracy on the Continuous Performance Task in healthy adults (e.g. Aman et al., 1984; Ballard, 2001; Kahn et al., 2012). Furthermore, improvements over time in SART performance have even been reported (Helton et al., 2009). Importantly, such issues have also been reported in studies using the CTET (i.e. the task used in Experiments 1, 3, and 6 of this project). For example, although O'Connell et al. (2009) required participants to perform the vCTET for 10 blocks of 3 minutes and 5 seconds each (i.e. ~31 minutes total), these researchers observed no evidence of deteriorations in task performance over the course of an experimental session. Identical results were also reported by Berry et al. (2014), in which participants were required to perform the vCTET for 10 blocks of 4 minutes each (i.e. ~40 minutes total). Such observations of consistent task performance are surprising given the strength of deteriorations observed in my vCTET experiments. These results therefore raise the question: given that my vCTET methods were based on the previous studies of O'Connell et al. (2009) and Berry et al. (2014), why did I observe such different results regarding time-on-task deteriorations?

One possible factor is break duration. In my vCTET experiments, participants were allowed fixed duration breaks of just 40 seconds. This contrasts with Berry et al. (2014), in which breaks lasted 60 seconds, and O'Connell et al. (2009), in which each participant was allowed to choose their own break durations. Task block durations could also have played an important role, given that each block in my vCTET experiments lasted 4 minutes and 50 seconds. This compares to just 4 minutes for Berry et al. (2014) and ~3 minutes for O'Connell et al. (2009). However, it is striking to note that, although significant deteriorations in task performance were observed in my vCTET experiments, my task sessions were significantly shorter than both O'Connell et al. (2009) and Berry

et al. (2014) (i.e. ~20 minutes vs. ~31 & ~40 minutes). Consequently, even with a reduced session length of just 20 minutes, this project suggests that strong and reliable deteriorations in vCTET performance can be induced through the application of long blocks and short, fixed-interval breaks. Given that similarly reliable deteriorations in task performance were also observed in Experiment 2, in which a visual threshold detection task was used, this project also suggests that the application of long blocks and short breaks could be used as a model paradigm to study deteriorations in performance on a range of additional, sustained attention tasks.

FUTURE DIRECTIONS

Following this discussion of the theoretical interpretations of my results, I now consider a number of possible directions for future research. Some of these directions stem directly from limitations of my experiments. For example, given the focus of this thesis on the effects of alpha-tACS on relatively short-term changes in visual attention (e.g. occurring over ~15 minutes of task performance), future studies might benefit from assessing the effects of alpha-tACS long-term deteriorations in attention (e.g. >2 hours), in order to better determine the usefulness of this technique in real-world settings. Furthermore, given the focus of this thesis on alpha oscillations, future studies might also benefit from assessing the effects of tACS across a range of low frequencies (e.g. 1 – 25 Hz), in order to determine optimal stimulation parameters for improving sustained attention. Of relevance to the point is the idea that tACS might have greater effects on brain activity and behaviour when delivered at individualised alpha frequencies (e.g. as in Neuling et al., 2013; Zaehle et al., 2010). In addition, given that the *Starstim*® device, which I used to deliver tACS, allowed recording of EEG activity with just six electrodes, future studies may benefit from studying the effects of alpha-tACS on brain activity using higher-density EEG montages. The use of just six electrodes in this project arguably limited the quality of my EEG data given that, for example, I was not able to clean this

data using methods like independent components analysis. Furthermore, the use of just six electrodes arguably limited the ways in which I could analyse this data, given that methods like spatial localisation and phase-based connectivity require large EEG montages (Cohen, 2014a). However, as stated above, such future directions stem primarily from limitations of the current project. Future studies may also benefit from the pursuit of entirely new methodological directions.

Focal and individualised stimulation parameters

For example, a number of methods have recently been proposed to improve the efficacy and selectively with which electrical currents can be delivered to the brain. Specifically, the spatial resolution of tES may be enhanced by delivering tES through multiple, smaller electrodes (e.g. 1cm^2), positioned in precise configurations on the scalp (Ruffini, Fox, Ripolles, Miranda, & Pascual-Leone, 2014). In one example, researchers targeted lateral primary motor cortex by delivering tDCS through one electrode positioned directly over this area, and four others positioned around it in a square formation (Villamar et al., 2013). In addition, delivery of tES currents to specific areas of the brain may be improved by optimising stimulation parameters for each individual based on previously collected MRI scans. For example, through computational modelling approaches, optimal electrode positioning can be estimated, taking account of individual differences in skull thickness and cortical folding (e.g. Dmochowski et al., 2013). Consequently, where sustained attention tasks have been associated with haemodynamic activity in specific regions of the brain (e.g. Langner & Eickhoff, 2013), these methods of tES localisation and optimisation could be used maximise the effects of tACS on task performance. However, these results would not provide insights into the *mechanisms* by which tACS exerts such effects. To gain such insights, additional methods will be required.

Concurrent neuroimaging and pharmacological interventions

One clear possibility is to record fMRI data during the delivery of tACS. As described earlier in this chapter (see p.219), previous tACS-fMRI studies have shown varying effects of alpha-tACS on haemodynamic activity across the brain (e.g. Alekseichuk et al., 2016). Consequently, although the behavioural effects of alpha-tACS did not correlate with EEG alpha activity across the experiments of this thesis, future tACS-fMRI studies may instead observe correlations with haemodynamic changes in unexpected regions of cortex. For example, given that tES currents are delivered broadly across the brain, it is possible that the behavioural effects of alpha-tACS are mediated by haemodynamic changes in prefrontal regions, rather than changes in occipitoparietal cortex as one might predict. Such findings would provide a more detailed understanding of the neural effects of alpha-tACS, and may facilitate identification of specific brain region for targeting in future tACS studies. However, in addition to these methods of concurrent neuroimaging, the mechanisms by which alpha-tACS exerts its effects could be investigated through concurrent, pharmacological manipulations.

Bauer et al. (2012) recently reported that administration of a cholinergic agonist strengthens the lateralisation of alpha power in visual cortex when participants shift their attention to one side of visual space (while leaving power in all other frequency bands relatively unaffected; Bauer et al., 2012). It could therefore be interesting to measure the influence of cholinergic agonists on the neural and behavioural effects of alpha-tACS. For example, would such cholinergic agonists strengthen the ability of alpha-tACS to increase EEG alpha power? Or, conversely, would a cholinergic antagonist lead to suppression of such tACS-related effects? Such experiments could provide important insights into the neuropharmacological systems that underpin the neural and behavioural effects of alpha-tACS (e.g. cholinergic systems).

Alternative methods of manipulating alpha oscillations

In addition, it is also possible that new insights into the contributions of alpha oscillations to visual attention could be gained by using alternative methods of manipulating alpha oscillations. As described earlier (p 218), there are many difficulties and uncertainties associated with modulating brain activity using tACS. However, it is also possible to influence the phase and power of ongoing alpha oscillations through presentation of flickering images at alpha frequencies. Such flickers, when delivered at ~10 Hz, can entrain the phase of ongoing alpha oscillations, and can be used as in additional tool to assess causal associations between alpha phase and visual processing (e.g. Notbohm et al., 2016). For example, associations between alpha oscillations and rhythmic fluctuations in visual attention have been supported by studies finding that, when people are briefly shown ~10 Hz visual flickers, their ability to detect subsequently presented visual stimuli oscillates in phase with that flicker (Mathewson et al., 2012; Spaak et al., 2014). Given such findings, similar studies could be conducted in future to investigate some of the possible roles of alpha oscillations in visual attention proposed in Chapter 2 of this thesis (see p.44).

For example, as described before, a recent study by Sherman et al. (2016) suggested an intriguing role for alpha oscillations in communicating top-down predictions in visual cortex. In this study, researchers found that an intermediate alpha phase position (0°) was associated with a more liberal response bias to threshold visual targets when these stimuli were expected, but a more conservative bias when these targets were not expected. This finding suggests that prior expectation influence the association between alpha phase and visual target detection. To further investigate such effects, I suggest that a future study could be run in which ~10 Hz flickers are again presented before the delivery of threshold visual stimuli (e.g. as in Spaak et al., 2014). However, some superficial aspect of these flickers (e.g. colour) could signal the likelihood that a

threshold stimulus would subsequently be presented. If prior expectations do indeed influence the association between alpha phase and threshold visual detection, I would expect to observe anti-correlated alpha oscillations in stimulus detection performance following the presentation of visual flickers that indicate an upcoming stimulus is either likely or unlikely. Given the association between top-down processes and acetylcholine, one might also predict that this behavioural effect would be enhanced by administration of a cholinergic agonist (as in Bauer et al., 2012). Such a result would provide evidence that alpha oscillations are mechanistically involved in rhythmic communication of predictions to visual cortex. Furthermore, given that the delivery of flickering images is unlikely to cause distributed changes in neural activity in the same way as tACS, it is arguable that such findings would provide clearer evidence of causal associations between alpha oscillations and visual attention. For example, although the precise mechanisms by which visual flickers influences neural activity are unknown, it is unlikely that such flickers will exert effects on distributed neuropharmacological systems in the same way as tES (e.g. through blocking adenosine A1 receptors; Márquez-Ruiz et al., 2013).

ON THE USEFULNESS OF tACS IN REAL-WORLD SETTINGS

In this final section, I consider the implications of my experiments for achievement of the primary goal of this research project: the improvement of sustained attention in real-world settings. In general, these experiments provide some intriguing insights into the possibility of using tACS for protecting attention from deteriorations over time. In two quite different visual tasks (i.e. Experiments 1 and 2), alpha-tACS was found to limit the slope of deteriorations in task performance that otherwise occurred during control-tACS. Similar results were also observed in Experiment 6 in which, at least at a descriptive level, theta-tACS was found to limit the slope of increases in vCTET RTs over time. Such findings suggest that low-frequency tACS could be used to aid

performance on a diversity of visual tasks in real-world settings. Given that tACS was delivered across my experiments with little discomfort (as reflected in the effective stimulation condition blinding observed across experiments), my studies also suggest that tACS could be applied in real-world settings without causing overt distraction. Nevertheless, in addition to these encouraging conclusions, it must be stated that a number of additional facets of my results call into question the efficacy with which tACS could be used to improve sustained attention in real-world settings.

For example, it is important to note that, in addition to protecting visual attention from deteriorations over time, the results of Experiment 4 suggested that alpha-tACS could also limit the slope of performance *improvements*. Although it is unclear whether these results reflected true impairments in learning (Chapter 7; p.172), such findings suggest the important possibility that, although alpha-tACS may improve visual performance in certain settings, it may also impair performance in other settings. Of relevance to this point is the idea that cognitive enhancement with tES could be a zero-sum game, in which improvements in one cognitive faculty come at the expense of impairments in another (Brem, Fried, Horvath, Robertson, & Pascual-Leone, 2014; Iuculano & Cohen Kadosh, 2013; Sarkar et al., 2014). In addition to this question of collateral cognitive impairments, it is also interesting to note that alpha-tACS, despite supporting visual attention from deteriorations over time, exerted no such effects on auditory attention. This finding was interesting from a scientific perspective, as it suggested that the effects of alpha-tACS on task performance are specific to the visual domain. However, it is arguable that this finding was not ideal if one hopes that alpha-tACS could be used to improve attention in real-world tasks (i.e. which commonly require attention to a complex diversity of sensory inputs). For example, for a soldier on patrol in a hostile environment, their attention should ideally be sustained within all sensory modalities. Nevertheless, in addition to these potential issues around the side effects and modality-specificity of tACS, perhaps the biggest limitation of this method for the

purposes of real-world cognitive enhancement is the weakness with which tACS appears to influence brain activity and behaviour. Across the many experiments of this project, relatively large sample sizes (i.e. ~40) were required to detect relatively weak effects of alpha-tACS on task performance. Descriptively, average improvements in task performance observed in this project were quite small in magnitude. For example, in Experiment 1, alpha-tACS was found to improve task accuracy by ~5%. In Experiment 2, alpha-tACS reduced RTs by ~20 ms. If this method can only induce small improvements in task performance, in a small number of subjects, and within a limited range of contexts, it is arguable that alternative methods of cognitive enhancement may provide greater benefits with reduced costs. For example, it is interesting to note that McIntire et al. (2014) observed much greater and more consistently enhancing effects of caffeine and prefrontal tDCS on sustained attention over substantially longer periods of time (compared with sham controls).

CONCLUSIONS

In summary, this thesis shows that, despite many previous studies reporting consistently negative associations between EEG alpha power and visual attention, electrical stimulation of posterior cortex at 10 Hz does not consistently impair visual task performance. Instead, alpha-tACS appears to prevent changes in visual attention, regardless of whether those changes bring about improvements or deteriorations in task performance. As alpha-tACS was not found to influence rapid switching of attention between visual tasks (i.e. in Experiment 5), such stabilising effects of alpha-tACS on visual performance may only be observed on slow changes in attention that occur over extended periods of time (i.e. > 15 minutes). However, as alpha-tACS was found to impair visuoauditory switching accuracy in Experiment 5, it is also possible that alpha-tACS supports sustained visual attention by exerting instantaneous effects on neural processing that prevent transitions of attention away from the visual domain. Given that

theta-tACS was found to exert weak, but descriptively similar effects to those of alpha-tACS on visual task performance, it possible that the behavioural effects observed in this thesis reflect general consequences of low-frequency tACS (e.g. < 15 Hz), rather than of stimulation at alpha frequencies specifically. Furthermore, the fact that alpha-tACS was not found to enhance EEG alpha power reliably in my experiments means that my results cannot easily be used to infer the mechanistic involvement of alpha oscillations in visual attention. Nevertheless, as noted previously (see p.226), it is possible that several, simple modifications to the methods of this thesis could significantly enhance the effects of tACS on brain activity and behaviour (e.g. individually tailored stimulation parameters). In this way, I hope that the identified weaknesses of this project can help design future experiments in the field, and that the most positive effects of alpha-tACS observed in this thesis can prompt more targeted investigations of how this intriguing method of neuromodulation can be used to influence critical features of human cognition.

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