The efficacy of neuromodulatory techniques for enhancing episodic memory

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Thesis summary

The ability to recollect the personal past, known as episodic memory, is a fundamental aspect of everyday life and is critical to the sense of self. This capacity declines with age and is also affected by several conditions, such as Alzheimer's disease. There is therefore a need to investigate interventions which might enhance memory. This thesis investigates whether electroencephalography neurofeedback (EEG-NF), which involves self-regulation of a target brain state via real-time feedback of an individual's own brain activity; and audio-visual entrainment (AVE), whereby the brain naturally synchronises its dominant frequency with the rhythm of flickering lights and auditory tones, can enhance different aspects of episodic memory.

In **Chapter 2**, a systematic review on episodic memory in healthy and clinical adult populations revealed that protocols varied considerably, and many studies had inadequate design features. The meta-analysis, conducted on studies with an active control group and randomisation/counterbalancing of participants to conditions, revealed a small beneficial effect of EEG-NF on episodic memory. Empirical studies were conducted using EEG-NF (**Chapter 3**) and AVE (**Chapter 5**), during the consolidation period between study and test phases, with the experimental group focused on theta and the active control group on low beta. There was tentative evidence that EEG-NF might be beneficial for episodic memory, once non-responders were excluded, but no evidence for positive effects of AVE. **Chapter 4** explored responder characteristics from the EEG-NF experiment.

The results from this thesis suggest that, as interventions to enhance episodic memory, AVE is not effective with the experimental design and parameters used, but EEG-NF has potential. EEG-NF seemed to selectively enhance free recall and the recovery of contextual information from the study phase, but not old/new item recognition or confidence judgements. However, further research is required to work out the optimal parameters and who might be responsive to this technique.

Preface

Chapter 2

EEG-Neurofeedback has a small but positive effect on memory performance: A meta-analysis of controlled studies in healthy adults. *Online poster presentation at the British Neuroscience Association Festival of Neuroscience, April 2021*.

Jackson L.E., Han Y.-J., & Evans L.H. (2023). The efficacy of electroencephalography neurofeedback for enhancing episodic memory in healthy and clinical participants: A systematic qualitative review and meta-analysis. *Neuroscience & Biobehavioural Reviews*.

Chapter 3

Theta EEG-neurofeedback does not enhance episodic memory performance: Preliminary findings. *Poster presentation at the British Association for Cognitive Neuroscience Annual Meeting, Birmingham, May 2022*.

Chapter 5

No effect of theta audio-visual entrainment on episodic memory performance. *Data blitz presentation and poster presentation at the British Association for Cognitive Neuroscience Annual Meeting, Cardiff, September 2023*.

Contributors

For the systematic review and meta-analysis (Chapter 2), Dr Lisa Evans and Dr Yi-Jhong Han checked random samples of articles to ensure I had both adhered to the review inclusion criteria, and accurately extracted and coded the data, respectively. Dr Lisa Evans and Dr Yi-Jhong Han also contributed some of the writing to the published article.

For the empirical study investigating the effects of electroencephalography neurofeedback (EEG-NF) on episodic memory (Chapter 5), Dr Yi-Jhong Han designed the open-source EEG-NF system, and provided me with the bespoke training and support which enabled me to run the EEG-NF sessions, and collect and analyse the EEG data.

For the empirical study investigating the effects of audio-visual entrainment on episodic memory (Chapter 5), the collection and scoring of the data was shared between myself and Amber Jones. Collection involved participant recruitment and conducting a laboratory-based, computerised memory task, followed by an online memory task via Zoom. Amber and I both scored all the different memory measures independently for accuracy.

I performed all analyses and wrote the thesis.

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Chapter 1: General introduction

1.1 The importance of memories

Our memories play a fundamental role in our day-to-day functioning. Our ability to process and store information related to our experiences enables us to learn about ourselves and the world around us. Having access to our stored memories facilitates information-sharing between ourselves and others, and the ability to learn how to complete tasks and solve-problems. Unfortunately, our memories can sometimes let us down. For example, a person might struggle to remember where they put their car keys, the name of the dish they ordered and enjoyed at a restaurant, or information they previously studied for a presentation. Age-related cognitive decline can often lead to increased forgetfulness or delays in remembering information (Cansino et al., 2009; Prince et al., 2024). Such memory lapses can be a source of frustration and concern for an individual when they occur, especially if they involve a loss of a sense of 'self'. Furthermore, memory can be more severely impaired as a symptom of pathological conditions; for example, depression (Lemogne at al., 2005) and schizophrenia (Achim & LePage, 2005), traumatic brain injury caused by an accident or substance abuse (Fama et al., 2021; Paterno et al., 2018), severely deficient autobiographical memory (Palombo et al., 2015) and neurodegenerative disease such as mild cognitive impairment (Nordahl et al., 2005) and Alzheimer's dementia (Baudic et al., 2005; Greene et al., 1996). The current increase in life expectancy reported by the World Health Organisation (WHO) and the predicted escalation in dementia incidence to over 1.6 million by 2050 by Alzheimer's Research UK, both mean that there is a growing burden on the family and caregivers of those experiencing such memory deficits, and on the healthcare resources that support them. Therefore, given both the importance and fallibility of memory, there is a need to research interventions that could enhance it with the aim of improving these individuals' quality of life.

There currently exists a range of public health information and advice at our disposal regarding ways in which memory might be improved, from getting a good night's sleep (Rasch & Born, 2013) and eating a healthy diet (Huang et al., 2022), to being socially active (Hackett et al., 2019; Zahodne et al., 2019) and playing a musical instrument (Walsh et al., 2019), to the use of pharmaceuticals (Sharma, 2019) or 'nootropics' like Ginko biloba (Field & Vadnal, 1998). An alternative approach for maintaining or improving memory which has risen in popularity over the past decade is cognitive training, informally referred to as 'brain training'. This involves engaging with activities via apps and games (e.g. sudoku), that claim to 'sharpen the mind' by fine-tuning executive functions such as processing speed, attention and working memory. Some studies show positive results that support the effectiveness of cognitive training in young healthy adults (Edwards et al., 2017; Nouchi et al, 2013), gleaned from implementing mental activities such as mental arithmetic, naming items from a category, and game-playing e.g. Tetris. Cognitive training has also been used as part of treatment programmes for individuals experiencing episodic memory deficits, in cases of healthy age-related cognitive decline and forms of dementia, such as Alzheimer's disease (Mendonca et al., 2022). However, there is a lack of generalisable empirical support regarding which type of training works best for whom, and whether these effects transfer onto non-trained tasks or real-life scenarios (Boot & Kramer, 2014; Katz et al., 2018). Fundamentally, evidence regarding whether such brain training subsequently and indirectly enhances episodic memory performance, is mixed (Hampshire et al., 2019b; Simons et al., 2016). Overall, the lack of existing empirical support for a reliable method people can adopt to improve their memory, highlights an important need to investigate techniques for enhancing episodic memory.

The scope of this thesis is to focus on two interventions that propose to directly target the neural mechanisms hypothesised to underlie episodic memory processes. Electroencephalography neurofeedback and audio-visual entrainment are both non-invasive techniques which have been shown to successfully modulate individuals' brain activity via different means. Such interventions enable researchers to investigate and measure a more causal relationship between the intervention and memory performance, to thereby determine more reliably the efficacy of these techniques. Therefore, the main aim of this thesis will be to empirically investigate whether these two interventions can enhance episodic memory performance.

1.2 Electroencephalography neurofeedback

1.2.1 What is Electroencephalography neurofeedback?

Neurofeedback is a technique that utilises a brain-computer interface (BCI) to provide feedback to an individual that represents their real-time brain activity. Neurofeedback systems essentially include elements such as i) brain imaging technology to measure real-time brain activity, ii) a neurofeedback software program to perform online feature extraction of the target brain activity, iii) a computer interface that presents to users their real-time brain activity which is usually represented by visual or auditory means, or a combination of both, and finally iv) the individual themselves, known as ‘the learner’ who self-regulates the target brain activity (Enrique-Geppart, 2017). The aim of neurofeedback is for the individual to learn to generate a pattern of brain activity theoretically linked with a desired behavioural outcome via the process of operant conditioning (Skinner, 1945), described in more detail below (Section 1.2.3.).

Neurofeedback systems can use a range of different neuroimaging techniques to measure brain activity and subsequently modulate certain behaviours. Technological advances in neuroimaging methods have introduced to the neurofeedback domain real-time functional magnetic resonance imaging neurofeedback (rtfMRI-NF), functional near infrared spectroscopy neurofeedback (fNIRS-NF), and real-time magnetoencephalography neurofeedback (rtMEG-NF). Both rtfMRI-NF and fNIRS-NF are characterised by haemodynamic self-regulation i.e. blood oxygen level-dependent (BOLD) data is fed back to the learner which is indirectly associated with neural activity. These methods benefit from high spatial resolution, providing the means to target the more precise location of brain activity in deeper neuroanatomical structures that is linked with certain behaviours, but with low temporal resolution (1-2 seconds, plus 4-6 seconds haemodynamic delay). Accordingly, both rtfMRI-NF and fNIRS-NF have been used to successfully modulate neural activity associated with affect (Weiskopf et al., 2003), cognition (Marx et al., 2015) and motor ability (Mihara et al., 2012). The benefits associated with these techniques are that successful haemodynamic self-regulation effects are achieved quicker than neuromodulation of electrical brain activity, and that they provide more information about underlying function and neural connectivity (Thibault et al., 2016). This is similarly the case for rtMEG-NF which measures the amplitude of magnetic field signals generated by both superficial and deeper cortical areas, thereby providing higher temporal resolution for real-time feedback (on average in less than 50ms) and some degree of localisation of brain activity. rtMEG-NF has also been used to successfully increase source level activity at the primary sensorimotor cortex after three 40-minute sessions using motor imagery, relative to a no-feedback control (Boe et al., 2014). However, research regarding these methods is in its relative infancy and some studies lack replicability (Thibault et al., 2016).

The most extensively studied and long-standing neurofeedback technique is electroencephalography neurofeedback (EEG-NF), which is the focus of this thesis. EEG-NF involves electrodes being placed on the learner's scalp which record the real-time electrical activity generated by pyramidal neuronal cells within the brain's cortical regions (Berger et al., 1929). The target brain activity which is fed back to the learner can be calculated in real time in different ways; for example, this activity can be represented by event-related potentials such as slow cortical potentials (Kotchoubey et al., 2000, 2001), connectivity-based coherence (Kober et al., 2020), or more frequently by way of oscillatory power or amplitude. Neural oscillations are rhythmic patterns of activity, or waveforms, generated by the synchronous firing of neurons. They are characterised by their frequency which is measured in Hertz. Established frequency bands include delta (1-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (15-22 Hz) and gamma (25-100 Hz). There is evidence to support the functional role of different neural oscillations in memory processes (Fell & Axmacher, 2011; Klimesch et al., 1994, 1997, 1999, 2001; Nyhus & Curran, 2010) which can inform the target brain activity to be adopted in various EEG-NF training protocols. The first demonstration of neurofeedback in human participants involved them being trained to achieve alpha brain activity by rewarding them with the sound of a bell (Kamiya, 1968). These initial findings inspired subsequent research into EEG-NF which has increased exponentially over the past 20 years and provides some mixed evidence regarding the effectiveness of EEG-NF on behavioural outcomes. EEG-NF has been applied in the clinical domain to treat patients with a range of psychiatric and neurological disorders, including attention-deficit hyperactivity disorder, epilepsy, major depressive disorder, post-traumatic stress disorder and alcohol dependence (Marzbani et al., 2016; Thibault et al., 2016). It has also generated enhanced performance in healthy populations in areas such as mental rotation (Hanslmayr et al., 2005), music (Egner et al., 2003) and memory (Yeh et al., 2021). The key benefits of EEG-NF are that it offers high temporal resolution feedback from selective areas of the cortex and is cost-effective. Portable, user-friendly devices, or 'home-kits,' are already currently available (e.g. Muse, NeuroSky and Sens.ai). This makes EEG-NF a promising intervention for modulating desired behavioural outcomes in both research and domestic settings. However, while some of the research findings are promising these need to be examined in more detail and the design of the studies considered to ensure that the conclusions made are justified. In the following section some key methodological features of EEG-NF experiment are outlined, such as the use of a control group, blinding and training amount.

1.2.2 EEG-NF training and methodology

A crucial feature of any EEG-NF experiment is the use of a control group or condition, to compare the effects of EEG-NF training both on a neurophysiological and a behavioural level. More recently, it is being acknowledged that the use of an active control is key, whereby control participants have the exact same schedule as the experimental participants during which they are involved in an active task (Ros et al., 2020; Sorger et al., 2019). The different types of active control include: a contingent sham, whereby participants receive feedback of their own brain activity from a frequency that is not thought to be related to the target behaviour; a non-contingent sham, whereby participants receive feedback but not linked to their own brain activity e.g. often from a previous participant, known as 'yoked' feedback which ensures all participants receive the same feedback experience; an inverse sham, which involves participants receiving the inverse of the target brain activity to test whether this has the opposite effects to that expected of the brain activity of interest; and finally a non-EEG-NF control such as mental rehearsal or fitness activities (Thibault et al., 2016). These control features serve to maintain motivation and rule out the possibility that placebo and non-specific effects are driving any positive outcomes (Enriquez-Geppart et al., 2017; Thornton et al., 2018).

Due to the dynamic nature of the EEG-NF task, at least single blinding, whereby participants are unaware of whether they are in the experimental or control group/condition, is vital to avoid demand characteristics and placebo effects affecting participants' performance on the task. This is particularly important for non-contingent sham controls to ensure the participant does not guess they are in the control group by detecting a lack of agency during the task (Sorger et al., 2019; Thibault et al. 2016). Double blinding, whereby the experimenter is also unaware of whether the participant is being tested under the experimental or control condition, serves to avoid any biases occurring during participant-experimenter interactions during EEG-NF which may influence participants' performance. Both between- and within- participants experimental designs are used across EEG-NF studies, with some adopting robust features such as randomisation of participants to groups and counterbalancing conditions, respectively. These features are important to avoid the influence of other participant characteristics (e.g. age and gender) and selection bias when allocating participants to groups, and order effects (e.g. practice and fatigue) in a within-participants design. Whilst between-participants designs require more participants for sufficient statistical power, there is less risk of participant attrition as participants perform under only one condition. Within-participants designs, on the other hand, are statistically higher powered with less participants and inter-individual differences are controlled for. However, there is a higher risk of drop-out, and unblinding given that participants are required to perform under both the experimental and control conditions (Goodwin & Goodwin, 2018).

There is a high degree of variability in the study design features used in EEG-NF experimental research. An EEG-NF training session typically comprises approximately 30 minutes of neurofeedback, often divided into blocks of between 3 and 10 minutes with a rest between blocks. Some studies have included a single session (Escolano et al., 2014a; Rozengurt et al., 2017); however, many include a schedule of EEG-NF sessions which can span a few days a week, and last up to several weeks (Bearden et al., 2003; Deng et al., 2014). The timing of the EEG-NF training sessions often occurs immediately before the testing of neurophysiological and behavioural changes. Further tests can be administered at various time-points including 24 hours or one week following EEG-NF training, and up to several months, to test for any persistent effects. A baseline neurophysiological and behavioural measurement is normally taken pre-EEG-NF training to measure any positive or negative changes in these measurements following the intervention. In the case of episodic memory studies which aim to measure the retrieval of new information that is encoded prior to the intervention e.g. the EEG-NF takes place between the study and the test phase, absolute scores taken post-intervention represent performance.

The measurement of electrophysiological activity, for the purposes of both online feedback and offline analysis, involves different methods. Firstly, the electrodes used to measure the target brain activity during online feedback can range from one lead electrode to a cluster, depending on the cortical region/s in which the activity of interest is most active (Enriquez-Geppert et al., 2017). Electrode clusters can also serve to account for individual differences in activity, increase signal-to-noise ratio, and improve source localisation (Enriquez-Geppert et al., 2017; Song et al., 2015). Similarly, for offline data analyses of the electrophysiological data in experimental settings, standard whole head EEG recordings are taken using the international 10-20 system (Jasper, 1958), and montages specific to certain behavioural inquires. These provide better quality data representing the original signal for determining both the success of self-regulation during the EEG-NF training session and the neural correlates of the behaviour of interest following EEG-NF feedback (Acharya & Acharya, 2019). Online feature extraction of oscillatory activity can be calculated using fast Fourier transform, whereby the electrical signal captured by the EEG signal is transformed from the time-series domain to the frequency domain. This involves measuring the strength of the signal (e.g. amplitude or power) for each frequency unit (or band) of interest and can be displayed as the power spectral density (Baher et al., 2012; Jain et al., 2024). Wavelet transformation is a more sensitive method which achieves the same goal but provides flexibility in handling signals with sharp spikes and discontinuities, and by capturing information on when frequencies occur (Guo et al., 2022). The quality and precision of the signal measured and fed back to the participant can depend on several factors, and this can vary across studies (Rogala et al., 2016). These include the sample rate i.e. the resolution of the signal representing the underlying brain activity (Weiergraber et al., 2016); the length and time-smoothing of the windows used during fast Fourier transform to sample the signal (Ouyang et al., 2022; Pant et al., 2024); and the artefact control/rejection parameters used to increase the signal-to-noise ratio of the brain activity data e.g. ocular and body movement inhibit bars, and simple threshold values (Paluch et al., 2017).

The modality of the feedback can take the form of a visual computer display e.g. a 2D moving vertical bar or 3D rollercoaster, an auditory tone, or haptic sensations. This feedback can be continuous as a real-time stream of feedback information, or discrete such as a digital counter showing the number of times the threshold has been met. Threshold setting is a key feature within an EEG-NF protocol, as it determines at what point the learner receives positive feedback for generating the target brain activity. The pre-set threshold represents the goal that participants aim to achieve as per EEG-NF instructions. In some studies, this remains at a fixed level, often at 80-90 % of the value measured in the previous block, to allow headroom for an increase. However, in some EEG-NF studies the threshold is dynamically adjusted to account for how successful or not individuals are at self-regulating the target brain activity, and thereby decreases or increases to make it easier or harder to meet the threshold, respectively. It is important that the level of difficulty set by the threshold is appropriate and that the feedback is timely to optimise the success of EEG-NF training (Bauer et al., 2016; Davelaar, 2018), described in more detail in Section 1.2.4. A more in-depth evaluation of the use of various methodological features across studies examining the effect of EEG-NF on episodic memory performance, is provided in Chapter 2 of this thesis.

1.2.3 What are the underlying mechanisms of EEG-NF?

Operant conditioning is the predominant theory in the literature that attempts to explain the possible mechanisms underlying neurofeedback training. This theory also explains learning in a multitude of contexts outside of neurofeedback whereby it is proposed that the process involves three key elements: i) a discriminative stimulus, ii) a response, and iii) a reinforcer (Skinner, 1945). In relation to EEG-NF, individuals receive real-time positive feedback when their neural activity, detected by the EEG-NF system, reaches a pre-determined threshold. This threshold indicates the minimal amount of target brain activity required that is associated with the desired behavioural outcome. According to this theory, following repeated and timely positive feedback, the target brain activity is reinforced in response to the feedback during EEG-NF training, which in turn elicits the desired behavioural outcome.

This associative learning relies on the Hebbian principle that if the firing of a post-synaptic neuron repeatedly follows the firing of a pre-synaptic neuron, this strengthens the synaptic connection increasing transmission of information between the two – 'neurons that fire together wire together' – Hebb, (1949). This reinforcement is facilitated by the concept of 'prediction error' whereby as associative learning develops, as does expectation, and dopamine bursts are generated via the striatal system in response to both unexpected rewards and reward predicting stimuli (Daniel & Pollmann, 2012). Furthermore, spike-timing dependent plasticity relies on the precision of firing times of the presynaptic and postsynaptic neurons occurring simultaneous to the release of dopamine for optimal learning and behavioural modification (Ashby & Ennis, 2006). Specifically, within the context of EEG-NF, this example of long-term potentiation manifests as EEG-NF learners generating the optimal target brain activity the more it is reinforced by contingent positive feedback. On this basis, a crucial element of the EEG-NF training protocol is therefore the latency between the measurement of on-going target brain activity and the presentation of this to the individual by way of feedback. This stands EEG-NF in good stead, given the high temporal resolution of EEG.

In addition to operant conditioning, other theories have been proposed to explain the mechanisms underlying neurofeedback, which differ in the extent to which they claim the user is consciously aware of the learning process, as opposed to learning being unconscious, automatic or incidental (Sitaram et al., 2016). For example, the awareness theory (Black et al., 1977, cited in Beatty, 1983) suggests that the learner becomes aware of the physiological change in the brain in response to the feedback and has subsequent voluntary control over the response. The dual process theory (Lacroix et al., 1981) supports the contribution of both conscious and unconscious learning; a trial-and-error approach whereby learners consciously test the effectiveness of individual mental strategies until they find one that works i.e. receives the most positive feedback, at which point this strategy becomes automatic. These somewhat opposing theories bear relevance to the dichotomous debate surrounding whether the use of EEG-NF strategies is conducive to learning to self-regulate a target brain state i.e. conscious awareness of learning (Lubianiker et al., 2022) or whether self-regulation is more easily achieved by being guided by the feedback i.e. unconscious learning, detailed below in Section 1.2.4.

1.2.4 The phenomenon of EEG-NF non-responders

The fundamental element for successful self-regulation to occur, and for the desirable behavioural outcome to be achieved, is for the individual to be able to modulate their brain state in the first place. A key issue is that some studies report that approximately a third of individuals are unable to achieve the target brain activity during EEG-NF training (Enriquez-Geppert et al., 2014b; Zoefel et al., 2011). In truth, this estimation could be more given not all studies report this information (see Chapter 2). Herein exists a stumbling block regarding EEG-NF as an intervention. This reliance on the learnability of the individual creates an unknown quantity in EEG-NF research and the consequences are significant given non-responders either dilute the effect of EEG-NF training on behavioural outcomes, or need to be removed potentially increasing the number of participants who need to be tested to achieve adequate statistical power. Importantly, this issue renders the utility of EEG-NF questionable if it is not effective for a large proportion of individuals. It is not currently clearly understood why some learners are unable to self-regulate their brain activity during EEG-NF. This could potentially be attributed to the quality of EEG-NF training, such as methodological parameters and instructions/strategies (Autenrieth et al., 2020; Gruzelier, 2014b); individual differences, such as personality or cognitive abilities (e.g. attention) (Kadosh

& Staunton, 2019); or it could be the interaction between the learner and the training environment influencing outcomes, such as the individual's current state of mind (e.g. mood or motivation) (Kadosh & Staunton, 2019) or placebo effects (Thorton, 2018). A small amount of research has been undertaken regarding psychological traits, or states, that may contribute to one's ability to self-regulate their brain activity as well as the use of strategies during EEG-NF training, and this research is discussed in more detail below.

Fundamentally, EEG-NF is a learning exercise and requires the user to be engaged with the task; otherwise, it is unlikely that key mechanisms of the operant conditioning process required for reinforcing the desired behaviour will be effective. Flow state, described as an optimal state of effortless attention (Bruya, 2010), is achieved when goals of the task are clear, feedback regarding performance is received immediately, and the individual's subsequent perceived level of task difficulty and skill are balanced (Csíkszentmihályi, 1990). This state, the 'Goldilocks zone', is associated with a high level of learning and accuracy on a task (Wilson, 2019). Bauer et al (2016) demonstrated this during an EEG-NF task, by adjusting the feedback threshold to match the level of perceived difficulty as informed by participants' self-reported mental effort. Aligning the task with the users' perceived level of difficulty served to improve their ability to self-regulate their brain activity in line with the target frequency.

Other factors that may affect an individual's engagement with the task are mood and motivation. Theoretically, these have strong links with learning, based on the core elements of the classic trilogy-of-the-mind – 'cognition, conation, affect' (Hilgard, 1980). Motivational behaviour can be characterised as reward-seeking behaviour which forms the basis of operant conditioning involved in the EEG-NF process. Nijboer et al. (2008) revealed participants' ability to regulate sensorimotor rhythm (SMR) by visualising movement was positively associated with higher scores on the 'mastery confidence' subscale of the Questionnaire for Current Motivation (QCM; Rheinberg, 2001), whereas 'fear of incompetence' impaired their performance. Improved performance on the SMR-BCI task has also been linked with the two remaining subscales of the QCM: interest (Leeb at al., 2007) and perceived task challenge (Kleih et al., 2010). Mood has also been shown to influence EEG-NF training, with positive affect improving performance (Nijboer et al., 2008) and negative affect impairing it, such as participants' level of anxiety and depression (Gruzelier et al., 1999), and tension (Jeunet et al., 2015). However, this limited research involves some small samples in clinical populations and issues with replication, and some studies found no link between motivation and neurofeedback performance (Enriquez-Geppert et al., 2014b; Hammer et al., 2012). Further systematic investigation into the influence of mood and motivation on EEG-NF training performance is therefore needed to draw stronger conclusions.

In addition to state-based factors, the influence of fixed, trait-based factors such as attentional ability and personality on EEG-NF performance has been examined. Concerning the former, the assumption would be that being inherently able to sustain one's attention could increase EEG-NF self-regulation success. Daum et al. (1993) used the digit span (Ebbinghaus, 1885/1964) and block tapping (Corsi, 1973) tasks to measure drug-refractory epilepsy individuals' attention span and found that those who scored higher on these tasks were better able to control their slow-cortical potentials. Furthermore, Hammer at al. (2012) found that higher scores on the attitudes to work objective personality test AHA1 (Kubinger and Ebenhöh, 1996) was a significant predictor of SMR-BCI performance. Whilst these findings provide some insight, they are based on a clinical group of epilepsy patients which lacks generalisability, and an indirect measure of attention. A few personality traits have been linked with improved EEG-NF performance. Tipple (2024) used the NEO PI-R personality factors (Costa Jr & McCrae, 1992), self-regulation questionnaire (Brown et al., 1999) and the need for cognition scale (Cacioppo et al., 1984) to measure participants' psychometric traits. Frontal-midline theta responders scored higher on the personality trait of conscientiousness, and on the decision-making and goal-setting subscales. Furthermore, self-regulation ability was associated with fluid intelligence in a gamma EEG-NF protocol (Khodakarami & Firoozabadi, 2020) and self-reliance in a SMR-BCI task (Jeunet et al., 2015). Finally, locus of control i.e. one's belief in their ability to control the visual or auditory stimuli reflecting their brain state, was found to improve their ability to move an on-screen cursor using motor imagery (Burde & Blankertz, 2006); however, Witte et al. (2013) revealed a negative effect in a similar EEG-NF task. The variability in these findings (see review by Kadosh & Staunton, 2019) prevents strong conclusions being made with regard to the influence of trait-based factors on responder ability, warranting further exploration.

The effect of neurophysiological factors on individuals' EEG-NF responder ability have also been investigated. Chikhi et al. (2023) reported that the resting amplitude of high alpha frequency predicted an amplitude increase during training, and in other studies a similar result was found for the alpha (Nan et al., 2018; Wan et al., 2014), beta (Nan et al., 2015; Reichert et al., 2015) and SMR (Reichert et al., 2015) target frequency bands. Another study found that resting state theta amplitude measured at the left dorsolateral prefrontal cortex was associated with a reduction in the target slow brain waves using a multisensory neurofeedback device called AutoTrainBrain (Eroglu et al., 2018). However, a study by Gevensleben et al. (2009) found that initial increases in theta activity, rather than resting state theta activity, predicted subsequent self-regulation success (see reviews: Alkoby et al., 2018; Weber at al., 2020). Further exploration is required to determine if resting state activity can be a reliable factor to pre-determine whether an individual will respond positively to EEG-NF training of target frequency bands.

Finally, strategies have been suggested during EEG-NF training to help individuals self-regulate the target band (Eschmann et al., 2020; Rozengurt et al., 2017). However, research investigating which strategies increase participants' ability to self-regulate their brain activity is limited and inconclusive (Autenrieth et al., 2020; Chikhi et al., 2023; Kober et al., 2013). Subsequently there is no official empirical guidance to determine which strategies facilitate the operant conditioning process during EEG-NF training. Critically, findings relating to successful strategies could depend on the specific EEG-NF protocol. For example, Autenrieth et al. (2020) found in a single SMR-NF session the most efficient strategies reported by participants fell under the categories of breath ('conscious breathing or the active control of breathing'), relax ('the feelings of turning off different body parts or the stream of thoughts, the search of a comfortable sitting position and relaxing of the face, neck and other body parts'), and cognition (the occurrence of thoughts, imagery, and memories not related to the task). Chikhi et al. (2023) found that certain strategies were linked to improved self-regulation of higher alpha amplitude, namely those under the banner of ‘cognitive’ (i.e. the participant performs a task requiring cognitive effort such as mental calculation, course recall) and ‘memories’ (i.e. the participant remembers past events). Furthermore, relaxation and mental arithmetic have been associated with increased theta activity, whereas beta activity has been associated with concentration levels (Rozengurt et al., 2017).

Interestingly, Chikhi et al., (2023) also included a ‘no strategy’ condition which favoured the EEG-NF ‘Learner’ group. This finding suggests that more effective self-regulation from EEG-NF training can be experienced when participants engage with the implicit learning processes of operant conditioning, rather than become overloaded with different strategies to try (Hardman et al., 1997; Kober et al., 2013). This is supported by Davelaar et al. (2018) whereby non-learners described their experience as more deliberate and effortful, whereas learners were guided more by their senses. In contrast, Lubianiker at al. (2022) propose that explicit representational learning whereby learners develop an awareness of the link between internal actions (i.e. mental strategies) and subsequent reward, can enhance EEG-NF success.

The research detailed above demonstrates that many factors and their effect on EEG-NF responder ability have been examined but there are only a small number of studies focused on each and the findings are mixed. Furthermore, a critical issue is that there is no agreed operational definition of what is a responder and what is a non-responder. This can depend on the measurements and contrasts used to calculate successful self-regulation; for example, an increase in target activity during or post EEG-NF training, and by what magnitude. This is an essential consideration to be able to generalise findings relating to responder ability, and ultimately address the important question regarding EEG-NF in terms of who are the optimal learners, and what are the factors that predict learnability? This is key to improving the success of EEG-NF training (Friedrich et al., 2014). The issue of non-responders and what factors might be associated with responder ability is considered in Chapter 4.

In conclusion, there is still debate surrounding the efficacy of EEG-NF training on target brain activity, and in turn behavioural effects. To monitor and assure the validity and effectiveness of an EEG-NF protocol, EEG-NF success can be indexed by two measures: band specificity and cognitive specificity/interpretability (Gruzelier, 2014a, 2014b). Band specificity or 'trainability' requires that during EEG-NF training there should be predicted changes in the trained EEG frequencies, while EEG frequencies which are not used as feedback frequencies, should not be affected by the training i.e. 'independence' (Zoefel et al., 2011). Cognitive specificity/interpretability requires that expected changes are observed in cognitive ability (or desired behaviour) based on the proposed role of frequency bands in such behaviours e.g. episodic memory. Although reviews have been undertaken to define, synthesise and evaluate the various study and protocol characteristics to untangle and draw conclusions about what is effective, or ineffective, in EEG-NF empirical research (Enriquez-Geppart et al., 2017; Gruzelier, 2014a, 2014b; Ros et al., 2020 – also see Chapter 2 of this thesis), questions remain surrounding the impact of the various factors and ultimately who does EEG-NF work for?

Overall, there is an important need to build on the existing empirical evidence to determine the efficacy of EEG-NF training on indices of both successful self-regulation of the target brain state and the enhancement of the desired behaviour in line with previous findings. Further research is required adopting more robust experimental procedures and by gathering more information on EEG-NF responders to inform the future development of targeted, effective protocols which could optimise the beneficial effects of EEG-NF for both healthy and clinical populations.

1.3 Entrainment of oscillatory activity

1.3.1 Neural entrainment

Rhythmic activity is a fundamental feature of both our internal and external environments; from our breathing and heart rates, and sleep-wake cycles (i.e. circadian rhythms) to how we receive and process sound and light from the physical world around us (Lakatos et al., 2019). Oscillatory activity in the brain is known to play a functional role in a variety of mechanisms that underlie our daily interactions with our environment. Theoretically, having control over this oscillatory activity could therefore influence these interactions and our subsequent behaviour.

An alternative technique to EEG-NF which also aims is to modulate neural oscillatory activity is neural entrainment. Neural entrainment occurs when a population of neurons in a stimulated region adopts the phase of an entraining stimulus. As the strength and phase alignment of the oscillatory activity coupling the external stimulus and the internal rhythms increases, so does the entrainment effect (Hanslmayr et al., 2019). Brain entrainment differs from classical phase synchronisation in that it is unidirectional (i.e. internal rhythms are driven by external rhythms), and the internal rhythms being entrained are self-sustained oscillators (i.e. they already naturally exist) (Lakatos et al., 2019). Entrainment can be achieved using non-invasive techniques such as transcranial electric and magnetic stimulation (tES and tMS, respectively). During tES, weak electrical currents are administered via scalp electrodes, and magnetic pulses applied during tMS via a coil which induces electrical activity in the targeted neural tissue. Deep brain stimulation (DBS) is an invasive technique which involves electrical stimulation of both cortical and subcortical regions via depth electrodes already inserted into the brains of neurological or psychiatric patients, such as in epilepsy or major depressive disorder. An alternative, more user-friendly and non-invasive technique for entraining the brain is sensory stimulation. This method can be used to entrain the brain via stimulation via one of more of the senses. For example, stimulation can be auditory, visual, or haptic (Hanslmayr et al., 2019).

1.3.2 Audio-visual entrainment

Audio-visual entrainment (AVE), which is the focus of the second intervention examined in this thesis, refers to the observation that oscillatory activity in the brain will naturally synchronise its dominant frequency with the rhythm of periodic external stimuli, such as flickering lights and auditory tones. Visual flicker involves a light stimulus flashing at a specific frequency and auditory flicker constitutes regular beats of a single tone at a specific frequency, known as isochronic tones (Siever & Collura, 2017). If the stimuli occur repetitively at a rate high enough to sustain power i.e. the event-related potential generated by the stimulation does not revert to baseline levels, the elicited feedforward response which can be detected by Fourier analysis, is called a steady-state evoked potential, or field for magnetic fields measured by MEG. In contrast to spectral changes engendered by EEG-NF, steady-state evoked responses have excellent signal-to-noise ratios, relative immunity to artifacts due to their high spectral specificity, and are almost instantaneous (Regan, 1989). The effect of entrainment, in terms of the intensity of a neural signal induced by an external stimulus, can be measured by the power of certain frequencies, or frequency bands, of interest. These frequencies can be entrained by manipulating external stimuli. For example, cartesian gratings induce sustained narrowband gamma band activity (30–70 Hz) in the visual cortex (Gulati & Ray, 2024), or as with AVE, the frequency of both flickering light and auditory tone stimuli can be set to pulsate at the desired entrainment frequency.

In support of both the immediate and short-term effects of AVE, Teplan (2006) revealed using EEG measurements that stimulation at narrowband theta frequency (4 Hz) over 25 sessions increased this frequency 25-fold during AVE, and cross-hemisphere theta coherence (4-6 Hz) significantly increased in central and parieto-occipital areas post-AVE, both compared to pre-AVE levels. This provides support for not only the strength and reliability of the entrainment response, but also possible cortical spread of theta oscillations, in theory via the thalamus, that originally present within sensory regions in the form of steady-state evoked potentials when audio and visual stimuli are received via the retina and cornea, respectively. Furthermore, human intracranial EEG (iEEG) - an invasive yet more precise measurement whereby electrodes are surgically affixed to the surface of the brain to measure electrical activity from the cortex - has detected power and phase synchronisation changes during monaural and binaural beat stimulation, where these rhythms are not exclusively induced in sensory regions but are also transmitted downstream to deeper brain regions, for instance the hippocampus (Becher et al., 2015). Such cortical spread can be explained by the concept of ‘travelling waves’, where theta and alpha oscillations have been shown to propagate across the cortex (Mohan et al., 2022). Moreover, auditory and visual flicker at gamma frequency (40 Hz) has been shown to have a suppressive effect on β-amyloid plaques and modification of microglia, demonstrating that visual stimulation at this frequency can modulate activity at a cellular level, although these findings need to be replicated in humans (Iaccarino et al., 2016).

The emergent therapeutic technique that is AVE is supported by some empirical findings, demonstrating positive effects on a range of behaviours (see review by da Silva et al., 2015). Golovin et al. (2015) showed a significant increase in cognitive functions such as attention switching and visuo-motor response speeds in track and field athletes after daily 25-minute sessions of 3-13 Hz AVE across three months, compared to a control group. Promising results were also revealed after four weeks of 30-minute nightly AVE sessions in reducing self-reported symptoms of insomnia and chronic pain (Tang et al., 2014). AVE has similar benefits to EEG-NF, whereby this technique can induce neural activity in a safe way and is portable, user-friendly and relatively affordable. Commercial AVE devices which are currently available for use within a domestic setting, are the DAVID devices (https://mindalive.com). It is claimed that these devices can enhance a range of physiological and psychological functions, such as concentration, alertness, mood, relaxation and sleep. These outcomes are proposed to be achieved by selecting an inbuilt program, such as: ‘brain booster’ to improve mental functioning and memory (30 mins of left side: 14-10 Hz, right side: 19-10 Hz); ‘sharpen the mind’ to energise (20 mins of 19-21 Hz); ‘mood booster’ to reduce negative emotions (4 mins of left side: 10 Hz, right side: 18 Hz); ‘coffee break alpha’ to facilitate relaxation (15 mins of 10 Hz) and ‘Delta’ to assist sleep (45 mins of 3.5 Hz). Users are required to sit or lie down in a comfortable position in a darkened room and attend to the lights and sounds delivered via a custom eyeset and headphones. This can involve individuals keeping their eyes open or closed, depending on the level of comfort. The duration and frequency of each entrainment session depends on the needs of the user and can be set manually. For the purposes of research, this is a useful feature given that sessions can be customised to ensure experimental participants are entrained by the specific frequency of interest, and control participants are entrained by an unrelated frequency. To provide proof of concept and evidence of entrainment of the desired frequencies, individuals' brain activity can be monitored via EEG during the entrainment session. Subsequent analysis of the power spectral density can therefore demonstrate whether entrainment of a certain frequency indeed generated a significant increase or 'peak' in the frequency of interest.

This technique therefore holds promise as one which can be tested as an intervention to improve a range of human behaviours in both healthy and clinical populations. The device I opted to use in this study (https://mindalive.com/products/david-live) and versions thereof are the products of over 20 years of research and development, with studies conducted during that period demonstrating its positive effects on a range of behavioural outcomes. For example, the effects of AVE have been investigated for: chronic pain management (Boersma & Gagnon, 1992); the treatment of various phobias (Wolitzky-Taylor et al., 2008) and seasonal-affective disorder (Berg & Siever, 2009); executive function in children with autism (Naeeimi et al., 2013), attention and concentration in chronic fatigue syndrome (Trudeau et al., 1999); and memory enhancement in ageing adults (Palmquist et al., 2014). Some studies involved input from the founder and company selling the devices (https://mindalive.com); therefore, more independent investigation is needed to provide an objective and unbiased reflection of the efficacy of these devices to support their current application.

1.4 Episodic memory

1.4.1 Stages of memory processing

As discussed, our memories are important for many aspects of day-to-day human functioning, including learning new information, undertaking practical tasks and problem-solving. Our understanding of how we achieve this is based on a long history of memory research. According to the multi-store memory model (Atkinson & Shiffrin, 1968), fundamentally, the memory system is made up of a sensory, a short-term and a long-term memory store. The three stages of information processing in the memory system are: encoding, storage and retrieval. During the initial stage of encoding, information is received via the senses and processed by way of visual or acoustic coding i.e. sensory memory. These sensory representations can then be stored in short-term memory for between 15 and 30 seconds, with a capacity of 7 (+/- 2) items at any one time (Miller, 1956). In the absence of rehearsal or encoding into long-term memory, information held in short-term memory is susceptible to interference and decay given its transient nature (Atkinson & Shiffrin, 1971). However, one benefit of the durability and accessibility of this memory store is that it enables information stored therein to be manipulated in real-time to facilitate mental operations such as problem solving and reasoning, known as working memory. This is a self-contained, multi-component system, that includes the central executive, visuospatial sketchpad, phonological loop, and episodic buffer (Baddeley & Hitch, 1974; Baddeley, 2003). Crucially, for information to survive beyond short-term memory, it must be transferred to long-term memory via the process of consolidation during the retention period (Atkinson & Shiffrin, 1971). This can be achieved via mnemonic exercises such as rehearsal of information, or elaborative encoding which involves associating new information with existing information (e.g. the memory palace). The latter utilises semantic coding and thereby creates a deeper level of information processing (Craik & Lockhart, 1972). Consolidation can also occur during sleep or a relaxed waking brain state (Carr et al., 2011; Rasch & Born, 2013). Once information is stored in long-term memory, it can last indefinitely and forms the core basis of our ability to learn.

1.4.2 Long-term memory – what is episodic memory?

Our long-term memories consist of different types which are defined by their specific functional roles in our day-to-day lives. An influential theory of memory suggests that there are three types of long-term memory: episodic, semantic, and procedural memory (Tulving, 1972). Episodic memory is a type of explicit, declarative long-term memory which involves conscious recollection of experiences and events, or 'episodes', in our personal past; including what we did, where and with whom (Tulving, 1972). By processing and storing both temporal and spatial contextual information relating to an experience or an event, we create a coherent narrative structure which is key to developing our representation of our 'self' in subjective time - including the past, the present and the future. The key feature that separates episodic memory from other types of memory is that it is characterised by ‘autonoetic consciousness’, which is a form of self-knowing that enables behaviours such as mental time travel, self-projection and episodic future thinking via the reflection of our own memories which can subsequently influence our behaviour (Tulving, 1985).

Episodic memory differs from semantic memory, another type of explicit, declarative long-term memory, which is our memory of specific facts, concepts and general knowledge which we have acquired during our lives (Squire, 1992b). In contrast, semantic memories are not tied to a particular time or place i.e. they have no temporal or contextual structure. Given they are shared across individuals, by their nature they are directly opposed to episodic memories which are exclusive or unique to an individual’s experience i.e. autobiographical content (McRae & Jones, 2013). Semantic memory is supported by ‘noetic consciousness’ which is an awareness of the internal and external world in which we exist (Tulving, 1985). The third type of long-term memory is procedural memory, which differs from both episodic and semantic memory in that it is implicit i.e. no conscious effort is involved. This ‘anoetic consciousness’ or ‘non-knowing’ underscores the automatic nature of procedural memory which is generated by stimulus/response behavioural associations on the sensory level (Tulving, 1985). Procedural memory therefore involves ‘knowing how’ to complete different tasks i.e. our memory of motor skills (informally, ‘muscle memory’). In this regard it is prescriptive rather than declarative, ‘a blueprint’ for determining future behaviour (Tulving, 1985).

Both episodic and semantic content can be simultaneously accessed during long-term memory retrieval. For example, we might recall bumping into a friend who was also walking their dog in the local park which was unusually busy, and the weather was bright but chilly (episodic content). We might also remember it was 26th December, which is Boxing Day, and our friend was George from work who was walking his labradoodle called Hugo, a far bigger dog breed than our chihuahua called Keith (semantic content). Our procedural memory in this scenario is facilitating both our ability to talk to George and walk whilst controlling a dog on a lead.

1.4.3 Neural mechanisms of episodic memory

In terms of neural structures, it is known that episodic memory processes take place in the medial temporal lobe - including regions such as the hippocampus, and the entorhinal, perirhinal, and parahippocampal cortices - the retrosplenial cortex, left lateral parietal cortex, posterior cingulate, precuneus, and medial prefrontal cortex (Ranganath & Blumenfeld, 2008; Simons et al., 2022). Whilst these core regions collectively enable us to vividly re-experience previously encoded and stored personal events, research shows that certain areas and connections are activated depending on the specific type of retrieval (e.g. whether or not contextual details are recalled beyond simple recognition) or how memory is evaluated (objective vs subjective measures), as covered in more detail below. According to hippocampal memory indexing theory (Teyler & DiScenna, 1986), the hippocampus is responsible for storing and indexing the various patterns of neocortical activity (e.g. visual, auditory representations) associated with each event. During encoding of episodic events experienced by the individual, each pattern of neocortical activity is generated by the simultaneous firing of a unique sub-population of neurons representing that event, also called an ‘engram’. Synaptic plasticity strengthens the connections between these neurons leading to ‘pattern completion’ in the CA3 subfield of the hippocampus, known as the ‘autoassociator’ and regeneration in CA1 (Rolls, 2013). This stage represents the binding of information where temporal and spatial associations are formed between features of an event experienced. Strong (intrinsic neuronal excitability) or repeated signals are more likely to be strengthened, and this forms the basis of memory formation and learning. Stronger stimuli can be those more ‘emotionally salient’ due to creating an arousal response (positive or negative), hence involvement of other parts of the limbic system, such as the amygdala, in memory formation (Faul & Labar, 2020).

Consolidation of episodic memories, defined as the progressive stabilisation of a memory trace over time, is thought to occur during slow-wave ripple bursts at 150 – 250 Hz in the hippocampus during the awake state (Carr et al., 2011; van de Ven et al., 2016), similar to the consolidation process which happens during sleep (Rasch & Born, 2013). During the awake state, this activity needs to be measured when an individual is immobile and when the theta/delta power ratio is low, to distinguish it from movement-related patterns of activity (Carr et al., 2011; van de Ven et al., 2016). The process of consolidation involves the sequential reactivation of hippocampal place neurons associated with a previous experience and behavioural trajectory, followed by the redistribution from temporary to long-term storage i.e. from the hippocampus to the neocortex, respectively (Carr et al., 2011; Rasch & Born, 2013). A recent account proposes that the consolidation of memories occurs due to a lack of retroactive (post-encoding) interference, whereby processing of new or overlapping information or hippocampal activity following encoding disrupts the binding of information during the retention period (Yonelinas et al, 2020). Thus, it is proposed that protection from interference thereby reduces forgetting.

During episodic retrieval, the presence of a single feature of the original event, whether deliberate or incidental, can activate the other neurons associated with the event, allowing recollection of all details of the original event (Teyler & Rudy, 2007). This is demonstrated in studies investigating the single ‘concept’ neuron response to certain famous people and landmarks being presented to participants. For example, when presented with a picture of Jennifer Anniston (‘Rachel’ from the TV series, Friends), participants also recalled Lisa Ludlow (‘Phoebe’), a co-star from the same series (Quiroga et al., 2005; 2009). This reactivation process has been demonstrated using iEEG, revealing activation in the hippocampus during reconstruction of the cued content, particularly temporal and spatial, followed by an increase in activity in medial parietal, medial prefrontal, and lateral parietal areas, during elaboration of the more specific features, such as faces, objects, and scenes associated with the original event (Simons et al, 2022; Treder et al, 2021). Moreover, both reactivation and re-experiencing of the original event create a duplicate copy of the initial representation, further reinforcing the original, unique pattern of neocortical activity via long term potentiation (Rowland, 2014).

1.4.4 Familiarity and recollection: Single- and dual- process accounts of recognition memory.

Recognition memory is a subcategory of episodic memory which enables an individual to recognise previously experienced people, objects and events. There is debate amongst the memory literature regarding what specific processes underlie our recognition memory. The initial explanation for this was based on a single process account. According to signal detection theory (Egan, 1958; Yonelinas, 1994), recognition memory operates on a continuum whereby successful retrieval of individual episodic memories is dependent on the strength of the original memory. Specifically, increasing memory strength correlates with an individual's ability to recollect information beyond merely a sense of familiarity associated with an item and event. Subsequent accounts built on this theory, largely superseding it with the predominant current view that recognition memory is served by more than one process.

Dual process theories of recognition memory (Atkinson & Juola, 1974; Jacoby, 1991; Mandler, 1980; Yonelinas, 2002), propose that recognition memory is supported by two functionally distinct processes: familiarity and recollection. The former involves a recognition judgement concerning whether something has been previously encountered or not i.e. an individual's ability to discriminate between old and new items. Recollection involves conscious recall of contextual detail previously studied i.e. an individual's ability to retrieve not just whether something has been encountered before or not but also some details from the encoding episode. Familiarity is conceived as a fast, automatic process, whereas recollection, is a slower, more deliberate process. The reason for this is that familiarity is often based on matching surface-level, perceptual details, whereas recollection involves a more controlled search of elaborative, qualitative details i.e. temporal and spatial context associations with items or events (Yonelinas, 2002).

Considering recognition could involve both familiarity and recollection, certain memory paradigms have been designed to generate separate scores to represent these processes. As is used in this thesis, the source memory design involves an old/item recognition judgement followed by a question probing participants' memory for contextual details e.g. the gender of the speaker. Alternatively, the Remember/Know procedure (Tulving, 1985), involves participants subjectively deciding whether their recognition of an item (‘know’) is accompanied by retrieval of contextual details presented at the study phase (‘remember’). Thus, such tests enable researchers to measure these processes in isolation on a behavioural level to explore any differential effects interventions might have on the constituent parts of recognition memory: familiarity and recollection.

The separation of these two processes is also supported to some extent by neurophysiological and neuroimaging studies. For example, EEG studies have identified event-related potential indices which appear to distinguish, and map onto, recollection and familiarity processes. For example, during retrieval, familiarity-based responses are related to an early frontal-central scalp positivity (mid-frontal ERP old/new effect), whereas recollection is related to a later left-parietal positivity (left parietal ERP old/new effect). The timing of these responses, 300-500 ms and 400-800 ms, respectively, supports the notion that familiarity is a faster process than recollection (Curran & Cleary, 2003). Thus, the neural indices of recollection and familiarity have been revealed by EEG work to temporally, topographically and functionally dissociate, suggesting two distinct processes underlie recognition memory (see Wilding & Ranganath, 2012 for more details).

The functional dissociation between familiarity and recollection processes is also supported by fMRI neuroimaging studies, where subregions of the medial temporal lobe are linked to the different processes. Specifically, the perirhinal cortex (located in the anterior parahippocampal gyrus) supports familiarity by encoding and retrieving specific item information. During recollection, the parahippocampal cortex (located in the posterior parahippocampal gyrus) facilitates encoding and retrieval of contextual information, whereas the hippocampus serves to bind the item and context information (Rangathan et al., 2010). This is supported by studies including patients with focal brain legions that have caused amnesia. Hippocampal damage preferentially impairs responses that are based upon recollection of qualitative information about the study event, leaving familiarity-based responses relatively unaffected (for reviews see Montaldi & Mayes, 2010; Yonelinas et al., 2010). In contrast, damage to the surrounding medial temporal lobe, such as the perirhinal cortex leads to deficits in familiarity. If this is selective to the perirhinal or entorhinal cortex and does not influence the hippocampus this will result in the individual having selective familiarity issues (see review see Kohler and Martin, 2020).

Moreover, Vilberg & Rugg (2008) conducted a meta-analysis of fMRI studies that reported the brain regions that indicate retrieval effects associated with both familiarity and recollection, represented by MNI (Montreal Neurological Institute) coordinates from voxel-wise analyses. The findings revealed familiarity effects present in the superior region of lateral parietal cortex centred around the intra-parietal sulcus, whereas recollection effects were localised to the posterior region of inferior parietal cortex. Based upon existing knowledge regarding the roles of these regions i.e. top-down attentional control and in the detection of behaviourally relevant stimulus events (Corbetta & Shulman, 2002; Kastner & Ungerleider, 2000) and sustained focusing of attention on the contents of working memory (Ravizza et al., 2004), respectively, this led the authors to propose the contribution of these regions in the context of recognition memory. For example, in the case of familiarity, distinguishing between old and new items is considered akin to detecting the infrequent or novel stimuli during an oddball task. However, during the process of recollection, inferior parietal cortex acts as an interface between the retrieved memory representation and the executive systems that monitor and control on-line processing, akin to the multi-modal 'episodic buffer' introduced by Baddeley (2000).

An important finding discussed is that inferior parietal recollection effects are insensitive to changes in indices of response confidence or familiarity memory strength (Montaldi et al., 2006; Yonelinas et al., 2005), which further supports a process-pure role of recollection as opposed to existing on a continuum of memory confidence or strength as offered by the single-process account described above. However, whilst there are regions of the brain which are more associated with recollection than familiarity and vice versa, there are many regions which are involved in both. To provide an explanation for this, Skinner & Fernandez (2007) propose that the distinction between familiarity and recollection is less informed by these individual brain regions, and more determined by the strength of the connections between the hippocampus and frontal, parietal and surrounding temporal regions that are active during episodic memory retrieval. This further supports the notion that memory processes rely on communication within networks of brain regions with dedicated individual functional roles, and that these networks can be flexibly activated in response to memory task demands. Therefore, there is a strong rationale for examining whether interventions such as EEG-NF and AVE will differentially enhance performance depending on the type of memory being measured.

1.4.5 Subjective and object memory performance

Another key aspect of memory processing which is studied in the literature, is the objectivity of memory performance. Our ability to retrieve our memories can be measured objectively by way of different episodic memory tasks. For example, recognition memory via old/new item discrimination judgements, or source memory via recollection of contextual details associated with an item previously experienced, generate accuracy scores reflecting objective performance. However, subjective measures of participants' own performance on these memory tasks, such as when they provide confidence ratings, provide another perspective on the processes involved in the retrieval of episodic memories. However, differences have been observed between individuals' scores on objective and subjective measures of episodic memory (Mendonca et al., 2022; Yazar et al., 2014).

Further research on this topic has reinforced a neuroanatomical dissociation between objective and subjective recollection of personal events, spurred on by the discovery that activity in lateral parietal regions in the brain, specifically the angular gyrus, was greater when participants made subjective memory confidence assessments than when they made objective recognition memory decisions (Chua et al, 2006). A subsequent study investigated both recognition and source memory performance in patients with bilateral parietal lesions (Simons et al., 2009). During a surprise memory test, participants were required to judge whether a sentence being read out was one they previously heard during the study phase, and if so, whether the reader’s voice had been male or female. Following this, a subjective confidence rating was made regarding their judgment for both the recognition and source memory tasks. The results showed that whilst recollection remained intact, participants’ subjective confidence ratings were lower for their performance on the source memory task, relative to the control participants. This suggests that these participants’ assessment and monitoring processes that contribute to subjective aspects of recollection were impaired.

Another study used continuous theta burst stimulation in healthy participants to disrupt the functioning of specific left parietal subregions, i.e. the left angular gyrus, prior to administering a battery of episodic memory tests (Yazar et al., 2014). This method allowed for conclusions to be drawn regarding a possible cause and effect relationship between the functioning of this brain region and successful memory performance for a range of memory types. In accordance with previous studies, the researchers found that whilst participants achieved high source recollection accuracy, there was a selective reduction in their rated source confidence. Furthermore, research has revealed a distinction between enhanced activity in both the dorsal and ventral posterior parietal cortex for objectively measured memory precision and subjective recollection, respectively (Fandakova et al., 2021). Specifically, the latter i.e. subjective memory involved activation of angular gyrus and the precuneus, both of which are associated with autonoetic consciousness. Moreover, meta-cognitive monitoring was associated with activation in dorsal anterior cingulate cortex and anterior insula, whereas evaluation of retrieved content in the context of current task demands generated activity in the lateral prefrontal cortex (Fandakova et al., 2016). Research supporting this potential dissociation between subjective and objective memory performance warrants further investigation into these phenomena and under what conditions they can be differentially affected. These findings provide compelling evidence that objective and subjective measures of episodic memory recruit distinct brain regions, indicating separate processes are at play. This is important to consider in relation to how neuromodulatory techniques such as EEG-NF and AVE might enhance these different aspects of episodic memory.

1.4.6 Oscillations and memory

Understanding the neural mechanisms underlying episodic memory processes is key for informing more targeted interventions aimed at enhancing episodic memory performance. Whilst there is evidence to support the contribution of a range of frequencies to episodic memory (Klimesch et al., 1997, 1999, 2001), there exists substantial evidence to support the functional role of theta oscillations (4-8 Hz) in the encoding, consolidation and retrieval of episodic memories.

1.4.6.1 Memory encoding

Findings from EEG studies, whereby successful memory performance is compared against trials that were not associated with successful memory performance, have shown an increase in frontal theta oscillations during encoding and this increase is related to items that are later successfully recalled (Cruzat et al., 2021; Hanslmayr et al., 2009; Klimesch et al., 1997, 2000). To rule out a possible attentional effect favouring the remembered items, Klimesch et al. (1996) demonstrated a similar outcome when controlling for participants' attentional levels during encoding, further reinforcing theta's role in this stage of memory processing. Furthermore, one study that used iEEG confirmed that theta oscillations generated from within the prefrontal cortex predicted episodic encoding success (Sederberg et al., 2003). Moreover, source modelling used in a MEG study detected increased theta power in the medial temporal regions immediately before presentation of an item that was subsequently recalled (Gruber et al., 2013). These findings suggest that increased theta activity immediately prior to study stimuli serves to facilitate the encoding of new information, allowing for enhanced retrieval success of the content studied. Importantly, the latter two studies provide evidence of theta activity in brain regions associated with episodic memory processes, namely the medial temporal lobe and the pre-frontal cortex.

1.4.6.2 Memory consolidation

Theta oscillations have been proposed to support rapid eye-movement (REM) sleep-dependent processes of memory consolidation. During this stage of sleep, ponto-geniculo-occipital waves inhibit the processing of external stimuli resulting in an internal, fluid state that is conducive to reorganising and shaping hippocampal memory representations (Ramirez-Villegas et al., 2020b). Reactivation of these representations could facilitate synaptic plasticity and further consolidation of information and experiences, due to theta's role in spike-dependent plasticity (Albers et al., 2013; Rasch & Born, 2013). In further support of this, in another study, scalp-recorded EEG theta activity was enhanced during REM sleep following learning of paired associates (Fogel et al., 2007) and was correlated with consolidation of emotional memories, specifically over the right prefrontal cortex relative to the left (Nishida et al., 2008). These findings reinforce theta's role in the consolidation of episodic memories.

1.4.6.3 Memory retrieval

Some studies have also reported links between theta power and the retrieval of episodic memories. Recognition memory studies have shown that theta power is higher during correct recognition of studied items than during correct rejection of non-studied items (Burgess & Gruzelier, 1997; Klimesch et al., 2001). Furthermore, theta activity during retrieval has also been found to play a selective role in the recollection of contextual details relating to information previously studied (Gruber et al., 2008; Guderian & Düzel, 2005). For example, Addante et al. (2011) found that frontal-midline theta activity preceding a retrieval cue was predictive of correct source but not item information (e.g. an old/new recognition judgement) and correlated with post-stimulus parietal activity and successful source retrieval. Furthermore, a study using a Remember/Know paradigm found that early theta synchronisation during the post-stimulus window of 250–375 ms predicted knowing i.e. familiarity, and increased theta power during the later post-stimulus window of 500–625 ms predicted remembering i.e. recollection (Duzel et al., 2003). These findings suggest not only a role of theta in episodic memory retrieval, but also infer that the timing of this activity is related to distinct processes within recognition memory such as familiarity and recollection (as discussed in Section 1.4.4).

1.4.6.4 Cortico-hippocampal link

In line with hippocampal memory indexing theory (Teyler & DiScenna, 1986), the encoding and retrieval of episodic memories is facilitated by communication between the medial temporal lobe and pre-frontal regions by phase synchronisation of both theta and gamma oscillations (Nyhus & Curran, 2010). A MEG study revealed increased theta phase coherence between the prefrontal cortex and the hippocampus for memory associations successfully encoded (Backus et al., 2016). Furthermore, this is supported by Cohen (2011) who measured the integrity of white matter tracts connecting the hippocampus and the prefrontal cortex using diffusion tensor imaging. Participants with higher hippocampal-prefrontal cortex connectivity were found to have enhanced long-term memory and exhibited higher levels of delta and theta frequencies in frontal regions as measured by scalp EEG.

1.4.6.5 Theta-gamma coupling

Also known as induced theta-gamma coupling, one of the first observations of this mechanism was during an iEEG study by Mormann et al. (2005). The researchers measured oscillatory activity from depth electrodes already implanted in epilepsy patients during a continuous word recognition task. The theta cycle at approximately 6 Hz was found to modulate changes in power in the gamma frequency range (40 Hz–50 Hz) in the hippocampus which was more pronounced during the correct recognition of words presented earlier i.e. old items. Research has since further supported this recruitment of gamma frequencies during the theta phase and the link with episodic memory retrieval (Colgin, 2014; Fell & Axmacher, 2011). It is proposed that during this process the two oscillatory frequencies become ‘phase synchronised’, whereby depolarisation can facilitate timely pre- and post-synaptic action potentials, leading to increased neural communication and synaptic plasticity. Crucially, spike–field coherence has been shown to occur for oscillations in the theta and gamma frequency ranges in the hippocampus and neocortex, regions that are both relevant and active in episodic memory processes (Colgin, 2014; Fell & Axmacher, 2011).

Together, gamma and theta frequency oscillations execute different functions during episodic memory processes (Nyhus & Curran, 2010). Gamma oscillations (~40 Hz–100 Hz) can create connections across the cortex to bind perceptual features of a stimulus with contextual information gathered from diverse brain regions, to feed into episodic representations developed in the hippocampus, and facilitates the transfer of information during bottom-up and top-down processing (Nyhus & Curran, 2010). Complementing this, it is proposed that theta oscillations play a specific role in the binding of contextual information during encoding (Herweg et al., 2020) and in top-down control from the frontal cortex to the hippocampus whereby it serves to temporally order the individual memory representations during both the encoding and retrieval of episodic memories (Hsieh & Ranganath, 2014; Kawasaki et al., 2010). The timing of this activation is important for the induction of plasticity in the hippocampus i.e. spike-timing plasticity and the development of long-term memories.

Together, this evidence supports a functionally significant role of theta oscillations in episodic memory processes, both during encoding and when people try to remember the contextual details of a previous encounter i.e. recollection. This previous research provides grounds for the use of interventions which specifically target theta to improve memory performance.

1.5 EEG-NF and episodic memory

A growing body of research over the past couple of decades has shown that EEG-NF can have a beneficial effect on episodic memory in healthy volunteers. Significant improvements in episodic memory have been found in a handful of studies that tested the effects of a theta EEG-NF protocol (4-8 Hz). The theta frequency is a promising contender for enhancing episodic memory considering that enhanced theta activity has been found during the encoding, consolidation and retrieval of episodic memories (see Section 1.4.6). A study by Eschmann et al. (2020) revealed a significant increase in source memory for ratings of animacy and pleasantness assigned to 200 words at the encoding stage but not for an old-new recognition judgement of the words themselves, relative to an active control. This effect was observed at a second testing timepoint, which occurred 13 days following seven, 30-minute daily sessions of individualised theta EEG-NF training. This finding supports the use of theta EEG-NF for selectively enhancing recollection in healthy adults, as opposed to familiarity processes alone. Rozengurt et al. (2017) found that a single 30-minute session of theta EEG-NF (4-8 Hz) significantly increased immediate free recall performance for 30 object pictures studied prior to the EEG-NF training, compared to both an active low beta control, and a passive movie-watching group. This effect increased at both 24 hours and 1 week later testing timepoints. Interestingly, this less common study-test design also showed positive results for visuo-spatial memory after a single 30-minute session of theta EEG-NF implemented during the retention period (Shtoots et al., 2020). These findings provide further support for the beneficial effects of theta EEG-NF, implemented during the consolidation period, on the recollection of previously encoded information.

The alpha band has also been adopted in some EEG-NF studies based on its association with relaxation and the cortical inhibition of the sensory cortex (Klimesch et al., 2007). Hsueh et al. (2016) found that twelve 36-minute sessions of alpha (8–12 Hz) upregulation significantly increased performance in a word pair task undertaken by 25 healthy adults, relative to an active control. This finding was subsequently replicated using a portable device, in a slightly smaller sample and following slightly less EEG-NF training (Wei et al., 2017). A meta-analysis by Yeh et al. (2021) reported a moderate to large (d = .77) overall effect of alpha EEG-NF on episodic memory in healthy adults, a value which includes some studies that found no effect and those with small sample sizes (Yeh et al., 2021). One clinical study by Lavy et al., (2021) investigated the effects of ten 30-minute sessions of individual upper alpha EEG-NF on episodic memory performance in 15 patients with mild cognitive impairment, a precursor to Alzheimer's dementia. No significant improvement in scores was observed on either verbal or non-verbal delayed recall tasks, when compared to an active control. However, mild-cognitive impairment patients significantly enhanced both verbal and non-verbal immediate recall following alpha EEG-NF training, and this effect persisted for 30 days. This finding could instead support other studies that have observed beneficial effects of alpha EEG-NF on short-term/working memory (Escolano et al., 2014b; Wei et al., 2017), and for treating symptoms of attention-deficit hyperactivity disorder (Bussalb et al., 2019).

The effect of SMR on episodic memory has also been commonly tested using EEG-NF training, generating a mixture of results. SMR (12 – 15 Hz) falls into the low beta frequency band category and involves the use of electrodes selectively targeting the sensory-motor cortex. The rationale for this is that previous evidence indicates that higher levels of SMR activity reduce sensorimotor interference, and thereby maintain an internal, alert state which subsequently promotes cognitive processing (Pfurtscheller, 1992; Sterman, 1996). Kober and colleagues have conducted several studies, investigating the effects of SMR EEG-NF training on a range of cognitive measures, including episodic memory, in both healthy and clinical populations (Kober et al., 2015a, 2015b, 2016, 2017a, 2017b, 2019, 2020). In Kober et al., (2015b)'s study, the SMR group (n = 10) performed significantly better on a verbal and visual memory subtest called 'construction' (VVM2 construction 2), which assesses long-term memory of visuo-spatial and verbal material, following EEG-NF training compared to the pre-test. No improvement was observed in the active control group following EEG-NF training. Findings regarding the remaining measures, and from their other studies, are mixed. Marlats et al. (2019) found 20 sessions of SMR EEG-NF protocol in their pilot study significantly enhanced episodic memory in 20 older adults with mild cognitive impairment, but they did not include a control group rendering the result inconclusive given these changes cannot be confidently attributed to the EEG-NF protocol used.

Considering the variability in frequency bands that have featured in EEG-NF studies, it is difficult to conclude which one predominantly supports episodic memory processes. Some findings suggest that upregulation of alpha, SMR and theta frequencies can facilitate episodic retrieval, and some studies have tried to link these two things together by showing significant correlations between increased target brain activity and episodic memory performance (Eschmann et al., 2020; Hsueh et al., 2016; Kober et al., 2015b, 2017b; Rozengurt et al., 2017). However, this is not always the case: claims of positive effects of EEG-NF are often made without neurophysiological data being reported. For example, Guez et al. (2014) showed that 5 weeks of two 30-minute sessions per week of (i) upper alpha (10-12 Hz) EEG-NF significantly increased scores on an associative memory test, and (ii) SMR (12-15 Hz) EEG-NF training significantly increased scores on an item memory test. Therefore, Guez et al. (2014) claim that their findings demonstrate a selective effect of upper alpha and SMR EEG-NF on recollection and familiarity memory processes, respectively. However, they report no data relating to neurophysiological changes that occurred during the EEG-NF training to support this claim. In this vein, many EEG-NF studies only report neural activity regarding the frequency bands of interest, therefore there is not a clear picture about the specificity of the effects of different bands, or how others interact and therefore contribute to the overall reported effects on memory.

While the EEG-NF literature contains some positive findings, some are less conclusive and this is commonly attributed to a lack of consistency in the EEG-NF designs and protocols employed, and in some cases, small sample sizes. An important factor that could affect the success of EEG-NF training and its impact on episodic memory performance, is the amount of EEG-NF training. It is noted that some studies report no evidence of significant self-regulation until the 3rd or 4th session of EEG-NF training (Hsueh et al., 2016; Pei et al., 2018; Wei et al, 2017), whereas other studies demonstrate significant increases in target band activity within a single session (Reiner et al., 2014; Rozengurt et al., 2017). Single case studies have shown positive results which are unique to the individual and their range of symptoms, and therefore lack generalisability. A range of memory paradigms are also used across studies, with varying types and numbers of stimuli being presented to participants to remember. Crucially, different types of control groups or conditions are used as a baseline from which to statistically compare these scores. As discussed in Section 1.2.2, the choice of control group could impact these results depending on whether it is a convincing sham scenario thereby controlling for demand characteristics or placebo and other non-specific effects, or whether it is a contingent sham involving self-regulation of an alternative band, thereby controlling for the effect of other frequencies. Subsequently, it is clear that a review and meta-analysis is required to determine whether EEG-NF does have a beneficial effect on episodic memory and what might affect this relationship – this is what has been conducted in Chapter 2.

1.6 AVE and episodic memory

AVE is another focus of this thesis, in terms of investigating the efficacy of neuromodulatory techniques for increasing both theta activity and episodic memory performance. Empirical studies have directly tested the effects of visual and/or auditory stimulation, which is delivered at the theta frequency, on episodic memory. Considering its relative infancy, the literature base is limited. However, some studies show promising results.

Koster et al. (2019) used EEG to measure the effects of visual flicker and found that stimulation at individual theta frequency during encoding elicited clear steady-state visually evoked potential signals over the visual cortex. Moreover, this evoked activity predicted enhanced episodic memory performance on a Remember/Know task, which measured whether participants could consciously recollect the items (i.e. remember), if the item was simply familiar indicated by an old recognition judgement (i.e. know), or if the item was novel (i.e. new). The findings from this study observed a higher number of subsequently remembered items and a lower number of subsequently forgotten items in the theta group, relative to a control group who were stimulated at individual alpha frequency. The number of subsequent know responses remained unaffected by the stimulation. This supports the idea that visual stimulation of individual theta during encoding selectively enhanced recollection processes, not familiarity.

Simultaneous presentation of both auditory and visual stimulation during encoding has also been linked with enhanced episodic memory performance. Wang at al. (2018) found that the higher the phase synchronisation of entrained theta oscillations at 4 Hz in the visual and auditory cortex, modulated by the luminance and amplitude of the video and sound stimuli, the higher were the scores on an associative memory task (Clouter et al., 2017; Wang et al., 2018). This supports the importance of the phase and timing of rhythmic audio-visual stimulation at the theta frequency in enhancing episodic memory performance. Both theta and alpha oscillations have since been implicated in flexibly modulating the specific direction (spatial) and timing (phase) of neuronal spiking and excitability, across brain networks responsible for episodic memory encoding and retrieval (Mohan et al., 2022). A recent review by Wang et al. (2024) further supports the important role that both the phase of hippocampal theta oscillations, and the timing of the action potentials between pre- and post-synaptic neurons, play on both synaptic plasticity (i.e. long term-potentiation) after rhythmic sensory stimulation, and subsequent memory processes. Moreover, a study conducted on mice showed that auditory and visual flicker at gamma frequency (40 Hz) can have a suppressive effect on β-amyloid plaques, suggests that sensory entrainment might also affect subcortical activity in the hippocampus and thereby potentially reduce Alzheimer’s pathology and improve memory performance (Martorell et al., 2019).

The studies described above demonstrate a link between stimulation of theta frequencies during the encoding of episodic information and the subsequent enhancement in retrieval of this information. A study by Roberts et al. (2018) used a similar design to Rozengurt et al. (2017)’s study but instead of engaging in theta EEG-NF, participants received 36 minutes of either theta (5.5 Hz) or low beta (14 Hz) AVE during the consolidation period between study and test, using a commercially available device (DAVID PAL 36, MindAlive Inc., Edmonton, Canada MindAlive Inc.). During the study period, participants viewed 200 words and for half of them indicated whether they considered that the word referred to an ‘alive’ item and for the other half they completed a ‘man-made’ judgement. At the retrieval stage, participants viewed the same words, plus another 100 lures, and for each word made an item (i.e. old/new recognition judgement) and source (i.e. ‘alive’ or ‘man-made’) decision. Roberts and colleagues reported enhanced source memory in the theta group compared to the low beta control, but no difference in item-only memory scores immediately following AVE. This effect was found when scores in the experimental theta (5.5 Hz) group were compared in two different experiments to different control groups: one 14 Hz low beta and the other white noise. These findings further support the selective effect of theta AVE on recollection, and not familiarity, memory processes. An increase in the targeted frequency for both conditions was measured by EEG during AVE, with topographical maps depicting 4-6 Hz activity in the theta group localised in occipital regions, and 14 Hz low beta activity in the control group more globally dispersed. Furthermore, significantly higher theta power was measured during retrieval in the 5.5 Hz theta group in frontal and parietal regions which are associated with episodic memory. While increased theta activity would be expected during successful retrieval, this was higher in the theta group compared with the 14 Hz low beta control group. This latter group difference could suggest a resonance of induced theta activity generated by theta AVE with endogenous theta oscillations in locations involved in episodic memory retrieval.

Together these findings stand both audio and visual stimulation in good stead as effective methods for increasing targeted oscillations involved in episodic memory retrieval. The observed consolidatory effects of theta entrainment via AVE aligns with theta's functional role in facilitating long-term potentiation and thereby possibly generating lasting effects of entrainment. However, empirical evidence to support the persistent effects of AVE is lacking. The current body of evidence in this area demonstrates a need for more research to be conducted to support the efficacy and application of AVE, as a portable, user-friendly device, for producing long-lasting positive effects on episodic memory performance.

1.7 Aims of the thesis

The broad aim of this thesis is to investigate the efficacy of two neuromodulatory techniques – EEG-NF and AVE – and whether they can be successfully applied to both increase theta oscillatory activity and subsequently enhance episodic memory performance in healthy young adults. Theta was chosen as the target frequency for modulation given its widely reported functional role in episodic memory processes. These interventions were applied during the retention period between the study and retrieval of new information.

Chapter 2. The efficacy of electroencephalography neurofeedback for enhancing episodic memory in healthy and clinical participants: A systematic qualitative review and meta-analysis.

The thesis begins with an in-depth analysis of the research investigating the effects of EEG-NF on episodic memory in adults in both healthy and clinical populations. The reason for this, as outlined above, is that there is a mixture of findings regarding whether there is an effect of EEG-NF on episodic memory. A key question that I wanted to address in this thesis is whether EEG-NF can benefit episodic memory. Therefore, a systematic review was conducted of the area. This allowed me to gain an overview of the kinds of studies which had been conducted and the parameters they had used in their neurofeedback design. Only studies which had adequate design features e.g. an active control group or condition were included in a meta-analysis to determine if EEG-NF could enhance episodic memory. In addition, given the wide variety of parameters in these experiments, such as frequency band trained and the number of feedback sessions, these were included in the analyses to determine which design characteristics might be more likely to lead to beneficial memory performance. This chapter contributes the first systematic review and meta-analysis examining the effectiveness of EEG-NF on episodic memory performance and has been published in the Neuroscience and Biobehavioral Reviews journal.

Chapter 3. Examining the effect of theta EEG-NF on episodic memory performance.

In this chapter, an empirical study was conducted examining the effects of theta EEG-NF during the retention period between encoding and retrieval of new information, compared to an active control group (low beta), on episodic memory performance. The experimental design is very similar to the one used by Rozengurt et al. (2017). This study aimed to replicate Rozengurt's finding of significantly enhanced free recall, both immediately and 24 hours later, following 30 minutes of theta EEG-NF. However, I also wanted to examine the memory benefit of this intervention in a more nuanced way by including a variety of objective memory measures which tap specific process, such as recollection and familiarity. Based on previous research it was hypothesised that free recall and recollection of source information would be selectively enhanced, not familiarity. Moreover, I wanted to include subjective measures relating to these types of recognition memory, considering self-reported confidence has not been examined in previous EEG-NF studies.

Chapter 4. EEG-NF responders: Exploration of individual differences.

In this chapter I explored what factors are associated with an individual's ability to successfully self-regulation target frequency activity, considering existing empirical evidence examining these relationships is limited and inconclusive. To achieve this, I examined questionnaire and cognitive task data that were collected in the study conducted for Chapter 3 by investigating whether there are any relationships between these individual factors and EEG-NF responder ability. The strategies used by responders is also reported. The aim was to see if such findings could inform the development of an EEG-NF responder profile, to both optimise the recruitment of sufficient samples in future EEG-NF research and to maximise the effectiveness of EEG-NF in enhancing episodic memory in targeted individuals.

Chapter 5. Examining the effect of theta audio-visual entrainment on episodic memory performance.

In the final empirical chapter, I examined whether an alternative neuromodulatory technique, audio-visual entrainment (AVE), could enhance episodic memory. The rationale for exploring this technique was the relatively passive nature of the user's role to achieve the desired effects of neuromodulation. In theory, this would avoid the issue of EEG-NF non-responders as described previously. The exact same memory paradigm was adopted as in Chapter 3. This research aimed to replicate the existing finding that theta (5.5 Hz) AVE applied during the retention period significantly enhanced contextual recollection but not familiarity of information previously learnt (Roberts et al., 2018). Furthermore, this study aimed to extend this finding by testing whether the positive effects of theta AVE persisted 24 hours following the encoding of new information, given this has been found in EEG-NF studies (Eschmann et al., 2020; Rozengurt et al., 2017). This would provide supporting empirical evidence for the use of this technique as an intervention to enhance episodic memory in healthy adults.

1.8 Statistical approach - Overview

Chapter 2. The efficacy of electroencephalography neurofeedback for enhancing episodic memory in healthy and clinical participants: A systematic qualitative review and meta-analysis.

To determine the overall effect of EEG-NF on episodic memory in adults across the healthy and clinical human populations, a meta-analysis was conducted. This involved calculating an individual effect size (standardised mean difference) using data extracted from each relevant finding contained within each study that met the inclusion criteria. Subsequently, a pooled mean population effect size was generated using robust variance estimation to allow for the inclusion of multiple effect sizes within a study. Appropriate adjustments were made to account for small sample sizes, study design and outliers.

To investigate whether certain factors moderated the overall mean population effect size, a series of meta-regressions were performed. Both categorical and continuous moderators were investigated, e.g. both the amount and successfulness of EEG-NF training, the type of episodic memory tested, and the type of active control used within the study design. Additional meta-analyses were conducted for each factor to demonstrate the spread of effects.

Chapter 3. Examining the effect of theta EEG-NF on episodic memory performance.

Episodic memory performance

To test whether theta EEG-NF enhanced episodic memory performance, scores were compared between the Theta group and the Low Beta (active control) group for the memory tests: free recall (both immediately following EEG-NF and 24 hours later), cued recall and source recollection (gender identification of the speaker). Significance testing was achieved using one-tailed, independent groups parametric tests (or the Mann-Whitney non-parametric equivalent in cases of violation of normality of data distribution).

Further exploratory analyses using two-tailed independent groups parametric tests (or the Mann-Whitney non-parametric equivalent) were conducted to investigate any differences in performance between the Theta group and the Low Beta group for corrected recognition (old/new item discriminability), and subjective confidence ratings for both old and new recognition and source recollection. The analyses were repeated for sub-groups of EEG-NF responders, defined as those who increased their theta/low beta at least 5% from resting baseline to the average of the six active EEG-NF blocks.

Given the same research question was tested for different outcome measures thereby increasing the family-wise error, multiple comparisons were corrected using the Benjamini and Hochberg False Discovery Rate. This method is considered to provide a good balance between discovery of statistically significant results and limitation of false positive outcomes (Jafari & Ansari-Pour, 2018). Bayes analyses were conducted to assess the strength of evidence in favour of the alternative hypothesis for the group comparisons. Graphical representation of the behavioural data includes violin plots to compare scores between the Theta group and the Low Beta group for each memory test.

EEG-NF success

EEG-NF performance or ‘respondability’ was calculated using different measures: theta/low beta power ratio, theta relative power (for the experimental group) and low beta power (for the active control group). Two-tailed independent groups parametric tests (or the Mann-Whitney non-parametric equivalent) were conducted to investigate any differences in EEG-NF performance or ‘respondability’ between the Theta group and the Low Beta group. The primary contrast representing EEG-NF success was the percentage change between an individual’s resting baseline measurement and the average of the six active EEG-NF blocks. The difference between resting baseline and post-EEG-NF resting block was also explored to determine any change in tonic EEG. Correlational analyses were also conducted to determine the relationship between the percentage change in theta/low beta ratio from baseline to average of all six NF blocks and the various memory scores.

Graphical representation of the EEG-NF data includes violin plots to compare EEG-NF performance or 'respondability' between the Theta group and the Low Beta group for each EEG-NF measure, and line graphs to depict any learning trajectories or correlations.

Chapter 4. EEG-NF responders: Exploration of individual differences.

Exploratory analyses were conducted to investigate whether any individual factors were associated with EEG-NF respondability. Individual factors included in these analyses were current motivation and current mood, flow state, locus of control, task difficulty, personality traits, sustained attention and resting state EEG prior to EEG-NF training. Respondability was measured as the relative percentage increase in target band activity from an individual's baseline to the average of the six EEG-NF training blocks.

Two types of analyses were run: (i) independent groups parametric tests (or the Mann-Whitney non-parametric equivalent) to compare scores for each factor between Responders and Non-responders (i.e. those who were able to increase the target brain activity above zero from baseline to the average of the six active EEG-NF blocks), regardless of whether the target band participants had been assigned to upregulate was theta or low beta; and (ii) correlational analyses between each factor and participants' respondability represented by a z-score transformation. All analyses were performed on the full sample (i.e. the theta and low beta groups were collapsed), and separately for the theta and low beta groups to determine whether any relationships were specific to the target band. Group comparisons are presented visually using violin plots, and correlations are presented using line graphs.

The Benjamini and Hochberg False Discovery Rate multiple comparisons correction was applied to the data. Bayes analyses were also conducted to assess the strength of the evidence supporting the hypotheses, all of which were two-tailed/correlated except for task difficulty which was one-tailed/negatively correlated.

EEG-NF strategy use was explored descriptively by way of frequency counts for each strategy. The effectiveness of each strategy is represented as the percentage of responders that used each strategy. Both strategy use and effectiveness are presented using bubble charts for the full sample and for the theta and low beta groups separately.

Chapter 5. Examining the effect of theta audio-visual entrainment on episodic memory performance.

The same behavioural scoring, statistical analyses and graphical representations were used for this data as what was used in Chapter 3.

Regression to the mean

Regression to the mean is a statistical phenomenon that can manifest in a within-participants experimental design. It is therefore an important consideration in the interpretation of some findings in this thesis whereby participants' performance (measures of both memory and oscillatory activity) is measured pre- and post the EEG-NF training intervention.

Regression to the mean can occur after a participant initially obtains an extreme score by chance, and scores obtained at timepoints thereafter increasingly shift towards the mean value. This can be misinterpreted as an effect of the intervention that is applied following the initial measurement, rather than chance. Acceptable methods for mitigating the issue of regression to the mean is random sampling of participants and the use of a control group. The latter would serve to help evaluate the extent of changes caused by regression to the mean or isolate the effects of the intervention in the experimental group.

Chapter 2: The efficacy of electroencephalography neurofeedback for enhancing episodic memory in healthy and clinical participants: A systematic qualitative review and meta-analysis.

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2.1 Introduction

The ability to remember events or “episodes” from our personal past is known as episodic memory (Tulving, 1972). It includes details about what happened, when and where. For example, try to remember your last birthday. Perhaps you can recall what you did, who celebrated it with you and what presents you received. These are all features of episodic memory. The ability to go back and figuratively relive past experiences is a fundamental aspect of everyday life and is critical to our sense of self. In everyday life we sometimes have memory lapses, where we fail to remember an important detail about an event, and this can become more prevalent in older age (Cansino et al., 2009). Moreover, deficits in episodic memory are a hallmark feature of certain disorders, such as mild cognitive impairment (Nordahl et al., 2005) and Alzheimer’s disease (Green et al., 1996). There has been a growing impetus in recent years to develop and test interventions to determine if they can enhance memory performance.

One technique that has emerged which may hold promise is neurofeedback. This is a self-regulatory technique where an individual is given feedback about certain patterns of brain activity which are proposed to be linked to a target behaviour. The assumption is that through this real-time feedback an individual can change their brain activity to the pattern desired and this will result in enhancements in behaviour. It is a non-invasive procedure which is based upon operant conditioning. There are several imaging modalities which can be used to measure different brain signals, such as functional Magnetic Resonance Imaging (fMRI), which measures changes in blood oxygenation and flow to selected cortical regions and magnetoencephalography (MEG), which indexes the amplitude of magnetic fields (see review by Thibault et al., 2016). The technique which has been researched the most, and will be the subject of this paper, is electroencephalography (EEG), which measures electrical activity generated by pyramidal cells perpendicular to the scalp. The benefit of EEG for neurofeedback is its prevalence and accessibility, with low-cost headsets available that could be used in participant's homes.

The standard and most prevalent approach using EEG is to examine brain oscillations (Buzsaki, 2006), which arise from the synchronised activity of a population of neurons within a selected frequency band and feedback the power of this signal to the participant. However, several other approaches have emerged in more recent years. For instance, network or connectivity-based neurofeedback has been employed with EEG, which focuses on inter-electrode phase coherence over certain frequency bands. This can provide an estimate of the functional interactions between neural systems operating in a frequency band (e.g. see Kober et al., 2020). Another approach is low resolution electromagnetic tomography (LORETA; Pascual-Marqui et al., 1994), which utilises multi-channel scalp-recorded EEG data and inverse solutions to estimate underlying brain electrical activity. LORETA neurofeedback targets the regulation of activity in specific brain regions using scalp-recorded multi-channel EEG data (e.g. see Bauer & Pllana, 2014; Congedo et al., 2004). Very recently machine learning algorithms have been proposed for use in EEG neurofeedback paradigms, for example, to train autobiographical memory (see Luján et al., 2021). This approach involves identifying the training targets and features from the multiple-channel data in real-time. As the majority of studies use a standard power-based oscillatory approach, that measurement is the focus of this study.

Moreover, from the memory literature there is good reason to think that EEG-Neurofeedback (EEG-NF) may be effective as there is now substantial evidence delineating a functional role for brain oscillations in episodic memory. For example, numerous studies using intercranial electrodes in patients with epilepsy and scalp recorded EEG and MEG have found this link, with several frequency bands being investigated, including theta (4-8 Hz), alpha (8-12 Hz) and gamma (25-100 Hz) (Duzel et al., 2003; Fell et al., 2003; Guderian & Duzel, 2005; Klimesch et al., 1997; 2001; Lin et al., 2018; Martin-Buro et al., 2020; Mormann et al., 2005). Research is currently determining the exact functional significance of these frequency bands and their interaction with each other in promoting episodic retrieval (Hanslmayr et al., 2016; Herweg et al., 2020; Nyhus & Curran, 2010).

There have been a few studies which have examined the effects of EEG-NF on episodic memory. One of the first studies completed in healthy volunteers was by Berner et al. (2006) who was interested in the links between sleep, neurofeedback and memory performance. In their study a sample of 11 participants, who had previously been found to be able to regulate their brain activity, took part in four 10-minute neurofeedback sessions where they were required to upregulate sigma/beta activity (11.6-16 Hz) or were given pseudo feedback which was provided randomly from an inactive EEG channel (within-participants design, sessions counterbalanced and one week apart). After the neurofeedback session participants were required to encode word-pairs by imagining a visual relationship between the two words. Participants were given a cued recall test in the evening around 10-15 minutes after the encoding phase and then another test in the morning. Neurofeedback had no significant effects on memory performance on either test. In contrast other studies have found significant effects of neurofeedback on episodic memory. For example, in a study by Rozengurt et al. (2017), they asked healthy volunteers to upregulate their theta for 30 minutes in the period between participants learning object pictures and having to subsequently free recall them. In comparison to active (who upregulated low beta, 15-18 Hz) and passive control groups the participants who completed theta neurofeedback had significantly better memory performance immediately following the intervention and also one day and one week later. Thus, there are differences between studies in their conclusions as to whether EEG-NF has a beneficial effect on memory and there is heterogeneity in terms of neurofeedback testing protocols, such as which EEG frequency band is targeted.

The issue of whether EEG-NF can enhance episodic memory has also been examined in the context of various clinical conditions, such as mild cognitive impairment, sleep disorders, epilepsy, and stroke. Lavy et al. (2019) conducted a pilot study in 11 individuals who had a diagnosis of mild cognitive impairment. Neurofeedback training was ten 30-minute sessions which were delivered over five weeks and asked participants to increase the power of their individual upper alpha band. There was no control group in this study. Participant's performance was examined before the intervention, immediately afterwards and at a 30-day follow-up. Participants were given a standardised battery of tasks measuring a variety of cognitive functions as well as an item-association memory task. In the standardised battery, one of the measures, the composite memory score, was found to improve from before the intervention to afterwards and then was maintained at the 30-day follow-up. However, this reflected improvements in immediate recall, likely more akin to working memory. Participants did not show any enhancement for the item-association task, a measure of episodic memory, for either words or images. Nevertheless, there are other clinical studies which have demonstrated enhancements of episodic memory. Escolano et al. (2014) tested 60 participants with major depressive disorder, who were not randomly allocated to the neurofeedback group and a non-interventional control group. The neurofeedback protocol was targeted at increases in individual upper alpha power, with participants completing eight sessions of 20-minutes neurofeedback training, spread over five weeks. For the measure of episodic memory there was an improvement in the number of words recognised from pre to post intervention in the neurofeedback group which was not seen in the control group. In parallel with the findings from healthy volunteer studies there is mixed evidence as to whether EEG-NF is advantageous for episodic memory, and this is complicated further by the range of clinical disorders that have been examined.

The small number of studies discussed above also highlight two critical design issues which need to be considered when determining the efficacy of EEG-NF. One is the presence of an active control group/condition (Enrique-Geppart et al., 2017; Ros et al., 2020; Sorger et al., 2019). This allows the researcher to determine the extent to which any improvement seen in the experimental group is specifically due to the neurofeedback intervention and not other general factors, such as: participant-experimenter interaction, motivation, and repetition-related effects. In the context of EEG-NF experiments there are three general options for an active control: i) non-contingent, where there is no link between the participant's brain activity and the feedback they receive, such as when they receive the same feedback as a participant in the experimental group or artificially generated feedback, ii) contingent, where the participant receives feedback from an alternative frequency band that is not hypothesised to be linked to the target behaviour, and iii) non-neurofeedback, where participants complete a task that they need to engage with that does not require neurofeedback. For all control conditions the participants should have the same schedule as those in the experimental group, including visits to the lab and being actively engaged with a task for the same duration. Moreover, in between-participants designs participants should be randomly allocated to the experimental or control group (or in within-participants designs the conditions should be counterbalanced) to minimise bias by the experimenter or participant. In EEG-NF studies this would also mean that studies which allocate 'non-responders', i.e. those participants who are unable to regulate their brain activity in the desired way, to the control group do not meet this criterion. Therefore, the quality of studies needs to be examined, particularly the presence of an active control group and randomisation of participants to groups.

Given the potential promise of EEG-NF to enhance episodic memory function there is now a need to review, evaluate and quantify the research in this area. The first aim was to conduct a systematic review into the literature on episodic memory and EEG-NF to understand what research has been conducted in this area. This review included both healthy and clinical populations and three key areas were examined: i) sample characteristics, ii) study design, and iii) neurofeedback protocols utilised. This is the first systematic and qualitative review which has been conducted examining both healthy and clinical populations specifically with respect to episodic memory and will provide information concerning the scope of currently published studies. The second aim was to complete a meta-analysis to determine whether EEG-NF can enhance episodic memory performance. Importantly for this aim the analysis was restricted to only those studies where there was an active control group/condition and participants were randomly allocated or counterbalanced to the experimental and control groups/conditions. Furthermore, given the heterogeneity of neurofeedback protocols it was examined whether there would be moderators of memory performance. The essence of EEG-NF is that it is participants' success in modulating their brain activity which results in the behavioural improvement. I therefore also included a measure of EEG-NF success in the moderator analysis to examine this. My goal with this meta-analysis was to provide critical information for future studies on episodic memory as to whether EEG-NF can enhance memory and what might be the optimal training parameters.

2.2 Methods

2.2.1 Study searches and inclusion criteria

The search for studies was completed in two rounds. The initial search took place on 1 February 2021, followed by a fresh search which was conducted on 4 March 2022 to ensure the review included newer publications. This was conducted within the databases PsychInfo, PubMed, Scopus (Elsevier), Web of Science, CINAHL and ProQuest using the key word search string: ((EEG OR electroencephalograph*) AND (biofeedback OR neurofeedback OR "bio feedback" OR "neuro feedback") AND (memor* OR cogniti*)). A filter was added to include English language articles only. Following the removal of duplicate studies, the searches generated 2086 potential studies that ranged from published books and articles to conference proceedings, randomised controlled trials, dissertations and theses.

The initial screening process involved scanning the titles and/or abstracts of each study generated by the search, followed by more detailed scrutiny of the remaining 211 full-text studies to ascertain eligibility. Screening was performed by the first author and a random sample containing approximately 10% of the full-text studies was screened by one of the other authors, to check consistency of eligibility judgements. Raters achieved 90% alignment and discussed and agreed on the eligibility status of the remaining studies. To be eligible for inclusion to the qualitative review the study needed to meet the following criteria. First, the study needed to involve neurofeedback, which was measured using EEG. Second, the study needed to examine the effects of EEG-NF on episodic memory. A variety of tasks can be used to do this, including recall and recognition and could be of verbal or visual information. Third, the participants were adult healthy volunteers or those with a clinical condition. Studies which had tested animals, or children i.e. those aged 15 or younger, were not included. Importantly, in this paper, the question being examined is whether EEG-NF has an effect on episodic memory and not whether there is a difference between healthy and clinical groups. For the qualitative review the final study set was 46.

Additional criteria were applied for completion of the meta-analysis. First, studies had to have an active control group or control condition, which was attended according to the same schedule as the experimental group. Second, studies needed to have randomised participants to the experimental or control groups if it was a between-participants design or to counterbalance the conditions if it was a within-participants design. Finally, the study needed to have sufficient data available for calculating effect sizes. The final study set for the meta-analysis was 21. See Figure 1 for an overview of study screening and selection.

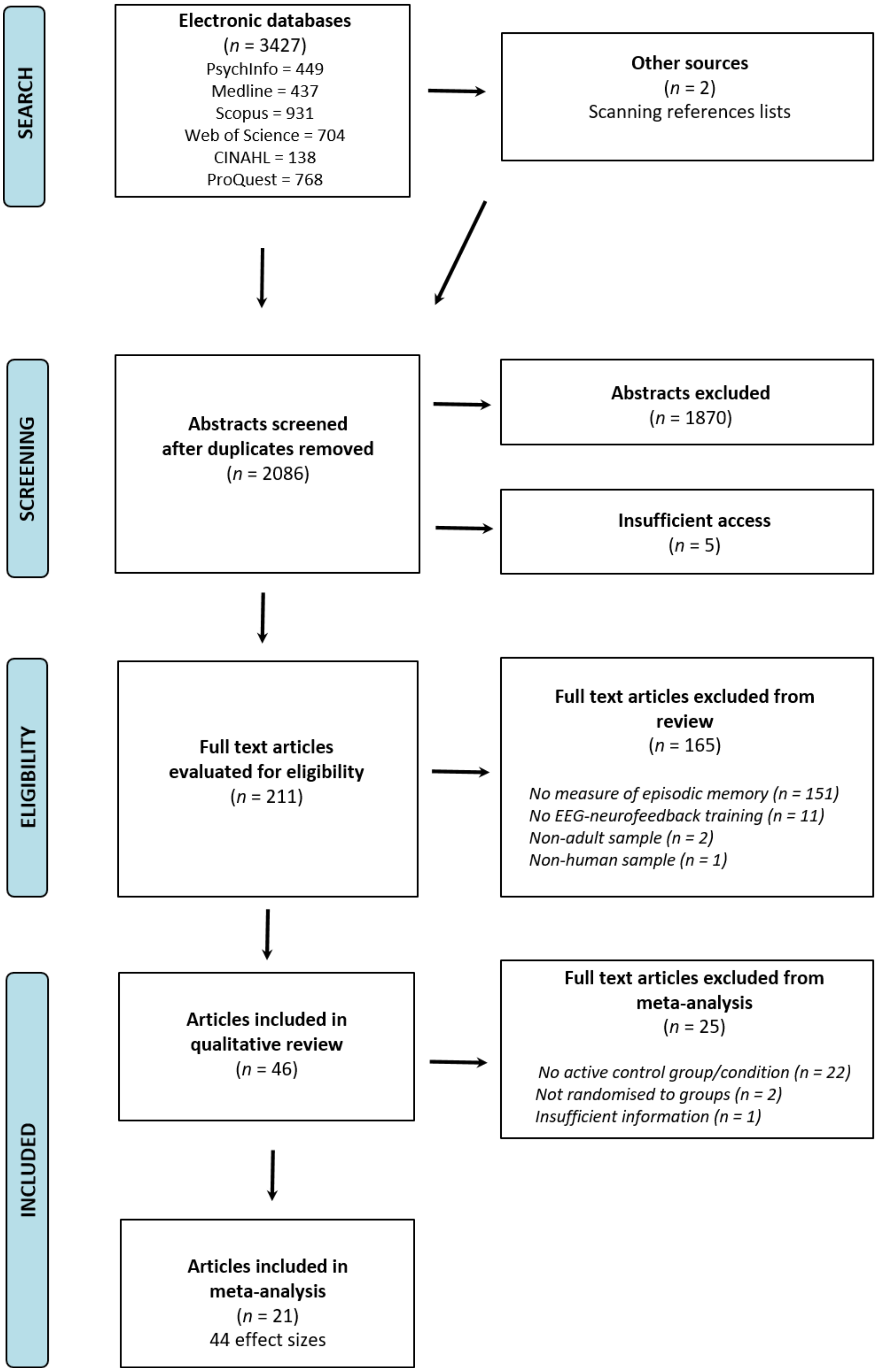

Figure 1. Flow diagram of the study selection process following PRISMA criteria (Moher et al., 2009).

2.2.2 Data extraction and study coding

Data were extracted by the first author and a random sample containing approximately 10% of the eligible studies was completed by one of the other authors to check consistency of data extracted. The following variables were coded:

2.2.2.1 Sample characteristics

This included the number of participants in each study, and per group or condition. The mean age of participants was also recorded including the age range, if reported in the study. The population type was defined as healthy volunteer or a clinical group. In addition, the number of participants who were unable to self-regulate the target band during neurofeedback i.e. non-responders, was also noted if reported.

2.2.2.2 Study design

Whether the study was within-participants (a cross-over design where all participants were tested under both the experimental and control conditions), or between-participants (participants were allocated to either the experimental or control group/condition) was noted. Single-case and single-group experiments, where no control condition was included in the design, were labelled as such where only within-participant changes are noted before and after the neurofeedback. The presence of a control group/condition was coded with the following general categories used: i) no control; there is only a neurofeedback condition, with nothing to compare this to i.e. pre-post only designs, ii) non-active control; there is a control group or condition but participants do not receive any training, this would include waitlist control groups in clinical studies, and iii) active control; there is a control group or condition where the participant does a task according to the same schedule as the neurofeedback group.

For the meta-analysis only studies which had an active control group/condition were included and this category was further split into the following three groups: i) non-contingent, where there is no link between the participant’s brain activity and the feedback they receive, ii) contingent, where the participant receives feedback from an alternative frequency band that is not hypothesised to be linked to the target behaviour, and iii) non-neurofeedback, where participants complete a task that they need to engage with that does not require neurofeedback. A study using inverse contingency, where the active control group regulated target band in the opposite direction, was coded as contingent as well. Studies were also coded as to whether they randomised participants to groups, if it was a between-participants design. This included pseudo-randomisation where participants were matched across groups e.g. for demographic factors such as age, gender and education. For within-participants design it was examined whether the order of the experimental and control conditions was counterbalanced. Finally, it was also coded as to whether blinding measures were included in the experimental design. There were three classifications of blinding: none, single (the participant does not know which study group they are in) or double (the participant and experimenter do not know which group the participant has been assigned to).

2.2.2.3 EEG-neurofeedback training

There were several aspects of the neurofeedback training protocol that were coded. Across different studies the neurofeedback training is structured in different ways, some have many testing sessions, whereas others have only one. Therefore, one variable that was coded is the number of separate neurofeedback testing sessions. Related to this is the total duration of time that participants spend completing neurofeedback training. Therefore, the number of minutes each participant spent performing neurofeedback training was also quantified for each study, excluding resting. A variety of EEG frequency bands can be used for neurofeedback. The following were coded: slow cortical potentials (0.1-1 Hz), theta (4-8 Hz), alpha (8-12 Hz; this also includes the mu rhythm, 8-13 Hz), beta (12-30 Hz; this also includes the sensory-motor rhythm, 12-15 Hz and sigma, 11.6-16 Hz), and gamma (30-100 Hz). Clinical studies where participant's feedback was based on their resting baseline quantitative EEG were coded as qEEG. This method measures localisation, frequency, and connectivity of brain activity for every individual, which informs their live z-score training in relation to the normative/clinical database (Ko et al., 2021). Neurofeedback is measured from certain electrode sites positioned over the scalp. These were grouped into: frontal, central, or parietal and occipital sites. In addition, the number of feedback electrodes used to measure target activity was recorded. The neurofeedback the participant receives can come from different modalities, coded into: visual, auditory and both. Finally, it was coded whether in each study participants were given instructions for how they should go about regulating their brain activity. This was coded as yes if any were given, even if they were vague, and a no if no explicit instructions were provided to the participant i.e. they were instructed to simply relax and let the feedback guide them.

2.2.2.4 Episodic memory measure

To examine whether EEG-NF affected episodic memory performance in the meta-analysis, an effect size was calculated to reflect the magnitude of change in memory scores pre- and post- EEG-NF in the experimental group, relative to the control group. Episodic memory was further sub-categorised into recognition and recall in the moderator analysis to determine whether the effect of EEG-NF was moderated by these memory types. A measure of recognition memory was obtained from memory paradigms or neuropsychological tests that required participants to make an old/new decision. A measure of episodic recall was acquired where participants were required to recall information studied at least 15 minutes prior (e.g. delayed memory or source recollection tasks). Group means (M), standard deviations (SD) and sample sizes (n) were extracted from the text or alternatively from figures using WebPlotDigitizer (Version 4.3, Rohatgi, 2020). Alternatively, F and t statistics were used to calculate the effect size. If insufficient data were reported, this was requested by contacting the corresponding author via email, if no response was received, these studies were excluded from the meta-analysis.

2.2.2.5 Neurofeedback success measure

To generate a measure of participants’ overall ability to self-regulate target brain activity, a binary code was assigned to each study, whereby ‘1’ indicates that EEG-NF success was reported and ‘0’ indicates there was no evidence of EEG-NF success. Self-regulation of target brain activity was evidenced by a range of different measures across studies, including absolute and relative power or amplitude, and band-ratio such as theta/low beta. EEG-NF was considered a success when the authors reported a statistically significant increase in the EEG-NF group relative to the control group. This could be reported by way of: i) a significant between-groups p-value ($p < 0.05$), ii) a significant group effect or interaction between groups and time in an ANOVA, or iii) a significant within-subjects pre-post EEG-NF comparison (e.g. baseline to EEG-NF training session) in the experimental group but not in the control group. This success measure is the same as used by Rogala et al. (2016). The same criteria were applied to each band where more than one band was investigated within a study.

2.2.2.6 Statistical analyses

A meta-analysis was conducted using the robu() function of the robumeta package in R, version 4.0.3. The output of the primary meta-analysis included the pooled mean population effect size (*g*) which represents the overall effect of EEG-NF on memory. Also reported is the standard error, a t-value representing the statistical significance of the combined effect size and 95% confidence interval. The proportion of heterogeneity observed across studies is indicated by I^2, and τ^2 represents an estimate of the standard deviation of the true effect size.

2.2.2.7 Effect size calculation

The standardised mean difference (*d*) was calculated for most studies using the d_{ppc2} formula (Morris, 2008). Alternatively, F and t statistics were used in equivalent formulas, and appropriate transformations and corrections applied for studies using within-participants designs (Morris & DeShon, 2002). Individual effect sizes were converted from *d* to Hedges’ *g* using the bias correction formula (Hedges, 1981), which produces a relatively unbiased estimate of the population standardised mean difference effect size. The small sample correction was applied to studies with a sample size of 50 or less (Hedges & Olkin, 1985).

2.2.2.8 Outliers and influential cases

Outliers, or ‘extreme effect sizes’, can contribute disproportionately to the effect size estimate in a meta-analysis. Consequently, if these are included in analyses, the reported pooled effect size estimate could be somewhat greater or smaller than the true effect size. Many different methods exist to detect outliers; however, a common method used to detect outliers in a meta-analysis is to calculate whether the confidence interval of each study effect size overlaps with the confidence interval of the pooled effect size estimate. If either the lower or upper boundary of the former does not overlap with the upper or lower boundary of the latter, respectively, the study effect size is considered an outlier (Viechtbauer & Cheung, 2010). In the current meta-analysis, reported are the pooled effect sizes that were calculated following the removal of outliers detected using this method.

2.2.2.9 Publication bias

Egger’s Regression Test (ERT) was used to test for possible influence of publication bias on the analyses (Egger et al., 1997). This test aims to measure any significant relationship between the effect size and its precision, whereby such a relationship might indicate that larger effect sizes are driven by small-study effects, i.e. studies that are less precise. A modified version of the ERT was used in this meta-analysis, whereby the effect sizes were regressed against the sample variance ($\sqrt{W}$) rather than the standard error, as the latter can overestimate the significance of funnel plot asymmetry when using SMD effect size estimates (Pustejovsky & Rogers, 2019; Rogers & Pustejovsky, 2021).

2.2.2.10 Data synthesis

Robust variance estimation (RVE) was used to account for the dependency between multiple effect size estimates within each study (Hedges et al., 2010; Tanner-Smith & Tipton, 2014). Accordingly, this method firstly applies an appropriate correlated weight and standard error to each effect size estimate to allow the balanced inclusion of multiple outcomes in the meta-analysis. Sensitivity analysis was performed to estimate the correlation between the effect sizes within-studies (p) based on the fact a random effects model was used. A small sample correction was applied because less than 40 studies were included in the meta-analysis (Tipton, 2015).

2.2.2.11 Moderator analyses

To investigate the relationship between individual moderators and the overall mean population effect size, a meta-regression was performed with RVE. Categorical moderators were dummy coded to compare two sub-levels within a factor. Multi-level factors were contrast (sum) coded to compare the mean effect size of each level with the grand mean of the factor (e.g. the difference between the mean effect size for studies employing alpha band as the experimental EEG-NF protocol, and the grand mean of all EEG-NF protocol mean effect sizes). Both the coefficient (*B*) and the p-value are reported for each comparison, as well as the degrees of freedom (*df*). Continuous moderators consisted of numerical data which could be directly correlated with effect sizes via a linear regression model with RVE. Similarly, the coefficient (*B*) of the slope is reported along with the *df* and *p*-value, to reflect the magnitude and direction of the relationship (e.g. between the amount of EEG-NF training received by participants and their subsequent memory performance). Categorical moderators that contained less than 5 effect sizes were excluded from all analyses. This resulted in the omission of the active non-EEG-NF condition from the control condition analysis (1 effect size), the gamma band frequency (2 effect sizes) being removed from the target frequency band analysis, and the auditory variable (4 effect sizes) being excluded from the modality analysis.

2.3 Results

2.3.1 Sample characteristics

The systematic review included 46 studies with a total of 1127 participants (1192 observations), details of these studies can be found in Table 1. Of these studies just under half had been conducted in healthy volunteers (n = 22) with the rest in clinical populations or looking at the effects of a medical condition (n = 24). A wide variety of conditions have been examined but for many only a single study has been conducted in that area: Alzheimer's disease (n = 1), alcoholic dependence syndrome (n = 1), COVID-19 (n = 1), epilepsy (n = 1), insomnia (n = 2), mild cognitive impairment (n = 3), major depressive disorder (n = 1), multiple sclerosis (n = 2), obsessive compulsive disorder (n = 1), stroke (n = 5), and traumatic brain injury/concussion/brain tumour (n = 6). For all studies reviewed the sample sizes range from single-case studies up to 79 participants in total, with a maximum of 40 participants in the experimental group (excluding single-cases, mean = 16, median = 11). For healthy volunteer studies, where there were no single-case studies, the mean number of participants in the experimental condition of interest is 13.9 (median = 10). In the clinical domain there are a significant number of studies which only have one participant in the experimental condition (n = 8), excluding these studies results in a mean number of participants in the experimental condition of 19.4 (median = 15).

In neurofeedback experiments some participants cannot regulate their brain activity in the desired way. Thus, positive effects on memory cannot be expected in these individuals if they are unable to complete the intervention. There is no standard definition of what would constitute a non-responder, but it has been estimated that the rate of these is between 16-57% (Alkoby et al., 2018). After excluding studies with one or two participants in the experimental condition it was found that 28 (80%) did not report information regarding how many participants were non-responders. In the 7 studies (including one study with two conditions) that did report the number of non-responders in the experimental condition the percentage ranged from 0 to 33.3 with an average of 17.7% for healthy participants and 30.6% for clinical patients.

2.3.2 Study design

A total of 17 studies (37%) included no control measure i.e. there was not a group or condition to compare the effects of the neurofeedback training on memory to. These were largely single-case studies and pilot work. Five of the studies (2 healthy volunteer, 3 clinical) used a non-active control. In all these studies there was a control group, but this group did not do anything instead of the neurofeedback intervention and did not attend the lab according to the same schedule. Twenty-four of the studies did include an active control group or condition. Of the studies with a control condition or group (active or non-active) 3 of these had a within-subjects design (10.3%) and 26 (89.7%) had a between-participants design. All 3 studies with a within-subjects design counterbalanced the conditions, and for the between-subjects design, 22 studies randomised participants to the experimental and control groups. This meant that 4 studies did not implement randomising or were not clear when reporting this information. A further design feature that studies can apply is blinding. Of those studies with a control group or condition in 14 (48.3%) of them participants were blinded to their group allocation, or the condition under which they were being tested. Double blinding was implemented in seven studies (24.1%), whereby both participant and experimenter were unaware of who was in what condition. No blinding measures were included in eight studies (27.6%), or this information was not clearly reported.

2.3.3 EEG-neurofeedback training

The number of feedback sessions included in EEG-NF training schedules ranged from one single session to 42 sessions, with the total amount of training provided to participants ranged from 25 minutes to 17.5 hours, with four studies failing to report this latter information. As might be anticipated and can be seen from Table 1 there seems to be a difference between single-case and group studies in the number and duration of neurofeedback. The median number of sessions in single-case studies is 19 (mean = 19.8) with a median duration of 8.75 hours in total (mean = 9.18 hours). In group studies there are a median of 10 sessions (mean = 10.8) and these have a median total duration of 3.5 hours (mean = 4.61 hours). Thus, the number and duration of neurofeedback sessions has a lot of variability across studies, even when single-case studies are excluded these range from 1-40 sessions, ranging from a few minutes to 16 hours.

Forty-six studies were included in the qualitative review and 7 of these investigated more than one frequency band (besides the neurofeedback control condition). Therefore, *k* refers to the number of protocols rather than to the number of studies (total k = 53). The EEG-NF protocols used across studies included alpha (8-12 Hz), beta (12-30 Hz), theta (4-8 Hz), gamma (30-100 Hz), slow cortical potential (SCP) and qEEG. All protocols involved up-regulation of the target frequency band unless otherwise stated. The protocol used the most in neurofeedback studies on memory in this review was beta (k = 22). In addition to general broadband beta (k = 4), this includes 16 sensorimotor rhythm (SMR) protocols, 1 up- and down-regulation of SMR coherence, and 1 sigma band. Most of the beta protocols (k = 20) used centrally located electrodes. Fourteen protocols examined alpha, comprising broad band alpha protocols (k = 6), 2 peak alpha frequency (PAF) protocols, 5 upper alpha (UA) and 1 mu (alpha rhythm that is typically localised over bilateral sensorimotor cortex). As might be anticipated alpha was mainly measured at parietal sites (k = 5), with two additional protocols combining parietal with occipital sites. Occipital (k = 3) and central (k = 4) areas were also targeted with alpha. Theta was the focus of 5 protocols and featured in 1 protocol which involved down- instead of up-regulation. Electrode placement was generally at frontal regions (k = 4). A minority of protocols looked at gamma (k = 3), SCP (k = 2) and qEEG (k = 2). Five studies used protocols combining different frequencies. Across all protocols an average of 1.7 electrodes were used (median = 1), with a range of 1 to 6 electrodes. See Figure 2 for an overview of EEG-NF protocols and electrode locations.

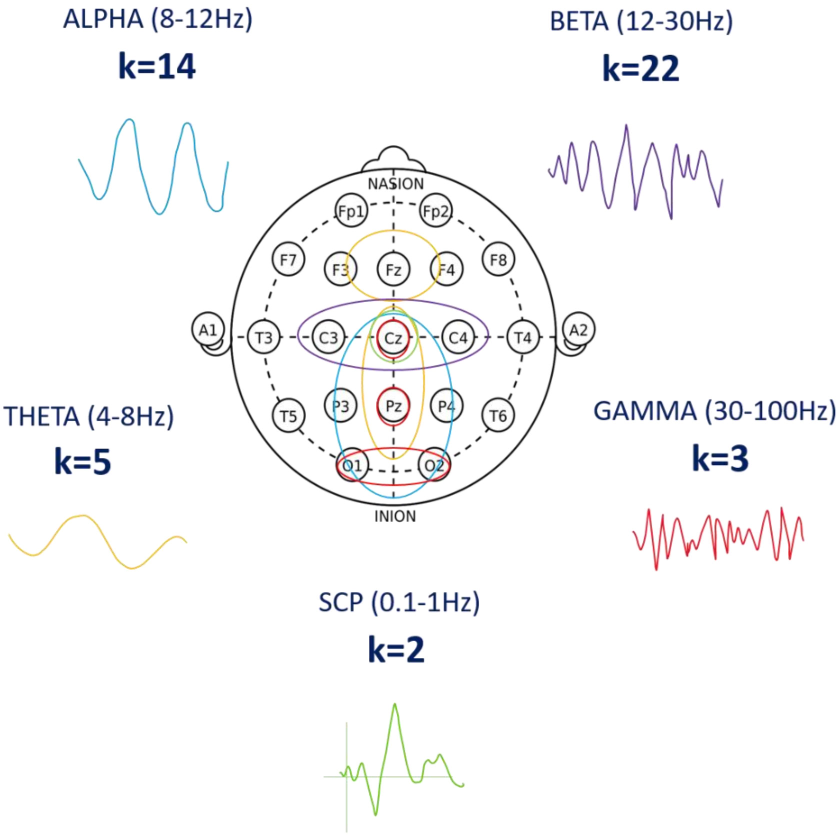

Figure 2. Diagram depicting the number of protocols of each frequency band type and the predominantly used electrode/s location for each.

When participants receive neurofeedback, it can be delivered in different modalities. The studies in this review mainly presented feedback just visually (n = 22), this was typically a bar graph where participants had to try to keep the bar above a line (e.g. Kober et al., 2015b; Rozengurt et al., 2017) but also included richer displays like a rollercoaster (e.g. Eschmann et al., 2020; Wang & Hsieh, 2013). A combination of visual and auditory feedback was also popular (n = 18), and this could be achieved by presenting participants with a short acoustic tone and increasing the clarity of the picture. Less popular was solely auditory feedback (n = 3), where the aim was simply to increase the rate of the tone occurrences. Three studies did not report which modality was used to deliver neurofeedback.

In the majority of studies (n = 36) participants were not provided with explicit instructions on how to self-regulate target brain activity. In these studies participants are generally told that the feedback that they receive is determined by the characteristics of their EEG and they need to work out what mental state provides positive feedback and to maintain that, or this information was not clearly reported. Eight studies provided participants with suggested strategies to modulate target brain activity. One study (Byers et al., 1995) introduced instructions for the second part of the protocol but not the first, so is not included in the totals above. Some of these instructions were quite general e.g., to use a combination of relaxation techniques and positive thought (Hoedlmoser et al., 2008), whereas others gave specific strategies for target bands e.g. relaxation for theta and concentration for low beta (Rozengurt et al., 2017) and motor imagery for SMR (Kober et al, 2020).

2.3.4 Meta-analysis

2.3.4.1 Sample characteristics

For the meta-analysis only studies where the relevant data were available, and which had an active control condition and who randomised participants to this or the experimental condition (or counterbalanced in a within-participants design) were included. This reduced the sample to 21 studies, with 361 participants across all these studies in the experimental condition/group. Most of these studies were on healthy volunteers with only 2 conducted in clinical populations. The mean age of participants was 32.8 years (range 20 to 75.3). Some of the studies had multiple memory measures or looked at several target frequency bands and so generated a total of 44 effect sizes (range of 1 to 8 per study).

2.3.4.2 Publication bias

The possible influence of publication bias on the analyses was estimated using a modified version of Egger's Regression Test for funnel plot asymmetry (ERT; Egger et al., 1997; Pustejovsky & Rogers, 2019, 2021). This revealed significant funnel-plot asymmetry when testing the initial study set ($n = 21$; $k = 44$; $t = -3.23$, $p = 0.011$). However, on removal of all identified outliers (5 effect sizes from four studies: Guez et al., 2015; Hord et al., 1975; Hsueh et al., 2012; Shtoots et al., 2020) the result of the ERT was not significant: $t(9.13) = -2.38$, $p = 0.147$. Therefore, the final study set included in the meta-analysis constituted 20 studies with 39 effect sizes.

2.3.4.3 Primary analysis: Effect of EEG-NF on episodic memory.

A statistically significant, small effect (Cohen, 1988) of EEG-NF on episodic memory performance was revealed: $g = 0.31$, $SE = 0.09$, $t(17.1) = 3.49$, $p = 0.003$, 95% CI [.12, .49][1, 2] - see Figure 3. A small amount of heterogeneity ($I^2 = 18.2\%$, $\tau^2 = 0.03$) was detected between the studies analysed. Further exploration of this variance was conducted by way of moderator analyses and their individual estimates to examine the dispersion of effects.

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[1] The result of the meta-analysis on the study set before outliers were removed was still significant but with a smaller effect size: $g = 0.28$, $SE = 0.11$, $t(19.3) = 2.55$, $p = 0.019$, 95% CI [.05, .50].

[2] The meta-analysis was performed on a study-set including solely healthy participants i.e. Lavy et al. (2021) and Schabus et al. (2017) were removed. This was to preclude possible anomalies in the effects of EEG-NF training on clinical patients. A statistically significant, and slightly bigger effect size was generated: $g = 0.35$, $SE = 0.09$, $t(15.6) = 3.82$, $p = 0.002$, 95% CI [.16, .55].

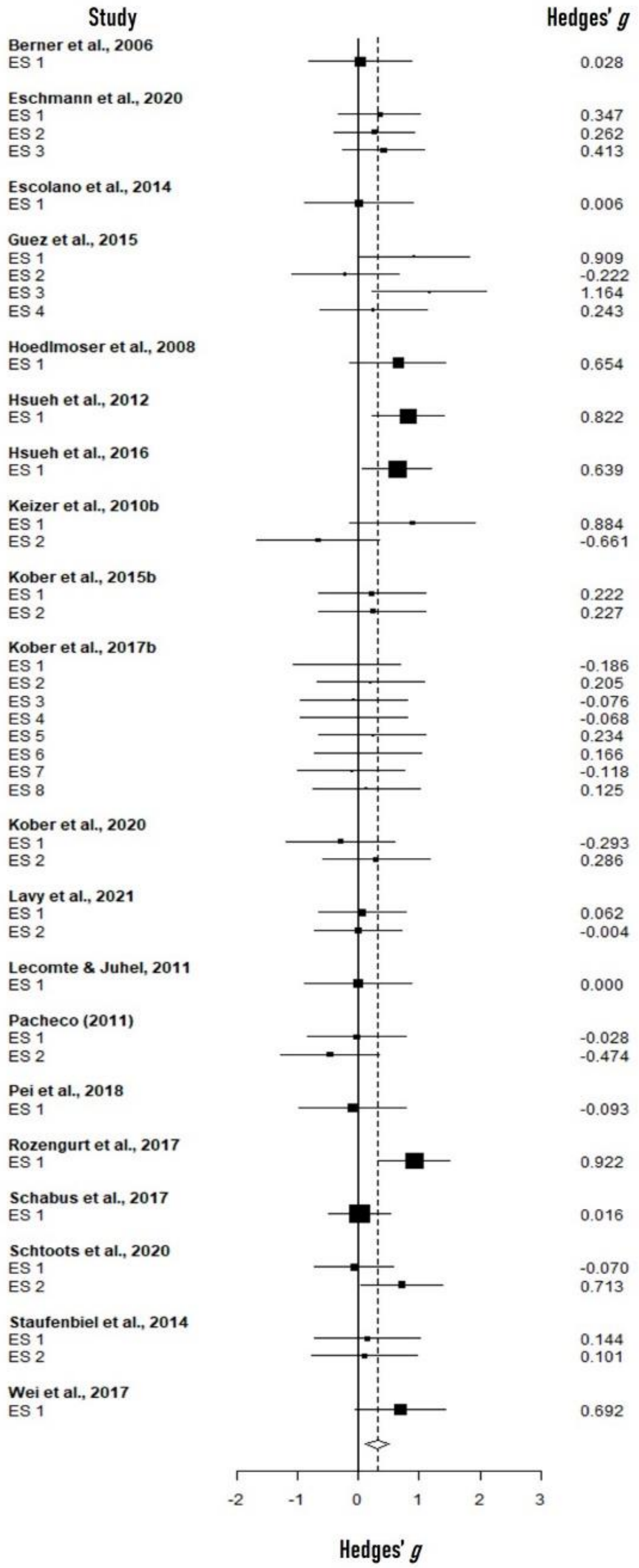


Figure 3. Forest plot showing the overall effect of EEG-NF on episodic memory performance and the distribution and weighting of effect sizes across studies, represented by the size of the square. Error bars represent the 95% confidence interval of the effect. Squares to the left of zero indicate a negative effect of EEG-NF on memory. Squares to the right of zero indicate a

positive effect of EEG-NF on memory. The white diamond and dotted line represent the pooled effect size.

2.3.4.4 Moderator analyses

Several moderator analyses were conducted to examine the effects of the sample, study design and EEG-NF training parameters and type of episodic memory measures. The results for all these analyses, including individual effects for each group, are summarised in Table 2.

EEG-NF success significantly moderated the effect of EEG-NF on episodic memory ($B = 0.46$, $p = 0.007$), such that where studies reported significant modulation of brain activity in the EEG-NF group relative to the active control group, a highly significant, approaching medium size effect on memory performance was revealed ($g = 0.47$, $t(11.2) = 0.472$, $p < 0.001$). In studies where no such modulation was reported, no effect was observed on memory performance.

Memory type (i.e. whether recognition or recall was being measured) was not a significant moderator of memory performance overall. However, at the sub-group level EEG-NF had a highly significant, small size effect on participants' ability to recall information ($g = 0.34$, $t(15.1) = 3.54$, $p = 0.003$). The analysis revealed no significant effect on recognition performance.

Memory modality (whether verbal or visual memory was being measured) significantly moderated the overall effect size ($B = -0.34$, $p = 0.032$). A significant, small size effect of EEG-NF on verbal memory was revealed ($g = 0.37$, $t(13) = 3.65$, $p = 0.003$), whereas it had no significant effect on visual memory.

There was no significant moderation effect of control condition on episodic memory performance. However, on a sub-group level, studies using a contingent control generated a highly significant, small size effect ($g = 0.31$, $t(17.1) = 3.49$, $p = 0.003$), whereas the effect was not significant for studies using a non-contingent control.

Another factor that was explored was whether the EEG-NF training instructions given to participants moderated the overall memory effect size. Whether or not participants were given instructions regarding how to achieve the target brain state did not significantly influence overall memory performance. However, a small effect on memory performance was found in the sub-group analysis for those who received no in structions ($g = 0.23$, $t(12) = 2.22$, $p = 0.047$) and those who did ($g = 0.44$, $t(4.7) = 2.66$, $p = 0.048$). The modality of the neurofeedback did not moderate memory performance. However, on a sub-group level, protocols delivered visually did ($g = 0.36$, $t(10.2) = 3.02$, $p = 0.013$). In studies where a combined visual and auditory protocol was used, there was no significant effect of EEG-NF on memory performance.

There was no evidence that target frequency band, either in the moderation or sub-group analyses, had any impact on memory performance. Similarly, the amount of EEG-NF, whether measured by the total time or number of sessions, did not affect memory.

Interactions between EEG-NF training band and the amount of training (both the number of EEG-NF training sessions and EEG-NF training time) were explored, to determine whether the amount of EEG-NF training differed according to the target frequency band (alpha, beta, and theta). The interactions between both measures of training amount and all three protocols were significant; however, these results cannot be trusted given in all cases the degrees of freedom were too small (i.e. below 4) – See Table 3. This indicates that for these contrasts there were an insufficient number of studies per group. More studies conducted in this field could better elucidate any relationships between the amount of EEG-NF training required to self-regulate certain frequency bands.

Table 1. *Sample, study design and EEG-NF training characteristics of all studies included in the systematic review.*

Study	NF sample size	Age (mean)	Population	Number of non-responders	Design	Control	Randomised /Counter-balanced	Blinding	No. of training sessions	Training time (mins)	Target frequency band	Electrode site	EEG-NF modality	Instructions
A. Studies included in the meta-analysis														
Berner et al. (2006)	11	20.8	Healthy	0	Within - participants	Active (NCS)	Y	NR	1	40	Sigma +	Cz	Both	N
Eschmann et al. (2020)	17	23	Healthy	NR	Between - participants	Active (CS)	Y	Single	7	210	Theta +	Fz	Visual	Y
Escolano et al. (2014a)	10	25.1	Healthy	NR	Between - participants	Active (NCS)	Y	Double	1	25	Upper alpha +	P3, Pz, P4, O1 & O2	Visual	N
Guez et al. (2015)	SMR: 10 UA: 10	23.6	Healthy	NR	Between - participants	Active (NCS)	Y	Double	10 10	300 200	SMR + Upper alpha +	C4 Pz	Both	N
Hoedlmoser et al. (2008)	16	23.6	Healthy	NR	Between - participants	Active (CS)	Y	Single	10	240	SMR +	C3	Both	Y
Hord et al. (1975)	7	20	Healthy	1	Between - participants	Active (NCS)	Y	Single	7	630	Alpha +	O2	Both	N
Hsueh et al. (2012)	SMR: 23 Mu: 25	21	Healthy	NR	Between - participants	Active (CS)	Y	NR	12 12	432 432	Mu + SMR +	C3, C3a-p; Cz Cza-p; C4, C4a-p	Visual	N
Hsueh at al. (2016)	25	21.3	Healthy	5	Between - participants	Active (CS)	Y	Single	12	432	Alpha +	C3, C3a-p; Cz Cza-p; C4, C4a-p	Visual	Y
Keizer at al. (2010)	Gamma: 8 Beta: 9	22.6	Healthy	NR	Between - participants	Active (CS)	Y	Double	7 7	210 210	Gamma + Beta +	Oz Oz & Fz	Auditory	N
Kober et al. (2015b)	10	24.4	Healthy	NR	Between - participants	Active (NCS)	Y	Double	10	180	SMR +	Cz	Visual	N
Kober et al. (2017b)	SMR: 10 Gamma: 10	46.4	Healthy	NR	Between - participants	Active (CS)	Y	Single	10 10	180 180	SMR + Gamma +	Cz Cz	Both	N
Kober et al. (2020)	10	24.9	Healthy	NR	Between - participants	Active (CS)	Y	Single	10	180	SMR coherence +/-	Cz & CPz	Visual	Y
Lavy et al. (2021)	15	71.9	Clinical (MCI)	NR	Between - participants	Active (CS)	Y	Single	10	300	Alpha (PAF)	Pz	Both	N
Lecomte & Juhel (2011)	10	75.3	Healthy	3	Between - participants	Active (No-NF)	Y	NR	4	120	Alpha + & slow beta +	C3 & C4	Both	N
Pacheco (2011)	12	26.1	Healthy	NR	Between - participants	Active (NCS)	Y	Single	10	300	SMR +	Cz	Visual	N
Pei et al. (2018)	10	22	Healthy	NR	Between - participants	Active (CS)	Y	Single	5	180	Alpha +	Fz & C4	Visual	N
Rozengurt et al. (2017)	25	29.8	Healthy	6	Between - participants	Active (CS)	Y	Single	1	30	Theta +	Fz	Visual	Y
Schabus et al. (2017)	30	38.6	Clinical (insomnia)	NR	Within - participants	Active (CS)	Y	Double	12	360	SMR +	C3	Visual	Y

Shtoots et al. (2020)	18	23.5	Healthy	NR	Between - participants	Active (CS)	Y	Double	1	30	Theta +	Fz	Visual	N
Staufenbiel et al. (2014)	Gamma: 10 Beta: 10	67.8	Healthy	NR	Between - participants	Active (CS)	Y	Double	8 8	240 240	Gamma + Beta +	Fz	Auditory	N
Wei et al. (2017)	15	26	Healthy	NR	Between - participants	Active (CS)	Y	Single	12	300	Alpha +	C3	Visual	N

B. Studies included in the systematic review only

Afsar et al. (2021)	1	25	Clinical (TBI)	NA	Single - case/group	No	NA	NA	20	600	Alpha +	O1 & O2	Both	N
Bearden et al. (2003)	1	52	Clinical (stroke)	NA	Single - case/group	No	NA	NA	42	1050	Theta -	P3; T3-C3	Both	N
Bennett et al. (2013)	1	31	Clinical (TBI)	NA	Single - case/group	No	NA	NA	20	NR	Alpha + & theta +	O1 & O2	NR	N
Byers et al. (1995)	1	58	Clinical (concussion)	NA	Single - case/group	No	NA	NA	12 19	NR	SMR + Beta +	Cz T3 – C3	Both	Y N
Deng et al. (2014)	40	26.7	Clinical (OCD)	NR	Between - participants	Not - active	Y	NR	40	960	Alpha +, SMR + & theta +	NR	NR	Y
Escolano et al. (2014b)	40	51.6	Clinical (MDD)	NR	Between - participants	Not - active	N	Single	8	160	Upper alpha +	P3, Pz, P4, O1 & O2	Visual	N
Ghosh (2014)	1	39	Clinical (ADS)	NA	Single - case/group	No	NA	NA	10	400	Alpha + & theta +	NR	Visual	N
Hershaw et al. (2020)	38	33.4	Clinical (concussion)	NR	Single - case/group	No	NA	NA	15	450	qEEG	NR	Both	N
Kober et al. (2015a)	SMR: 11 UA: 6	65	Clinical (stroke)	SMR:3 UA:2	Between - participants	Active (No-NF)	N	NR	10 10	180 180	SMR + Upper alpha +	Cz Pz	Both	N
Kober et al. (2016)	2	40.5	Clinical (MS)	NA	Single - case/group	No	NA	NA	10	180	SMR +	Cz	Both	N
Kober et al. (2017a)	2	72.5	Clinical (stroke)	NA	Single - case/group	No	NA	NA	10	180	Upper alpha +	Pz	Visual	N
Kober et al. (2019)	14	38.9	Clinical (MS)	NR	Single - case/group	No	NA	NA	10	180	SMR +	Cz	Visual	Y
Kotchoubey et al.(2000)	27	40.7	Healthy	NR	Single - case/group	No	NA	NA	4	43.72	SCP +/-	Cz	Visual	N
Kotchoubey et al.(2001)	34	35.2	Clinical (epilepsy)	NR	Between - participants	Active (No-NF)	N	No	35	676.6	SCP +/-	Cz	Visual	N
Lagravinese et al.(2021)	1	49	Clinical (brain tumour)	NA	Single - case/group	No	NA	NA	15	525	Beta +	Cz	Both	N
Lavy et al. (2019)	11	70	Clinical (MCI)	NR	Single - case/group	No	NA	NA	10	300	Alpha (PAF)	Pz	Both	N
Luckos et al. (2021)	1	48	Clinical (COVID-19)	NA	Single - case/group	No	NA	NA	30	NR	Beta1 + & SMR +	C3 & C4	NR	N

Luijmes et al. (2016)	10	75.5	Clinical (AD)	NR	Single - case/group	No	NA	NA	30	600	qEEG	Fz, Cz, Pz and P4	Both	N
Martlats et al. (2020)	20	76.1	Clinical (MCI)	NR	Single - case/group	No	NA	NA	20	900	SMR +	Cz	Both	N
Reddy et al. (2013)	30	29.5	Clinical (TBI)	NR	Between - participants	Not - active	Y	NR	20	NR	Alpha +	O1 & O2	Visual	N
Reichert et al. (2016)	1	74	Clinical (stroke)	NA	Single - case/group	No	NA	NA	10	180	SMR +	Cz	Visual	N
Schabus et al. (2014)	24	34.8	Clinical (insomnia)	8	Within - participants	Active (CS)	Y	Single	12	240	SMR +	C3	Visual	N
Toppi et al. (2014)	2	45	Clinical (stroke)	NA	Single - case/group	No	NA	NA	10	180	SMR +	Cz	Visual	N
Tseng et al. (2021)	17	21.6	Healthy	NR	Between - participants	Not - active	Y	Single	3	90	Theta +	Fz	Auditory	Y
van Eijk et al. (2017)	10	78.6	Healthy	NR	Between - participants	Not - active	N	NR	10	210	SMR +	Cz	Both	N

Note. Abbreviations: AD = Alzheimer's dementia; ADS = Alcoholic Dependency Syndrome; COVID-19 = Coronavirus disease of 2019; MCI = mild cognitive impairment; MDD = major depressive disorder; MS = multiple sclerosis; OCD – obsessive compulsive disorder; TBI = traumatic brain injury; CS = contingent sham; NCS = non-contingent sham; No-NF = No-neurofeedback; NA = not applicable; NR = not reported.

Table 2. *Moderator analysis results for all categorical and continuous factors included in the meta-analysis*.

Category	Moderator	Level	Moderator analysis			Sub-group effect size			Heterogeneity		
			B	*df*	*p*	*ES*	*g [95% CI]*	*p*	I^2	τ^2	*df*
Brain activity	Self-regulating success		0.46	7.9	**0.007**						
		Yes				26	0.47 [.26, .68]	**<0.001**	0.00	0.00	11.2
		No				12	-0.009 [-.24, .22]	0.920	0.00	0.00	4.6
Episodic memory	Memory type		-0.19	4.5	0.407						
		Recognition				8	0.12 [-.38, .61]	0.543	19.05	0.05	3.8
		Recall/source				31	0.34 [.14, .54]	**0.003**	14.48	0.02	15.1
	Memory modality		-0.34	10.2	**0.032**						
		Verbal				26	0.37 [.15, .59]	**0.003**	6.06	0.01	13.0
		Visual				13	0.02 [-.20, .23]	0.854	0.00	0.00	7.5
Study design	Control group		-0.29	6.1	0.131						
		Contingent				39	0.31 [.12, .49]	**0.003**	18.25	0.03	17.1
		Non-contingent				10	0.09 [-.27, .45]	0.537	0.00	0.00	4.0
EEG-NF training	Instructions provided		0.21	10.5	0.303						
		Yes				9	0.41 [-.12, .94]	0.048	33.66	0.05	4.7
		No				30	0.23 [.004, .46]	**0.047**	9.11	0.02	12.0
	Target frequency band	**GM: 0.33**									
		Alpha	-0.07	8.4	0.608	8	0.24 [-.17, .66]	0.197	0.00	0.00	5.2
		Beta	-0.15	11.7	0.271	23	0.20 [-.11, .50]	0.184	25.95	0.06	9.0
		Theta	0.22	3.1	0.255	6	0.55 [-.35, 1.45]	0.120	44.97	0.09	2.0
	Modality		0.15	8.7	0.393						
		Visual				18	0.36 [.10, .62]	**0.013**	31.08	0.06	10.2
		Both				17	0.21 [-.11, .53]	0.155	0.00	0.00	4.8
	Total time (mins)		<.0001	6.7	0.656						
	Total number of sessions		0.005	7.4	0.868						

Note. Significant (p < .05) moderators and individual estimates in bold. Dummy-coded categorical moderators: *B* represents the difference between estimated effects for each group. Contrast(sum)-coded categorical moderators: *B* represents the difference between estimated effects for each group and the grand mean of that category. Continuous moderators: *B* represents effect size change relative to one-unit moderator change. Abbreviations: CI = confidence interval; df = degrees of freedom; ES = effect size; g = Hedges' g; GM = grand mean; I^2 = I-squared measure of heterogeneity; p = probability value; τ^2 = Tau squared.

Table 3. *Analysis of interactions between EEG-NF training amount and target frequency band*

EEG-NF training amount	Target frequency band	*B*	Standard Error	t-value	df	p-value	95% CI
Number of Sessions	Alpha	0.804	0.023	35.4	2.91	<0.001	0.73, 0.87
	Beta	0.780	0.044	17.5	1.49	0.010	0.51, 1.05
	Theta	0.689	0.050	13.8	1.00	0.046	0.06, 1.32
Training time	Alpha	0.026	0.001	21.8	2.44	0.001	0.02, 0.03
	Beta	0.026	0.001	22.0	2.86	<0.001	0.02, 0.03
	Theta	0.023	0.002	13.8	1.00	0.046	0.002, 0.04

Note. B represents effect size change relative to one-unit moderator change for each category; CI = confidence interval; df = degrees of freedom; p = probability value.

2.4 Discussion

This is the first systematic review and meta-analysis which examines the effect of EEG-NF on episodic memory in both healthy and clinical populations. The first aim of the systematic review was to provide a qualitative overview of the literature based on several factors, such as the participants, study design and neurofeedback protocols to understand what research has been conducted in this area. Forty-six studies were found with approximately equal numbers conducted in healthy volunteer and clinical groups. The second aim was to conduct a meta-analysis solely on studies with an active control condition or group, which contained randomised or counterbalanced participants, to determine if EEG-NF can enhance episodic memory and whether success in modulating brain activity affected this result.

The meta-analysis, which included 20 studies (39 effect sizes), revealed a small beneficial effect of EEG-NF on episodic memory performance. This finding is in line with the meta-analysis by Yeh et al. (2020) on six episodic memory studies. However, their effect size was much larger than ours (0.77 versus 0.31). This is likely because in the Yeh et al. (2020) analysis the effect size was calculated using only post-neurofeedback memory performance and one outcome per study was included. In the current meta-analysis, the calculations took into consideration participants' pre-neurofeedback memory performance, to provide an adequate baseline of their ability, thereby generating a more accurate effect size (Morris & DeShon, 2002). Also, multiple outcomes per study were included to avoid selection bias which can occur when choosing only one outcome when multiple outcomes are available. Therefore, the analysis was more inclusive and based upon more studies as I included all frequency bands and episodic outcome variables were included, and both healthy volunteers and clinical populations were examined.

The finding that EEG-NF does improve episodic memory performance provides some incentive to conducting further research in this area, to determine if this technique could be developed as an intervention to enhance memory functioning in individuals. Given that it is low-cost, portable and could be conducted by the individual in their home it would be ideally suited to this. However, there are further issues which would need to be considered. One, which is the same for any intervention, is about how long behavioural benefits are seen for? Many of the studies in this review tested performance immediately after training, those who do look at longer intervals typically test after one to two weeks (e.g. Eschmann et al., 2020; Rozengurt et al., 2017). It is unknown if improvements are maintained over a longer timescale. Furthermore, there is very little research completed on training generalisability. If neurofeedback can enhance memory for the task tested in the protocol will this also lead to a boost in memory capabilities in everyday life? The transfer of learning beyond the specific task tested to other tasks and to more ecologically valid activities is rarely examined. The second major question concerns the mechanisms and brain structures underlying episodic memory that neurofeedback is acting on. In this regard neurofeedback using other imaging modalities, such as functional Magnetic Resonance Imaging (fMRI), might provide complementary information to EEG, due to its higher spatial resolution and ability to access deeper brain structures which are known to be important to memory, such as the hippocampus. Research in this domain is very much in its infancy, with very few studies. A proof-of-concept study by Hohenfeld et al. (2017, 2020) used real-time fMRI-based neurofeedback training of visuo-spatial memory in older adults and those with Alzheimer's disease. After three sessions of training, which targeted the parahippocampal gyrus, there was potentially some improvement in the delayed recall condition of a different visuo-spatial task. Thus, even if EEG-NF can enhance memory a better understanding of the neural basis and more data on the longevity and transfer of the effect is required.

Although the moderator analysis was not significant, at the sub-group level it was found that EEG-NF had a small size, significant effect when participants free recalled or remembered source/contextual details but the effect on recognition was not significant. The majority of tasks administered to participants were bespoke tasks delivered on a computer, but a few gave standardised neuropsychological tasks which tend to be given in paper format (e.g. Rey Auditory Verbal Learning Test, RAVLT; Rey, 1964). These bespoke tasks encompass several different types of paradigms, such as paired associates, where participants learn pairs of items and then at test are given one of the items and have to recall the other (e.g. Berner et al., 2006; Hsueh et al., 2012; 2016); the Remember/Know paradigm, which taps participants' subjective ability to distinguish between being able to recover any contextual details from the encoding episode (a Remember response) or being aware that an item was previously presented but without any of these details (a Know response) (e.g. Keizer et al., 2010; Staufenbiel et al., 2014); and tasks where participants have to indicate if a test item is new or old, and if old, the encoding task that was completed on it (e.g. Eschmann et al., 2020). The memory tests administered can vary substantially in the number of items and the duration of the test. For example, Rozengurt et al. (2017) asked participants to encode 30 items and gave a free-recall test which took approximately 5 minutes; whereas other studies ask participants to encode and retrieve a few hundred items which takes much longer (e.g. in Eschmann et al., 2020, 200 words were studied and 300 were in the test phase). There are also differences in the design of studies and how the memory tasks are administered. Rozengurt et al. (2017) was specifically interested in how neurofeedback could enhance consolidation, so participants studied items, received the neurofeedback and then their memories were tested in the same session, 24 hours later and a week later. Other studies (e.g. Eschmann et al., 2020) look at transfer effects whereby participants complete a baseline study and test memory task, receive neurofeedback (typically over several days), and then learn new items and are tested on them. Thus, there is great variety in the characteristics of the memory tasks used.

One way that these seemingly different tasks can be thought of is in terms of process. According to dual-process models of memory (e.g. Jacoby, 1991; Yonelinas, 2002) familiarity describes a fast and relatively automatic process that involves recognition of having previously encountered something i.e. participants' ability to discriminate between old and new items. In contrast, recollection is a slower, more effortful process, that involves conscious recollection of previously studied contextual detail i.e. participant's ability to retrieve source information. Thus, tasks which require participants to free-recall or recover details from the study phase utilise recollection, whereas recognition tasks require familiarity (but can also be completed with recollection). This study's results suggest that EEG-NF may target recollection rather than familiarity. That is extremely useful as the decline in memory seen in aging (Friedman, 2013) and across clinical conditions such as Alzheimer's Disease and Mild Cognitive Impairment (Westerberg et al., 2006), and Depression (Dillon & Pizzagalli, 2018) all point to specific deficits in recollection. EEG-NF also appeared to have a specific effect on verbal memory for language-based stimuli e.g. words, but there was no effect on visual memory for spatial form e.g. objects, places, animals, and people. One explanation for this could be that retrieval of visual stimuli is known to be far more superior than that of verbal stimuli – the so-called picture superiority effect (Paivio, 1971) - so perhaps there was less capacity for participants to improve on this. It might also be that EEG-NF training might have less impact on more automatic visual stimuli-based tasks and instead facilitate communication between the more distributed networks across the left prefrontal and temporoparietal regions used in linguistic processing (Binder et al., 1997). It was not possible in this review, due to a paucity of studies, to examine whether neurofeedback targeting a certain frequency band and location would be more likely to enhance recollection and verbal stimuli, but future empirical work could address this.

A fundamental assumption of EEG-NF is that a participants' ability to successfully regulate their brain activity in the desired manner is related to a change in behavioural performance. The moderator analysis provided support for this by revealing that enhanced episodic memory performance was observed only in studies reporting a significant change in the target brain activity due to neurofeedback. In this meta-analysis, a binary code was used to represent self-regulating success; specifically, 'yes' if participants were able to achieve the target brain activity, and 'no' if not (as used by Rogala et al., 2016). A more robust approach could be to calculate an effect size to represent EEG-NF success and correlate this with memory performance effects. However, there is some variability in the units of measurements used to calculate changes in neural activity across studies (e.g. spectral power, time above threshold). Furthermore, the contrasts used to measure these differences can range from between pre- and post-EEG-NF resting blocks, or between rest/early active EEG-NF blocks and the average of all, or just later, active EEG-NF blocks. Together, this presents a challenge in synthesising these values appropriately in a meta-analysis. Nonetheless, this positive finding demonstrates the importance of the ability to self-regulate target brain activity to receive the associated benefits to memory.

One inherent issue when using EEG for neurofeedback is the production of eye and movement artefacts in the electrical signal during the training session. These artefacts can generate frequencies that overlap with the target brain frequency to be modulated. In the event artefacts are produced, it could be argued that any improvements in memory performance observed following EEG-NF may be due to artefact-feedback, as opposed to any real changes in target brain activity being fed back to the individual. Many protocols try to mitigate for these effects by using online real-time artefact detection processes, whereby when certain thresholds are exceeded; where eye and movement artefacts are usually seen, this causes the neurofeedback to be interrupted and paused until the level of artefacts are below the threshold. In addition, offline analyses can be implemented on the EEG data to detect artefacts and to correct or remove these to ensure when researchers quantify whether participants were able to successfully modulate their brain activity in the desired manner this is not contaminated by the effect of artefacts. The vast majority of studies included in the meta-analysis (all except two) reported implementing some form of control for artefacts. Even if these two studies are excluded from the moderator analysis, the result is still significant. Thus, the enhancements in memory performance, found when people can successfully modify their brain activity in the meta-analysis, are likely to be as a result of real changes in target brain activity rather than eye or movement artefacts driving neurofeedback success.

However, there are some individuals who cannot produce the target brain activity during neurofeedback. This has been reported to be approximately one-third of individuals (Enrique-Geppart et al., 2017), and this study's findings suggest up to a third of people. However, it was also found that the vast majority of studies did not report the number of non-responders, so this number might not be reliable, and practices around non-responders in many studies were not clear. This presents a couple of issues in EEG-NF research. First, the inclusion of non-responders might serve to diminish the overall observed effect of EEG-NF on memory performance at a group level. Second, the exclusion of non-responders from relevant analyses might render a sample insufficiently powered to detect the effect of interest. Furthermore, if studies do identify non-responders there is a lack of consensus as to what measure to use to do this and how to define a non-responder. For example, in Rozengurt et al. (2017) they described them as those who cannot increase their target band power ratio by at least 5% relative to baseline, whereas others have defined them as those whose total target band duration in the last session is not greater than 95% confidence intervals of the total duration in the first three sessions (Hsueh et al., 2016). Recent research has been undertaken to examine what individual differences predict responder ability. Psychosocial factors such as attention/concentration, motivation and mood have been linked to self-regulation ability (Kadosh & Staunton, 2019). Also, brain volume, fluid intelligence and alpha power at rest have predicted responders (Enriquez-Geppert at al., 2013; Khodakarami & Firoozabadi, 2020; Kober et al., 2017). Taken together, these points suggest that future research using EEG-NF could benefit from: the use of a widely adopted, operational definition of a responder; accurate reporting of the number of responders per study and by collecting informative participant data that may assist researchers in identifying non-responders.

Perhaps surprisingly it was not found that total time or the number of neurofeedback sessions that the participant completed moderated the effect of neurofeedback on episodic memory. There are a variety of explanations for this. One possibility is that what is important is the training intensity i.e. how many sessions participants complete over what period of time (Esteves et al., 2019; Rogala et al., 2016). Alternatively, a critical variable might be the extent to which participants can exert control and pace for themselves the training sessions rather than this being externally dictated (Uslu & Vogele, 2023). The target band frequency was also not found to be a moderator of memory performance. These results could be partly because there is ongoing debate regarding the specific role of different oscillations in memory but also the small number of studies per band (except beta), rendering us possibly underpowered to detect these effects. In any event, drawing confident conclusions about band specificity at a meta-analytical level remains a challenge given many studies do not report activity across the full power spectrum, only the target band.

Better transparency regarding this should elucidate the contribution from adjoining bands or coupled frequencies (Ros et al., 2020). Furthermore, some research shows enhanced effects of EEG-NF on both neural and cognitive outcomes with personalised feedback, such as individual peak alpha or individualised theta (Alkoby et al., 2017).

There is some debate in the literature regarding whether giving specific instructions to participants assists self-regulation of the target brain activity. The majority of studies in the qualitative review did not give explicit instructions to participants. In the meta-analysis there was tentative evidence of better memory performance when participants did not receive any instructions with respect to how they should achieve the target brain state. This aligns with a recent study (Chikhi et al., 2023) which explicitly tested this idea by giving one group of participants a list of mental strategies, based on previous studies which had trained the same target band, and another group no strategies. Contrary to expectations they found that giving participants instructions about strategies did not enhance their ability to modulate the target band frequency. They suggest that this might have been because the strategies given were too numerous or not relevant. However, they did find a link between certain self-reported strategies and higher target band activity, highlighting that specific strategies may play a role in how well participants can modulate their brain activity. Further work explicitly examining strategies and applying a more fine-grained classification of them would be useful (see Lubianiker et al., 2022) and might also help researchers to reduce the number of non-responders as these could be individuals who are unable to find or to implement an effective strategy.

The design quality varied across studies, with just over a third of studies not reporting a control group or condition, and of those that did, the majority randomised or counterbalanced participants. For those with a control group or condition, around three-quarters implemented some form of blinding, with the rest either failing to do this or report it. There was a suggestion in the moderator analysis, which only included studies with an active control group, that those studies which used a contingent control had a more beneficial effect on memory performance, which was not found when using a non-contingent control group. An explanation for this could be that participants in a contingent group are being trained to specifically regulate activity that is unrelated to the target frequency band, so there is potentially better separation in measured activity between the experimental and control group. Conversely, in a non-contingent group, participants could be upregulating frequencies within the target band, and thereby obscuring the effect. Non-contingent controls, where participants detect them, can be associated with negative effects, such as: frustration and decreased motivation due to the lack of control over the feedback received (Sorger et al., 2019; Witte et al., 2013) and risk unblinding the participants. Thus, in healthy volunteer research a contingent control condition might be best as participants can exert control over brain activity, which eliminates the negative issues arising from a lack of this and may allow the experimenter to demonstrate greater specificity in the neurophysiological mechanism (Sorger et al., 2019).

Finally, the analysis of the studies included in the qualitative review revealed that the sample size in many of these, even excluding single-case studies, was very low. A power calculation reveals that for a one-tailed test (alpha = 0.05, power = 0.8) comparing between two unmatched groups 21 participants would be required in each group to detect a large effect (d = 0.8) and 51 for a moderate effect (d = 0.5). Thus, many of the studies are insufficiently powered to detect a large effect size and none of the studies have sufficient participants to detect a moderate effect of neurofeedback on memory in a between-participants design. This review demonstrates the fundamental need for larger samples to be used in EEG-NF research to reliably reveal its true effect on episodic memory.

In conclusion, the meta-analysis based on actively controlled studies revealed a small-size, significant positive effect of EEG-NF on episodic memory performance. Effects of EEG-NF were larger for tasks requiring retrieval of details around the encoding episode, with enhanced performance in remembering verbal stimuli. Importantly, the overall effect was significant for studies reporting that participants were successful in self-regulation of the target frequency band. Therefore, the efficacy of EEG-NF to improve episodic memory shows promise. However, sufficiently powered studies with adequate study design features are required to provide stronger empirical support for this intervention. Moreover, there is a need to investigate the characteristics of responders and the specific effects of different EEG-NF protocols on underlying neural systems involved in memory processes.

Chapter 3: Examining the effect of theta electroencephalography neurofeedback on episodic memory performance.

3.1 Introduction

The review and meta-analysis conducted in the previous chapter indicates that EEG-NF has a small but significant effect on episodic memory performance. The aim of this chapter was to empirically examine this question by administering EEG-NF during the retention period following encoding of new information and determining if it has effects on different aspects of episodic memory in healthy adult volunteers. The benefit of this research would be to (i) strengthen the evidence relating to the efficacy of EEG-NF for use by healthy individuals to enhance episodic memory performance, and (ii) contribute findings regarding the timing of EEG-NF and the possible underlying mechanisms influencing episodic memory processes. Ultimately, this empirical evidence could contribute to research exploring whether this technique could subsequently assist ageing adults or clinical patients with memory impairments.

The meta-analysis did not reveal any significant effects of frequency band i.e. whether a certain band was more effective than others in enhancing memory. It is possible that this was due to the small number of studies per band which meant that this analysis was underpowered. However, there is compelling evidence from the broader memory literature that theta plays an important role in supporting episodic memory and particularly associative memory e.g. retrieving an item and a piece of source information, such as the location it was presented, likely reflecting the memory process of recollection (e.g. see review by Herweg et al., 2020). This research is reviewed in more detail in Chapter 1: General Introduction (Section 1.4.6).

There have been a couple of studies which have specifically explored the role of theta in neurofeedback. A study by Eschmann et al. (2020) investigated whether a 7-day schedule of 25 minutes of theta EEG-NF training could improve retrieval of source information compared to an active control group who trained randomly chosen frequency bands. Participants completed a source memory task where they had to remember the encoding task (animacy or pleasantness) that they had completed with the word. This was conducted in a pretraining session and twice after the training. Eschmann and colleagues found a significant and selective effect of theta EEG-NF on source memory in the second session, which happened 13 days following EEG-NF training. Moreover, participants' enhancement in memory performance from the pretraining session to the post-training sessions was predicted by the increase in theta during neurofeedback. There were no effects of the neurofeedback on item memory i.e. distinguishing old from new words. This study strongly supports the role of theta in episodic memory and the beneficial effect of neurofeedback in boosting this. However, in this study a significant amount of neurofeedback training was used, and this was spread over several days.

Alternatively, other researchers have utilised different designs to determine the effects of neurofeedback on memory. Rozengurt et al. (2017) gave their participants 3 study-test cycles to learn 30 object pictures and then participants were split into three groups, who did the following for 30 minutes: i) theta neurofeedback (experimental group), ii) low beta neurofeedback (active control group), or iii) watched a movie (passive control group). Participants then tried to free recall the objects immediately after the training, 24 hours later and a week later. The researchers found that both neurofeedback groups were successful in moderating their brain activity to the desired frequency. The theta neurofeedback group significantly improved immediate free recall of the objects, with this effect increasing at both the 24 hour and 1-week timepoints following the intervention, compared to both the active neurofeedback control condition and the passive movie viewing group. Similar to Eschmann et al. (2020) the greater the theta increase in this group, the larger the benefit to memory. This study indicates that even a single, short theta neurofeedback session can enhance memory.

The main aim of the current study was to replicate Rozengurt's finding that a single 30-minute session of theta EEG-NF performed during the retention period between study and test can improve free recall, with persistent effects observed 24 hours later. I also wanted to extend this work by determining whether an increase in theta induced by EEG-NF could also improve source memory, in subsequent cued recall and source recollection tests, as was found in the study by Eschmann et al. (2020) and was indicated in the meta-analysis conducted in Chapter 2. Finally, a more exploratory direction was to assess whether theta neurofeedback could affect subjective memory, by examining the confidence with which people made their decisions.

Importantly, a robust experimental design was adopted, including a sufficiently powered sample, an active contingent control and randomisation of participants to the experimental and control groups, to contribute reliable empirical data to the literature (Ros et al, 2020). Participants were randomly allocated to either a theta group or a low beta control where they received 30 minutes of theta or low beta EEG-NF respectively, after encoding 80 nouns. Following the intervention, participants completed several memory tests including free recall, recognition, cued recall and source recollection, some of these with confidence ratings. Scores were compared between groups to determine whether the theta group performed better than the control group on the memory measures.

On the basis of the studies by Eschmann et al. (2020), Rozengurt et al. (2017) and the meta-analysis in Chapter 2 it was hypothesised that participants in the Theta group will achieve significantly higher free recall (both immediately following EEG-NF and 24 hours later), cued recall and source recollection scores than participants in the Low Beta group. It was hypothesised that there will be no difference in recognition scores between the Theta group and the Low Beta group i.e. theta neurofeedback will have no effect on participants' ability to discriminate old from new items. No hypotheses were made about group differences in source and recognition confidence as this aspect was exploratory.

It was anticipated that there would be an increase in theta for those participants who received feedback on this band, compared to the low beta group, and an increase in low beta for the group that received feedback on this band compared to the theta group. This would indicate that the administration of the neurofeedback had been successful. As in previous studies it was predicted that there will be a positive correlation between the extent of increase of theta in this group and free recall performance.

3.2 Methods

3.2.1 Participants

Fifty-eight right-handed, native English speakers aged 18-30 years were recruited from the Cardiff University psychology undergraduate population. An a-priori power calculation based on conducting a between-participants t-test with a one-tailed hypothesis, $\alpha = 0.05$, power = 0.8, and the effect size generated by Rozengurt et al. (2017) of Cohen's $d = 0.922$ established that a minimum sample size of 16 per group was required to detect a similar effect (G*Power: Version 3.1.9.7). Participants had normal, or corrected to normal vision and hearing, and no reported history of any psychiatric or neurological disorders. All participants provided informed written consent to participate in the study which was approved by the School of Psychology Ethics Committee for Cardiff University. Participants were compensated for their time with course credits. Participants were randomly assigned to one of two groups: the Theta group and the Low Beta group. Two datasets were excluded from analyses due to technical issues. There were no significant group differences in mean age and gender ratio (Theta group: n=29, 27 females; mean age = 19.0); Low Beta group: (n=27, 25 females; mean age = 19.1).

3.2.2 Experimental Design

Figure 4 gives an overview of the experimental procedure with approximate timings. Each of these phases is described in more detail in the sections below.

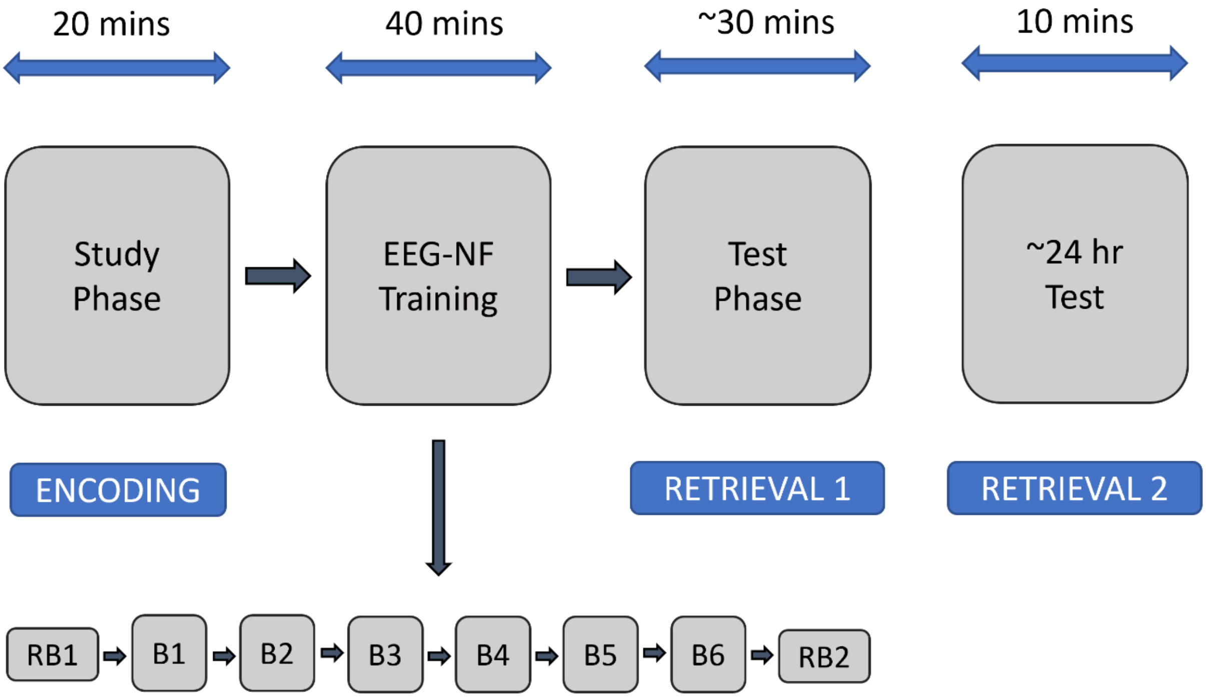


Figure 4. Schematic diagram showing an overview of the experimental design: The Study Phase, EEG-NF training, Test Phase and the 24-hour follow-up test. B1 – B6 = 5-minute active EEG-NF blocks; RB1 = 4-minute resting baseline; RB2 = 4-minute post-EEG-NF resting block.

3.2.2.1 The Behavioural Task

3.2.2.1.1 The Stimuli

Two hundred and forty nouns were selected from the Medical Research Council Psycholinguistics database (http://tinyurl.com/mrc-database). All words were between three and eight letters long with a Kucera-Francis written frequency of 20-100, and concreteness and imageability ratings of 500-700. Derivational variants were removed to reduce possible effects of memory interference. The nouns were randomised to make 120 word pairs and were filtered to ensure none contained alliteration or rhyming words. Auditory word pair stimuli were generated by an online text-to-voice computer application, creating English-speaking male and female versions of each word pair. The audio editing software, Audacity, was used to normalise the sound level and quality across the audio word pairs, and to ensure the time gap between the first and second noun was consistent at 500ms. Three study phase wordlists were rotated across participants to enable counterbalancing of the variables: word pair status (old or new) and gender of speaker (Jack or Chloe). Each wordlist comprised 80 old word pairs, with an equal number of word pairs presented by Jack and Chloe. For the test phase, 40 new words (the first words from the remaining word pair stimuli) were intermixed with the study phase cue words, thereby creating a list of 120 words. The response options for old/new and Jack/Chloe were reversed (left or right hand) for each wordlist, creating six counterbalanced test phase versions. All word stimuli were presented randomly with no more than four consecutive old or new words, or words spoken by Jack or Chloe.

3.2.2.1.2 The Memory Paradigm

Prior to both the study and test phases, participants received written instructions which the experimenter reinforced and answered any questions. A shortened version of both instructions also appeared on the screen before each task. The task described below is closely based on the one by Yazar et al. (2014) and was designed and implemented using E-Prime 2.0 software (Psychology Software Tools, Pittsburgh, PA).

In the study phase, a fixation cross was displayed on the screen (500ms), followed by a word pair (e.g. “BILLBOARD – FRIDGE”) presented both in the centre of the screen (3s) and auditorily via headphones. The name of the speaker also appeared on the screen above the word pair: ‘JACK’ or ‘CHLOE’, respectively. Next, the words ‘SPEAK SENTENCE NOW’ were presented (10s), during which participants generated a sentence that included both words from the word pair, and the name of the speaker, as per the instructions they had been given. Participants completed this sequence for all 80 word pairs, with two breaks included where participants were given agency to continue when they were ready by pressing any key – see Figure 5A which shows the study phase sequence.

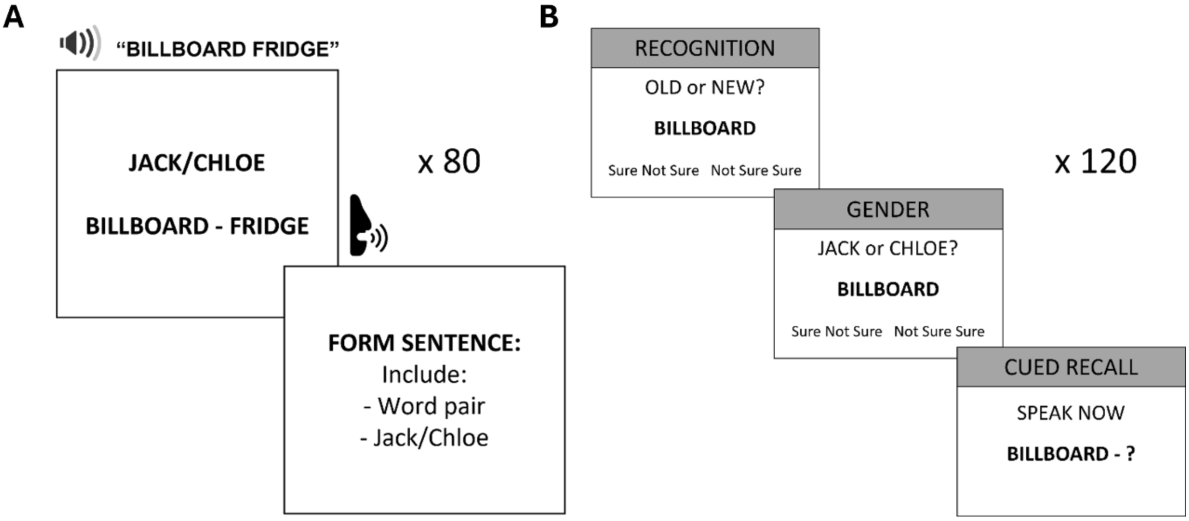


Figure 5: Schematic diagram representing an individual trial for A) The Study Phase where participants encoded randomly presented word pairs, and B) The Test Phase including a recognition (with confidence judgement), source recollection (with confidence judgement) and cued recall task, following a 5-minute free recall task.

The duration between the study and the test phase was approximately 45 minutes, during which the EEG-NF intervention took place (see Section 3.2.2.2.2). Following this, participants completed the test phase of the experiment which examined different aspects of memory. First, they were instructed to write down as many of the nouns presented to them in the study phase as they could freely recall within 5 minutes. Following this, participants completed a computerised task including three memory tests: a recognition judgement (old or new), source recollection i.e. the gender of the speaker (Jack or Chloe), and cued recall – Figure 5B shows the computerised task test phase sequence. Participants viewed a fixation cross (1s), followed by the first word of a word pair (e.g. “BILLBOARD - ?”). The stimulus word remained on the screen throughout the trial while participants completed all memory judgements. First, participants indicated whether they thought the word was presented in the study phase (“OLD” or “NEW”), and their confidence in that decision (“Sure” or “Not Sure”), by pressing the number on the response keypad (NA*t*A technologies Inc., 2006) that corresponded with the on-screen instructions. A “NEW” judgement terminated that trial and initiated the presentation of the next word from the wordlist. If participants responded with an “OLD” judgement, they were next prompted to indicate whether they thought the word was originally spoken by Jack or Chloe, and their confidence in that decision, in the same way as described above. Finally, the words “SPEAK NOW” appeared above the stimulus word, followed by a question mark. At this point, participants either said the word they remembered being paired with that word out loud, or ‘pass’ if they were unable to remember the target word. All spoken responses were recorded via E-Prime. Three breaks were included where participants were again given agency to continue when they were ready by pressing any key.

The follow-up test phase was conducted via a video conference call (Zoom Video Communications, Inc. 2021) approximately 24 hours following the study phase. Participants were sent a link to the memory task which was designed using an online survey software (Qualtrics, Provo, UT, 2021). Participants were provided with online instructions before they completed another free recall task where they were instructed to type as many of the nouns presented to them in the study phase as they could freely recall within 5 minutes.

3.2.2.2 The Neurofeedback Task

3.2.2.2.1 Electrophysiological recordings

Participants were prepared for EEG recording using a BioSemi Active Two system (BioSemi, Amsterdam, The Netherlands). Thirty-two silver-chloride, pin-type active electrodes were mounted in a fitted elastic cap according to the standard 10-20 system and in a standard memory montage. Conductive gel was used at electrode sites to facilitate a connection between the electrode and the participant’s scalp. Electrooculography recordings were taken using four flat-type active electrodes placed at the left and the right outer canthus sites to detect horizontal eye-movements, and at the infraorbital and supraorbital sites (1cm below and above the eye, respectively) to detect vertical eye-movements. Two additional flat-type active electrodes were placed on the left and the right mastoid bone, to which the data were re-referenced both during the online EEG-NF protocol and for offline EEG data analysis. The offset for each active electrode was kept between +/-40 mV to ensure sufficient electrode connection and signal-to-noise ratio. The raw EEG signal was recorded from 14 active electrodes at sites: Fp1, Fp2, F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, O1, Oz, and O2 during the 4-minute resting block, the six active EEG-NF blocks, and the post-EEG-NF resting block for those who completed it and stored for offline analysis (see Section 3.2.3). Participants were instructed to sit comfortably and remain still during all EEG recordings to minimise eye and body movements.

3.2.2.2.2 Online EEG-NF protocol

Participants completed a 4-minute eyes-open resting block where they stared at a white fixation cross in the middle of a 22” computer monitor black screen, followed by 30 minutes of EEG-NF, which was divided into six 5-minute blocks. Real-time EEG-NF was delivered online and recorded as described above using BrainBay neurofeedback software (BrainBay V2.6; Veigl, & Wilkerson, 2021) in parallel with the BioSemi Active Two EEG system. The lead electrode used for EEG-NF was Fz, which was also used by Rozengurt et al. (2017), given this position is where frontal-midline theta activity is maximal and has been implicated in episodic memory processes (Yamaguchi et al., 1990b; Mitchell et al., 2008; Hsieh & Ranganath, 2014).

In line with Rozengurt et al., (2017), the online EEG-NF signal was averaged and referenced to the two mastoid electrodes, band-pass filtered at 0.5-30 Hz (order 8) using an alpha bessel butterworth filter and sampled at a rate of 2048 Hz. Absolute EEG spectral power was calculated using fast Fourier analysis with epoch duration of 4096 ms, 50% overlapping, and time-smoothing with the Hann window for the frequency bands of interest: theta (4-8 Hz) and low beta (15-18 Hz) for the experimental groups, and delta (0.5-2 Hz) and beta2 (22-45 Hz) for the artefact rejection inhibit bands. Low beta was used as the active control frequency band to enable the Low Beta group to engage with a comparable EEG-NF experience as the Theta group by receiving a feedback frequency not considered to play a key functional role in episodic memory processes (Rozengurt et al., 2017). The Theta group received positive feedback for increasing their theta/low beta power ratio, and the Low Beta group participants received positive feedback for increasing their low beta/theta power ratio (Rozengurt at al., 2017; Shtoots et al. 2020; Tseng et al., 2021).

Positive feedback was provided to participants by way of a vertical bar displayed on the screen, the height of which increased and decreased according to the target-band power ratio. A horizontal criterion line was situated half-way between the minimum and maximum height of the bar (0 and 100, respectively). Participants were provided with written and verbal instructions to raise the bar as high as possible above the criterion line, and for as long as possible. It was explained to participants that the height of the bar represented the amount of target brain activity they were generating in real-time, detected by the EEG system. The same suggested strategies were provided to all participants, such as mental operations, focussing on raising the bar, imagining past or future events, thoughts of movement, relaxation or imagining feeling a certain emotion. They were instructed to use a 'trial and error' approach initially, and then to continue using a strategy that appeared to successfully increase the height of the bar.

Inspired by Rozengurt et al. (2017), a 90% adaptive threshold was applied to each of the six active EEG-NF blocks. This meant that the minimum target band activity (e.g. theta/low beta ratio power) participants needed to generate during each block to receive positive feedback (i.e. for the top of the bar to reach the goal horizontal criterion line) was manually set to 90% of that generated in the previous block. In the case of the first active EEG-NF block, the threshold was set to 90% of the participant's preceding resting baseline target ratio power. The threshold value for each EEG-NF block was calculated in MATLAB (Version R2021a). The rationale for this adaptive thresholding was to both calibrate the difficulty level to the individual's performance and to raise the ceiling to facilitate learning. A coefficient was also applied to the calculation to ensure that the proportional vertical movement of the bars in both conditions was matched visually.

To minimise ocular and muscle movement artifacts, positive feedback was interrupted (i.e. the vertical bar froze) during each active EEG-NF block if participants simultaneously increased delta (0.5-2 Hz) or beta2 (22-45 Hz) band power, respectively (Eschmann et al., 2020; Paluch et al., 2017) by more than 120% of that measured during the resting baseline block. This value served to raise the ceiling to account for potentially increased artifactual activity during the active EEG-NF blocks. The threshold also aimed to strike a balance between allowing too many artifacts in the feedback data and withdrawing too much feedback; the latter of which could make the task of upregulation too difficult, thereby causing participants to feel frustrated and demotivated. Positive feedback was also interrupted when participants' EEG activity exceeded the 100 μV artefact-rejection simple threshold. Participants were informed that if the bar froze momentarily, it was because too many artifacts had been detected in their EEG activity, and they were asked to try and minimise any eye and/or body movements that might have caused these artifacts during the EEG-NF task.

3.2.3 Offline EEG-NF analysis

The raw signal for the 14 EEG data channels was preprocessed using EEGLAB (Delorme, & Makeig, (2004) toolbox in MATLAB. The data were re-referenced to the mastoid reference electrodes, down sampled to 256 Hz and an IIR butterworth band-pass filter applied at 0.03 – 40 Hz (order 8). The band pass frequency range was initially selected in anticipation of event-related potential (ERP) analyses being conducted, had a significant effect of theta EEG-NF on episodic memory been found overall. The lower high pass cut-off frequency would serve to reduce the effect of filter distortion which has been observed using 0.3 Hz and above (Tanner et al., 2016). In relation to this study, the early mid-frontal old/new effect (FN400) could be affected, which provides a neurophysiological measure of familiarity memory processing. The issue of using different parameters for online and offline processing of the EEG-NF data is acknowledged and discussed further in this and Chapter 4, and the General Discussion, Section 6.4.1. Independent component analysis was performed on the data to detect and remove ocular and channel artifacts, which were identified using SASICA plugin for EEGLAB (Chaumon et al., 2015). Artifact rejection was then applied to the data with the following parameters: simple voltage threshold at 75 μV, 50 μV at the low frequency (0-1 Hz) signal component, and 35 μV at the high-frequency (20-35 Hz) component (Rozengurt et al., 2017). Offline absolute and relative theta and low beta power were calculated using wavelet transform with the following parameters: epoch duration of

4096 ms, 50% overlapping, and time-smoothing with the Hann window. These measures were used to calculate the target band power ratio for the resting baseline and post-EEG-NF resting block, and each of the six 5-minute active EEG-NF blocks.

3.2.4 Statistical analyses

All statistical analyses were performed in jamovi (Version 2.2.5, 2021).

3.2.4.1 Episodic memory performance

To test whether theta EEG-NF enhanced episodic memory performance, scores were compared between the Theta group and the Low Beta group for the memory tests. Scores obtained at both timepoints were compared: immediately after EEG-NF, and approximately 24 hours later for free recall. Free recall scores reflected the number of individual nouns participants remembered from all 80 word pairs presented in the study phase, out of a total of 160 nouns. Corrected recognition (i.e. old/new item discriminability) scores were calculated by deducting the proportion of each participant's false alarm rate from their hit rate. Recognition confidence ratings were based on the number of times participants responded 'sure' for (i) OLD recognition judgements as a proportion of recognition hits, and (ii) NEW recognition judgements as a proportion of correct rejections. Source recollection was calculated as the number of items where participants correctly recalled the gender of the speaker (JACK or CHLOE), as a proportion of recognition hits. Source confidence was based on the number of times participants responded 'sure' for their source judgement, regardless of gender, as a proportion of source accuracy. Cued recall scores represented the number of correctly recalled paired words, out of a total of 80.

To determine whether the Theta group performed significantly better than the Low Beta group for free recall, cued recall, and source recollection, one-tailed independent groups t-tests were conducted, or the non-parametric equivalent Mann-

Whitney and Welsch's tests in cases where the assumption of normality or equal variances was violated, respectively. Two-tailed tests were conducted to establish any significant group differences based on old/new item discriminability (i.e. corrected recognition scores), and both recognition and source confidence. The Benjamini and Hochberg False Discovery Rate multiple comparisons correction was applied to the data, and all p-adjusted values are reported in the text along with any change in significance.

In addition, Bayes analyses were conducted on the data in jamovi. The calculated value is a ratio of the likelihood of an alternative hypothesis to a null hypothesis, and therefore indicates the relative strength of the evidence for an alternative hypothesis (Dienes, 2014). To allow interpretation of Bayes factors in this regard strength thresholds recommended by Lee and Wagenmakers (2014) were adopted, see Table 4.

Table 4. *Lee and Wagenmaker (2014)'s summary of Bayes Factor values and strength of evidence terminology.*

BF_{10}	**Support for hypothesis**
<.01	Decisive evidence for H0
.01-.03	Very strong evidence for H0
.03-.10	Strong evidence for H0
.10-.33	Substantial evidence for H0
.33-1	Anecdotal evidence for H0
1	No evidence
1-3	Anecdotal evidence for H1
3-10	Substantial evidence for H1
10-30	Strong evidence for H1
30-100	Very strong evidence for H1
>100	Decisive evidence for H1

Note. Abbreviations: BF = Bayes Factor; H0 = Null hypothesis; H1 = Alternative hypothesis

3.2.4.2 EEG-NF self-regulation ability

Target band activity is reported using two separate measures: (i) power ratio where the theta/low beta ratio was calculated by dividing theta absolute power by low beta absolute power (and vice-versa for low beta/theta ratio), and (ii) relative power which represents theta or low beta absolute power as a proportion of the total absolute power measured across the frequency spectrum i.e. 1 Hz–128 Hz. The former provides a measurement of the target band activity as a ratio that accurately reflects the feedback signal provided to participants during EEG-NF. The latter provides a measure of the target band activity generated in relation to all other frequencies, to explore the extent of band specificity as a product of the EEG-NF training.

Change in target band activity was calculated as a percentage increase: (i) from the resting baseline block to the average of all six active EEG-NF blocks (i.e. during EEG-NF), and (ii) from the resting baseline to the post-EEG-NF resting block (i.e. tonic EEG). The EEG-NF learning trajectory is represented by depicting the target band activity measure for each of the six individual EEG-NF blocks.

Independent t-tests were conducted on the EEG-NF data to examine whether there was a significant difference in target band activity following EEG-NF between the Theta group and the Low Beta group. Paired t-tests were conducted to determine whether there was a significant change in target band power following EEG-NF in each group. Non-parametric equivalents were used where there was violation of the data normality assumption; namely, Mann-Whitney and Wilcoxon paired signed rank test, respectively.

Correlational analyses were also conducted using Kendall's Tau correlation for both the Theta group and the Low beta group to determine any relationships between respondability (i.e. percentage change in theta/low beta ratio from participants' resting baseline measure to the average of the six active EEG-NF training blocks) and memory performance. The theta/low beta ratio was used to represent theta-change here because this measure is what comprised participants' online EEG-NF training.

All statistically significant analyses were set at $p < 0.05$, means (M) and standard deviations (SD) are reported using violin plots, error bars represent the standard error of the mean (SEM) in line graphs, and n represents the number of participants. All p-adjusted values following multiple corrections are reported in the text plus any change in significance.

3.3 Results

3.3.1 EEG-NF effects on episodic memory performance

To test whether theta EEG-NF enhanced episodic memory performance, memory scores were compared between the Theta group (n = 29) and the Low Beta group (n = 27). Participants were tested immediately following EEG-NF for all memory measures, and approximately 24 hours later for the free recall test. Two additional participants' scores are missing for the source recollection calculation and one for the cued recall, recognition and subjective measures, both in the Theta group. This is due to technical issues with ePrime that occurred during these sessions.

Participants in the Theta group performed better numerically than the control participants on all memory measures. However, one-tailed independent groups t-tests revealed that this difference was not significant: Free recall ($t(54) = 1.31$, $p = 0.100$); Cued recall ($t(53) = 0.05$, $p = 0.480$); and Source recollection ($t(52) = 1.42$, $p = 0.080$). Participants' old/new item discriminability ($t(53) = 0.13$, $p = 0.901$) did not differ significantly between the groups. Participants' scores also did not significantly differ for any of the confidence ratings: Old item confidence ($U = 302$, $p = 0.279$); New item confidence ($t(52) = 0.14$, $p = 0.893$), and Source confidence ($U = 356$, $p = 0.883$). Finally, the Theta group did not significantly out-perform the Low Beta group when tested 24 hrs later ($t(54) = 0.46$, $p = 0.323$) - see Figure 6. Participants' performance in both the recognition (Corrected recognition = 0.708) and source recollection (Conditionalised source = 0.734) tests was sufficiently above floor level i.e. > 0 for recognition and > 0.5 for source recollection, but quite a bit less than ceiling, ruling these issues out.

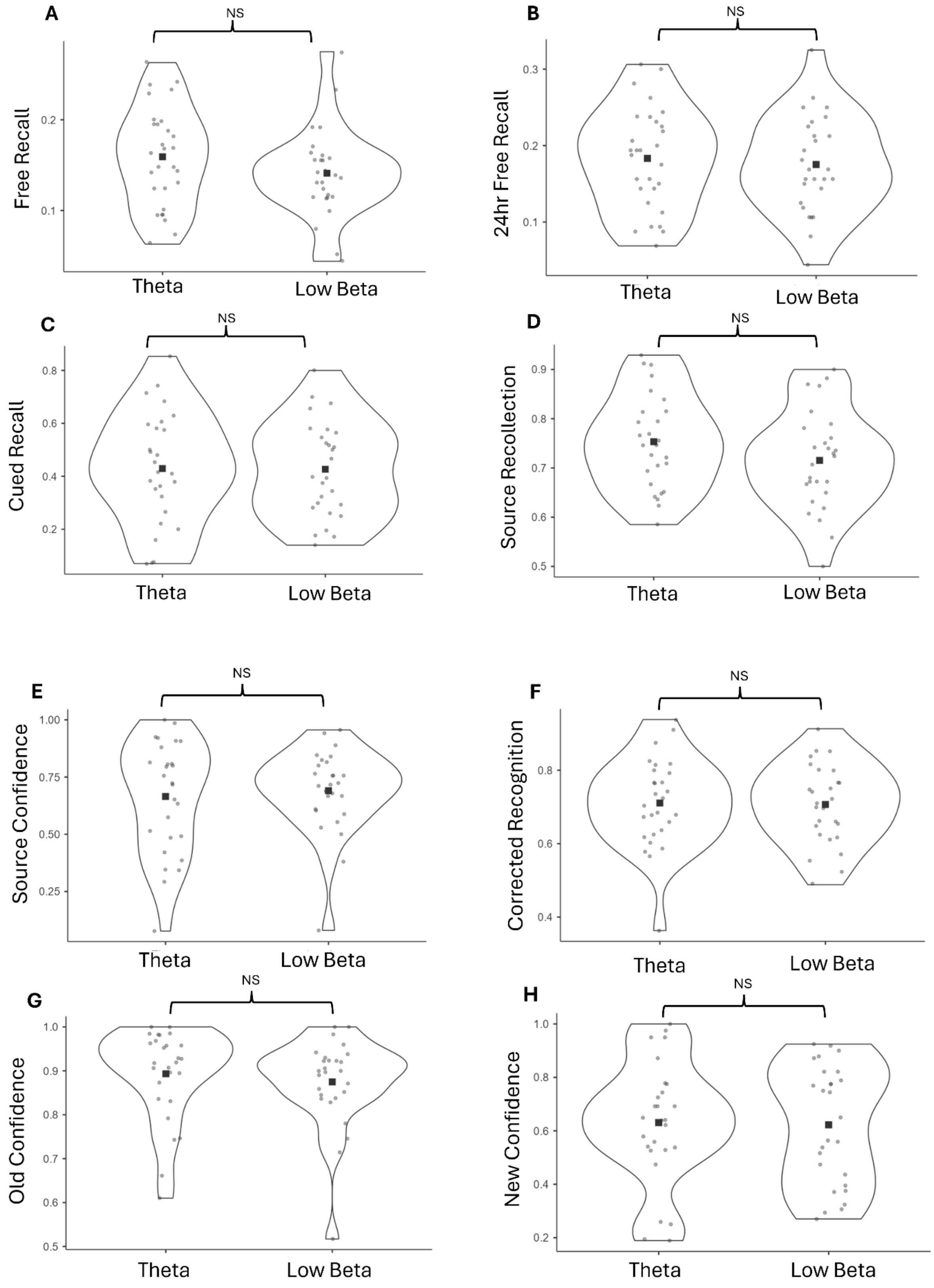


Figure 6. Violin plots display performance in all memory measures for the Theta group (n = 29) and the Low beta group (n = 27): A) Immediate free recall; B) 24hr free recall; C) Cued recall; D) Source recollection; E) Source confidence; F) Corrected recognition; G) Old item confidence; H)

New item confidence. The black square depicts the mean and the grey dots represent the distribution of data points.

3.3.2 EEG-NF effects on modulation of target band power

To determine whether participants were successful in up-regulating the target frequency band, percentage increase in theta/low beta ratio power was compared between the Theta group and the Low Beta group. Relative power in the target band is also reported for both the Theta group and the Low Beta group.

3.3.2.1 Neural activity during EEG-neurofeedback

Oscillatory activity was compared between the resting baseline and the average of the six active EEG-NF blocks. Participants in the Theta group did not increase their theta/low beta ratio significantly more than the Low Beta group (U = 367, p = 0.696) – see Figure 7A. There was a non-significant increase in theta/low beta ratio (6.4%) in the Theta group (W = 273, p = 0.238), also a non-significant increase in theta/low beta ratio (4.5%) in the Low Beta group (W = 244, p = 0.194) – see Figure 7B. Baseline measurements of theta/low beta ratio did not differ between the groups (U = 389, p = 974).

There was no significant difference in relative theta power increase between the Theta group and the Low Beta group (U = 313, p = 0.203) – see Figure 7C. Relative theta power reduced non-significantly in both the Theta and the Low Beta groups, by 17.1% (W = 135, p = 0.076) and by 3.6% (W = 191, p = 0.981), respectively – see Figure 7D. Baseline measurements of relative theta power also did not differ between groups (U = 333, p = 0.342)

Relative low beta power increase also did not differ significantly between the Theta group and the Low Beta group (U = 288, p = 0.091) – see Figure 7E. Relative low beta in the Low Beta group decreased non-significantly by 3.9% (W = 160, p = 0.984), whereas it decreased significantly in the Theta group by 21.6% (W = 87, p = 0.015) - see

Figure 7F. Baseline measurements of relative low beta power also did not differ between groups (*U* = 346, *p* = 0.455).

In summary, when looking at the difference in neural activity between the resting baseline and the subsequent neurofeedback blocks there was no significant evidence that the theta group had been able to upregulate this band or that the low beta group were successful in increasing their low beta levels.

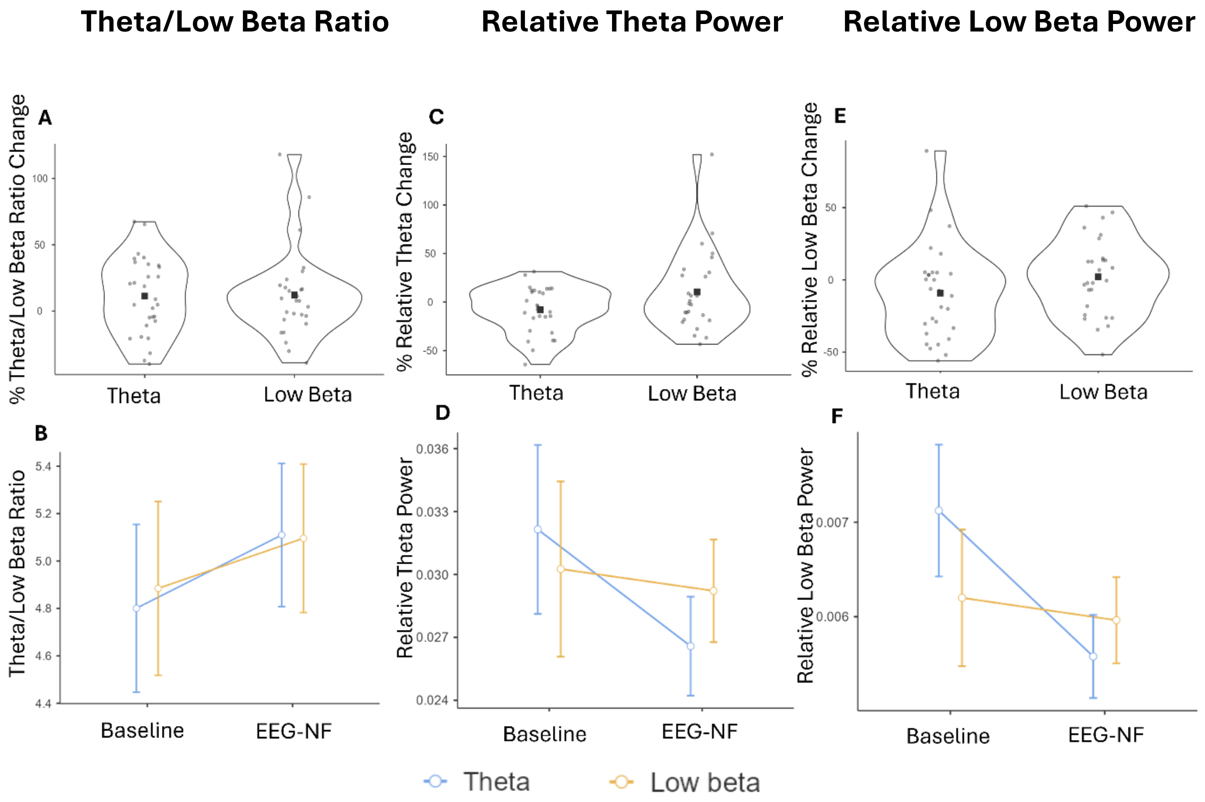


Figure 7. Violin plots depict the neural activity percent change from resting baseline to the average of all active EEG-NF blocks in the Theta group and the Low beta group displayed for: A) Theta/low beta ratio power, C) Relative theta power, and E) Relative low beta. The black square depicts the mean and the grey dots represent the distribution of data points. Line graphs show learning trajectory from resting baseline to EEG-NF average for the same measures (B, D, and F, respectively). Error bars represent +/- SEM.

3.3.2.2 Tonic EEG – pre- and post-EEG-NF resting blocks

Neurofeedback success was also examined in a complementary way. Oscillatory activity was compared between the resting baseline and the post-EEG-NF resting block, for all participants who completed a post-EEG-NF resting state block (n = 45). Theta/low beta ratio power increase did not significantly differ between the Theta group and the Low Beta group (W = 234, p = 0.693). There was a non-significant increase in theta/low beta ratio power in both the Theta group and the Low Beta group, by 1.7% (t(20) = 0.273, p = 0.788) and 7.7% (W = 172, p = 0.546), respectively – see Figure 8A. Baseline measurements of theta/low beta ratio power in participants' resting baseline did not significantly differ in this sample (U = 215, p = 0.410).

There was no significant difference in relative theta power increase between the Theta group and the Low Beta group (U = 183, p = 0.120). Relative theta power reduced non-significantly in the Theta group by 19.7% (W = 85, p = 0.304) and increased in the Low Beta group by 5.6% (t(23) = 0.750, p = 0.461) – see Figure 8B. Baseline measurements of relative theta power also did not differ between groups (U = 201, p = 0.251).

Relative low beta power increase also did not differ significantly between the Theta group and the Low Beta group (U = 195, p = 0.199). Relative low beta in the Low Beta group increased non-significantly by 4.8% (t(23) = 0.626, p = 0.538), whereas it decreased non-significantly in the Theta group by 18.0% (t(20) = -1.32, p = 0.202) – Figure 8C. Baseline measurements of relative theta power also did not differ between groups (U = 234, p = 0.682).

In summary, when examining neurofeedback ability by comparing the difference in target band frequency between the resting state prior to the training and after the neurofeedback there was no significant evidence that at a group level participants had been able to upregulate their brain activity in the desired manner. Whether this measure of neurofeedback success is examined or the one in the prior section they both indicate that the neurofeedback training, of either theta or low beta, was not successful at the group level.

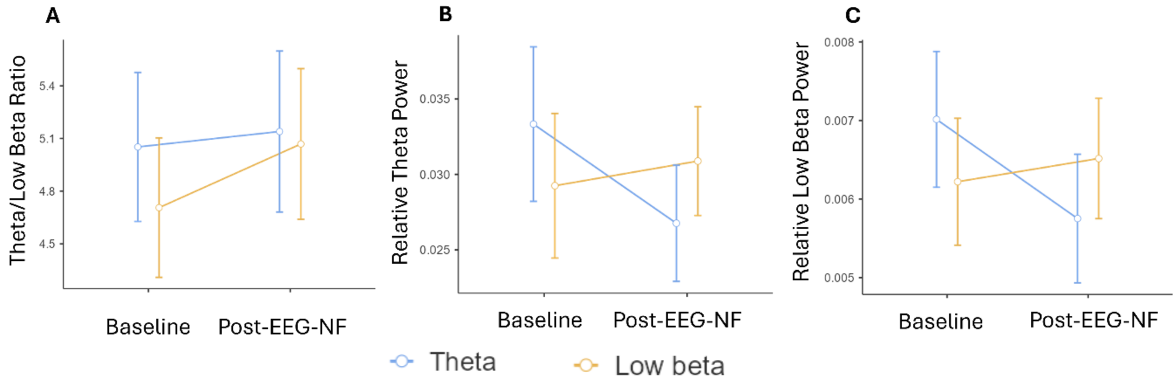


Figure 8. Line graphs display neural activity from resting baseline to post-EEG-NF for A) Theta/low beta ratio power, B) Relative theta power, and C) Relative low beta. Error bars represent +/- SEM.

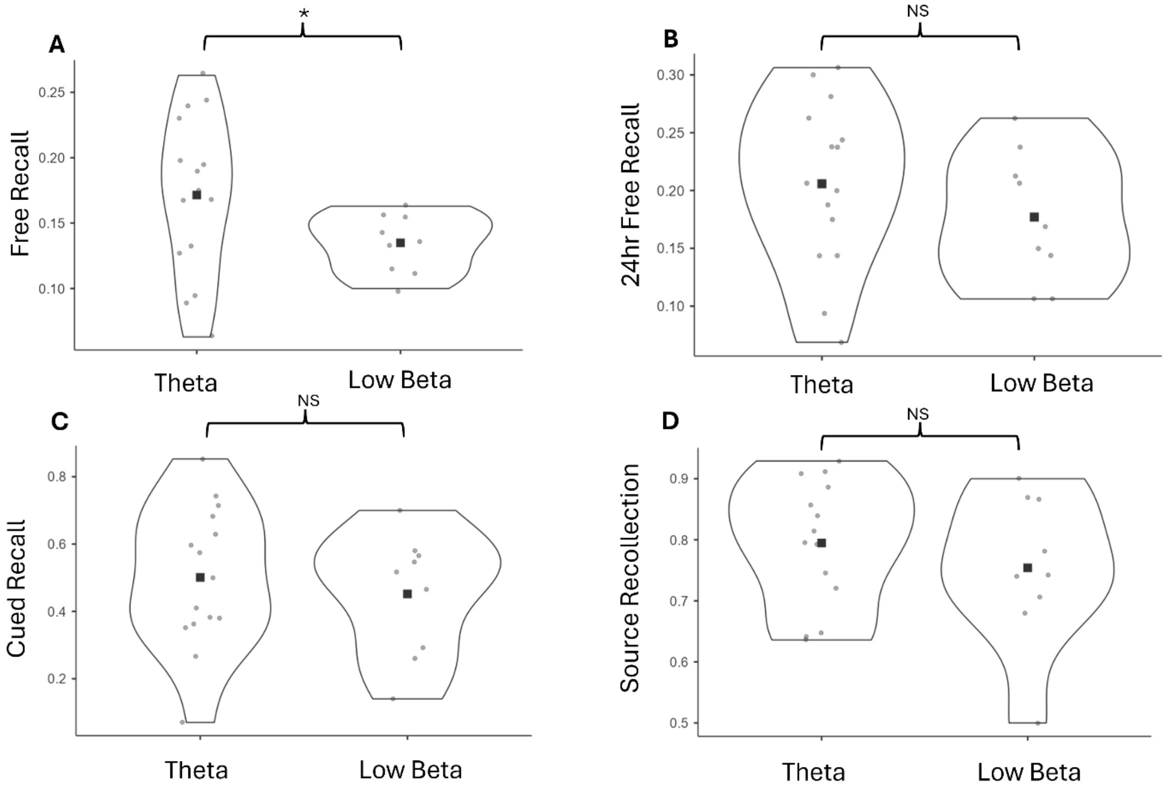
3.3.3 EEG-NF responders v non-responders: Effect on episodic memory performance

3.3.3.1 Theta Responders vs Low beta Responders

The analyses conducted above on the EEG-NF data indicated that at the group level the intervention was not successful: those in the theta/low beta group did not significantly enhance their levels of the target frequency band. It is known that a certain proportion of participants are not able to regulate their brain activity - called non-responders. Therefore, for the following analyses the non-responders were excluded. EEG-NF responders were defined as those participants who were able to increase target band power i.e. theta/low beta ratio in the Theta group and low beta/theta ratio in the Low Beta group, by at least 5% when comparing the average of the six active EEG-NF blocks to their resting baseline (this threshold is taken from the paper by Rozengurt et al., 2017). This resulted in a high proportion of non-responders in each group: 48% non-responders in the Theta group (n = 14) and 67% (n = 18) in the Low beta group compared to Rozengurt et al. (2017): 24% and 48%, respectively. Thus, in the subsequent analyses which have been performed there are 15 participants in the Theta group and 9 in the Low beta group.

Again, participants in the Theta group performed better numerically than the control participants in all memory measures. Welch's t-test revealed that Theta group responders performed significantly better than Low beta group responders in solely the immediate free recall test (t(19.3) = 2.12, p = 0.02 – Figure 9A. However, the Theta group did not significantly out-perform the Low Beta group in free recall when tested 24 hours later (*t*(22) = 1.03, *p* = 0.157). There were no significant differences in any measures of subjective confidence: Old item confidence (*U* = 55.5, *p* = 0.659); New item confidence (*U* = 47.0, *p* = 0.328); and Source confidence (*U* = 56.5, *p* = 0.705). Participants' old/new item discriminability also did not differ significantly between the groups (*t*(22) = 0.53, *p* = 0.599) - see Figure 9.

Multiple comparisons corrections using the Benjamini and Hochberg False Discovery Rate method were conducted which resulted in there no longer being a significant difference in immediate free recall scores between the Theta and Low beta responder groups: p(adjusted) = 0.08.



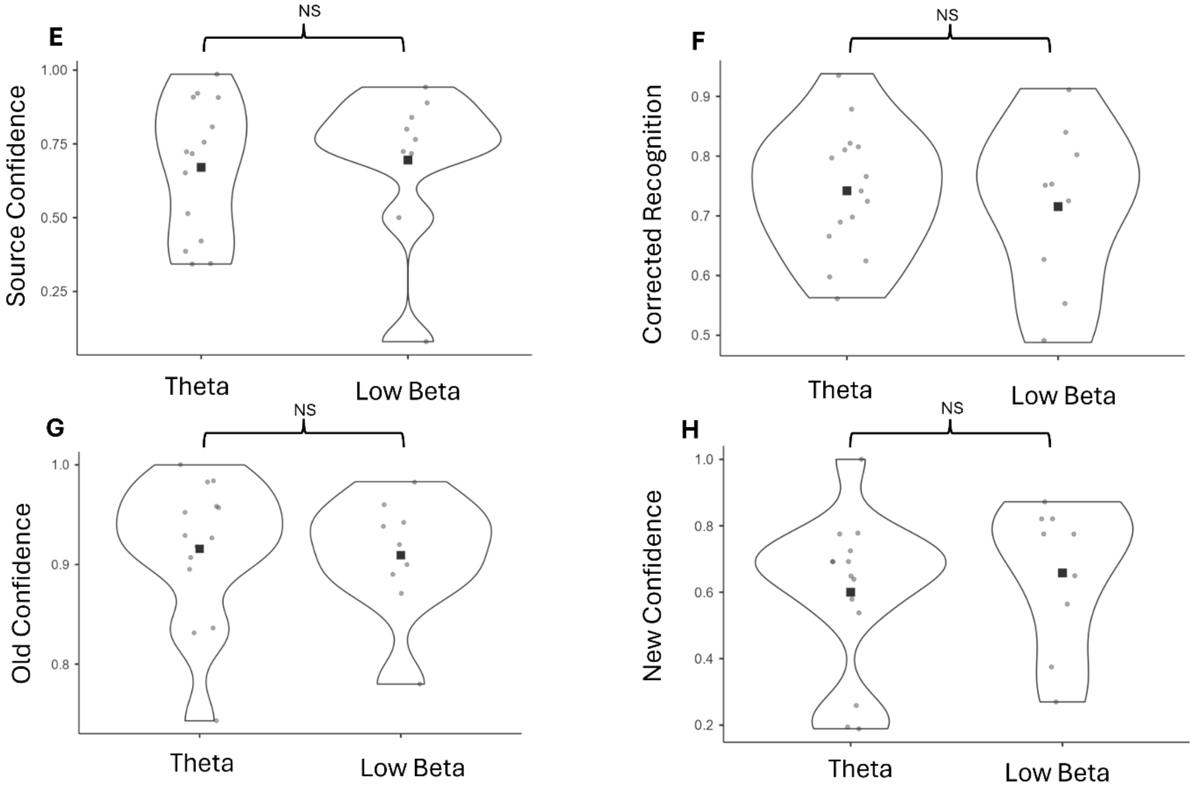


Figure 9. Violin plots display performance in all memory measures for Theta responders (n = 15) and Low beta responders (n = 9) for: A) Immediate free recall; B) 24hr free recall; C) Cued recall; D) Source recollection; E) Source confidence; F) Corrected recognition; G) Old item confidence; H) New item confidence. The black square depicts the mean and the grey dots represent the distribution of data points. * = p < .05; NS = non-significant.

To complement the frequentist statistics which had been completed, Bayes Factors were calculated to determine the strength of evidence for the alternative hypothesis that there would be differences between groups. As can be seen from Table 5 this indicates that there is anecdotal evidence for there being a difference in immediate free recall between the theta and the low beta responder groups and anecdotal evidence for the null hypotheses for the remaining measures.

Table 5. *Bayes factors for all memory measures comparing Theta responders to Low beta Responders.*

Memory measure	Bayes Factor
Immediate free recall	1.98
24 hours free recall	0.90
Cued recall	0.59
Source recollection	0.76
Source confidence	0.39
Corrected recognition	0.42
Old item confidence	0.39
New item confidence	0.44

3.3.3.2 Theta responders vs Theta non-responders

Finally, exploratory analyses were conducted on solely the Theta group, this time comparing Theta responders and Theta non-responders. The purpose of this was to directly compare the effect of theta EEG-NF on episodic memory between responders and non-responders who were self-regulating the same target band. This served to potentially rule out any effects of self-regulating different target bands. In the Theta responder group, there were 15 participants and 14 in the Theta non-responder group.

Independent t-tests revealed that Theta responders scored significantly higher than non-responders in both cued recall (t(26) = -2.06, p = 0.025) and source recollection (t(25) = -2.58, p =0.008). Theta responders also performed significantly better than non-responders at the 24 hours follow-up free recall test (t(27) = -2.01, p = 0.027), but not at the immediate free recall test (t(27) = -1.27, p = 0.108). Participants' scores did not significantly differ for any of the confidence ratings: Old item confidence (U = 78.5, p = 0.560); New item confidence (t(25) = 0.73, p = 0.474); and Source confidence (t(25) = -0.11, p = 0.910). Following multiple comparisons corrections using the Benjamini and Hochberg False Discovery Rate method, there remained a significant difference between Theta group responders and Theta group non-responders for the measures of source recollection (p(adjusted) = 0.032) and at the 24 hours follow-up free recall test (p(adjusted) = 0.036), but the difference in cued recall score was no longer significant (p(adjusted) = 0.05). Immediate free recall scores remained non-significant: p(adjusted) = 0.108.

Participants' old/new item discriminability (corrected recognition) also did not differ significantly between the groups: (t(26) = -1.51, p = 0.143) – see Figure 10. Bayes factors indicated anecdotal to moderate evidence in support of the alternative hypothesis for immediate free recall, 24hr free recall, cued recall and source recollection. Bayes factors indicated anecdotal evidence in support of the null hypotheses for the remaining measures – see Table 6.

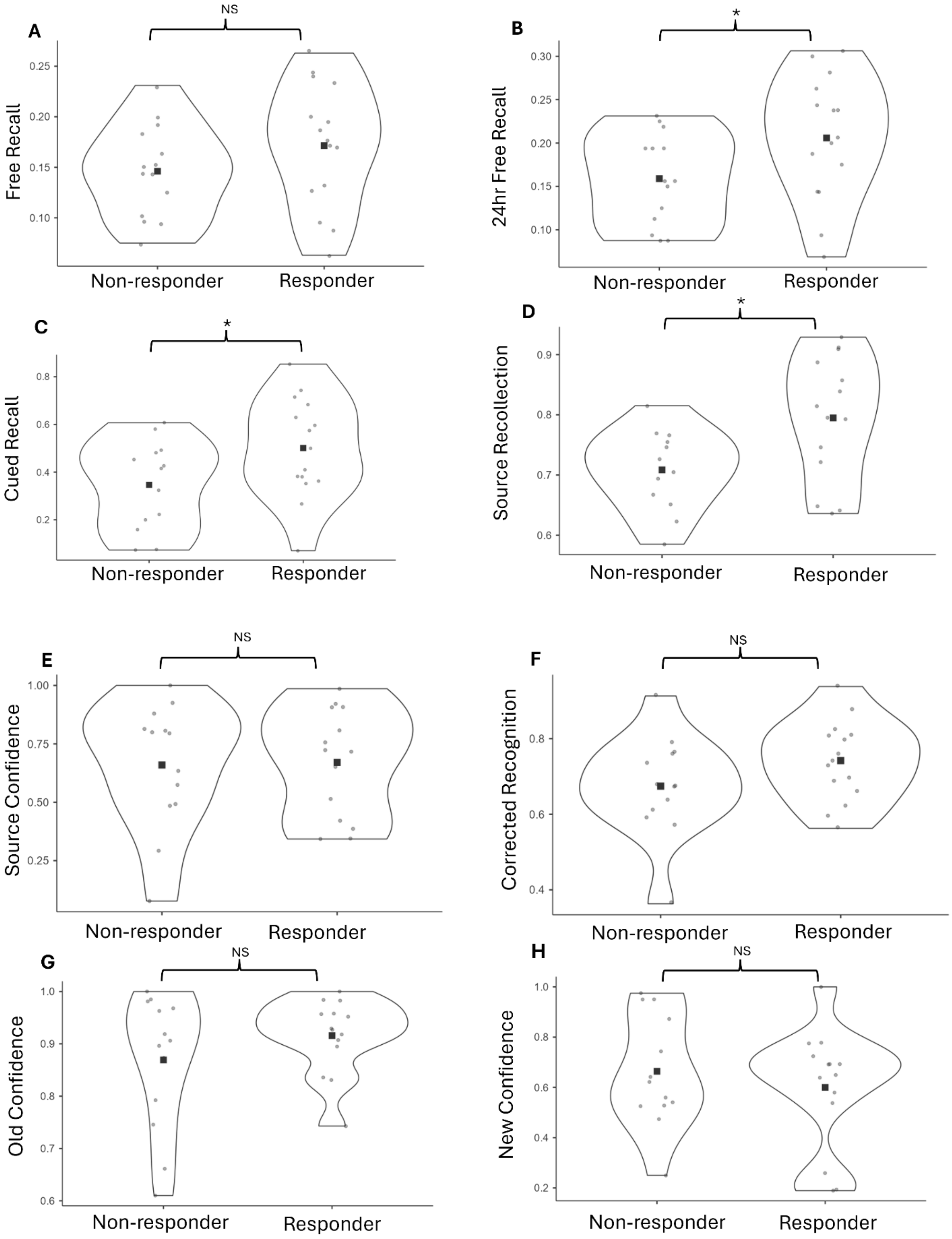


Figure 10. Violin plots display performance in all memory measures for Theta responders (n = 15) and Theta non-responders (n = 14): A) Immediate free recall; B) 24hr free recall; C) Cued recall; D) Source recollection; E) Source confidence; F) Corrected recognition; G) Old item confidence; H) New item confidence. The black square depicts the mean and the grey dots represent the distribution of data points. * = p < .05; NS = non-significant.

Table 6. *Bayes factors for all memory measures comparing Theta Responders to Non-responders.*

Memory measure	Bayes Factor
Immediate free recall	1.09
24 hours free recall	2.89
Cued recall	3.10
Source recollection	7.12
Source confidence	0.36
Corrected recognition	0.82
Old item confidence	0.60
New item confidence	0.44

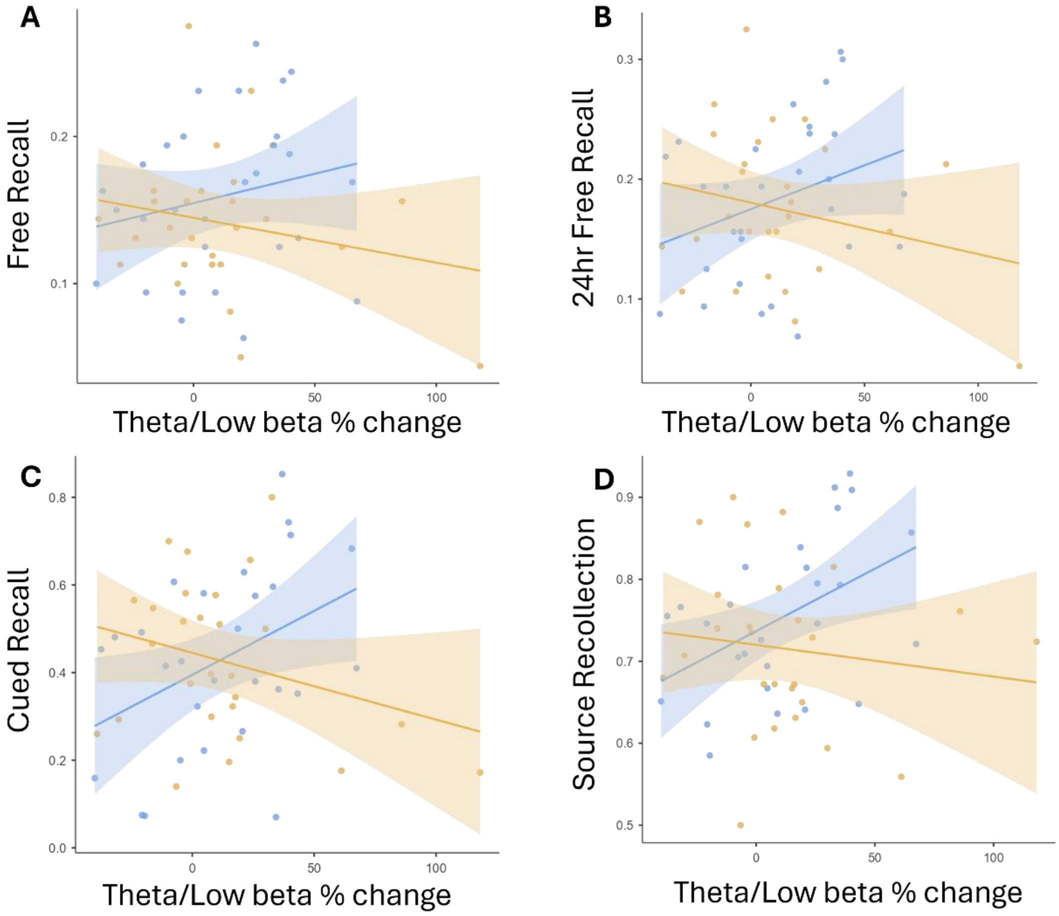
Correlational analyses were also conducted using Kendall's Tau correlation for both the Theta group and the Low beta group to determine any relationships between respondability and memory performance.

In the Theta group, there was a significant, positive correlation between theta/low beta ratio change and source recollection (τ_b = .285, p = .037), but no significant correlations with cued recall (τ_b = .249, p = .066), free recall both immediate (τ_b = .145, p = .276) and 24 hours later (τ_b = .206, p = .119), old item confidence (τ_b = .148, p = .278), new item confidence (τ_b = .043, p = .754) and source confidence (τ_b = .048, p = .741). Participants' old/new item discriminability (corrected recognition) also did not differ significantly between the groups (τ_b = .219, p = .105). However, following correction for multiple comparisons using the Benjamini and Hochberg False Discovery Rate method, the correlation between theta/low beta ratio and source recollection was no longer significant: p(adjusted) = 0.148.

In the low beta group, there were no significant correlations between theta/low beta ratio percentage change and any of the memory measures: Free recall (τ_b = 0.000, p = 1.000), 24 hour follow-up free recall (τ_b = -.043, p = .754), cued recall (τ_b = -.162, p = .246), source recollection (τ_b = -.149, p = .278), old item confidence (τ_b = -.149, p = .278), new item confidence (τ_b = -.100, p = .465) and source confidence (τ_b

= .003, p = .983). Participants' old/new item discriminability (corrected recognition) also did not differ significantly between the groups (τ_b = -.032, p = .818).

Overall, these analyses reveal a positive relationship between increased theta activity and most of the memory measures in the Theta group, and tentative evidence that theta may play a role in source recollection processes; however, this is before multiple comparisons corrections. Contrastingly, most memory scores are negatively correlated with increased theta activity in the Low beta group; however, these correlations are all non-significant.



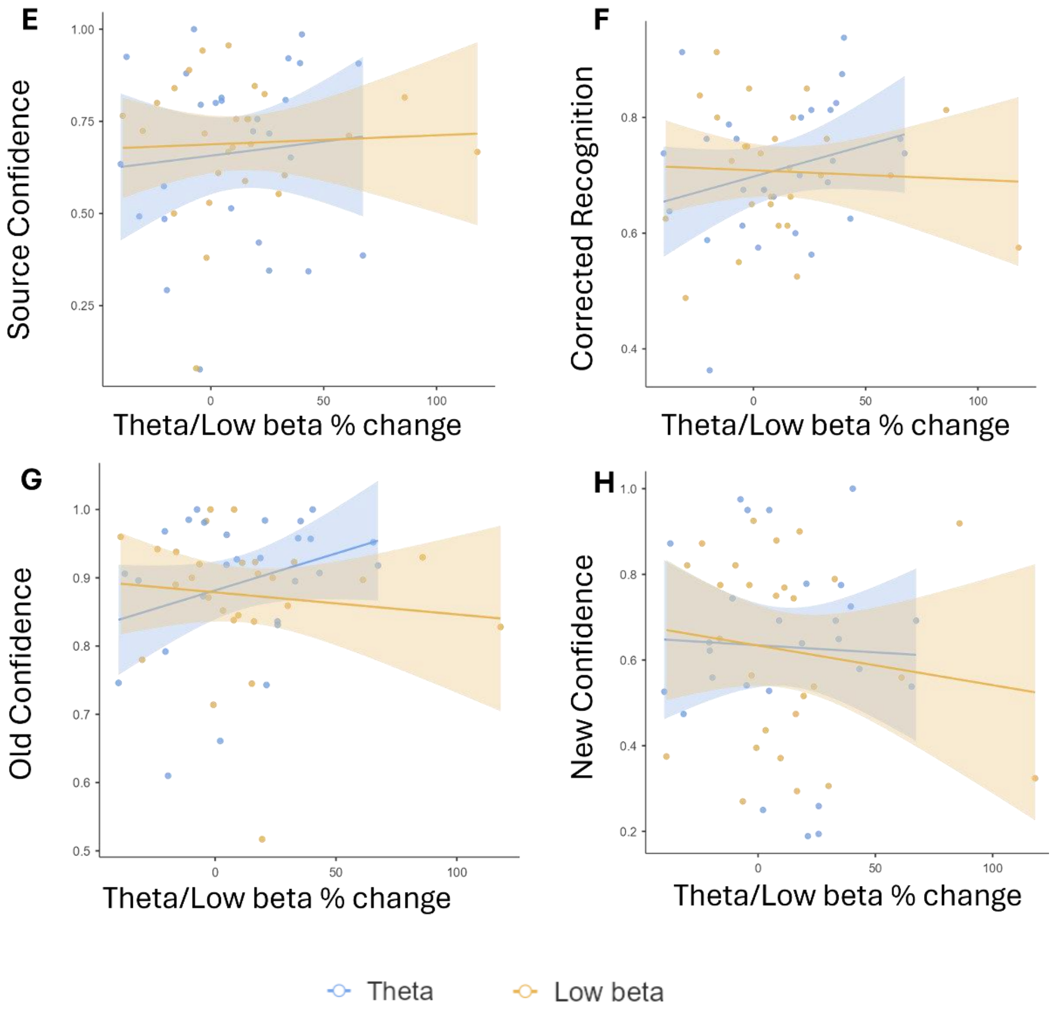


Figure 11. Line graphs showing the relationships between participants' percentage theta/low beta change in both the theta and low beta groups and all memory measures: A) Immediate free recall; B) 24hr free recall; C) Cued recall; D) Source recollection; E) Source confidence; F) Corrected recognition; G) Old item confidence; H) New item confidence. Shaded areas represent the standard error.

3.4 Discussion

3.4.1 Episodic memory and electrophysiological findings

This study investigated whether a 30-minute single session of theta EEG-NF immediately following the study phase, improved participants' ability to recollect this new information by examining various aspects of episodic memory tests, relative to an active Low Beta control group. Contrary to my hypothesis, and to a previous study with a similar design (Rozengurt et al., 2017), participants in the Theta group did not perform significantly better in any of the tests which tapped recollection: free recall, cued recall, and source recollection, as expected. Furthermore, participants' subjective confidence in both their recognition and source recollection scores did not differ significantly between the groups. Examination of the EEG data revealed that overall, the Theta group was not successful in upregulating more theta activity relative to the Low Beta group, using measures comparing theta activity both during and post-EEG-NF, to participants' individual resting baseline. In fact, subsequent examination of individual participants' data revealed that a high number of participants across groups were not able to upregulate the target band.

In this study the proportion of remaining responders i.e. 52% and 33% for the Theta group and the Low Beta group, respectively, is significantly smaller than the average proportion of approximately two-thirds, as reported in the literature (Enriquez-Geppert et al, 2014b; Zoefel et al., 2011). Moreover, the proportion of responders in Rozengurt's sample was 76% and 52% for the Theta and Low Beta group, respectively. In their study, Rozengurt and colleagues demonstrated enhancement of free recall performance following 30 minutes of theta EEG-NF for the entire sample, and a larger effect was revealed for their sub-sample of EEG-NF responders. This might provide some explanation as to why an effect was not found at a group level in the current study, as the larger number of non-responders in the full sample are likely to have diluted such effects if they were present.

Considering this, analyses were conducted focussed solely on EEG-NF responders – defined as those participants who increased target band ratio power during EEG-NF by at least 5% relative to their resting baseline, in both the Theta group and the Low Beta group. The purpose of this was two-fold: (i) to investigate the potential effects of theta EEG-NF on episodic memory performance in a sub-sample where the intervention was successful, and (ii) to control for psychophysiological factors, such as the effects of positive reward, by ensuring participants in both groups received a comparable experience of successful EEG-NF upregulation. The same analyses revealed that the Theta group out-performed the Low Beta group in the immediate free recall measure only. This result provides some evidence that theta EEG-NF upregulation between study and test enhances free recall ability and supports Rozengurt et al. (2017)'s finding with the same memory measure but in a small sample. However, following multiple comparisons corrections, this finding was no longer significant. Bayes factors indicate the data provide anecdotal evidence in support of theta EEG-NF enhancing immediate free recall.

One consistent observation across both studies, is that the Low Beta group included a very small number of responders compared to the Theta group. To overcome this, further exploratory analyses were conducted where the Theta group were divided into responders and non-responders and memory performance was compared between the two groups. In this alternative contrast, the Theta non-responder group thereby served as a control group but with a larger sample size. The benefit of this contrast is that it also removed any potential anomalies associated with upregulation of low beta in the Low Beta group. The results of these analyses revealed significantly enhanced performance in the 24-hour follow-up free recall test, thereby partially replicating Rozengurt et al. (2017)'s findings. Furthermore, the results also included significant improvement in source memory i.e. cued recall and source recollection scores, supporting previous EEG-NF research (Eschmann et al., 2020). These findings survived multiple comparisons corrections, albeit cued recall bordered significance at p(adjusted) = 0.05. Specifically, this contrast demonstrates that participants who were able to increase their theta activity benefited from enhanced recollection, as opposed to those whose theta activity remained unchanged by the intervention. However, and notwithstanding again the clear issue with sample power, the lack of randomisation of participants to groups means this comparison also introduces a potential confound in that non-responders might have felt frustration during the task which could have impaired their performance. Consequently, these findings present tentative evidence that theta EEG-NF can enhance episodic memory, but this interpretation is made with caution considering these issues. As a result of the small number of responder participants correlational analyses were not conducted between theta activity and free recall memory performance.

3.4.2 Does theta EEG-NF enhance memory?

When analyses were conducted in participants who could successfully modulate their brain activity in the desired manner there was some evidence that increased frontal-midline theta activity immediately following the encoding of new information specifically enhanced performance in the free recall tasks, and in both cued recall and source recollection tests. This could provide some support for the functional role of theta phase synchronisation during recollection processes, and more specifically in associative memory processes involved in the retrieval of source information (Clouter et al, 2017; Herweg et al., 2020). Considering that no differences were found between groups in recognition memory scores (i.e. old/new item judgements), this study's findings infer a dissociation in recollection and familiarity processes and thereby support the dual process theory of memory (Jacoby, 1991; Yonelinas, 2002).

An important distinction to consider when interpreting these results, regarding the possible mechanisms by which theta EEG-NF enhances recollection processes, is the timing and schedule of EEG-NF training. Given the EEG-NF intervention took place during the retention period in a study-NF-test design, this study's findings could support the idea that increased theta activity during this period facilitated consolidation of the new information previously learnt, mirroring the waking state consolidatory processes that occur during sleep (Rasch & Born, 2013; Rozengurt et al., 2017). Other studies have also found strong effects of a single session of theta EEG-NF during the retention period for different types of memory, such as visuo-spatial memory (Shtoots et al, 2020) and procedural memory (Rozengurt et al, 2016). Alternatively, it is possible that persistent effects of theta post-EEG-NF could be responsible for enhancing retrieval processes at the test phase (Addante et al., 2011). This explanation could also account for the findings by Rozengurt et al. (2017) and potentially the current study. Exploration of the EEG data recorded during the test phase could elucidate whether the theta group experienced increased theta during the retrieval stage which might have contributed to enhanced memory performance. It would also be useful to know for how long the increase in theta activity is sustained for after neurofeedback training.

The correlational analyses show a less clear picture regarding theta's role in memory. In the theta group the relationships are positive and show tentative evidence for a significant role of theta in source recollection; however, this correlation is non-significant following multiple comparisons corrections. Furthermore, increased theta/low beta in the low beta generally depicts a negative relationship with participants' memory performance. Given the high non-responder rates, refining of the protocol and increasing responder rates could serve to provide a more accurate representation of theta's role in episodic memory performance following EEG-NF training.

3.4.3 Self-regulation ability – the issue with EEG-NF non-responders

A striking finding in the current study is the large number of people who were unable to upregulate their brain activity in the target frequency. However, it is important to note that in the review which was conducted in Chapter 2 it was found that 80% of studies failed to report information on this issue, so it is difficult to know whether the numbers in this study are representative or not. Some methodological factors are discussed here which may have contributed to the higher-than-average number of non-responders in the current study.

3.4.3.1 Provision of instructions/strategies

In the current study, the same list of strategies was given to all participants regardless of group membership. Participants were instructed to adopt a 'trial and error' approach and to be guided by the bar. One potential issue with this design is that it is not clear at what stage during the EEG-NF training participants move beyond experimenting with the different strategies and commit to using the strategy they deem is successful in raising the bar. This means that if participants were struggling to find a strategy that worked, prolonged time spent in the 'trial and error' stage could have served to render the upregulation ineffective due to trying too many strategies and running out of time. Eschmann et al. (2020) make a clearer distinction in their EEG-NF task design between the 'variable strategy phase' when participants could experiment with the provided strategies or introduce their own, and the 'constant strategy phase', when participants were required to use their preferred strategy. Interestingly, Eschmann et al. (2020) found frontal midline theta activity was significantly higher in the theta group compared to the Low Beta group in the constant strategy phase only. The EEG-NF training schedule in their study allowed participants three full EEG-NF training sessions to trial different strategies, whereas perhaps a single session, as used in the current study, is insufficient time to find one that works effectively when provided with many options. In Rozengurt et al.'s study (2017), participants were given specific recommended strategies to facilitate upregulation of target band power ratio (i.e. relaxation for theta and concentration for low beta), which could explain the higher number of responders in their study. However, some findings suggest that more effective self-regulation from EEG-NF can be found when no suggested strategies are provided at all (Chikhi et al., 2023). It has been proposed that participants may engage more directly with the implicit learning processes involved in operant conditioning, rather than be overloaded with, or confused by, different strategies to try (Hardman et al., 1997; Kober et al., 2013). EEG-NF strategies are discussed in more detail in Chapter 4.

3.4.3.2 The EEG-NF protocol: artefact rejection and feature extraction

The current study adopted the use of the ‘beta2’ (22-45Hz) inhibit bar for the detection of muscle artifacts based on a study which deemed this frequency band effective in removing online artefacts during EEG-NF with high signal-to-noise quality (Paluch et al., 2017) and as an alternative to high beta (18 Hz–22 Hz), used by Rozengurt and colleagues, which was considered a potential issue regarding upregulation of low beta due to the flanking frequency bands (Ros et al., 2013). However, as this was used in conjunction with the delta (0.5 Hz–2 Hz) inhibit bar to control ocular artifacts (Eschmann et al., 2020; Escolano et al, 2014a) it is possible that the combined thresholds set for these inhibit bars, along with the 100 μV artefact-rejection simple threshold, may have been too harsh for some participants who are prone to more frequent blinking or habitual body movements during the EEG-NF training. These participants may have triggered the threshold more often and thereby technically received less EEG-NF training overall. This issue could possibly be diminished if the initial threshold was set relative to an active EEG-NF block, as opposed to the resting baseline, to account for artifact inducing behaviour during the task which may be more prominent than during rest, and thereby leaving more headroom for movement. Furthermore, if participants were able to visually monitor the inhibit bars on-screen, they might be better able to control the onset of artefacts caused by such movements, as has been done in some EEG-NF studies (Kober et al., 2015b, 2017b). However, it could be argued that such visual displays might detract attention from the target visual feedback. Further research investigating the optimal methods for adequately controlling for artifacts during EEG-NF training is needed to better inform the protocols used in future EEG-NF experiments.

3.4.3.3 Importance of the control group

Despite the points discussed above, the analyses show that a proportion of the sample was able to self-regulate their brain activity by engaging with the EEG-NF intervention. One issue with associating any observed enhancement in recollection with this successful increase in theta activity in the sub-samples of responders, would be the nature of the control condition. It is acknowledged that the feedback protocol used in this study allows for the specific effects of theta EEG-NF to be demonstrated solely relative to low beta - the online protocol does not account for the possibility that participants are modulating other frequencies along with theta (or low beta) during EEG-NF training, barring delta and beta2 which were controlled by way of inhibit bars. Notably, calculation of relative theta and low beta activity reveal that both decrease during EEG-NF training compared to resting baseline. This suggests that other frequencies across the spectrum also increased during EEG-NF, reducing the prominence of the target band power. Other studies have also reported simultaneous modulation of non-target frequency bands (Ros et al., 2013). This is an important consideration, especially given studies using alpha- and SMR- based EEG-NF protocols have also revealed enhancement in episodic memory performance (Escolano et al., 2014a; Hsueh et al., 2016). More detailed exploratory analysis of the full spectrum of brain activity would determine whether band training independence has been achieved (Gruzelier et al., 2014a, 2014b; Zoefel et al., 2011) thereby isolating the specific effects of increased theta on episodic memory performance, or whether other frequencies may be at play.

As noted above, trainability of the low beta/theta ratio was less successful, demonstrated by the comparably low number of responders in the Low Beta group. Van Son et al. (2020) found no overall upregulation effect after 25 minutes of beta/theta ratio EEG-NF training, albeit using the broader beta band (12-30Hz). It could be that this band is generally difficult to self-regulate, especially given that increased low beta/theta has been attributed more to a reduction in theta as opposed to increased low beta (Nan et al., 2015). Interestingly, the correlational analyses, although non-significant, indicate a positive relationship between theta/low beta ratio power and some of the memory measures (immediate and 24 follow up free recall, cued recall and source recollection); however, in the low beta group this relationship is negative. Therefore, despite an increase in theta/low beta, memory performance is lower. Given that an increase in theta/low beta ratio power is the opposite of what participants' goal was in the low beta group – which was instead to increase low/beta ratio power – it is possible that poor memory performance could have been a result of frustration and demotivation due to not succeeding at the task and subsequently receiving no positive reward.

It could also be questioned whether the Fz electrode is the optimal site for low-beta feedback. The rationale for this electrode is heavily weighted towards training frontal midline theta, given theta's maximal activity recorded at this site (Yamaguchi et al., 1990b; Mitchell et al., 2008). The beta/theta EEG-NF protocol, used by Van Son et al. (2020), commonly utilises more centrally located electrodes at Cz, C3 or C4 or a combination thereof, where activity in the beta band is maximal. This brings into question whether a low beta/theta active contingent control is the best control to use in an EEG-NF study, especially low beta's association with alert focus and concentration (Gruzelier, 2014a; Ray & Cole, 1985) – this is discussed in more detail in Chapter 6, Section 6.4.3. To preclude potential interference from cognitive functions associated with a particular frequency band, it may be more effective for participants in the control group to upregulate randomly selected frequency bands. This has been successfully used for EEG-NF training programmes that extend beyond a single session (Eschmann et al., 2020; Wang & Hsieh et al., 2013). However, in these studies, no data is reported regarding whether participants in the control group were successful in upregulating the various individual frequency bands. If not, the control participants could potentially have experienced similar frustrations as both the Low Beta group and Theta non-responders in the current study. Another alternative option is a non-contingent control, or 'sham' control condition where participants are provided with yoked feedback from another participant experiencing successful self-regulation. Again, there is no clear guidance in the literature as to the optimal EEG-NF control group or condition to inform EEG-NF research.

Finally, it is possible that given the experiment took place during the COVID-19 pandemic with increased safety measures such as masks and visors, this could have caused a lack of engagement with the task due to increased levels of anxiety, thereby negatively affecting some participants' ability to successfully upregulate their brain activity, and in turn benefit from the proposed effects of EEG-NF on their memory performance. Thus, it might have been hard for the participants to relax and to concentrate, which are usually associated with theta and low beta bands respectively, given the broader climate in which the research took place. Measures of participants' current motivation and mood were recorded prior to the EEG-NF task to investigate whether these factors may have contributed to the high number of non-responders. These findings are discussed in Chapter 4.

3.4.4 Study improvements and future research

Potential improvements to the current study's design and methodology could be proposed based on the limited body of research in existence exploring the use of EEG-NF as an intervention for improving episodic memory. The current study's findings highlight the consistent and prominent issue of EEG-NF non-responders in the literature and foreground a need to focus on increasing the number of responders to strengthen both the power of the sample, and the reliability of the findings that potentially link increased theta oscillatory activity with episodic memory performance.

Firstly, the methods used to process EEG-NF data and determine respondability must be valid and robust. It is acknowledged that the use of different parameters (e.g. band pass filter frequency cut-off frequencies) for online and offline processing of the EEG-NF data may have affected the measures of EEG-NF success, although both band pass ranges comfortably contained the frequencies of interest. As a result, there is a possible disparity between the amount participants successfully upregulated the target band power ratio and that represented by the offline EEG-NF data. The implications for this and investigating EEG-NF responder ability is discussed in Chapter 4, Section 4.4.7, and generally in Chapter 6, Section 6.4.1. Furthermore, optimising the EEG-NF protocol could be achieved by ensuring that the online ocular and muscle artefacts are controlled for, but not so much so that EEG-NF training is rendered ineffective for some participants (Paluch et al., 2017). Given there are no solid recommendations regarding this in the literature, further research could involve collecting such data and identifying an appropriate threshold to inform future EEG-NF experiments, or by establishing this at the piloting stage of an experiment. Moreover, EEG-NF protocols based on individuals' peak activity at resting baseline may enhance upregulation ability, as opposed to feeding back the general broad band, which has been shown to be effective in some EEG-NF studies (Eschmann et al., 2020; Escolano et al., 2014b).

Secondly, there is some evidence in the literature pertaining to individual differences in ability to self-regulate brain activity during EEG-NF. For example, research suggests that a higher resting baseline predicts better EEG-NF performance in the target band (Nan et al., 2015; Wan et al., 2014). Other factors such as current mood and motivation, attention and personality have also been shown to effect participants' ability to self-regulate their brain activity (review by Alkoby et al., 2018). Finally, some studies have explored whether specific strategies are linked with brain trainability (Autenrieth et al., 2020; Kober et al., 2013). Further research in this area could serve to develop an EEG-NF 'responder profile' which could serve to streamline recruitment of suitable participants in studies researching the various effects of EEG-NF, and to optimise the use of EEG-NF as an intervention. Data collected during this experiment relating to these factors is reported on in Chapter 4 of this thesis to address this gap in the research. Fundamentally, there is currently no strong empirical evidence reliably informing researchers of systematically tested factors that affect EEG-NF responder ability. However, EEG-NF and its effect on episodic memory is a relatively new area of research, and the expectation is that such questions will be addressed over time as empirical support grows and becomes more robust.

It is also worth noting that there is a difference between the current study and Rozengurt's et al.'s (2017) memory paradigm in terms of the encoding phase. Rozengurt and colleagues included the development of a learning curve where participants in both the Theta and the Low Beta group repeated the same free recall test three times pre-EEG-NF training. This strategy of strengthening encoding by repeatedly testing deliberately served to align memory performance levels in the two groups pre-EEG-NF, so that subsequent changes in post-scores can be attributed more reliably to the EEG-NF intervention. In the current study, participants' baseline memory performance was unknown therefore possible group differences in baseline memory performance may have obscured the beneficial effects of theta EEG-NF in this case. However, participants were initially randomised to the two groups which is a commonly accepted method for avoiding confounding the results with such individual factors.

Finally, the number of participants recruited for this study was based upon the effect size obtained by Rozengurt et al. (2017) of d = 0.922. This was used for the power analysis given the aim to replicate Rozengurt et al. (2017)'s study using a similar experimental design. However, it is noted that this effect size of EEG-NF on episodic memory is larger than that reported in Chapter 2 (g = 0.31) which represents all studies included in the meta-analysis. A power analysis conducted based on the meta-analysis's effect size instead results in 130 participants per group being required to achieve sufficient power. This renders the current study underpowered to find a small effect such as that generated by the meta-analysis. However, the broader issue is whether EEG-NF as an intervention, which has such a small positive effect on episodic memory performance, is viable. This is discussed further in Section 6.3 of the General Discussion in this thesis.

3.4.5 Conclusion

In this chapter a positive effect of theta EEG-NF on the different measures of recollection was not found at a group level. However, on further inspection of the EEG-NF data, a high number of EEG-NF non-responders was discovered. By conducting further analyses focussed on solely EEG-NF responders, there was some evidence that theta EEG-NF did enhance performance on recollection memory scores. Due to the small sample size, generally only anecdotal evidence from the Bayes Factors and lack of randomisation of participants in some of these analyses, the results are interpreted with caution. It is noted that the findings differ somewhat according to whether the theta group is compared to the low beta group of responders or theta non-responders, in terms of which recollection measures might be enhanced. This highlights an existing issue regarding the importance of the active control group, whereby in this case, comparable experience may be lacking in the non-responder group due to the lack of positive feedback received. This study's findings suggest possible support for the effect of theta EEG-NF during the retention period on objective recollection of new information studied. However, future experiments would benefit from richer empirical support guiding methodical features such as the optimal EEG-NF control condition and the recruitment of participants able to self-regulate targeted oscillatory activity. This could strengthen the empirical support for the use of theta EEG-NF to enhance episodic memory and inform future research in this area.

Chapter 4: Electroencephalography neurofeedback responders - Exploration of individual differences

4.1 Introduction

The key assumption underlying the validity of EEG-NF is that a link exists between self-regulation of the target brain state and the desired behavioural outcome. Therefore, it is imperative that individuals can successfully self-regulate their brain activity to experience the subsequent and behavioural benefits of EEG-NF training. However, one initial challenge when considering this is that, as reported in Chapter 2, many EEG-NF studies do not report evidence of self-regulation or 'learning', so it can be unclear if this link is present in studies. While various methodological features of the EEG-NF procedure could be related to the extent that individuals can self-regulate (Enriquez-Geppert et al., 2017; Gruzelier et al., 2014b) it is important to also consider the person as they play an active role in the EEG-NF process. Previous research has indicated that a substantial number of individuals are seemingly unable to significantly modulate their brain activity during EEG-NF training to achieve the target brain state (Alkoby et al, 2016) and this is what was found in Chapter 3. However, there is little information regarding why this is the case. It is therefore important that research tries to understand the characteristics of the learner, and the interplay between the learner and the EEG-NF process, to explain the variability in individuals' ability to self-regulate.

The aim of the work in this chapter was to explore a range of factors to determine if they are related to participants' ability to successfully regulate their brain activity. An enhanced understanding of the personal attributes that promote effective self-regulation would benefit the EEG-NF literature two-fold by: (i) streamlining the recruitment of participants to include solely EEG-NF responders which could serve to increase sample power and the likelihood of finding an effect in EEG-NF experiments, if one exists, or allow for direct comparisons to be made between responders and non-responders; and (ii) enabling more tailored application of EEG-NF training based on individual characteristics which could improve the efficacy of EEG-NF by optimising behavioural outcomes.

As outlined in detail in Chapter 1 (Section 1.2.4) there are a few studies which have looked at various state and trait characteristics of the learner that might be influencing self-regulation ability. Initially, it would be anticipated that being engaged with the EEG-NF task could be conducive to increased chance of EEG-NF success. Some studies have looked at the effects of motivation and mood and found higher motivation levels and positive mood are more likely to be associated with EEG-NF success (Kleih et al., 2010; Leeb et al., 2007; Nijboer et al., 2008), although other studies have failed to find these links (Enriquez-Geppert et al., 2014; Hammer et al., 2012). Similarly, finding the task to be not too difficult or easy would also be vital to neurofeedback success and generally research supports this assertion (Bauer et al., 2016). A core feature underpinning this ‘sweet spot’ of perceived task difficulty is that of being in a state of ‘flow’. Broadly theorised as being conducive to learning (Csíkszentmihályi, 1990; Wilson, 2019), flow state – one of ‘effortless attention’ (Bruya, 2010) - has been shown to be induced by EEG-NF training and associated with subsequent memory benefits (Eschmann et al. 2020). However, it is unknown whether an existing state of flow during EEG-NF training could facilitate enhanced reinforcement learning i.e. self-regulation ability itself. It also follows that trait-based attentional ability might be associated with task engagement and better self-regulation performance; however existing positive findings are based on a unique sample of drug-refractory epilepsy patients (Daum et al., 1993) and an indirect measure of attention (Hammer at al., 2012). Further exploration is clearly required to determine whether these factors relating to task engagement influence responder ability.

Furthermore, some studies have investigated potential links between individual personality traits and EEG-NF responders (see review by Kadosh & Staunton, 2019). Research conducted on these measures has revealed some links to traits such as conscientiousness, decision-making and goal setting (Tipple, 2024), fluid intelligence (Khodakarami & Firoozabadi, 2020) and self-reliance (Jeunet, 2015); however, other findings are mixed (Hammer et al., 2012; Kleih et al., 2010; Witte et al., 2013). These findings suggest that more positive and productive personal attributes like planning and organising could be conducive to successful self-regulation. However, more data is needed to draw strong conclusions regarding the influence various personality traits have on EEG-NF responder ability. There are also mixed findings regarding whether one's belief in their control of the EEG-NF feedback (e.g. the stimuli goal) relates to their ability to successfully self-regulate their brain state. Burde and Blankertz (2006) found that participants with higher locus of control scores were better able to move an on-screen cursor using motor imagery; however, this finding was not replicated in a similar follow-up study (Witte et al., 2013). Moreover, findings by Kikkert (2015) revealed that locus of control was found to solely relate to greater beta increases in participants for phasic learning, highlighting the important question as to whether the influence of these factors is dependent on the specific target frequency characterising the EEG-NF protocol. A few studies have also looked at the effect of individuals' neurophysiological state measured by EEG and found their resting state to be a predictor of subsequent EEG-NF training success (Eroglu et al., 2018; Chikhi et al., 2023; Nan et al., 2015, 2018; Reichert et al., 2015; Wan et al., 2014). However, these findings relate to a range of EEG-NF protocols. The current study aims to extend these findings to explore the effects of resting state on self-regulation of the theta and low beta bands.

Finally, research investigating the effect of strategies on individuals' ability to self-regulate their brain activity is inconclusive regarding whether certain strategies work best, or none. For example, breathing exercises, relaxation, and cognition have all been linked to efficient self-regulation of SMR and high alpha (Autenrieth et al., 2020; Chikhi et al, 2023). Contrary to this, a direct comparison demonstrated that adopting no strategy was found to be more effective than using strategies (Chikhi et al., 2023). Subsequently there is no official empirical guidance to determine which strategies facilitate the operant conditioning process during EEG-NF training (Pigott et al., 2018). Again, it could be argued that the existing findings related to effective strategies might depend on the specific EEG-NF protocol. For example, relaxation and mental arithmetic have been associated with increased theta activity, whereas beta activity has been associated with concentration levels (Rozengurt et al., 2017). More systematic testing and precise classification of the various strategies might serve to elucidate the beneficial effects of different strategies on self-regulating specific brain states (Lubianiker et al., 2022). The current study uses pre-defined strategies for participants to select and try, rather than them being required to randomly explore strategies which are later categorised during the analysis stage based on participants' self-reports.

As can be seen from the forgoing discussion there is only a relatively small number of studies which have looked at the characteristics associated with successful EEG-NF. For some factors significant results found in some studies have not replicated in other studies. This could be due to several factors, such as lack of power, as many studies have been conducted with small sample sizes; differences in the populations that have been examined e.g. clinical groups or healthy volunteers; and there could be differences in what factors are associated with neurofeedback success depending upon what frequency band is being trained. The neurofeedback study conducted in Chapter 3 offered an excellent opportunity to explore questions about what participant characteristics and strategies might be associated with neurofeedback ability, due to the large number of participants who were non-responders, and because a large battery of questionnaires and tasks were administered to the participants to examine these questions. Thus, the aim of this chapter was to examine these data to explore the active role of the learner and to determine for whom EEG-NF training works.

Initially, this involved for the whole sample investigating if there were any differences between responders and non-responders on a variety of individual differences factors, including: self-reported quantifiable measures of motivation and mood, flow state and task difficulty, personality traits, attentional ability, and a neurophysiological measure (EEG resting baseline activity). As continuous variables have more statistical power than binary ones, correlational analyses were also conducted in relation to these variables. Instead of looking at responder versus non-responder, a measure of the extent to which the participant had elevated the target frequency band was examined. Descriptively it was also assessed what strategies participants had used to regulate their brain activity. In addition to these analyses parallel ones were conducted but rather than looking at the whole sample these were split by the target frequency band i.e. theta and low beta. This is due to some studies e.g. Kikkert (2015) finding that some participant characteristics were related to neurofeedback success when certain frequency bands were trained.

There is compelling evidence from previous studies that the levels of perceived task difficulty will be related to neurofeedback success. It was therefore predicted that Responders will report significantly lower levels of perceived task difficulty than Non-responders in relation to the EEG-NF task.

In terms of the other individual differences factors the following hypotheses were tentatively made as the research is more mixed in its findings and/or limited in what has been conducted. It was therefore examined if responders and non-responders would differ significantly (or there would be a significant correlation with increased target band) on the following variables: i) current motivation (specifically the subscales of challenge, interest, probability of success and anxiety), ii) positive and negative mood, iii) flow state, iv) locus of control, v) sustained attention, and vi) resting baseline target band activity.

Hypothesis 1: Responders' scores for the current motivation sub-scales of Challenge, Interest, Probability of Success and Anxiety will differ significantly from those of Non-responders.

Hypothesis 2: Responders' positive and negative mood will differ significantly from that of Non-responders.

Hypothesis 3: Responders and Non-responders will differ significantly on their measure of flow state.

Hypothesis 4: Responders' level of perceived control over the bar will differ significantly from that of Non-responders in relation to the EEG-NF task.

Hypothesis 5: Responders' scores of sustained attention will differ significantly from those of Non-responders.

Hypothesis 6: Responders' EEG resting baseline will be significantly different to Non-responders for the target EEG-NF band.

It is unclear whether the differences predicted above would be affected by the frequency band trained, so these analyses split by theta and low beta are exploratory.

4.2 Methods

4.2.1 Participants

The behavioural data were collected from the same participants who completed the EEG-NF experiment reported on in Chapter 3 of this thesis. The sample comprised: Responders (n = 30, 27 females; mean age=18.9) of which 18 were Theta group participants and 12 were Low beta participants, and Non-responders (n=26, 25 females; mean age=19.2) of which 11 were Theta group participants and 15 were Low beta participants. A post-hoc sensitivity analysis was calculated to examine the difference between the two independent groups for a two-tailed hypothesis, α = .05, power = 0.8, and revealed a sample of this size is sufficiently powered to detect an effect of Cohen's d = 0.764, which is approaching a large effect size (G*Power: Version 3.1.9.7). A post-hoc sensitivity analysis for a correlation, with the same parameters as above, could detect an r = 0.356, which is a moderate effect. A one-tailed test with identical parameters could detect Cohen's d = 0.674 and r = 0.319. Thus, the correlations might be better placed to detect significance if relationships exist.

4.2.2 Design

All participants in the sample were divided into two groups: Responders and Non-responders, where responders were defined as those whose theta/low beta ratio (or low-beta/theta for the control group) increased by more than 0% from baseline to the average of the six active EEG-NF blocks. This operational definition of a responder differs from that used in Chapter 3 (i.e. more than 5% increase in target band from baseline to the average of the six active EEG-NF blocks), as the current contrast results in a larger, and more even, number of participants in each group to compare. Responders and non-responder scores were compared for all factors, informed by existing findings in the literature, for the full sample and exploratory analyses conducted within the Theta and Control group separately.

4.2.3 Procedure

Throughout the EEG-NF experiment, participants were provided with several questionnaires (Qualtrics, QX), and a cognitive test which was implemented and presented online using the PsyToolkit platform (Stoet, 2010, 2017), to gather behavioural data related to individual differences and specific EEG-NF strategies participants used to self-regulate the target brain activity – see Figure 12. Participants were provided with specific instructions for each questionnaire and the task, which were built into the online programme. Participants were instructed to provide honest answers to all questions and to balance speed and accuracy whilst undertaking the task. The questionnaires and the cognitive task are summarised below.

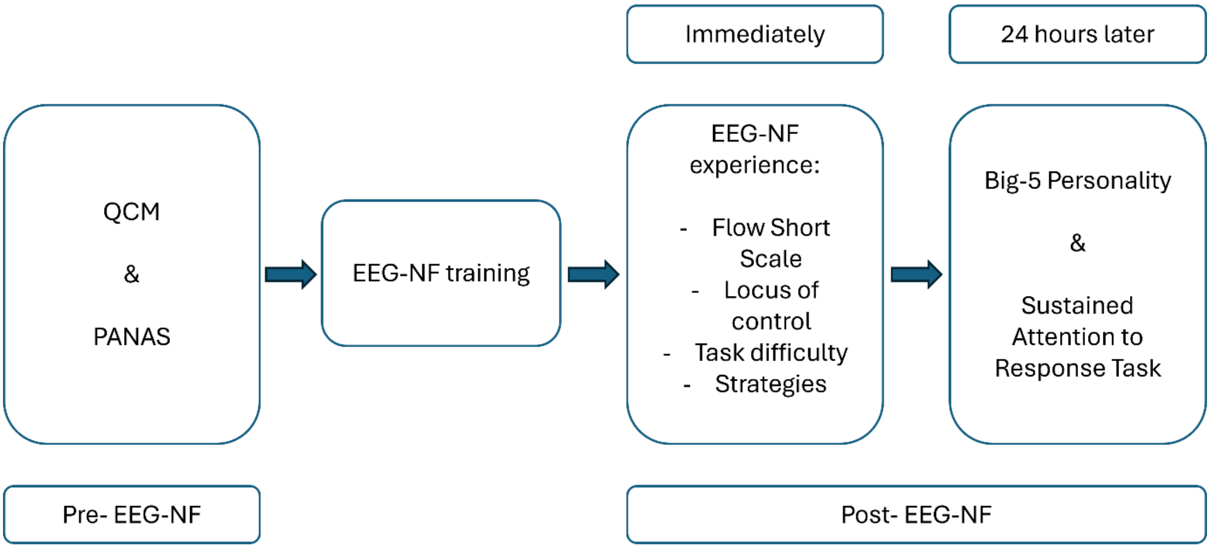


Figure 12. Schematic diagram showing the time-points when participants completed the questionnaires and cognitive task relative to EEG-NF training. QCM = Questionnaire for Current Motivation; PANAS = Positive and Negative Affect Scale.

4.2.4 Materials

4.2.4.1 The Questionnaire for Current Motivation (QCM)

In this questionnaire, participants indicated the degree of motivation they felt in anticipation of completing the EEG-NF training task. The version used for this experiment was an English adaptation (Vollmeyer & Rheinberg, 2006) of the original German version (Rheinberg, et al., 2001). The questionnaire comprises 18 statements, incorporating four subscales: “Anxiety” which represents a fear of task failure (5 statements e.g., “I feel under pressure to do this task well”; “Challenge” which refers to the degree of relevance and ease the responder attributes to the task (4 statements e.g., “This task is a real challenge for me”); “Interest” which reflects the responder’s level of positive affect and evaluation regarding the task (5 statements e.g., “I would work on this task even in my free time”); and “Probability of success” which is how likely the responder feels it is they will perform well at the task balancing their perceived ability versus the perceived task difficulty (4 statements e.g., “I think everyone could do well on this task”). Each item is rated on a 7-point Likert scale from 1 - Strongly disagree to 7 - Strongly agree. A higher score reflects positive alignment with each factor, accounting for two statements which are negatively worded. The range of scores for challenge and probability of success is 4–28 points, and for anxiety and interest the range is 5–35 points. The internal reliability estimates for the subscales are: Cronbach's alpha 0.79, 0.66, 0.82 and 0.72, respectively (Freund et al., 2011) and the validity of the scale has been demonstrated in various studies (Rheinberg et al., 2001; Vollmeyer & Rheinberg, 2006; Freund et al., 2011). The approximate duration of the questionnaire was between five and ten minutes.

4.2.4.2 The Questionnaire for Current Mood – Positive and Negative Effect Schedule (PANAS)

The purpose of this questionnaire was to gauge participants' current mood prior to engaging with the EEG-NF task. The internationally reliable short form version of the questionnaire (I-PANAS-SF) was used for this experiment (Thompson, 2007; Watson et al., 1988). The questionnaire comprises 10 items where each is composed of the same question beginning with: "Thinking about yourself and how you feel right now, to what extent do you feel....?", and ending with one of five positive ('alert', 'inspired', 'determined', 'attentive', and 'active') or five negative ('upset', 'hostile', 'ashamed', 'nervous' and 'afraid') adjectives relating to affect. Responders rate how they are currently feeling on a 5-point Likert-type scale: "1 - Strongly disagree" to 5 - "Strongly agree". Higher scores reflect a higher level of engagement with each affect, with a scoring range of 5 – 25 for both positive and negative affect. The internal consistency of this scale for positive affect is α = 0.75 and is α = 0.80 for negative affect (Thompson, 2007). The cross-cultural validity of this scale is supported (Karim et al., 2011). The approximate duration of the questionnaire was five minutes.

4.2.4.3 Flow State

The Flow Short Scale questionnaire measures an individual's functional state or 'flow'. The version used for this experiment was an English adaptation (Vollmeyer & Rheinberg, 2006) of the original German version (Rheinberg et al, 2001), and the wording was amended to refer specifically to the EEG-NF task. The test consists of 13 items, with 10 items measuring flow state characterised by (i) a challenge-skill balance, (ii) merging of action and awareness, (iii) unambiguous feedback, (iv) concentration on the task at hand, (v) time transformation, and (vi) fluency of action e.g., “My thoughts/activities run fluidly and smoothly”. The remaining 3 items measure the responder’s level of worry e.g., “I am worried about failing”. Responders rate to what degree they agree with each statement on a 7-point Likert-type scale: “1 - Strongly disagree” to 7 - “Strongly agree”. Higher scores reflect higher levels of both flow state and worry, factoring in one worry statement positively worded to reflect a lack of worry. The scoring range for flow state is 10 – 70, and for worry is 3 – 21. The scale is reliable (Cronbach’s α = 0.90) and standardised (T-norms; Rheinberg, 2004). The approximate duration of the questionnaire was one minute.

4.2.4.4 Locus of Control

Participants were also asked to reflect on the degree that they believed they had control over the bar during the EEG-NF task. This part of the questionnaire comprised of a single statement: “I felt like I had complete control over the height of the bar” and was scored using a 7-point Likert-type scale: “1 - Strongly disagree” to 7 - “Strongly agree”. A higher score indicated a higher level of confidence the responder had in their ability to autonomously increase the height of the bar in the desired direction. The scoring range was 1 – 7 (Enriquez-Geppert et al., 2013).

4.2.4.5 Task Difficulty

Participants’ perception of the EEG-NF task difficulty was measured by their response to a single statement: “I found achieving the goal of the EEG-neurofeedback training to be difficult” on a 7-point Likert-type scale: “1 - Strongly disagree” to 7 - “Strongly agree”. The scoring range was 1 – 7 (Enriquez-Geppert et al., 2013).

4.2.4.6 The Big 5 Personality Questionnaire

The Big 5 is an evidence-based personality questionnaire (Goldberg, 1990) based upon identified and categorised common personal attributes across a large sample of individuals by way of factor analysis. It is therefore considered to be a reliable measure of different aspects of an individual's fixed personality traits (Goldberg, 1992). The questionnaire consists of 50 items taken from the International Personality Item Pool (Goldberg, 1999, 2006; https://ipip.ori.org/) with 10 items representing each of the Big-Five Factor Markers of personality: openness (how open a person is to new experiences and ideas), conscientiousness (how organised, goal-oriented, and dependable a person is), extraversion (how outgoing and energised by social interactions a person is), neuroticism an individual's level of emotional stability), and agreeableness (how much a person prioritises others' needs and interests over their own). Participants were asked to rate each statement on how true it is in relation to their own personality, on a 5-point scale: 1 – disagree to 5 - agree. The scoring range for each trait is 5 – 50 points. The approximate duration of the questionnaire was ten minutes.

4.2.4.7 Sustained Attention to Response Task

The sustained attention to response task (SART) (Manly & Robertson, 2005) is a continuous performance task designed to measure participants' level of sustained attention whilst inhibiting distractions. During the task, a random series of 225 single digits (1 - 9), including 25 no-go trials are presented on a computer monitor at a regular rate of 1 per 1.15 seconds (18 digits for the practice run). The responder is instructed to press a single response key (the space bar) following each presentation except for a nominated no-go digit (i.e. 3), to which no response should be made. Scores represented accuracy of response (i.e. response to go trials and no response to no-go trials) with a maximum of 225. The duration of the task was approximately five to ten minutes.

4.2.4.8 EEG-NF Strategies

Participants viewed the same list of suggested strategies that were provided to them prior to the EEG-NF task and selected the strategies they had used and felt worked best to move the bar. The strategies were: “Mental operations” - mental arithmetic, counting backwards in increments and thinking about how to solve mathematical problems; “Emotions” - imagining feeling a certain emotion; “Concentration”- focusing on raising the bar; “Future thinking” - imagining what/where they would like to be in the future; “Memories” - childhood memories, re-living any vivid memories; “Thoughts of movements” such as their journey to university or work, or doing exercise; “General relaxation” - adopting a comfortable posture, relaxing their muscles, controlling their breathing or other meditation techniques; and “Other” where participants were asked to describe what they did. The final option was ‘No strategy’.

4.2.5 Statistical analysis

For the first set of analyses, the original Theta (experimental) and Low beta (control) groups were collapsed; namely, participants were categorised as Responders or Non-responders irrespective of whether their target band was theta or low beta i.e. this is the full sample. The second set of analyses were conducted separately for both the Theta and Low beta groups to investigate the effect of each factor on upregulation of the different frequency bands.

Independent groups t-tests (or the parametric equivalent where the assumption of normality was violated) were performed on all the individual questionnaire and task measures to establish whether there were any significant differences between Responders and Non-responders. In addition, Kendall’s Tau correlational analyses were conducted to determine any significant relationships between the various factors and EEG-NF responder ability, as represented by a z-score transformation of relative percentage increase from baseline to the average of the six blocks in both the Theta and the Low beta groups. All tests were completed two-tailed due to the exploratory nature of the hypotheses, except for perceived difficulty of the task where there is more compelling evidence to support one-tailed testing. The Benjamini and Hochberg False Discovery Rate multiple comparisons correction was applied to the data. Bayes Factors were calculated to assess the strength of the evidence for both between-groups and correlational analyses. All statistically significant analyses were set at $p < 0.05$, means (M) and standard deviations (SD) are reported using tables and violin plots, error bars represent the standard error of the mean (SEM) in line graphs, and n represents the number of participants.

The frequency of use for each EEG-NF strategy was counted for both the full sample and for the Theta and Low beta group individually. The proportion of responders that used each strategy was calculated to represent the effectiveness of each strategy, and this was presented as a percentage. For instances when participants selected the "Other" category, scores were then allocated to the relevant strategy according to participants' description, if this had not already been selected. Two more strategies were also created from participants' descriptions: "Verbal recall" and "Auditory".

4.3 Results

All the results from the full sample combined can be found in Table 7, for the Theta group in Table 8 and the Low beta group in Table 9. The tables contain the observed p-values prior to the application of the Benjamini and Hochberg False Discovery Rate multiple comparisons correction, with an asterix indicating those that survived correction. All adjusted p-values following correction are including in the text. Any significant findings regarding the relationship between task difficulty and respondability remain, given this is the only factor that is based on a one-tailed hypothesis and is therefore not subject to multiple comparisons correction.

4.3.1 Current motivation

Responders' and Non-responders' scores did not significantly differ for the measures of challenge, interest, probability of success, or anxiety, and correlations also revealed no significant relationships. Bayes Factors indicated between anecdotal and substantial evidence for the null hypotheses for these variables.

There was a significant difference between Theta Responders and Non-responders on the interest subscale, with Non-responders indicating more interest in the task than Responders (t(24.6) = -2.32, p = .029) – see Figure 13A. The Bayes Factor indicated anecdotal evidence for the alternative hypothesis in relation to this group difference. This result suggests that more motivation inspired by an interest in the EEG-NF task negatively affects an individual's ability to self-regulate their brain state in the desired way. However, following multiple comparisons corrections, this result is no longer significant (p(adjusted) = .218).

Low beta Responders scored significantly higher than Non-responders on the probability of success subscale (t(25) = 2.34, p = 0.028) – see Figure 13B, with the Bayes Factor indicating anecdotal evidence for the alternative hypothesis regarding this group difference. This would suggest that participants in the Low beta group who have a mindset of self-efficacy in relation to the task, as declared before the task, do indeed tend to perform better. However, following multiple comparisons corrections, this result is no longer significant (p(adjusted) = .420).

All other results not mentioned were non-significant, with Bayes Factors indicating anecdotal evidence for the null hypotheses.

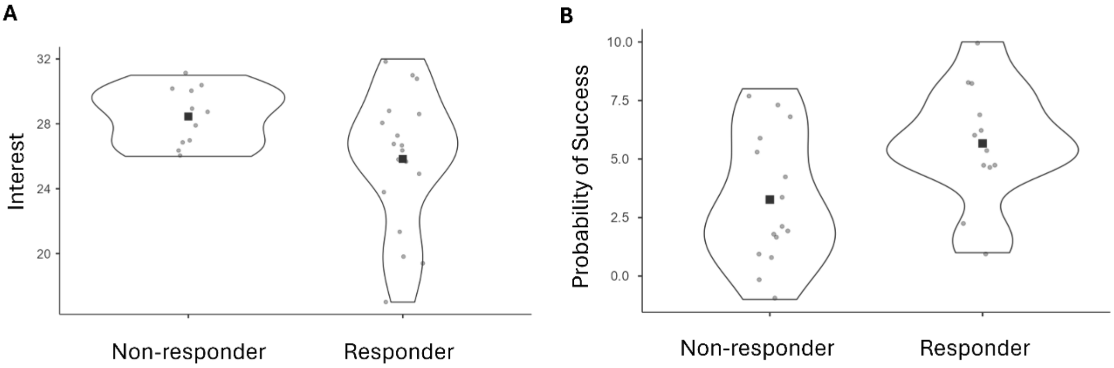


Figure 13. Violin plot showing scores for A) Theta Responders (n = 18) and Non-responders (n = 11) in the Interest subscale of the QCM and B) Low beta Responders (n = 12) and Non-responders (n = 15) in the Probability of Success subscale of the QCM. The black square depicts the mean and the grey dots represent the distribution of data points.

4.3.2 Current mood

There were no significant differences between all Responders and Non-responders for both positive and negative mood, or significant correlations. Bayes Factors indicated between anecdotal and substantial evidence for the null hypotheses.

When examining the Theta and Low beta sub-groups and correlations, the only significant results were for the Theta group. There was a significant difference between the Responders and Non-responders for positive mood ($t(27) = -2.10$, $p = .045$) and a significant correlation ($\tau_b = -.287$, $p = .039$) – see Figure 14A & 14B. The Bayes Factor indicates anecdotal evidence for the alternative hypothesis in terms of both the group difference and a correlation between positive mood and participants' ability to self-regulate theta. The direction of this correlation suggests that responder ability is negatively affected by an individual's positive mood immediately before undergoing EEG-NF training. However, following multiple comparisons corrections, these findings were no longer significant: group difference (p(adjusted) = .225); and correlation (p(adjusted) = .293).

All other results relating to mood were non-significant, with Bayes Factors indicating anecdotal to substantial evidence for the null hypothesis, suggesting that negative mood did not determine responder ability.

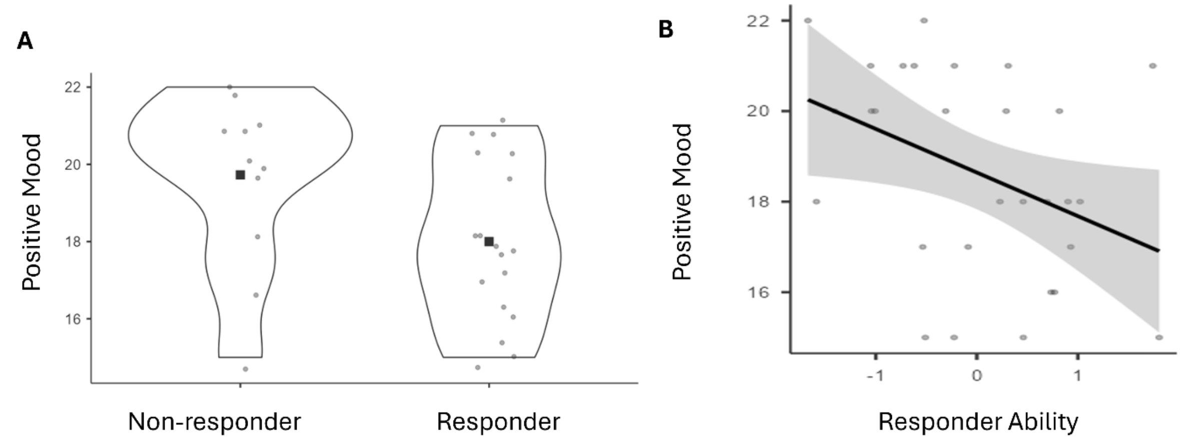


Figure 14. A) Violin plot showing the scores for Theta Responders (n = 18) and Non-responders (n = 11) in the Positive Mood subscale of the PANAS. The black square depicts the mean and the grey dots represent the distribution of data points. B) Line graph showing a negative correlation between Positive Mood and Responder Ability (z-scores). Shaded areas represent the standard error.

4.3.3 Flow state

Responders and Non-responders did not differ significantly on scores representing their flow state, and there was no significant correlation with responder ability. This was also the case for both the Theta and Low beta sub-groups. Bayes Factors indicate between anecdotal and substantial evidence for the null hypothesis for the subscale of flow. This suggests that being in a flow state is not associated with better performance on the EEG-NF task.

4.3.4 Locus of control

There were no significant differences between Responders and Non-responders in perceived control over the bar during the EEG-NF task, or significant correlations with responder ability. The same outcome applied to the Theta and Low beta sub-groups for this variable. Bayes Factors indicate between anecdotal and substantial evidence for the null hypothesis. These data suggest that an individual’s locus of control does not affect their ability to self-regulate their brain state.

4.3.5 Task difficulty

Non-responders reported a significantly higher difficulty level in relation to completing the EEG-NF task when compared to Responders (U = 275, p = .035). Bayes Factors indicate anecdotal evidence for the alternative hypothesis in relation to this group difference. There was also a significant negative correlation between participants’ perceived task difficulty and EEG-NF responder ability τ_b = - .272, p = .004 – see Figure 15. Bayes Factors indicate strong evidence for a negative correlation between task difficulty and responder ability.

Examination of the sub-groups revealed a significant, negative correlation between this variable and responder ability in both the Theta and Low beta sub-groups (Theta group: τ_b = -.270, p = .033; Low beta group: τ_b = -.302, p = .023). Only Low beta Non-responders reported significantly higher perceived task difficulty than Responders (t(25) = -1.74, p = .047). The results for task difficulty are displayed in Figure 15. Bayes Factors indicate anecdotal evidence for both the alternative hypothesis in the Low beta group, and the null hypothesis in the Theta group for this variable in terms of group differences. For the correlational analyses, Bayes Factors indicate anecdotal evidence for a negative correlation between task difficulty and participants’ ability to self-regulate theta; however, the evidence for this correlation is substantial in relation to self-regulating low beta. These findings suggest that Non-responders’ inability to effectively self-regulate the target brain activity is reflected in their increased level of perceived task difficulty, and this is more prominent in the Low-beta group.

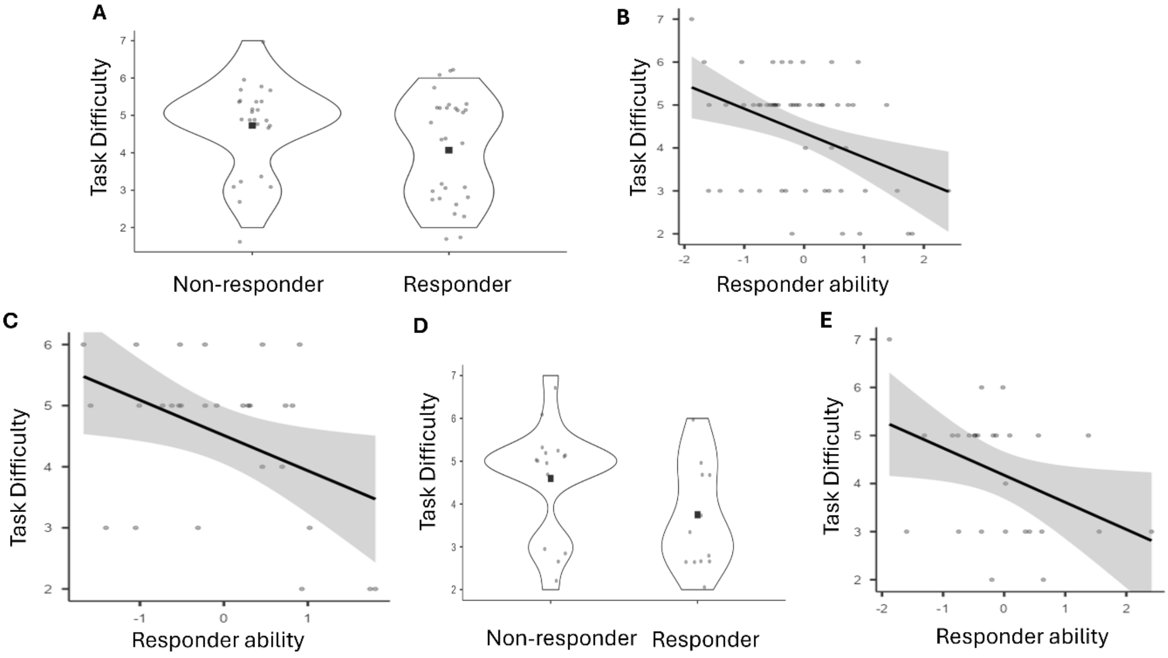


Figure 15. A) Violin plot showing the difference in perceived Task Difficulty between Responders (n = 29) and Non-responders (n = 26) and B) Line graph showing a negative correlation between Task Difficulty and Responder Ability (z-scores) for the full sample; and in the C) Theta group and E) Low beta group. D) Violin plot showing the difference in perceived Task Difficulty between Low beta Responders (n = 12) and Non-responders (n = 15). The black square depicts the mean and the grey dots represent the distribution of data points. Shaded areas represent the standard error.

4.3.6 Personality

There were no significant differences between Responders and Non-responders for any of the sub-factors of personality, and no significant correlations with responder ability. Bayes factors indicate anecdotal to substantial evidence supporting the null hypothesis for all sub-factors. These null results were mirrored in both the Theta and Low beta sub-groups, indicating that Responders and Non-responders were not distinguishable based on their personality traits, irrespective of the target frequency band during EEG-NF training. One exception to this was the subscale of agreeableness, whereby anecdotal evidence for a positive correlation was indicated by the Bayes Factors in both the full and theta-only samples.

4.3.7 *Sustained attention*

Responders did not differ significantly from Non-responders on scores of sustained attention, and there was no significant correlation with responder ability. This was also the case for the Theta and Low beta sub-groups. Bayes Factors indicated anecdotal to substantial evidence in support of the null hypothesis in all cases. These data suggest that individuals' trait-based attentional ability is not associated with responder ability during EEG-NF training.

4.3.8 *EEG resting baseline*

There was a highly significant difference between Theta Responders' and Non-responders' resting state theta/low beta power ratio ($t(27) = -4.68$, $p = <.001$), and a significant negative relationship between the Theta group's resting EEG baseline activity and their subsequent EEG-NF responder ability: $\tau\_b = -.399$, $p = .002$ – see Figure 16A & 16B. The Bayes Factors indicate decisive evidence for the alternative hypothesis in terms of a group difference and strong evidence for the correlation. Following corrections for multiple comparisons, these findings remained significant: group difference (p(adjusted) = .015); and correlation (p(adjusted) = .030).

Low beta responders' EEG resting baseline low beta/theta power ratio was lower than Non-responders; however, this difference did not reach significance. Bayes Factors indicate anecdotal evidence for the alternative hypothesis. However, there was a significant negative correlation between Low beta Responders' EEG resting baseline activity and their subsequent EEG-NF responder ability: $\tau\_b = -.362$, $p = .008$, with the Bayes Factor indicating substantial evidence for this correlation – see Figure 16C. However, following multiple comparisons corrections, these findings were no longer significant: group difference (p(adjusted) = .225); and correlation (p(adjusted) = .293).

These findings suggest that theta EEG-NF responder ability is linked with individuals' who have a low theta/low beta power ratio during resting state pre- theta

EEG-NF. However, it is acknowledged that this outcome could be influenced by regression to the mean.

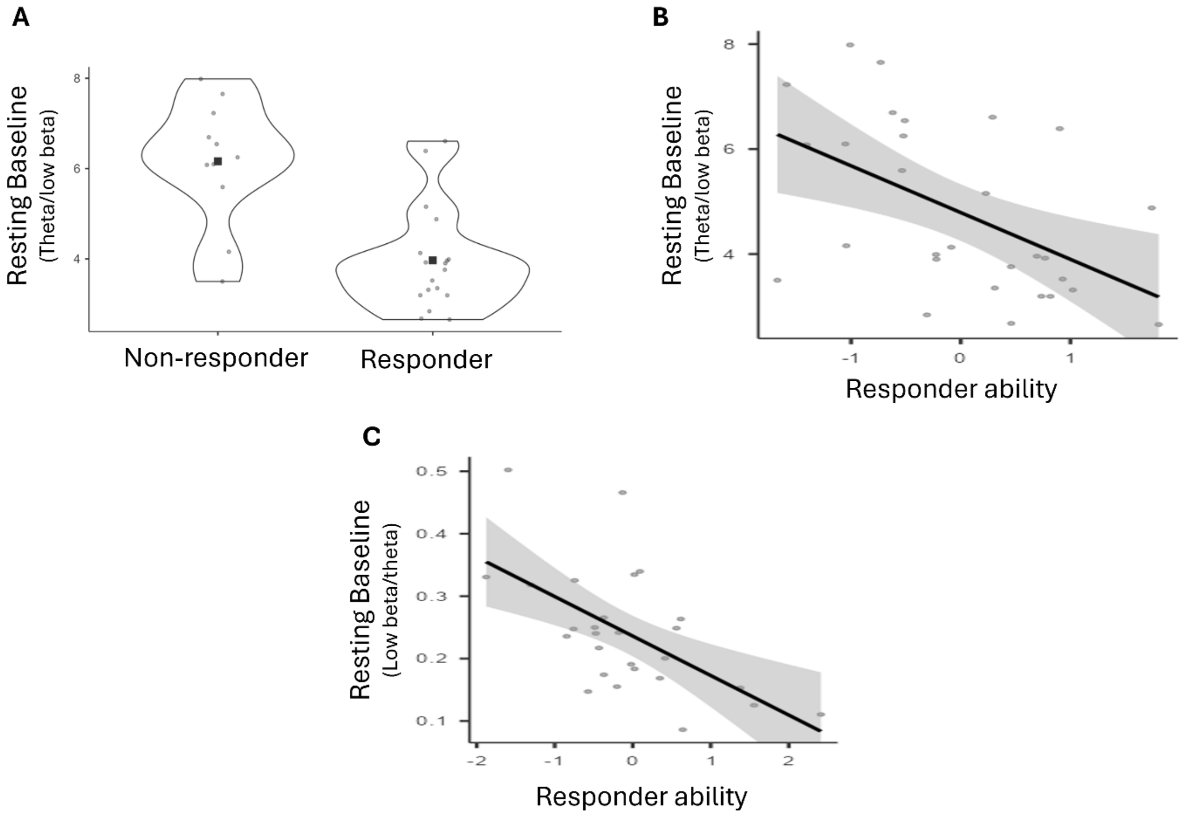


Figure 16. A) Violin plot showing the difference in resting baseline theta/low beta power between Theta Responders (n = 18) and Non-responders (n = 11). The black square depicts the mean and the grey dots represent the distribution of data points. Line graphs showing a negative correlation between B) Resting baseline theta/low beta power and responder ability (z-scores) in the Theta group and C) Resting baseline low beta/theta power and responder ability in the Low beta group. Shaded areas represent the standard error.

Table 7. *Full sample means, standard deviations and significance test values for all individual difference factors.*

Measure	**Responder**		**Non-responder**		**Between-groups**			**Correlation**		
	Mean	**SD**	**Mean**	**SD**	**t/ U**	**p**	**B**	**Tau**	**p**	**B**
Challenge	22.43	2.70	22.23	1.88	.33	.744	.282	-.001	.994	.174
Interest	26.23	3.81	27.46	2.90	313	.202	.391	-.075	.433	.241
Probability of success	4.20	2.96	3.58	2.64	.83	.413	.359	.059	.535	.213
Anxiety	15.83	5.25	16.46	4.39	-.48	.632	.298	-.113	.228	.366
Positive mood	18.73	2.08	19.58	1.88	305	.158	.862	-.119	.223	.397
Negative mood	9.77	3.00	9.96	3.22	-.23	.816	.277	-.060	.531	.214
Flow state	45.59	8.92	44.04	9.09	.64	.527	.322	.129	.169	.455
Locus of control	3.86	1.55	3.73	1.43	355	.710	.269	.140	.164	.536
Task difficulty	4.07	1.33	4.73	1.19	**275**	**.035**	**1.80***	**-.272**	**.004***	**23.4**
Extroversion	24.96	8.89	25.12	7.11	-.069	.946	.275	.046	.627	.199
Agreeableness	32.32	4.53	31.35	3.82	.85	.398	.370	.190	.050	1.320
Conscientiousness	24.36	5.55	23.96	5.81	.26	.799	.282	.033	.731	.188
Neuroticism	57.75	8.37	59.85	6.04	-1.05	.300	.432	-.119	.209	.390
Openness	25.54	5.06	24.69	5.90	.57	.575	.313	.062	.515	.220

Sustained attention	231.91	5.90	231.32	6.36	-.31	.758	.318	.098	.379	.300

Note. Significant (p < .05) factors in bold. All between-groups tests are two-tailed, except for task difficulty which is one-tailed (i.e. non-responders were hypothesised to generate higher scores). All correlations are non-directional, except for task difficulty which is uni-directional (i.e. task difficulty was hypothesised to correlate negatively with responder ability). Between-groups: t = student parametric test statistic; U = Mann Whitney non-parametric test statistic; B = Bayes Factor; Tau = Kendall’s non-parametric correlation coefficient. Abbreviations: SD = standard deviation. * = Significant findings retained following corrections for multiple corrections (if required).

Table 8. *Theta group means, standard deviations and significance test values for all individual difference factors*.

Measure	**Responder**		**Non-responder**		**Between-groups**			**Correlation**		
	Mean	**SD**	**Mean**	**SD**	**t/ U**	**p**	**B**	**Tau**	**p**	**B**
Challenge	22.61	2.83	22.64	1.57	-.031	.976	.356	.039	.776	.250
Interest	25.83	4.25	28.45	1.75	**-2.32**	**.029**	**1.379**	-.162	.233	.497
Probability of success	3.22	2.90	4.00	2.53	-.73	.469	.436	.003	.985	.239
Anxiety	15.56	5.87	16.27	4.41	-.35	.730	.373	-.206	.123	.782
Positive mood	18.00	2.11	19.73	2.20	**-2.10**	**.045**	**1.739**	**-.287**	**.039**	**2.356**
Negative mood	9.67	3.03	9.09	3.78	.45	.655	.385	.008	.955	.240
Flow state	43.65	8.94	41.45	6.38	.70	.488	.432	.162	.234	.490
Locus of control	3.53	1.70	3.73	1.01	-.39	.703	.376	.117	.416	.351
Task difficulty	4.29	1.40	4.91	1.04	69.5	.120	1.30	**-.270**	**.033** *	**2.47**
Extroversion	22.83	9.71	25.36	5.77	.78	.442	.447	-.025	.851	.243
Agreeableness	32.06	4.78	31.45	3.24	.37	.716	.375	.230	.091	1.044
Conscientiousness	24.56	5.87	25.00	4.80	-.21	.834	.362	-.005	.970	.239
Neuroticism	58.28	7.52	59.55	6.38	-.47	.645	.386	-.087	.511	.296
Openness	25.28	5.49	24.91	5.68	0.17	.864	.360	.063	.637	.268

Sustained attention	231.23	6.00	233.14	4.78	-.73	.478	.492	.027	.870	.289
EEG resting baseline	3.97	1.14	6.16	1.36	**-4.68**	**< .001***	**269**	**-.399**	**.002***	**20.1**

Note. Significant (p < .05) factors in bold. All between-groups tests are two-tailed, except for task difficulty which is one-tailed (i.e. non-responders were hypothesised to generate higher scores). All correlations are non-directional, except for task difficulty which is uni-directional (i.e. task difficulty was hypothesised to correlate negatively with responder ability). Between-groups: t = student parametric test statistic; U = Mann Whitney non-parametric test statistic; B = Bayes Factor; Tau = Kendall’s non-parametric correlation coefficient. Abbreviations: SD = standard deviation. * = Significant findings retained following corrections for multiple corrections (if required).

Table 9. *Low beta group means, standard deviations and significance test values for all individual difference factors.*

Measure	**Responder**		**Non-responder**		**Between-groups**			**Correlation**		
	Mean	**SD**	**Mean**	**SD**	**t/ U**	**p**	**B**	**Tau**	**p**	**B**
Challenge	22.17	2.59	21.93	2.09	.26	.797	.369	.030	.832	.253
Interest	26.83	3.13	26.73	3.39	89.5	1.00	.382	.018	.899	.250
Probability of success	5.67	2.50	3.27	2.76	**2.34**	**.028**	**2.445**	.170	.230	.521
Anxiety	16.25	4.37	16.60	4.53	-.20	.841	.365	.021	.883	.250
Positive mood	19.83	1.53	19.47	1.68	.59	.564	.408	.169	.247	.514
Negative mood	9.92	3.09	10.60	2.69	73.0	.414	.459	-.143	.319	.418
Flow state	48.33	8.51	45.93	10.46	.64	.527	.419	.093	.503	.309
Locus of control	4.33	1.23	3.73	1.71	1.021	.317	.528	.188	.203	.286
Task difficulty	3.75	1.22	4.60	1.30	**-1.74**	**.047** *	**1.981**	**-.302**	**.023** *	**5.08**
Extroversion	28.80	5.79	24.93	8.15	1.29	.209	.681	.142	.325	.494
Agreeableness	32.80	4.24	31.27	4.30	.88	.389	.494	.165	.259	.486
Conscientiousness	24.00	5.21	23.20	6.51	.33	.748	.388	.071	.623	.289
Neuroticism	56.80	10.10	60.07	6.01	-1.017	.320	.543	-.155	.282	.451
Openness	26.00	4.42	24.53	6.26	0.64	.528	.433	.078	.590	.296
Sustained attention	232.89	5.97	230.25	7.10	0.90	.379	.524	.142	.378	.409
EEG resting baseline	.200	.08	.247	.10	55	.093	1.390	**-.362**	**.008**	**7.09**

Note. Significant ($p < .05$) factors in bold. All between-groups tests are two-tailed, except for task difficulty which is one-tailed (i.e. non-responders were hypothesised to generate higher scores). All correlations are non-directional, except for task difficulty which is uni-directional (i.e. task difficulty was hypothesised to correlate negatively with responder ability). Between-groups: t = student parametric test statistic; U = Mann Whitney non-parametric test statistic; B = Bayes Factor; Tau = Kendall's rank non-parametric correlation coefficient. Abbreviations: SD

= standard deviation. * = Significant findings retained, following corrections for multiple corrections (if required).

Following correction for multiple comparisons, EEG resting baseline for the Theta group is the only factor that remains significant. This outcome suggests that there is a significant difference in resting theta/low beta power ratio between theta Responders and theta Non-responders. The significant negative correlation between resting theta/low beta power ratio and percentage change in theta/low beta power ratio following theta EEG-NF training suggests the lower an individual's resting theta activity is to begin with, the more successful they will be in increasing their theta activity during EEG-NF training. However, this finding is interpreted with caution given the potential issue with regression to the mean, as discussed in Section 4.4.5.

4.3.9 Strategies

All participants used at least one strategy during the EEG-NF task i.e. no participants just let the EEG-NF training guide them. The average number of strategies used by participants was 3.57. The order of strategies according to frequency of use, ranking from high to low was: 'memories' > 'mental calculations', 'concentration' > 'emotions' = 'future thinking = 'movement' > 'relaxation' > 'semantic recall' > auditory. Strategies ordered according to the proportion of responders that used each strategy, from high to low was: 'mental operations' > 'memories' > 'imagination' > 'concentration' > 'movement' > 'relaxation' = 'semantic recall' > 'auditory' – see Figure 17. The most frequent and effective strategy used by the Theta group responders was mental operations and for the Low beta responders group it was memories – see Figure 18.

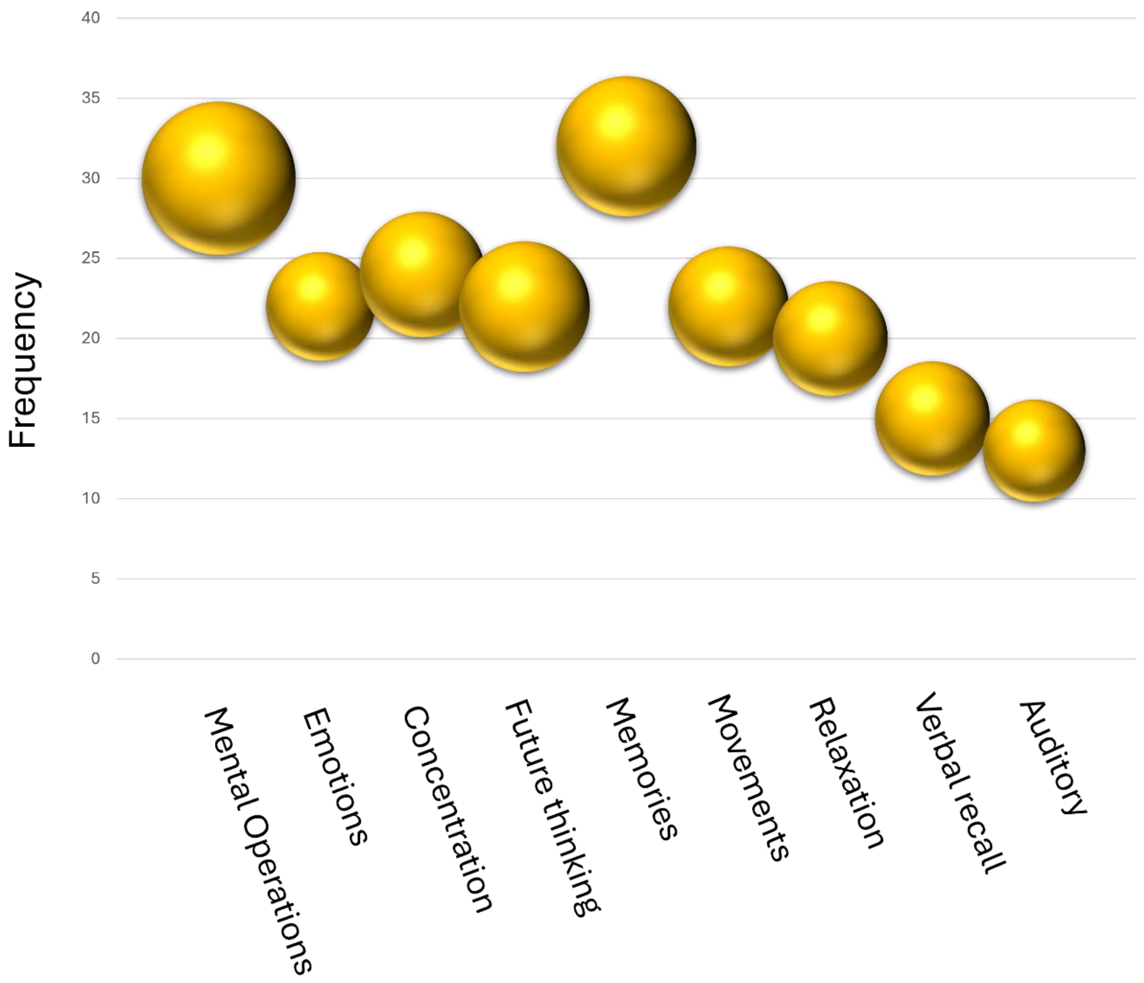


Figure 17. Bubble chart showing the frequency of use for each EEG-NF strategy for the full sample (n=56). Bubble size represents the percentage of Responders that used each strategy.

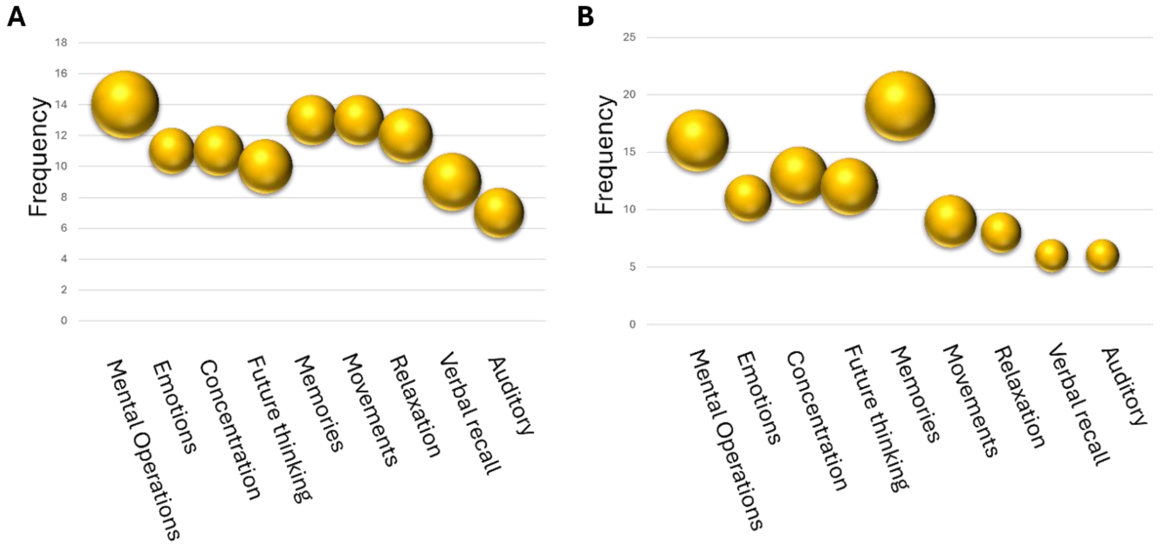


Figure 18. Bubble charts showing the frequency of use for each EEG-NF strategy for A) the Theta group (n=29) and B) the Low beta group (n=27). Bubble size represents the percentage of responders that used each strategy.

4.4 Discussion

The aim of this study was to investigate individual differences between EEG-NF responders and non-responders. To achieve this, responders and non-responders were compared across several factors, and correlations were investigated between each measure and EEG-NF responder ability. Considering that the full sample includes participants effectively trying to upregulate different frequency bands, analyses were conducted separately for the Theta group and the Low beta group, to determine whether individual factors differentially effected responder ability depending on the target frequency band.

Given the exploratory nature of this chapter and the number of factors tested, multiple comparisons corrections were conducted. It is therefore acknowledged that the following discussion points are speculatory in nature given most findings no longer remained significant following application of the Benjamini and Hochberg False Discovery Rate multiple comparisons correction.

4.4.1 Task Difficulty

Firstly, for the full sample i.e. collapsing participants into Responders and Non-responders irrespective of the target frequency band they were trying to upregulate, Non-responders reported a significantly higher level of difficulty in relation to completing the EEG-NF task than Responders. This sheds light on the experience of Non-responders, suggesting that they understood the goal of the EEG-NF training but were acutely aware that they were not performing well. Furthermore, there was a significant negative correlation between participants' perceived task difficulty and EEG-NF responder ability. Both of these findings support the hypothesis that Non-responders would score higher than Responders on task difficulty. Perceived task difficulty was also higher in the non-responder group for both theta and low beta, although this difference was more pronounced in the low beta group, providing an explanation in part for the high number of non-responders in the EEG experiment (Chapter 3) and suggesting that low beta could generally be a more difficult brain state to self-regulate. This is supported by the relatively lower number of low beta responders in Rozengurt et al. (2017)'s EEG-NF study whereby low beta was also used as an active control. The issue with perceived task difficulty experienced by participants supports the notion that conscious monitoring is actively present during the EEG-NF training task and therefore any difficulties experienced by individuals might be disrupting the operant conditioning process of reinforcing the desired brain state. Research has shown that task difficulty is associated with frustration (Csíkszentmihályi, 1990) and that aligning the EEG-NF parameters (e.g. the feedback threshold) according to participants' reported level of difficulty can enhance responder ability (Bauer et al., 2016). However, these results do not reveal why non-responders found the task difficult in the first place.

4.4.2 Current motivation and mood

Group comparisons of Theta responders versus Theta non-responders revealed that non-responders scored higher on the current motivation subscale of 'Interest', and reported more positive current mood, prior to EEG-NF training. Correlational analyses revealed a negative correlation between positive mood and increased theta upregulation following EEG-NF training.

Whilst these findings support the two-tailed hypothesis that Responders and Non-responders would differ on these measures of motivation and mood, the direction of the results contradicts studies that found a positive link between motivation and mood and EEG-NF success (Leeb et al., 2007; Nijboer et al., 2008). Furthermore, theories on motivational learning such as the Cognitive-Affective-Motivation Model of Learning (McGrew et al., 2004) leans towards a positive interaction between mood, motivation, and learning (Hilgard, 1980; McGrew, 2021) implying that these psychological aspects facilitate the learning process. Specifically, interest in a topic or task has been shown to have a beneficial effect on learning outcomes (Herpratiwi & Tohir, 2022; Krapp, Hidi, & Renninger, 2014). However, it is noted that these theories are generally applied to the field of education, where positive motivation and mood is characterised by more conscious goal-orientated thought and positive mood, and individuals are considered 'agentic contributors' i.e. more actively involved, according to Bandura's (1986) social cognitive theory on motivation. It could be argued that these factors may have differential effects on EEG-NF training whereby the goal is to modulate one's brain state. Specifically, the influence of these effects on EEG-NF may depend on the frequency band being trained. In the studies by Leeb et al. (2007) and Nijboer et al. (2008), a positive effect of interest and mood, respectively, was found on upregulation of the SMR band. However, in another study by Kikkert (2015) motivation was found to be negatively correlated with theta amplitude.

Given theta's association with relaxation (Rozengurt et al., 2017) the conscious cognitive aspects of increased motivation and mood might serve to contrastingly disrupt the process of achieving a theta brain state of 'effortless attention' (Bruya, 2010). The findings in this Chapter support this notion as interest and positive mood were found to have a negative effect on EEG-NF performance in the Theta, and not the Low beta sub-group. Low beta responders reported that they were more motivated by 'probability of a successful outcome' from the task, than non-responders, as measured by the Questionnaire for Current Mood. This supports Nijboer et al. (2008) who revealed that participants' ability to regulate SMR by visualising movement was positively affected by higher scores obtained on 'mastery confidence' - a subscale equivalent to the one used in the current study. The Questionnaire for Current Mood measures factors that are associated with achievement motivation, which according to the APA definition is characterised by a desire to perform well and be successful in a task. Furthermore, individuals motivated by achievement persevere more when faced with difficult challenges and are more likely to perform better. Accordingly, it could be that individuals who possess more confidence in their ability to succeed were more likely to overcome the challenge of upregulating low beta, and to subsequently respond better to training. In contrast, the performance of others tackling the same task was hindered by their perceived difficulty in completing the EEG-NF task.

It follows that to up-regulate low beta requires a more conscious effort to be invested in the EEG-NF training task by the participant. This aligns with research which demonstrates that beta oscillations are associated with active thinking and concentration. For example, in Rozengurt's study participants in the low beta control group were specifically instructed to use the strategy of concentration to raise the vertical bar and increase low beta activity. Furthermore, the study by Kikkert (2015) found that low beta enhancement within an EEG-NF session was positively correlated with participants adopting an analytical cognitive style. Taken together the evidence suggests that successful upregulation of low beta might involve conscious alertness, goal maintenance, and self-efficacy. This further supports the notion that certain individual approaches to an EEG-NF training task could be more or less conducive to EEG-NF self-regulation success depending on the target frequency itself.

4.4.3 Personality traits

Whilst these measurements characterise psychological aspects relating to individuals' state during the EEG-NF training task, some studies have investigated trait-based factors and found personality traits such as conscientiousness (Tipple, 2024) and self-reliance (Jeunet et al., 2015) were associated with frontal-midline theta and SMR responders, respectively. However, these findings are limited, with the current study's analyses revealing no links between any of the personality traits measured using the Big 5 personality questionnaire and individuals' ability to self-regulate brain activity, thereby contradicting the hypothesis. This could suggest that engagement with the EEG-NF task is more of a dynamic process, rather than reliant on fixed traits.

4.4.4 Attentional ability

A fundamental prerequisite of the EEG-NF training process is that the 'learner' must be fully engaged with the task itself for the key mechanisms of the operant conditioning process to take effect by way of reinforcing the desired behaviour. Subsequently, inherent attentional ability is a factor that has been studied in relation to EEG-NF responders, to determine how variation across individuals might influence EEG-NF self-regulation success. This research has found that high attentional ability is associated with individuals responding positively to EEG-NF training (Daum et al., 1993, Hammer et al., 2012). In contrast, this chapter's findings revealed no differences in sustained attention scores between responders and non-responders, or correlations with responder ability.

One important observation in relation to these mixed findings is the use of different tests of attention. Whilst the SART has been used for over 20 years as a measure of sustained attention, there are some studies that bring into question whether it could be partially measuring other psychological mechanisms, such as response inhibition and motor control. For example, it has been shown that a higher proportion of 'go' trials increases participants' motor response, reducing their ability to withhold their response to 'no go' trials (Wilson et al., 2016). Furthermore, directive instructions for participants to either prioritise speed or accuracy during the task can also influence performance (Mensen et al., 2021). These findings suggest that the SART might be also a measure of response strategy as opposed to sustained attention. It is also noted that the tasks used in Daum et al. (1993)'s study, namely digit span and block-tapping, are widely used as tests of working memory. It could be argued that given no motor response is involved in most EEG-NF feedback tasks, such vigilance tests of sustained attention may not be the most appropriate test of concentration required in the context of EEG-NF training. Indeed, working memory might be more directly involved in strategy use and self-monitoring during EEG-NF training.

4.4.5 EEG resting baseline

The influence of individual neurophysiological factors has also been investigated in the context of EEG-NF responders. For example, higher baseline levels of the target frequency have been found to predict subsequent EEG-NF self-regulation success (Chikhi, 2023; Nan et al., 2015; Reichert et al., 2015; Wan et al., 2014), although this finding is not consistent (Weber et al., 2020). The findings in this chapter show a significant difference in target band pre-EEG-NF training resting state between responders and non-responders. However, they reveal instead that lower baseline levels of both theta and low beta activity are significantly correlated with subsequent upregulation of theta and low beta within the EEG-NF training session, respectively. These findings seem feasible given the lower the baseline measurement, the more headroom there is to increase activity levels. In contrast, there might be a ceiling effect when individuals' resting baseline activity is high; although this would not explain why other studies found the opposite relationship. These opposing findings could be due to the variability in study design and EEG-NF protocol adopted. For example, the previous studies mentioned above found high baseline levels predicted responder success after many EEG-NF sessions, whereas the current study uses a single session. Furthermore, different target bands i.e. alpha and SMR, in both healthy and clinical populations are measured and use different methods to calculate resting state activity. It is also possible that intra-individual differences exist regarding resting state levels, rendering this factor possibly transient and therefore a less stable predictor of subsequent responder ability in different contexts. More research is required to determine how an individual's resting state can reliably inform self-regulation success during EEG-NF training. More nuanced understanding is required regarding the type of engagement that is deployed for successful self-regulation during EEG-NF.

Finally, as mentioned in Chapter 1, Section 1.8, regression to the mean can be an issue when comparing performance at more than one timepoint. In this case, the highly significant negative correlation between participants' EEG-resting baseline measurement and the percentage change in target band activity during EEG-NF training shows that an extremely low resting baseline target band activity is followed by significantly high target band activity. Therefore, this finding could be attributed to regression to the mean; to this statistical phenomenon of chance, and not to the effect of EEG-NF training itself. The inclusion of a sham control could allow a comparison to ascertain whether changes in target band activity are due to the EEG-NF training or due to chance.

A recent study has investigated the effect of the biological trait, Sensory Processing Sensitivity, on the efficacy of fNRIS-NF training (Acevedo et al., 2023). Superior memory benefits were associated with participants who scored higher on the Highly Sensitive Person Scale. Although no direct evidence is provided by the authors directly linking this positive outcome with fNIRS-NF success, the effects of the intervention are nonetheless inferred. Also, a different neurofeedback technique to EEG-NF is used combined with cognitive training, however the fundamental feedback principles underlying the techniques are comparable. This builds on the idea that successful reinforcement of the target brain state, and subsequently the desired behaviour, could be dependent on the individual's ability to effectively process the stimulus rewards that are key for guiding their neurophysiological response. It seems, given the dynamic nature of EEG-NF training, whether it's driven by trait or state factors, successful self-regulation might be strongly influenced by the nuanced interaction between the individual, the EEG-NF task and the environment.

4.4.6 Strategies

The descriptive findings show that, overall, mental arithmetic was the strategy used by the most EEG-NF responders. Theta responders also benefitted most from using mental arithmetic which has been adopted as a recommended strategy in EEG-NF studies aimed at increasing theta activity (Enriquez-Geppert et al, 2014b; Eschmann et al., 2020), followed by thoughts of movement and memories. Low beta responders mostly used memories as a strategy, followed by mental arithmetic and concentration. These findings do not support the recommended strategies in Rozengurt et al. (2017)'s study i.e. relaxation for theta and concentration for low beta. Indeed, considerable overlap in strategy use is highlighted amongst these findings and with previous research which links 'breathing exercises' and 'relaxation' with SMR upregulation (Autenrieth et al., 2020), and 'cognitive' strategies such as mental calculations with alpha upregulation (Chikhi, 2023). Whilst these data provide some insight into what strategies were used by participants and what worked best for the different protocols, strong conclusions cannot be made regarding the contribution of individual strategies to self-regulation success in this study, given most participants trialled a few strategies. Individual strategies would need to be systematically tested to determine this.

Furthermore, some research supports the idea that avoiding the use of strategies altogether can improve performance on the EEG-NF task (Kober et al, 2013; Chikhi, 2023) by instructing participants explicitly not to force mastery and to instead adopt a state of effortless relaxation (Witte et al., 2013). This notion relates to the debate in the literature as to whether EEG-NF training is optimal when engagement with the EEG-NF training is conscious and deliberate (e.g. utilising strategies), or unconscious and passive (using no strategy) (Chikhi, 2023; Kober et al, 2013; Sitaram et al., 2016). The former would draw upon more top-down executive functions so individuals can monitor the effectiveness of their performance employing cognitive processes such as goal maintenance and decision-making. In contrast, the latter would facilitate implicit learning in the operant conditional process, whereby individuals let the feedback guide them. This speaks to a more effortless, bottom-up process whereby learning is not a conscious goal for the learner and individuals simply allow the receipt of reward via the senses to reinforce the desired behaviour - a 'letting go'. Whilst this could not be explored given no participants used no strategy at all, this could be investigated further to determine its effect on theta responder ability, especially in relation to theta given the evidence seems to show that this approach might be more effective for self-regulating target frequencies at the lower end of the spectrum that are characteristic of a more relaxed state, without the cognitive demands of employing various strategies (Kober et al, 2013; Rozengurt et al., 2017).

4.4.7 Limitations and future directions

Some improvements could be made to the study by adapting the measurement of some factors. A key issue regarding the use of different parameters (e.g. band pass filter frequency cut-off frequencies, artifact rejection/control) for online and offline processing of the EEG-NF data is that the offline EEG-NF data informs the measure of ‘respondability’ i.e. the percentage increase in target band power ratio from participants’ resting baseline to the average of the six active EEG-NF blocks. If the data is treated differently, there could be a possible mismatch between participants’ offline EEG-NF measures and online, real-time performance. This could have implications in relation to the operational definition of an EEG-NF responder, which is the sub-population of focus in this Chapter. It would therefore be beneficial in this regard to ensure that the same, optimal EEG-NF processing parameters are applied to both online and offline EEG-NF data.

In terms of behavioural data, the questionnaire for current motivation and the positive and negative affect scale could be completed during more than one timepoint throughout the session to gauge how these psychosocial factors temporally correspond to EEG-NF training performance. However, in the current study, time was a consideration given the duration of the experiment - inclusive of the study-test memory paradigm, the EEG-NF training intervention, the cognitive task, and the various questionnaires – was already lengthy. Any additional cognitive load and subsequent effects of fatigue might have overall resulted in diminishing returns. The short-form flow state questionnaire, whilst adopted from other studies, could be replaced by a more comprehensive questionnaire, such as the flow state scale (Jackson et al., 2010) which probes these factors with more questions thereby increasing the richness and sensitivity of information acquired. Finally, task difficulty could be probed further by questioning why non-responders perceived higher levels of task difficulty than responders to gain more insight into what it is more specifically participants find difficult about EEG-NF training.

Two-tailed analyses were deemed an appropriate course of action in this study given previous findings were broad ranging across several factors, with mixed outcomes. The findings in this chapter provide interesting insights into some factors that might influence EEG-NF responder ability. However, some caution should be taken when interpreting these results given the high number of factors analysed with few significant results following statistical correction. Also to consider is that statistical power in the full sample was limited to detecting large and moderate effects in the between-participants and correlational analyses, respectively. At the target band sub-group level, these would have lower power to detect effects given the smaller sample sizes.

The variable findings in this research also further elucidates the complexity of EEG-NF training. An important consideration is the context of the interaction between multiple factors pertaining to the individual (i.e. ‘the learner’), the EEG-NF protocol itself (e.g. target frequency band), and the environment in which the EEG-NF training takes place, including the instructions and strategies provided to individuals. Future research could benefit from focusing on the interaction between these features, rather than examining them in isolation, to contribute to the current understanding of how individual differences effect EEG-NF responder ability within different contexts.

4.4.8 Conclusion

This chapter’s findings identify some relationships between individual factors and EEG-NF responder ability. In summary, the findings reveal that participants perceived the EEG-NF training task to be difficult, which supports the relatively high number of non-responders in Chapter 3’s experiment. However, separate analyses conducted on the theta and low beta control group highlighted different correlations between some of the individual factors and EEG-NF self-regulation success. Namely that motivational and affective influences such as interest in the task and positive mood, respectively, might negatively affect upregulation of theta activity during EEG-NF. In contrast, the low beta band was perceived as difficult to upregulate by non-responders, which was overcome by individuals with a higher level of achievement motivation driven by self-efficacy, leading to successful upregulation. Finally, low resting baseline levels were associated with EEG-NF self-regulation success of both the theta and low beta bands. These findings could be useful when considering who might respond most successfully to EEG-NF training to upregulate theta and low beta frequency bands.

Chapter 5: No effect of theta audio-visual entrainment on episodic memory performance.

5.1 Introduction

The clear issue with the high number of EEG-NF non-responders, as reviewed in Chapter 2 and demonstrated in Chapter 3 of this thesis, warrants investigation into an alternative intervention that could more reliably modulate individuals' theta activity. As addressed in previous chapters, the issue with EEG-NF non-responders is that the learner assumes an active role in the process; subsequently, the success of the intervention relies on their ability to self-regulate their target brain activity during the EEG-NF training session. What is clear is that a sizeable proportion of people are not able to do this. In this chapter a different method to modulate brain activity was investigated where the participants play a more passive role. As discussed in the General Introduction, AVE refers to the observation that oscillatory activity in the brain will naturally synchronise its dominant frequency with the rhythm of periodic external stimuli, such as flickering lights and auditory tones. The aim of the current chapter was to determine if AVE, using a commercially available device which can entrain theta, enhances performance on an episodic memory task. If successful, these findings could present an alternative option for more people to experience the memory benefits from such an intervention, as opposed to EEG-NF, via the use of an accessible, portable, and non-invasive device.

The General Introduction (Section 1.3) outlines the research demonstrating that AVE does induce a change in brain activity. Teplan et al. (2006) demonstrated that, not only did theta (4 Hz) AVE increase theta activity 25-fold during stimulation, but cross-hemisphere theta coherence (4-6 Hz) significantly increased in central and parieto-occipital areas post-AVE, both compared to pre-AVE levels. This cortical spread beyond sensory regions was also observed by Becher et al. (2015) during monaural and binaural beat stimulation, to deeper brain regions involved in episodic memory processes, such as the hippocampus. This evidence suggests that AVE stimulation not only creates a sensory entrainment response in occipital-temporal regions, but this resonates with areas associated with memory. Studies including behavioural measures of episodic memory performance following AVE support this assertion, whereby audio and visual flicker, applied during encoding, has been shown to improve recollection of contextual details (Koster et al., 2019; Wang et al., 2018). Moreover, Wang et al. (2018; 2024) provide evidence of a link between the phase and timing of rhythmic audio-visual stimulation in the theta frequency and synaptic plasticity (i.e. long term-potentiation), suggesting potential longevity of theta AVE effects on the consolidation of episodic memories.

It is noted that key studies measuring the effect of AVE on episodic memory mainly focus on performance immediately following entrainment. A review by Huang & Charyton (2008) reveals some evidence of long-term effects of AVE on a range of psychological behaviours; however, during many of these experiments, participants engaged in several AVE sessions with behavioural measurements recorded immediately following AVE. Only one study (Patrick, 1996) revealed behavioural improvements in processing speed and attention beyond cessation of AVE in a sample of children with attention-deficit hyperactivity-disorder. This was due to evidence of participants modulating their own activity once the intervention had been slowly withdrawn. This, together with theta's role in synaptic plasticity during entrainment (Wang et al., 2018, 2024) and the effect of theta EEG-NF on free recall 24 hours later (Rozengurt et al., 2017), provides a rationale for testing the effect of theta AVE on episodic memory performance the next day following a single session of theta entrainment.

Two studies which are of key relevance to this chapter were conducted by Roberts et al. (2018) and are similar in design to Rozengurt's study (2017). In the Roberts et al. (2018) studies healthy young participants in the experimental group received 36 minutes of theta (5.5 Hz) and this group were compared to those who received white noise (study 1) or low beta (14 Hz, study 2) AVE using a commercially available device (DAVID PAL 36, MindAlive Inc., Edmonton, Canada MindAlive Inc.). This intervention happened in-between the study and test phase. In both studies it was found that the theta entrainment enhanced source memory performance i.e. recollecting the encoding task they did with the word, but it had no effect on item memory i.e. old/new discrimination. In the second study EEG data were also collected which revealed band-specific enhancement of theta using these devices. Thus, this paper provides evidence that auditory and visual flicker, synchronised at the theta frequency and presented to individuals via headphones and glasses, before retrieval of new information previously learnt, can enhance episodic memory and specifically source memory. However, it is unclear as to whether the effects of AVE on memory are persistent.

The aims of the current study were two-fold: (i) to replicate Roberts et al. (2018)'s finding by delivering 30 minutes of either theta (5.5 Hz) or low beta (14 Hz) AVE between study and test using a commercially available AVE device (DAVID LIVE app and SPECTRUM Eyeset, MindAlive Inc., Edmonton, Canada), and; (ii) to extend Roberts and colleagues' findings, by conducting memory tests 24 hours later to determine whether the positive effects of AVE on memory performance persisted the next day. This study was completed using the same memory paradigm as was utilised for the EEG-NF study covered in Chapter 3, with the following hypotheses:

Hypothesis 1: Memory scores in the free recall, cued recall and source recollection tasks will be significantly higher in the theta (5.5 Hz) group than the low beta (14 Hz) group after the 30-minute AVE intervention between the study and the test phase.

Hypothesis 2: Memory scores in the free recall will be significantly higher in the theta (5.5 Hz) group than the low beta (14 Hz) group approximately 24 hours after the 30-minute AVE intervention between the study and the test phase.

Hypothesis 3: There will be no difference in recognition scores i.e. item memory between the Theta group and the Low Beta group.

Analyses into the difference between groups in source and recognition confidence is exploratory.

Overall, if the hypothesised effects are revealed, findings from this study could provide supporting evidence for the efficacy of AVE as a portable, user-friendly, non-invasive intervention for enhancing episodic memory performance in healthy individuals, with persistent effects.

5.2 Method

5.2.1 Participants

Sixty-six native English speakers aged 18-35 years (mean = 19.9; SD = 1.51) were recruited from the Cardiff University psychology undergraduate population. This sample size was calculated a-priori based on a one-tailed hypothesis and a between-participants t-test being conducted, α = 0.05, power = 0.8, and the effect size generated by Roberts et al. (2018) of Cohen's d = 0.628 (G*Power: Version 3.1.9.7) a more conservative estimate using the smaller effect size of the two experiments (i.e. white noise control condition). The effect size for their second experiment using low beta as a control condition was Cohen's d = 0.709. All participants took part in the main laboratory experiment. One participant in the low beta group did not complete the online free recall test 24 hours later.

To ensure safe participation in the AVE procedure, participants had normal, or corrected to normal vision and hearing, were not currently using any drugs (prescription or recreational) or under the influence of alcohol; and had no reported history of any psychiatric or neurological disorders; in particular, epilepsy, photic epilepsy or any seizure disorder. Participants were also excluded if they had ever experienced a head injury or a seizure of any kind, or thought they might have migraines/headaches triggered by the lights. Standard MRI exclusion criteria also applied, such as metal implants or devices within the body, pregnancy, and having had any surgical intervention within one month before scanning. All participants provided informed consent to participate in the study which was approved by the School of Psychology Ethics Committee for Cardiff University. Participants were compensated for their time with either course credits or monetary reward. Participants were randomly assigned to one of two groups; Theta Group (n=33; mean age = 19.9; SD = 1.69; 29 females), Control Group (n=33, mean age = 19.9, SD = 1.33; 24 females).

5.2.2 *Experimental Design*

See Figure 19 for a schematic overview of the experimental procedure. As can be seen from the figure participants completed a MEG resting-state scan before any procedures had been completed and after the AVE part of the study, along with a structural MRI scan. These data were not the focus for this thesis so will not be discussed further. The same memory paradigm and subsequent analyses were used as described in Chapter 3 of this thesis.

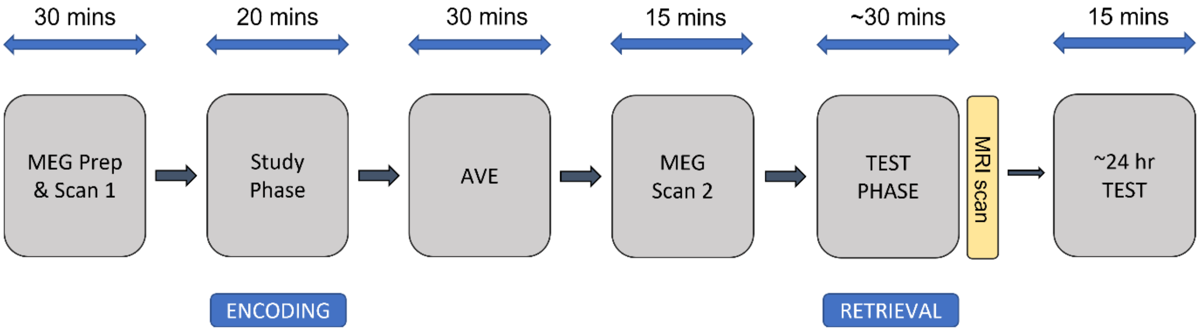


Figure 19. Schematic diagram showing an overview of the experimental procedure.

5.2.3 *AVE Procedure*

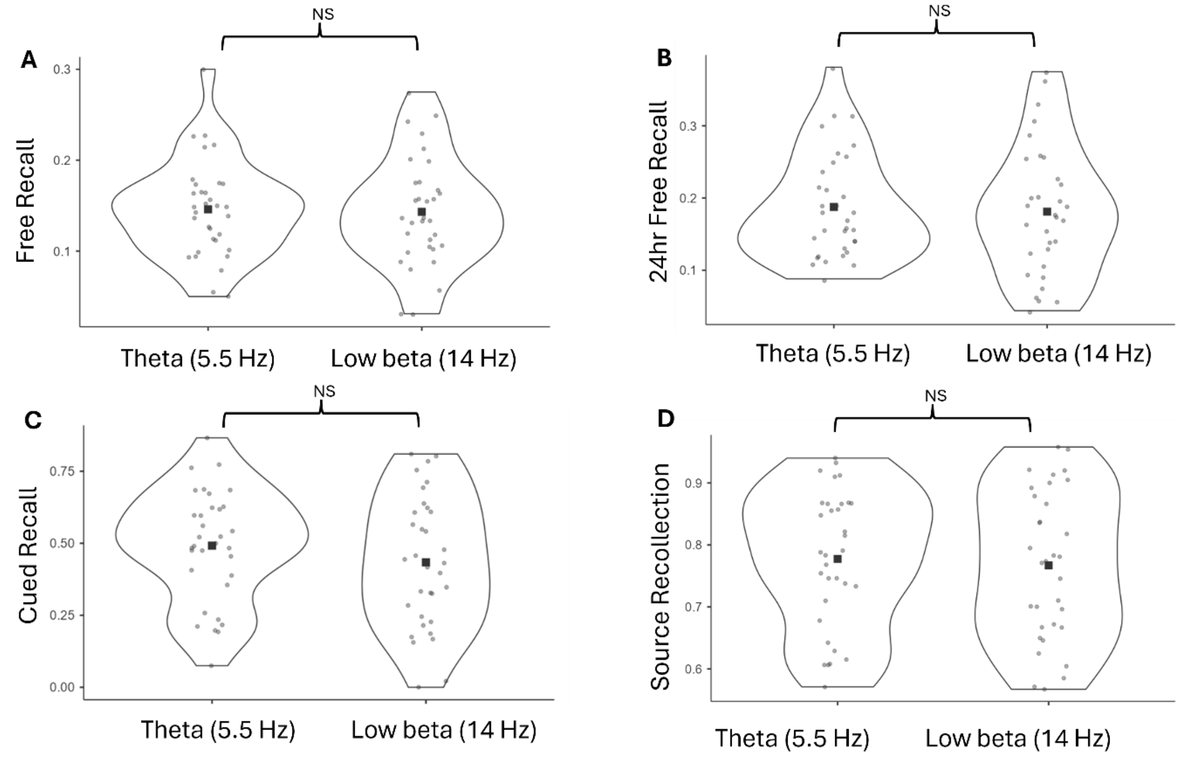
Brain entrainment involved participants engaging in 30 minutes of audio-visual stimulation between the study and test phases, where they remained seated in a dark room. The DAVID LIVE app (MindAlive Inc., Edmonton, Canada) was downloaded to a Windows 10 laptop and used to deliver rhythmic (isochronic) pulsing tones via high quality headphones (Sennheiser), phase-synchronised with sine-wave visual flicker delivered via LED lights inside darkened glasses (Spectrum USB Eyeset, MindAlive Inc., Edmonton, Canada), both of which were connected to the laptop. Participants received stimulation targeting frequencies of 5.5 Hz or 14 Hz, according to whether they had been allocated to the experimental Theta group or the control Low beta group, respectively. The brightness was set at 30% and the volume at 50% (within recommended safe sound levels), although these settings could be attenuated to suit participants' level of comfort. Throughout each session, the pitch was fixed at 170 Hz. Participants were instructed to relax and remain awake, and to attend to the lights and sounds, whilst keeping their eyes open if it was comfortable to do so.

Prior to conducting this study, a small pilot investigation was run to confirm that the AVE devices which were used for this study did entrain brain activity at the target frequency. Using EEG, it was found that when theta was entrained this resulted in an increase of this frequency (5.5 Hz) and the harmonics, and when low beta was entrained, there was an increase in low beta (14 Hz). The description and the results of this pilot can be found in Appendix 1.

5.3 Results

All statistical analyses were conducted in jamovi (Version 2.3.21, 2022). To test whether entrainment of theta activity enhanced episodic memory performance, memory scores were compared between the experimental group (5.5 Hz) and the control group (14 Hz). Scores obtained at both timepoints were compared: shortly after AVE, and approximately 24 hours later. Free recall scores reflected the number of individual nouns participants remembered from the 80 word pairs presented in the study phase, out of a total of 160 nouns. Corrected recognition scores were calculated by deducting each participant's false alarm rate from their hit rate. Cued recall scores represented the number of correctly recalled paired words, out of a total of 80. Source recollection was calculated as the number of items where the participants correctly recalled the gender of the speaker, as a proportion of recognition hits. Recognition confidence scores were based on the number of times participants responded with 'sure' with respect to correct recognition (old confidence) and correct rejection (new confidence). Source recollection confidence scores were based on the number of times participants responded with 'sure' relative to correct source recollection decisions. To determine whether the group differences were statistically significant, one-tailed independent groups t-tests (or the non-parametric equivalent Mann-Whitney tests in cases where the assumption of normality was violated) were conducted for the different memory measures: free recall, recognition, cued recall, and source recollection.

Participants in the theta group performed numerically higher than the control participants in all memory measures, except new recognition judgement confidence – see Figure 20. This difference was not statistically significant for any of the memory measures: free recall (t(64) = 0.20, p = 0.421), cued recall (t(64) = 1.12, p = 0.134), source recollection (U = 518, p = 0.369), corrected recognition (U = 476, p = 0.383), recognition confidence - old items (U = 462, p = 0.293), recognition confidence - new items (t(64) = -0.69, p = 0.491) or source recollection confidence (t(64) = 0.71, p = 0.482). Participants' performance in both the recognition (0.699) and source recollection (0.772) tests were above floor level i.e. > 0 for corrected recognition and > 0.5 for source recollection. Therefore, task difficulty is ruled out as a factor influencing the ability to reveal an effect. For the 24hr later follow-up test, free recall scores in the theta group were not significantly higher than the control group: (U = 507, p = 0.391). Bayes factors indicated anecdotal evidence in support of the null hypotheses for all measures – see Table 10.



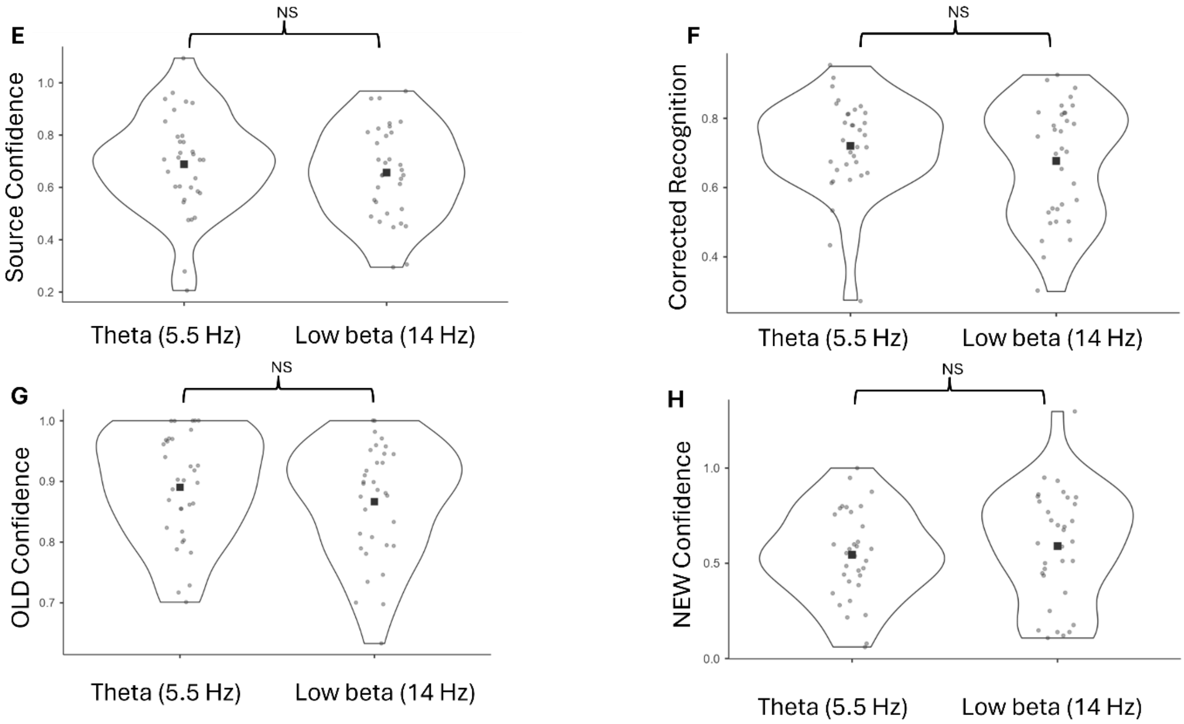


Figure 20. Violin plots showing scores for the Theta 5.5 Hz (n = 33) and Low beta 14 Hz (n = 33) groups: A) Free recall, B) 24hr free recall, C) Cued recall, D) Source recollection, E) Source recollection confidence, F) Corrected recognition, G) Old item recognition confidence and H) New item recognition confidence. The black square depicts the mean and the grey dots represent the distribution of data points.

Table 10. *Bayes factors for all memory measures comparing the Theta (5.5 Hz) group to the Low beta (14 Hz) groups.*

Memory measure	**Bayes Factor**
Immediate free recall	0.29
24 hours free recall	0.44
Cued recall	0.73
Source recollection	0.29
Source confidence	0.31
Corrected recognition	0.35
Old item confidence	0.50
New item confidence	0.31

5.4 Discussion

5.4.1 Can theta AVE enhance episodic memory?

In this experiment, participants' memory for word pairs that were studied before they received 30 minutes of AVE delivered at the theta frequency (5.5 Hz), relative to a low beta control (14 Hz) were compared. It was expected that enhanced memory performance in the theta group for source recollection would be observed, thereby replicating Roberts et al. (2018)'s findings. Based on some findings within the EEG-NF and AVE literature demonstrating the potential persistent effects of theta on memory, it was also expected that enhanced recollection would be observed when participants were tested approximately 24 hours later. However, contrary to my hypotheses, theta group scores were not significantly higher than the control group for free recall, source recollection, or cued recall. The same was the case for the free recall test conducted 24 hours later. No significant difference in corrected recognition scores were observed between the theta group and the control group. This was hypothesised, as the literature points to a selective relationship between increased theta and enhanced source memory (i.e. recollection) and not familiarity. Thus, the behavioural findings from this study do not support the use of AVE for enhancing episodic memory immediately following AVE or the next day.

5.4.2 Methodological variability

Whilst the study-test experimental design in the current study was similar to Roberts et al. (2018), there are also some differences to note which could explain why in the current study, a difference in memory scores was not found. A primary discrepancy is that Roberts et al. (2018)'s AVE device included 15 minutes of 'randomisation' in the pre-set theta program, where the lights and sounds were presented to participants at a range of different frequencies including theta, before they stabilized at 5.5 Hz for the remaining duration. Therefore, other frequencies within the randomisation could be responsible for the enhanced memory effect Roberts et al. (2018) found, which could explain why this result could not be replicated with a similar device which provided audio-visual stimulation consistently at 5.5 Hz or 14 Hz, for the theta and control group, respectively, for the full 30-minute period.

The duration between encoding and retrieval was approximately 15 minutes longer in the current study's experimental paradigm, compared to Roberts et al. (2018)'s study. This is because participants undertook a MEG scan immediately following the AVE intervention, and before their memory for the words encoded during the study phase was tested. This means that this study's participants would have been just starting the test phase at around the time participants in Roberts et al. (2018)'s study were coming to the final stages of the memory task. Furthermore, the memory paradigm in the current study tested more aspects of memory which rendered the testing session longer than the task completed by participants in Roberts et al.'s study. It is possible that the immediate effects of AVE had diminished somewhat by the time participants were tested, or had completed the testing session, consequently attenuating their beneficial effect on memory. Although the persistent effects of AVE are what was hoped to be observed, it is not clear from the literature how long these last and what are the underlying mechanisms, as many studies focus on measuring the neural response solely during AVE. According to Hanslmayr et al. (2019), direct entrainment effects slowly revert to baseline levels once stimulation has ceased, leaving an 'entrainment echo' of approximately 1.5 seconds. While Teplan et al. (2006) explored the transient effects of AVE on the EEG, this was limited to a 3-minute post-AVE resting state. However, it is acknowledged that Roberts et al. (2018) report increased theta power during the retrieval stage of their experiment which is beyond that tested by Teplan et al. (2006). While this would be expected due to theta's role in successful retrieval, Roberts and colleagues importantly show higher levels of theta in the theta group compared to the low beta group, over all trials with no difference for specifically source memory trials. This suggests either a persistent entrainment effect or that the action of entrainment is on more sustained memory processes. Therefore, further work is required to determine how long entrainment effects last for and how they might interact with more sustained memory processes.

5.4.3 Is there inter-individual variability in the neuromodulatory effects of AVE?

One of the rationales for using the AVE intervention was that the role of the receiver is relatively passive and the stimulation effect reliable and strong in comparison to EEG-NF closed-loop protocols. Whilst this is true, in a study by Attokaren et al. (2022), efforts were made to define a threshold that represented sufficient neural modulation following AVE, resulting in 10 out of a possible 22 meeting this threshold. However, they note that there still existed variability across participants within this sample. Some evidence suggests that the difference in the time it takes for auditory and visual information to travel via their respective pathways (King et al., 1985) can also vary across species and individuals (Attokaren et al., 2022). This could feed into Wang et al. (2018, 2024)'s findings regarding the importance of theta phase synchronisation and spike-timing dependent plasticity suggesting that, fine-tuning the synchronicity of the auditory and visual stimulation so that it is tailored to the individual, could enhance the ensuing entrainment effects.

Furthermore, and similar to EEG-NF, some research shows that participants' response to AVE can also depend on resting baseline conditions (Rosenfed et al., 1997). A study by Howard et al. (1996) showed enhanced effects of entrainment by beginning their protocol at 30 Hz and lowering it until participants were relaxed for 15 minutes and then applied the target frequencies of 8 to 14 Hz for seven minutes. This could serve to reset all participants' baseline to the same level before initiating AVE at the target frequency, thereby mitigating any individual differences in resting baseline activity. Furthermore, stimulus intensity has been shown to affect the strength of entrainment (Lakatos et al., 2019). In the current study, the brightness was adjusted according to participants' reported comfort levels, therefore it is possible that this reduced the effect of AVE for those with a lower brightness setting, although this was rare, and the brightness levels mostly remained at 30% which was used in the pilot study where a strong response was generated. In a similar vein, it is noted that whilst this constant, isochronic delivery of light and sound has generated positive effects on episodic memory (Koster et al., 2019; Wang et al., 2018), in these studies the 'flicker' was presented in short trials rather than consistently for an extended period such as in the current study. Mild side effects such as boredom, headache, and decreased focus have been reported by participants exposed to AVE in this way (Attokaren et al., 2022), some of which were echoed in this study's participant feedback, which could have affected both their neural response to audio-visual stimulation, and their performance on the tasks. However, these side effects are rare, and the direct effects of these issues would need to be systematically tested to draw conclusions about their effect on the intervention.

5.4.4 Limitations and future directions

A key limitation of the current study is that there is no measure of the direct AVE effect on the brain taken during AVE. This was not included in the current study's design due to the time and resource constraints, precluding EEG preparation and extra time in the MEG laboratory, respectively. Therefore, there is no evidence for the device successfully entraining the brain during the experiment. In its absence, it could be argued that the reason enhanced memory performance is not observed in the theta AVE group is because theta was not actually increased in the theta group because the intervention did not work. However, the efficacy of the AVE devices is supported by the EEG data recorded during AVE in the study performed by Roberts et al. (2018), which shows the power spectra including large 5.5 Hz and 14 Hz peaks in the theta group and beta group, respectively. Additionally, the EEG pilot data included in this study mirrors this strong entrainment effect measured during AVE whilst using the exact same devices subsequently used for the main experiment. Therefore, combining these empirical sources, it was deemed likely the AVE intervention was successful during the main experiment. However, replication of the study could benefit from either EEG or MEG recordings being taken during the AVE intervention to provide direct empirical evidence and useful data which could be analysed to further explore in detail the underlying neural mechanisms active during AVE entrainment.

Further analyses, which were beyond the scope of this thesis, could be conducted by looking at the resting state MEG data recorded both pre- and post- AVE. First, this could elucidate whether there were persistent effects of the entrainment on individuals’ resting state activity i.e. whether there was indeed more theta power in the theta group in post-AVE resting state MEG data, compared to the control group and prior to the AVE but with the benefit of being able to localise a more precise source of this activity. Furthermore, correlational analyses could determine whether there is a specific link between individuals’ theta power increase i.e. from pre- to post- AVE and source memory scores. Exploratory analyses of the resting state MEG data could also elucidate whether there are direct effects of AVE on functional connectivity in regions related to memory and whether these processes are associated with enhanced memory. This could provide additional empirical support for the idea that there might be a feedforward or ‘ripple effect’ of theta entrainment, from stimulus effect in sensory regions to cross-hemispherical coherence in the central and parieto-occipital regions (Teplan et al., 2006) and to stimulation of endogenous oscillatory activity within deeper regions associated with episodic memory processes, such as the hippocampus, via synaptic plasticity (Mohan et al., 2022; Wang et al., 2018, 2024). A more detailed understanding of these mechanisms could inform further research on the use of AVE for enhancing memory.

An important noteworthy point is that all participants received sensory stimulation at the same frequency (i.e. 5.5 Hz in the Theta group, and 14 Hz in the Low beta group). It has been shown that entrainment may be facilitated the smaller the difference is between the sensory input and naturally occurring brain frequencies (Lakatos et al., 2019). In the current study, it is therefore possible that for those participants whose individual theta frequency deviates from 5.5 Hz, entrainment might have been less effective. At this stage, there is currently no way of knowing what this deviation constituted. However, participants’ individual theta frequency can be calculated post-hoc from the resting state MEG data, and this could be used to determine whether there is a correlation between the ‘distance’ between a participant’s individual theta frequency and the theta entrainment frequency of 5.5 Hz, and their memory scores. The expectation here might be that the closer the 5.5 Hz entrainment is to their endogenous theta frequency, the greater the effect of the 5.5 Hz theta entrainment might have been on their memory performance. Therefore, modulation of brain rhythms could be optimised by targeting participants’ individual endogenous rhythms. Individualising neuromodulation techniques is discussed in more detail in Chapter 6 (Section 6.5.1) of this thesis.

5.4.5 Conclusion

In summary, the current study does not provide empirical support for the use of AVE as an intervention for modulating theta oscillations to enhance episodic memory. However, the sensory entrainment effects of AVE are supported by the EEG response measured during AVE in the pilot study (see Appendix A). A few possible explanations have been discussed regarding the lack of behavioural findings in the current study in relation to the current body of research that is focused on entrainment. It is proposed that further research and analyses involving neuroimaging methods could provide help in elucidating the complex interplay between the immediate sensory effects and the transient effects on individuals' endogenous rhythms, by providing insights into the precise neural mechanisms that take place between sensory entrainment and engagement of neural networks involved in cognitive functions such as episodic memory. Knowledge and understanding acquired in this area could inform and guide future AVE study design in terms of when AVE is best applied, i.e. during encoding or the retention period following study of new information, and whether effects can be optimised by tailoring the stimulation according to individual factors such as endogenous brain rhythms and audio-visual transmission speeds (Attokaren et al., 2022).

Chapter 6: General discussion

6.1 Overview of the thesis

Neural oscillations in the theta frequency (4-8Hz) play a key role in episodic memory, during the encoding, consolidation and retrieval of episodic content (Clouter et al., 2017; Fell & Axmacher, 2011; Herweg et al., 2020; Nyhus & Curran, 2010; Rasch & Born, 2013). Episodic memory processes facilitate learning and the pursuit of an individual's goal-directed behaviour via the successful recall of personal experiences. Therefore, a deficit therein can severely impact our quality of life both practically and psychologically by disrupting our day-to-day functioning and our sense of self (Tulving, 1972; 2002). This can be observed in age-related cognitive decline in healthy individuals (Cansino et al., 2009; Prince et al., 2024) and in conditions such as mild cognitive impairment (Nordahl et al., 2005) and Alzheimer's disease (Baudic et al., 2005; Green et al., 1996). This warrants investigation into interventions that could enhance episodic memory in both the healthy and clinical populations.

The aim of this thesis was to determine whether neuromodulatory techniques could enhance episodic memory. To achieve this aim, initially a review and meta-analysis was conducted on the existing published literature on EEG-NF and episodic memory in clinical and healthy participants (Chapter 2). Then two large-scale empirical studies were conducted. The first study used EEG-NF as the neuromodulatory intervention (Chapter 3), and the second study used AVE (Chapter 5). These interventions have preliminary support for their ability to enhance recollection when the intervention is implemented during the retention period following encoding of new information (Rozengurt et al., 2017; Roberts et al., 2018). As a large number of non-responders were found in the EEG-NF study, a chapter is devoted to this issue to determine if there are any characteristics associated with this profile (Chapter 4). Summaries of the results from this work are outlined below, before a wider discussion about the utility of neuromodulatory techniques for enhancing memory, as well as limitations of the work in the thesis and future directions.

6.2 Summary of findings

6.2.1 Review & meta-analysis (Chapter 2)

The body of literature investigating the efficacy of EEG-NF and its effect on episodic memory is small and characterised by mixed findings. A few studies provide promising support for this intervention whereas others found no effect at all (see Chapter 2). Furthermore, both the study design quality and the methodology adopted by researchers vary considerably across these studies. For example, not all studies have sufficiently powered sample sizes or implement adequate study control features, such as randomisation of participants to experimental conditions and having an active control condition. Moreover, a variety of different EEG-NF protocols have been implemented in healthy volunteers and a wide range of different clinical conditions. It is therefore difficult to establish a clear picture and draw reliable conclusions regarding the efficacy of EEG-NF as a tool for enhancing episodic memory. This creates an important need to conduct a more thorough and robust evaluation of the state of the EEG-NF literature, to provide empirical support for its use for the purpose of enhancing episodic memory.

The first aim of Chapter 2 was to provide an overarching and comprehensive systematic review of all existing studies that had investigated the effect of EEG-NF on episodic memory in human adults, within both clinical and healthy populations. An inclusive approach here enabled the identification and cross-examination of several variables under the broad categories of sample (size, age and population), study design (between- or within- participants, control measure, participant randomisation/counterbalancing, and participant/experimenter blinding) and EEG-NF training characteristics (frequency and duration of training sessions, target frequency band, lead electrode site/s, feedback modality, provision of instructions and the number of non-responders). The output of this systematic review provides a global and holistic overview of the variation across studies concerning these features, and the means for closer inspection. This chapter's second aim was to determine the effect of EEG-NF on episodic memory, and importantly whether successful self-regulation of the target frequency band moderates this effect, by conducting a meta-analysis on the relevant reported data. Effect sizes were calculated for all target frequency bands and episodic memory measures generating multiple outcomes. This served to avoid selection bias, a notable issue with a previous meta-analysis resulting in it representing only partial data (Yeh et al., 2021). Furthermore, the effect sizes generated in this meta-analysis were more precise given the calculation included both pre- and post- EEG-NF episodic memory scores (Morris, 2008). This methodology again improves on the prior meta-analysis which includes solely post-EEG-NF episodic memory scores in the effect-size calculation (Yeh et al., 2021). The inclusion criteria for this meta-analysis ensured that only the data from those studies with an active control and randomised/counterbalanced participants were analysed, thereby contributing to an overall more accurate quantitative representation of the effect of EEG-NF on episodic memory performance.

The findings from the meta-analysis revealed a small-size beneficial effect of EEG-NF on episodic memory performance, which was slightly larger when clinical studies were removed. Furthermore, this effect was moderated by participants' ability to self-regulate the target frequency band. There was some evidence to suggest a selective effect of EEG-NF on recollection in tasks such as free recall and those requiring participants to recall source or contextual detail. In contrast this effect was not found in tests of recognition i.e. discriminating old from new items. The effect of EEG-NF also seemed to be distinguishable depending on the nature of the test stimuli; namely, verbal memory was boosted by EEG-NF, whereas no improvement was observed in visual memory. These findings not only provide evidence of a positive link between successful generation of the target brain state during EEG-NF and subsequent memory performance, but that effective use of this intervention could be optimised for certain types of memory. In terms of the EEG-NF training itself, some tentative evidence suggests that visual feedback, as opposed to feedback consisting of both visual and auditory cues, facilitated its effect. Also, contrasting the EEG-NF training group with a contingent rather than a non-contingent control seemed to better reveal the beneficial effects of the intervention. The findings did not favour the use of any particular frequency band, or the inclusion of specific instructions, for enhancing the effectiveness of EEG-NF on episodic memory. Furthermore, no relationship was found between the duration of EEG-NF training and its ensuing effects, regardless of the training band, although for the latter there was an insufficient number of studies per group. Overall, the output from the systematic review contributes a broad and detailed overview of EEG-NF studies, confirming the extremely variable nature of the design quality of these studies and the methodology implemented. Importantly, the low average sample size used in EEG-NF studies meant many were insufficiently powered to find an effect in the first place, and there was a lack of studies that implemented adequate control measures, with just over a third of studies not reporting this information. These findings highlight the value of, and the need for researchers to implement, the recently published guidelines for conducting EEG-NF experiments (Ros et al., 2020) to determine the strength of empirical support for the efficacy of EEG-NF, as an intervention to elicit performance enhancement in areas such as episodic memory.

6.2.2 EEG-NF empirical study (Chapter 3)

Existing research findings suggest a potentially promising effect of theta EEG-NF on episodic memory, in particular the recollection of source/contextual information (Eschmann et al., 2020; Rozengurt et al., 2017). However, more empirical evidence is needed to strengthen support for this intervention. Although there is currently no concrete agreement on the oscillatory activity that most benefits different memory processes, there is increasing evidence to support theta's role in episodic memory (Clouter et al., 2017; Herweg et al., 2020). Furthermore, Rozengurt et al. (2017) showed that a single 30-minute session of theta EEG-NF training undertaken during the retention period following the encoding of new information, enhanced subsequent free recall of this information immediately following EEG-NF training, with increasing persistent effects observed both 24 hours and one week later, for healthy adult volunteers. This finding offers a unique perspective on the potentially optimal effects of theta EEG-NF applied during this period and thereby provides further support for theta's role in memory consolidation processes (Rasch & Born, 2013; Rozengurt et al., 2017).

However, the study’s finding is limited to one type of episodic retrieval i.e. free recall. Further research was therefore warranted to build on this finding and investigate whether the positive effect of theta EEG-NF implemented during the consolidation of new information, extended to different types of episodic memory, such as source memory (Eschmann et al., 2020) and to establish whether this differentially effected subjective memory (Yazar et al., 2014).

The first aim of Chapter 3 was to replicate Rozengurt et al. (2017)’s finding by testing participants’ free recall of previously encoded word pairs following 30 minutes of theta EEG-NF and by using a similar between-participants design i.e. contrasting performance on the task between the theta group relative to an active low beta EEG-NF control group. The second aim was to extend this finding by also testing participants on objective and subjective episodic memory tests, such as cued recall, item recognition and source recollection, including confidence measures of participants’ recognition and source memory accuracy (Yazar et al., 2014). It was hypothesised that the single session of theta EEG-NF would, in addition to free recall, significantly enhance cued recall and source recollection of encoded items, whereas no difference was expected in old/new item recognition judgements. Performance in free recall was also expected to increase when tested 24 hours later. Chapter 3 therefore aimed to provide unique insights into whether successful upregulation of theta activity during EEG-NF can facilitate the consolidation of new information for different types of recollection processes.

Chapter 3 study’s findings did not replicate Rozengurt et al. (2007)’s findings given that participants who received theta EEG-NF did not score significantly higher than the low beta control in any of the episodic memory measures, neither immediately following EEG-NF training, nor 24 hours later. Considering this, further analyses were conducted on the data at an individual level using Rozengurt et al (2017)’s operational definition of an ‘effective responder’ i.e. on those participants who were able to increase their target brain activity by at least 5% from resting baseline level to the average of the active EEG-NF training blocks. These analyses provided tentative evidence in favour of a positive effect of theta EEG-NF on immediate free recall, in line with Rozengurt’s finding, although only before multiple comparisons corrections were applied. The Bayes Factor indicated anecdotal evidence for an enhancement in memory for the theta group compared to the control. No other memory measures showed a difference between the groups. Further analyses, conducted on theta responders and non-responders, revealed a wider range of improvements for the theta group on a variety of recollection measures, including free recall, cued recall and source recollection. Thus, at the whole group level the alternative hypothesis was rejected as there was no evidence for theta benefiting episodic memory but there were a substantial number of people who could not successfully complete the intervention. Once these were excluded there was tentative evidence of some improvement in one objective measure of recollection, although this was not reflected in the correlations between theta activity and memory performance.

6.2.3 EEG-NF responders (Chapter 4)

About a third of individuals are unable to self-regulate the target brain state during EEG-NF training, who are labelled non-responders (Enriquez-Geppert et al., 2017). Non-responders pose a significant issue for researchers, given that they can dilute the true effect of EEG-NF on episodic memory in EEG-NF studies. Critically, removal of non-responders, depending on the number, could also potentially underpower the sample rendering it unable to detect an effect at all. There is therefore an important need to further investigate the phenomenon of EEG-NF responders. Some research has explored individual differences to elucidate which factors may influence responder ability (Alkoby et al., 2018). Furthermore, another factor that has become the focus of some research is EEG-NF strategies. Specifically, what strategies facilitate successful self-regulation, if any? (Chikhi et al. 2023; Kober et al., 2013). However, this research is limited and there is currently a lack of strong findings to guide future research in this area. Identifying individual characteristics and strategies associated with responder ability i.e. developing a ‘responder profile’, could serve to both increase recruitment of effective responders and allow tailoring of EEG-NF protocols to subsequently optimise its effects.

The first aim of Chapter 4 was to investigate a range of psychological factors to determine if there were any relationships with EEG-NF responder ability. During the EEG-NF experiment reported on in Chapter 3, participants rated their current motivation (Vollmeyer & Rheinberg, 2006) and mood (Thompson, 2007; Watson et al., 1988) prior to EEG-NF training, and their flow state (Vollmeyer & Rheinberg, 2006), perceived locus of control and task difficulty immediately afterwards by reflecting on their experience of the EEG-NF training. They also completed the Big 5 personality questionnaire (Goldberg, 1990) and the sustained attention to response task (Manly & Robertson, 2005). The score for each measure was compared between responders and non-responders using two-tailed between-participants tests, except task difficulty which was hypothesised to be associated with decreased responder ability. In addition, correlational analyses were conducted which tested the relationship between each factor and participants' level of target band increase. This chapter's second aim was to determine whether any specific strategies were associated with responder ability. Participants indicated which strategies, of those provided to them in preparation for the EEG-NF training, they used and which they thought were most successful in controlling the bar. The proportion of subsequent responders who used each strategy was calculated, to provide a general idea of what strategies seem to work best. This chapter therefore aimed to build on existing research by exploring factors that might distinguish responders from non-responders. However, it also extended analyses to determine whether responder ability differed depending on the target frequency band during EEG-NF training i.e. theta or low beta.

For many of the measures, there was no relationship with responder ability. However, one consistent finding was that non-responders found the EEG-NF task to be significantly more difficult. In this study, it was hypothesised that perceived task difficulty would be associated with participants' diminished ability to self-regulate the target band, given that previous studies had demonstrated this to be the case (Bauer et al. 2016; Wilson et al., 2019). Therefore, these findings echo this previous research. Analyses focused on the individual frequency bands provide tentative evidence that some measures differentially affect responder ability, depending on the target frequency band. For example, positive mood and interest in the task appeared to be associated with participants’ diminished ability to upregulate theta activity. Perceived difficulty regarding the EEG-NF task was more prominent in low beta than theta non-responders, which would support the higher number of low beta non-responders found in both this study and Rozengurt et al. (2017)’s study. Interestingly, low beta responders reported higher levels of probability of a successful outcome. Taken together these findings suggest low beta could be a harder frequency band to upregulate; however, individuals motivated by ‘probability of a successful outcome’ i.e. those with self-efficacy, were seemingly able to overcome this difficulty and successfully upregulate low beta. Finally, low resting baseline was strongly associated with higher responder ability. This chapter therefore contributes unique insights regarding how responder ability can differ depending on the properties of the individual’s brain state both before and during EEG-NF training and the target frequency band, and how these factors could be an important consideration for increasing the number of responders in future studies. However, given only a few findings survive multiple comparisons corrections, these results are interpreted with caution.

6.2.4 AVE empirical chapter (Chapter 5)

Brain entrainment is an alternative intervention to EEG-NF with the same end-goal: to modulate target oscillatory activity. The difference with entrainment is that it generates a largely automatic, and instant sensory response (Lakatos et al., 2019; Teplan et al., 2006) in users who remain relatively passive, standing this technique in good stead to mitigate the issue of EEG-NF non-responders. Some studies provide promising support for the effects of visual and auditory flicker (or a combination thereof) on episodic memory (Koster et al., 2019; Wang et al., 2018). Roberts et al. (2018) showed a strong effect of theta AVE, applied during the retention period after encoding, on the recollection of source/contextual details previously studied. Using EEG, their study demonstrated higher levels of theta activity during both the AVE session and the subsequent retrieval stage for the theta group following AVE. However, little is known about the persistent beneficial effects of AVE on episodic memory beyond the initial testing stage i.e. immediately following AVE. Positive effects would render AVE a promising contender for enhancing episodic memory performance in healthy individuals, as an accessible, portable device which can be used at home.

The aims of Chapter 5 were to replicate and extend Roberts and colleagues' findings by testing episodic memory at two time-points: both immediately following the AVE session and 24 hours later. Participants were tested using the same memory paradigm as Chapter 3, generating scores of both recognition and recollection, including the retrieval of source/contextual details. It was expected that 30 minutes of AVE applied during the retention period i.e. between the encoding and retrieval of new information, similar to Chapter 3, would significantly enhance performance in free recall and the retrieval of source/contextual details, but not item recognition. At the 24-hour later time point, scores in free recall were expected to increase in the theta group, based on Rozengurt et al. (2017)'s finding that not only was theta increased after a single 30-minute session on EEG-NF, but these effects also persisted into the retrieval stage. Therefore, this chapter aimed to observe whether these persistent effects would extend to the use of AVE. However, no positive effects on memory were observed either immediately following 30 minutes of AVE in any of the measures, nor an increase in free recall 24 hours later. This is contrary to what was hypothesised in both cases and so the findings from this study do not support the use of AVE as an intervention for enhancing episodic memory.

6.3 Could neuromodulatory techniques be used to enhance episodic memory?

6.3.1 Are widely available neuromodulatory techniques supported by research?

The work from this thesis, including the meta-analysis and the empirical study, suggests that there might be a small effect of EEG-NF on episodic memory, particularly recollection, but the empirical work is tentative. This stands in stark contrast to the current widespread availability and application of EEG-NF in both clinical and domestic settings. In the clinical domain, the efficacy of interventions and treatments are often measured against some benchmark of what is considered 'clinically significant'. For example, qEEG standardised indexing can assess an individual’s neural activity according to a normative database and use this contrast to inform the clinical goal of neuromodulation via EEG-NF (Ko et al., 2021). The same view could apply to the practical application of EEG-NF to enhance memory performance in healthy individuals. The findings in this thesis challenge whether a small effect is enough to warrant the use of EEG-NF. Moreover, the majority of studies included in the meta-analysis, and indeed the EEG-NF empirical study (Chapter 3), conduct EEG-NF training in the laboratory using technical and intricate EEG equipment, which is often costly and time-consuming. Therefore, these findings suggest that the small benefits of EEG-NF do not outweigh the resources invested, especially factoring in the potentially intense training that comes with it.

One could argue that the wave of ‘neurofeedback therapy at home’ EEG-NF headsets such as Muse, NeuroSky and Sens.ai which have entered the market within the past couple of decades, could partly mitigate this issue, given their accessibility. These companies, and subsequent product reviewers, claim several benefits can be achieved from consistent, regular EEG-NF sessions using these devices, ranging from improved sleep quality and relaxation to emotion regulation, sharper focus, and enhanced memory. However, empirical support for the specific positive effects on individuals’ memory performance is limited, with a stronger emphasis on subjective user testimonials. Importantly, only one study demonstrates a strong effect of alpha EEG-NF on retrieval of word-pairs using a portable, wireless EEG-NF device that operates via Bluetooth on a smartphone (Wei et al., 2017). This finding holds promise that EEG-NF training could be a feasible intervention accessed at home; however, more systematic testing on the effectiveness of such devices is required to draw stronger conclusions on their viability and beneficial effects of enhancing episodic memory.

Moreover, the null findings from Chapter 5, whereby the efficacy of AVE was instead tested with the specific aim of precluding the issue of EEG-NF non-responders, do not support the use of AVE as an intervention for enhancing episodic memory. It is noted that no neurophysiological recordings were taken during the AVE session in the main experiment, to evidence the effect of the intervention. However, the pilot data show strong entrainment effects following 15 minutes of AVE, for both theta and low beta activity. This, along with the EEG data from the Roberts et al. (2018) study, provides proof of concept for the AVE intervention in terms of successful targeted neuromodulation. These findings suggest that AVE could provide a more reliable method of achieving a target brain state; however, the effects on enhancing episodic memory are not supported by the current empirical work. Similar to EEG-NF, portable devices that provide audio-visual stimulation are currently available on the market which claim to improve well-being and cognitive functioning on a range of indices, including memory performance, such as Sens.ai and BrainTap, and the DAVID devices ((https://mindalive.com). Again, the availability of these devices is seemingly premature when there is limited empirical evidence to support their specific effects on various behaviour, including memory. Overall, these findings highlight the need for more robust and targeted research into neuromodulatory techniques such as EEG-NF and AVE to bridge the gap between the true state of the literature regarding their efficacy as an intervention, and their current accessibility and application within society.

6.3.2 Is there a dissociation in the types of memory that are enhanced by EEG-NF?

An important finding generated by the meta-analysis in Chapter 2, was that EEG-NF tended to enhance recollection but not familiarity of information previously learned. This supports the dual process theory of recognition which proposes a dissociation between these two memory processes (Atkinson & Juola, 1974; Jacoby, 1991; Mandler, 1980; Yonelinas, 2002). Furthermore, the tentative findings from Chapter 3 suggest that enhancement to episodic memory in EEG-NF responders was specific to objective, rather than subjective, measures of memory (i.e. free recall and confidence ratings, respectively). As previously discussed in the introduction to this thesis, research into the type of memory deficits experienced in healthy aging adults is related specifically to objective recollection (Cansino et al., 2009; Prince et al., 2024), whereas familiarity and subjective ratings of memory performance remain relatively intact. Importantly, the current research potentially supports EEG-NF as a suitable intervention for this population, given it seems to directly target these memory processes that deteriorate with age. It is worth noting that the effects generated by the meta-analysis were not controlled for age, and the participants recruited for the empirical studies were young adults. These participants are likely to perform very well on the tasks, which might suggest that beneficial effects of interventions could be larger for older adults as there is more capacity for them to improve.

In contrast to the findings of this thesis which tentatively suggest that EEG-NF could enhance recollection, a very recent study found that EEG-NF can impair memory (Campos-Arteaga et al., 2024). The study similarly investigated the effect of a single 30-minute session of EEG-NF on the consolidation of episodic memory in a study-EEG-NF-test design. However, instead of theta frequency band activity, the electrophysiological feedback comprised of each individuals' unique pattern of brain activity recorded during the encoding of specific stimuli i.e. pictures of either faces or houses. Adopting an old/new item recognition judgement memory task to test familiarity of these stimuli, the study's findings revealed impaired recognition accuracy up to one-week following EEG-NF of trained stimuli relative to untrained stimuli. Campos-Arteaga and colleagues' findings conflict with the vast majority of studies in this area, which tend to find beneficial or no effects of neuromodulatory techniques for enhancing episodic memory. Whilst their study does not provide any data relating to the effect of their EEG-NF protocol on recollection, significant impairment of familiarity processes poses a significant issue considering the evidence discussed prior that shows that this type of memory normally remains intact in healthy ageing adults.

On close inspection of the study, one key difference that could explain the contradicting results is the type of EEG-NF protocol used. In this thesis, as discussed, the theta frequency is deliberately chosen as the target neuromodulation given its role in the recollection of source/contextual episodic content. Instead, Campos-Artegea and colleagues experimented with a novel EEG-NF technique which involved feeding back to participants their pattern of brain activity measured during encoding of specific items (i.e. faces and houses). Whilst the aim of this was to selectively modulate the consolidation process of specific episodic content, the program used to classify basal brain patterns had a tendency to misclassify house- for face-related brain activity which may have caused more difficulty for participants in the house group. Furthermore, during the neurofeedback session, the researchers prompted participants to, "think about or recall some of the elements learned earlier or to recall known people and places" (Campos-Arteaga et al., 2014, page 3). Craig et al. (2014) showed that engaging in autobiographical memory recall impairs consolidation of previously encoded content due to triggering activation of the hippocampus during the retention period. Such interference of consolidation can cause subsequent noise during memory retrieval (Mednick et al. 2011) which could explain the memory impairment in Campos-Arteaga and colleagues' study.

Nonetheless, Campos-Artegea and colleagues' findings underscore the importance of scrutiny regarding both the type of EEG-NF protocol and the instructions provided to participants, to understand whether such nuanced features when implementing these interventions can influence memory consolidation in a different, and indeed opposite, way. It is therefore important to review and consider the conditions under which these alterations occur, and approach with caution future EEG-NF training experimental designs.

6.3.3 Can other techniques enhance theta and is there utility in combining interventions?

The lack of support for these neuromodulatory techniques presented in this empirical work leads to the consideration of alternative interventions for enhancing episodic memory. Neuromodulatory techniques such as EEG-NF and AVE constitute exciting areas of research given their reliance on advanced technologies that can alter our own brain states. However, there might be other ways of enhancing theta which could lead to benefits in memory. For example, EEG and MEG studies have revealed a link between meditation and increased theta oscillatory activity in brain regions associated with episodic memory, such as the right frontal and left parietal cortex and the hippocampus, respectively (Nyhus et al., 2019; Lardone et al. 2018). Furthermore, complex pre-frontal cortex-dependent cognitive tasks such as mental arithmetic have been shown to increase theta activity (Gartner et al., 2015), and the delayed matching to sample (Skinner, 1950), the Stroop (Stroop, 1935) and the n-back (Kirchner, 1958) tasks have all been successfully used to elicit theta activity to calculate individualised theta for EEG-NF protocols (Enriquez-Geppart et al., 2014b; Eschmann et al., 2020). Therefore, it could be argued that simply engaging with one of these tasks or activities during the retention period could have a beneficial effect on the consolidation of episodic memories, rather than trialing different strategies during EEG-NF training or sitting through 30 mins of pulsing lights and sounds. Some support for this comes from studies showing that meditation improved source memory discrimination in a Remember/Know task (Brown et al., 2016; Nyhus et al. 2019). However, it is noted that these studies implemented either encoding-based mindfulness, or four weeks of meditation practice as an intervention in a test-retest design, respectively.

Contrastingly, one study that tested the effect of meditation during the retention period between study and test found increased breath-focus during the meditation session resulted in decreased theta and impaired memory on a delayed verbal recall test (Collins & Wamsley, 2019). It is proposed that more cognitive engagement during the retention period might increase retroactive interference or competing demands on hippocampal and/or frontal executive attentional resources, thereby disrupting the consolidation process. A recent study by Shtoots et al. (2024) found that 20 minutes of theta transcranial alternating current stimulation - a passive entrainment which does not involve the engagement of mental strategies – during the retention period enhanced free recall of previously encoded objects, relative to both active and passive controls. Altogether, while these findings show promise, these tasks and activities would need to be systematically tested and compared in a multi-armed study to explore the relative effectiveness of different ways of modulating theta activity on subsequent memory enhancement.

As discussed in Chapter 1, cognitive training is a widely researched technique for enhancing various cognitive behaviours, including memory. One systematic review shows that there are positive, significant results that have been reported on the use of cognitive training for enhancing episodic memory for both healthy elderly individuals and those with clinical conditions (Mendonca et al., 2022). For example, the use of mnemonic strategies such as organisation and semantic categorisation, visualisation, and association to recall verbal content (da Silva & Yassuda, 2009; Willis et al., 2006) have shown positive results. However, it is unclear whether these beneficial effects on memory are stronger than those generated by EEG-NF.

Building on this, an alternative avenue of investigation has involved examining whether combining different techniques can increase the beneficial effect on memory (Hosseini et al., 2016). A review of studies using a four-week cognitive training programme in conjunction with NIRS neurofeedback (Matsuzaki et al., 2023) found a slightly larger overall effect (standardised mean difference = 0.38) on episodic memory than the meta-analysis focused solely on EEG-NF training reported on in Chapter 2. This outcome was based on two eligible studies: Nouchi et al., 2022 found healthy young adults in the combined cognitive training and NIRS group performed significantly better on the delayed WMS-R logical memory test, than the cognitive training alone or active control group. The second study (Acevedo et al., 2022) revealed an increase in older adults' verbal memory scores relative to an active control group. However, a systematic review of studies using combined EEG-fMRI protocols reports mixed findings and a lack of homogeneity in study designs (Ciccarelli et al., 2023). Of note is that empirical evidence related to alternative interventions, such as cognitive training and combined techniques, suffer the same issues concerning an insufficient number of quality studies, and variability in both the tools or tasks used to measure episodic memory, and subsequent evaluation of their effectiveness by adopting different control conditions (Mendonca et al., 2022).

A consistent theme amongst the studies examining the various techniques for enhancing episodic memory is the implementation of each intervention in isolation. Rather than a conjunctive approach to combining neuromodulation with cognitive training, a more integrative approach could be taken. A study by Parsons and Faubert (2021) examined whether reinforcement learning via EEG-NF could be linked to performance in the behaviour of interest i.e. perceptual learning. In this vein, they demonstrated enhanced learning in a 3-dimensional multiple object-tracking task relative to a standard learning paradigm, and an active sham control. In this experiment, online error-detection, which was based on brain activity and real-time adjustment, was provided in real time. A similar approach could be applied to a memory paradigm, whereby individuals' positive EEG-NF feedback is informed by their performance on the memory tasks. This could serve to simultaneously resolve the issue of lack of far transfer effects in both cognitive training and neuromodulatory models, by directly reinforcing and enhancing the behaviour of interest i.e. episodic memory, rather than ‘increasing cognitive reserve’ with games like sudoku and hoping this indirectly improves general cognitive functioning. Similarly, AVE also could be implemented during individuals’ engagement with relevant memory tasks, which could serve to simultaneously enhance theta in real-time during completion of the task and improve performance outcomes.

6.4 Limitations

6.4.1 EEG-NF Methodological limitations

As discussed previously, EEG-NF respondability is an important aspect underlying the findings in both Chapter 3 and 4 of this thesis. Although there is currently no formal definition of what constitutes an EEG-NF responder, and there are several ways that changes in target band activity can be measured, methods and rationales selected to define and measure EEG-NF respondability should be carefully considered, and ideally consistent.

In Chapter 3 EEG-NF, responders were defined as those participants who increased the target band activity by at least 5% from resting baseline to the average of the six active EEG-NF blocks (whereas this threshold was 0% in Chapter 4 to create larger, more even group sample sizes). These are valid definitions used in previous EEG-NF studies; however, averaging the EEG-NF training data across blocks could obscure important information whereby more detailed, nuanced investigations could take place looking at the pattern and trajectory of EEG-NF learning to inform measures of success.

In relation to the EEG data processing, different parameters were used to process the online and offline EEG-NF data (e.g. band pass frequency cut-offs and artifact rejection/control measures). As discussed, this occurred for various reasons:

potential issues relating to the high beta inhibit bar used in the previous study; adjustments made to the current study's band pass thresholds to account for potential ERP analyses; and due to the different EEG-NF software programmes used (e.g. adaptive thresholding was manually set in the current study). These differences could mean that the offline measurement of theta/low beta ratio power may slightly differ from that measured online during EEG-NF training. A consistent approach applied to processing both online and offline data could help to resolve this issue.

It is also acknowledged that the time-window of 4096 ms based on that used by Rozengurt et al. (2017), epoch overlapping of 50%, is quite large for online EEG-NF training. This could result in incomplete information regarding participants' actual theta/low beta ratio activity as it is generated which could impact the accuracy of feedback they subsequently receive in real time. Considering effective continuous feedback of the stimuli ideally requires more frequent updates between ~100 ms – 400 ms), studies broadly use smaller windows in EEG-NF studies to avoid such a latency lag in the extraction of the frequencies of interest in transformation from the time- to the frequency-domain (Huster et al., 2014).

6.4.2 Is one neuromodulatory session sufficient?

One important question is whether more sessions using such neuromodulatory techniques relates to a larger effect, or a more sustained increase in the target frequency, thereby increasing the chances of positive behavioural change. The low number of studies in Chapter 2 meant that a relationship between EEG-NF training amount and self-regulation success could not be reliably determined. However, some studies have found successful modulation of the target frequency after only a single session of EEG-NF (Escolano et al., 2014b; Rozengurt et al., 2017; Shtoots et al., 2020) and beneficial effects of AVE on memory were also found after a single session (Roberts et al., 2018). Thus, based on this work it was anticipated that effects would also be observed after one session for the empirical studies conducted.

In contrast to this, it is noted that a large proportion of EEG-NF studies have used long, intense training schedules with several sessions spread over a few weeks. EEG-NF training sessions range from three (Tseng et al. 2021) to 42 (Bearden et al., 2003) sessions. Furthermore, studies investigating the effects of AVE on various behavioural outcomes also rely on extended use over time; for example, improvements in both a range of cognitive functions including memory in older adults, and academic performance in students, were observed after 30 sessions of AVE using the DAVID devices (Budzynski, et al., 2007). Finally, cognitive training schedules used for treating episodic memory in healthy aging and patients with mild cognitive impairment and Alzheimer's disease included a minimum of five sessions and a maximum of 36 sessions (Mendonca et al., 2022).

It could be argued that prolonged use of these neuromodulation techniques results in stronger and more reliable effects over time. The beneficial implication of increased training schedules regarding these interventions is two-fold. Firstly, individuals might have a better chance of learning how to self-regulate during extended EEG-NF training, especially since they will have more time to figure out which strategy works for them. Eschmann et al. (2020) deliberately factored this into their experimental design by designating the first three sessions to strategy testing, with the last four sessions led by a constant strategy. Eschmann and colleagues observed significant self-regulating success during the constant strategy phase, where participants were encouraged to use their preferred strategy. Furthermore, Hsueh et al. (2016) found that participants' alpha amplitude only significantly increased after three or four 36-minute sessions. These findings reinforce the fact that EEG-NF is a learning process and that it can take time (Davelaar, 2023; Sitaram et al., 2016). In the studies in this thesis, no or weak effects and the large number of non-responders in the EEG-NF study, might have been a result of only conducting a single neuromodulatory session. Thus, this single session might not have been long enough for participants to learn to self-regulate and/or provided insufficient training of the relevant frequency band.

Secondly, once a strategy is found that works, the association between this and the neuromodulatory changes needs to be reinforced by way of repeated and timely positive reward, for operant conditioning to be successful (Skinner, 1945). In terms of

EEG-NF, initial activation of the neural networks associated with the goal, or chosen strategy, accumulates with increased positive feedback until it is fully activated (Davelaar, 2023). Over time, the cumulative strengthening of neural connections will lead to long-term potentiation via the principles of Hebbian plasticity (Hebb, 1949). Given that repeated audio-visual stimulation also leads to synaptic plasticity after cessation of the stimulation session (Siever & Siever, 2023), it follows that more training in both EEG-NF and AVE could optimise the long-term, on-going beneficial effects of these neuromodulatory techniques. However, it is currently unclear from the literature what is the optimal amount of time required for successful neuromodulation to occur, and whether this alters according to the specific target frequency band. More dedicated research is required regarding this to inform future studies and the application of these neuromodulatory techniques.

6.4.3 Responder ability and neuromodulatory techniques

Overall, there was no relationship found between responder ability and most of the individual factors explored in Chapter 4. Compounded with the lack of strong supporting empirical evidence, this means that currently the development of a reliable ‘responder profile’ to guide the identification of EEG-NF responders, is premature. Nonetheless, these findings together with those preceding, support the idea that EEG-NF responders (and non-responders) are a phenomenon worthy of further exploration and understanding, to maximise the number of individuals who can benefit from this intervention. Furthermore, consideration of the dynamic nature of EEG-NF and the complexities of self-regulation of different brain states is needed, which could inform what approach is best for ensuring individuals successfully achieve that state in the first place.

For example, this could involve the individual’s level of sensory processing determining how they interact with the training task and the environment, and ultimately how well they perform. A recent study has investigated the effect of the biological trait, Sensory Processing Sensitivity on the efficacy of fNRIS-NF training

(Acevedo et al., 2023). Superior memory benefits were associated with participants who scored higher on the Highly Sensitive Person scale. A different neurofeedback technique to EEG-NF is used combined with cognitive training, however the fundamental feedback principles underlying the techniques are comparable. This builds on the idea that successful reinforcement of the target brain state, and subsequently the desired behaviour, could be dependent on the individual’s ability to effectively process the stimulus rewards that are key for guiding their neurophysiological response. This could also be a factor to consider in relation to the application and efficacy of AVE, given contrastingly, older adults experience age-related sensory decline (Prince et al., 2024).

It is noted that the data relating to individual differences reported in Chapter 4 was predominantly measured using self-reporting questionnaires. This introduces the issue of subjectivity, which can be relatively flawed due to inaccuracies and inconsistencies in peoples’ meta-cognitive abilities (Somitori & Kunisato, 2022). Furthermore, Davelaar et al. (2018) revealed that the brain knows the difference between a sham and an experimental NF protocol, even when the individual does not. Specifically, a large sample of sixty participants were unable to detect whether they were in the alpha EEG-NF group or the sham group during a self-reported post-session debrief. However, a gradual reduction in relative theta power in the EEG-NF group only was a reliable predictor of group membership. This suggests that EEG-NF learning takes place at a physiological level, regardless of an individual's conscious awareness, further highlighting possible inaccuracies in self-reporting which could underpin participants’ responses in Chapter 3 where they were instructed to select what strategies they thought worked best to move the bar.

Interestingly, the strongest correlation amongst the various factors explored in Chapter 4 was participants’ resting state activity, an objective electrophysiological measurement representing the target frequency power ratio (e.g. theta/low beta) before they underwent EEG-NF training, although regression to the mean must also be considered when interpreting this finding. Nonetheless, this brings into question the value of self-reporting in the context of neuromodulation, barring the reporting of specific strategies they used which is informative (Davelaar et al., 2018). Also, it is noted that the relationship between several individual factors and responder ability were analysed on a linear basis. Subsequently, each measure, and its correlation with responder ability, was considered in isolation. This approach potentially undermines the complexity of processes underlying the EEG-NF task. Future research could adopt a more holistic approach to elucidate the interplay between the various factors and their individual weightings in terms of their ability to predict responder ability within the context of EEG-NF training.

One important measure that is absent from these data is the level of individuals' task engagement during the EEG-NF training session which has been proposed to correlate with learning ability generally, as it encompasses motivation and focus on the task at hand (Csíkszentmihályi, 1990; Wilson, 2019). The EEG-NF empirical study included a subjective measure of participants' current motivation before EEG-NF training, and an objective measure of their sustained attention during the SART. However, both are indirect measures of these factors outside of the EEG-NF training. Although EEG-NF self-regulation success is separately measured by the observed change in target brain activity, an objective measure of task engagement taken during EEG-NF training would serve to more reliably link this factor to performance on the EEG-NF task and subsequently allow exploration of individual differences regarding this. In this vein, Fairclough et al. (2013) investigated the utility of measuring psychophysiological signals representing intentional action or a change in state, using indices such as mental effort, positive and negative affect, and task motivation. This was in relation to mapping and maximising the accuracy between psychophysiological change and cursor control in an open-loop brain-computer interface. Such biomarkers could also potentially provide an objective measure of task engagement in closed-loop BCIs, such as EEG-NF. Similarly, in relation to AVE, some research has demonstrated a link between selective attention and entrainment effects (Calderone et al., 2014). Specifically, it has been shown that in primates, entrainment can be completely suppressed if a rhythmic stimulus stream is ignored (Lakatos et al., 2013; O'Connell at al., 2014). Therefore, measuring individuals' level of attention, or engagement during the AVE session could serve to uncover individual differences in AVE response in relation to this and identify possible ways to control this factor to further optimise the entrainment effects.

6.4.4 Is the beta frequency the optimal control measure?

An important issue to consider when evaluating findings relating to the efficacy of these neuromodulatory techniques is the choice of active control condition used to compare the results to. In this thesis, low beta frequencies were adopted (15-18 Hz for the EEG-NF study and 14Hz for the AVE study). Indeed, low beta has been selected as an active control in several EEG-NF studies (Rozengurt et al., 2016, Rozengurt et al., 2017; Shtoots et al., 2020) specifically due to its lack of association with the consolidation of long-term memories i.e. procedural, free recall, and visuo-spatial memory, respectively. However, while there is no empirical evidence directly linking increased low beta activity with episodic memory processes, the beta frequency is generally associated with alert focus and concentration (Gruzelier, 2014a; Ray & Cole, 1985), which might indirectly benefit memory processes. Furthermore, there is evidence for a potential role of ‘beta bursts’ in top-down control and working memory (Lundqvist et al., 2018; Schmidt et al., 2019). The theta/beta band protocol is commonly used to treat attention-deficit hyperactivity disorder (Van Doren et al., 2018), whereby an increase in this ratio is associated with inattention, therefore suppression (i.e. increased beta/theta) subsequently improves focus. In the current research, if the low beta control participants are benefiting from such enhanced attentional functioning, this could indirectly improve subsequent episodic memory performance by facilitating increased engagement with the EEG-NF or the AVE task. This would serve to diminish possible differences between the conditions.

In terms of AVE, the utilisation of 14 Hz stimulation for the control condition coincides with frequencies contained within the SMR band (12-15Hz) which is a common protocol used in EEG-NF studies to improve episodic memory. The rationale behind this is that, mechanistically, upregulation of SMR elicits a brain state which is conducive to more efficient stimulus processing by inhibition of interference caused by motion, resulting in subsequent improvements in cognitive performance (Sterman, 1996). It therefore could be proposed that participants in the AVE control group could have generated improved scores on this basis, closing the gap in performance and potentially significant differences between the experimental and control groups. However, one flaw with this argument is that in the EEG-NF studies, central electrodes measure SMR activity directly over the sensory-motor cortex, whereas AVE stimulation takes place via the occipital/temporal regions. It is unknown whether indirect beneficial effects transfer to the sensorimotor cortex by this technique, just as it is theorised that stimulation of 5.5 Hz within the theta band subsequently travels to brain regions known to play a role in episodic memory. These potential overlaps would need to be systematically tested to rule out any indirect effects of low beta on memory obscuring the results, and to determine whether low beta serves as an adequate control condition to reliably elucidate the true, relative effects of these neuromodulatory techniques.

Considering the quandary of using low beta as a contingent active control, a more neutral control might involve participants upregulating a range of 2Hz narrow bands outside of the frequency of interest, (e.g. 10–12 Hz, 12–14 Hz, 14–16 Hz) randomised across EEG-NF training trials. Although several sessions would be required here to average out any effects of specific frequencies, this could serve as an active control and prevent possible indirect influences of alternative frequency bands on cognitive functions (Eschmann et al., 2020; Wang & Hsieh et al., 2013). Similarly, in relation to the AVE task, a stimulation program involving randomised frequencies could constitute the control condition to avoid any indirect effects of 14 Hz stimulation on memory function.

It is noted that in the current experimental research, whilst the experimental design in both studies includes an active control condition for robust comparison between groups, it lacks a passive control group which is included in previous studies in the field (Rozengurt et al., 2016: Rozengurt et al., 2017; Schtoots et al., 2020). Unfortunately, limited time precluded the use of the same passive movie-watching control group in Chapter 3’s study, as used by Rozengurt et al. (2017). The inclusion of a passive control would provide a baseline to allow the observation that the intervention worked compared to no intervention at all. A passive control condition that involved the participant simply resting could also potentially attenuate cognitive engagement and indirect effects. However, it is difficult to control for what participants think about during rest, and studies show that they often engage in memories or future thinking (Collins & Wamsley, 2019) which could either increase theta or disrupt consolidation of encoded information due to interference (Craig et al., 2014), as discussed above in Section 1.4.3.

Finally, it is acknowledged that the use of low beta as a control condition in previous research (Rozengurt et al., 2017; Roberts et al., 2018) generated positive relative effects in favour of theta oscillatory activity's role is episodic memory retrieval. However, as discussed previously, low beta is also a seemingly difficult frequency band to self-regulate which could have rendered participants in the EEG-NF study frustrated and demotivated, disengaged from the EEG-NF task and subsequently under-performing on the memory tasks. This issue also underscores the importance of blinding and the impact of non-specific effects in considering an appropriate control condition. It remains a challenge in psychology to find the perfect control condition, especially in the case of studies investigating the effects of neuromodulation on cognitive function, such as episodic memory.

6.4.5 The memory paradigm

One of the limitations of the study-test memory paradigm used in both Chapter 3 and Chapter 5 (Yazar et al., 2014) is that because of its design whereby the intervention happened in-between the study and test phases, a pre-EEG-NF score could not be measured. Therefore, there are no baseline memory scores so that the change in memory performance after EEG-NF training can be examined. The randomisation of participants to the experimental and control groups would have served to mitigate this issue for the two studies, as the average baseline memory performance of the two groups should have been about the same and a relatively homogenous sample was used. However, this lack of data does preclude analysis of specific memory performance gains which could be correlated with target neuromodulation to determine the association between increased theta and the different episodic memory measures. Recording solely post-EEG-NF scores is a common feature of study-test designs, rather than two identical tests being conducted pre- and post- EEG-NF which would provide both scores. However, future research using this design could adopt the same approach as Rozengurt et al. (2017) by conducting a series of pre-tests whilst controlling for learning effects.

Secondly, it is acknowledged that there is a bias in the word stimuli given that the ratio of old items to new items is 2:1; a ratio which has been used in previous memory studies (Roberts et al., 2018; Eschmann et al., 2020). Participants were not informed about this, and certain design features were implemented to reduce encoding variability, such as word frequency and semantic pairing, and a limit was set to allow the presentation of a maximum of four sequential old/new words or Jack/Chloe to reduce habituation of participants' responses due to muscle memory.

However, it is possible that participants became acutely aware of the inequal weighting of old words which could have subsequently informed expected rates of old (target) and new (lure) items. This could result in participants initially being motivated to keep the false-alarm rate down and therefore respond new, before 'tracking and stabilising' based on the median set of recently tested items, and responding old. The latter refers to the heuristic principle of making more 'old' responses when the average familiarity of probes is high than when it is low, resulting in participants 'probability matching' in favour of old words, regardless of their recognition of the word (Rotello & Macmillan, 2007). Incorporating an equal number of old and new items may serve to resolve this potential issue. Also, signal detection analysis could be conducted on the behavioual response data to calculate the criterion location, a value that is the distance between the selection criterion (i.e. the threshold for giving a certain type of response) and the midpoint of the two distributions. This provides a measure of the bias caused by participants' tendency to give one type of response: 'yes' bias = old, 'no' bias = new (Rotello & Macmillan, 2007).

6.5 Future directions

6.5.1 Targeting the benefits of individualised EEG-NF protocols

Individualised frequencies are becoming the focus of more recent research into optimising the effects of neuromodulatory techniques on target oscillatory activity and behavioural outcomes, such as episodic memory performance. This approach seems to take a step in the right direction to specifically target modulation of an individual's naturally occurring oscillatory activity, rather than adopting a blanket approach by targeting general broadband frequencies, or randomly chosen individual frequencies within a designated band. Recent research demonstrates that individual neural oscillatory states can optimise learning and brain plasticity during brain entrainment (Michael et al., 2022) and transcranial brain stimulation (Bjekic et al., 2022). Specifically, Michael et al., (2022) delivered visual flicker to participants at their individual alpha frequency calculated previously using EEG and found that entrainment was significantly enhanced in terms of alpha power, phase alignment in the pre-stimulus period, and resulted in shorter latency of early visually evoked potentials. Importantly, a deviation of only +/- 1 Hz from the individual alpha frequency reduced this effect.

An individual's endogenous frequencies can be measured in a few ways, although this differs across specific frequency bands. For example, given that alpha waves present on the EEG more prominently when our eyes are closed, individual alpha peak frequency, occurring between 8-12 Hz, can be measured by calculating the difference between eyes-open resting baseline and eyes-closed resting baseline (Klimesch, 1999; Wan et al., 2014). In another study, Baba-Rebelo et al. (2021b) revealed enhanced upregulation of alpha with real-time calculation and adjustment of the individual peak alpha feedback parameter during the EEG-NF training session. Calculating individual theta frequencies presents a slightly more complicated process, since natural theta rhythms are not easily detected in the resting state EEG. Alternatively, individuals are required to undertake one or more cognitive tasks which are known to increase theta activity, such as intentional source memory tasks, the delayed matching to sample task (maintaining stimuli during the retention period), task switching (switch condition) tasks, the three-back task (updating condition), the stop-signal task (stop condition), and the Stroop-task (incongruent condition) (Enriquez-Geppert et al., 2014b; Eschmann et al., 2020; Huster et al., 2013). Specifically, higher levels of frontal midline theta are associated with high task difficulty and encoding and retrieval recruiting top-down control processes (Addante et al., 2011; Enrique-Geppart et al., 2014b; Eschmann et al., 2020; Koster et al., 2014). In the case of AVE, audio-visual flickering has been used to determine individuals' strongest response (e.g. power/amplitude) to 3 second trials of individual frequency flickering within the theta frequency band (4-7 Hz) (Wang et al., 2018). The resulting value obtained from any of these methods is subsequently used as the training parameter during the neuromodulatory intervention. This has been used successfully in both EEG-NF (Eschmann et al., 2020, Escolano et al., 2014b, Tipple et al., 2024) and sensory stimulation (Koster et al., 2014; Wang et al., 2018) studies.

On this basis, the current neuromodulatory investigations potentially could have benefited from the implementation of individualised theta frequencies within these interventions. Maximised resource allocation was the determining factor for not adopting this approach, given the duration of the memory paradigm plus the additional time-consuming practical constraints involved in both the EEG and MEG set-ups. Considering the lack of effects found for both EEG-NF and AVE enhancing episodic memory in Chapter 3 and Chapter 5, respectively, it is possible that an EEG-NF protocol individually tailored to each participant's natural theta rhythm might serve to increase self-regulation success rates, to allow a more robust evaluation of the effects of these interventions on different type of episodic memory processes. Moreover, as discussed in Chapter 4, even though AVE appears to be a more reliable method for neuromodulation, it remains unclear what are the mechanisms at play between stimulation at sensory regions of the brain and resonance with deeper structures involved in the consolidation and retrieval of episodic memories. Future work involving analysis of the resting state MEG data, which was outside the scope of this thesis, could provide insight into these mechanisms and potentially reveal whether, in addition to how, tapping into individuals' endogenous theta oscillatory activity could facilitate and optimise this transfer, thereby increasing the likelihood of enhancing episodic memory performance.

6.5.2 Considering the role of other frequencies on the spectrum.

While it is important to systematically test theta in isolation to empirically determine the role it plays in episodic memory processes the contribution of other frequencies to these processes needs to also be considered to facilitate a more holistic understanding of the mechanisms at play. For example, oscillatory activity in the delta, theta and gamma frequency bands is predominantly implicated in memory reactivation and consolidatory processes during both the sleep and active awake state (Headley & Pare, 2017). Therefore, when designing neuromodulatory protocols for interventions such as EEG-NF and AVE, it is plausible that inclusion of these additional frequencies could potentially enhance the overall effect on episodic memory by better reflecting and capturing the precise and complex oscillatory mechanisms underlying different episodic memory processes.

As discussed in the General Introduction, a growing area of research is investigating the interaction between theta and gamma frequencies, and the role this plays in episodic memory. Crucially, phase-amplitude theta-gamma coupling has been observed in the entorhinal-hippocampal system (Colgin et al., 2014), and phase-synchronisation has been measured between pre-frontal theta and parietal gamma oscillations (Koster et al., 2014). It is proposed that gamma oscillatory activity assists in perceptual binding and information transmission between these regions (Fell & Axmacher, 2011; Nyhus & Curran, 2010). The phase of theta activity modulates gamma power and is responsible for temporal ordering and cognitive control of the memory representations (Brookes et al., 2020). Specifically, research findings support the role of phase-amplitude theta-gamma coupling in working memory tasks (Abubaker et al., 2024; Tamura et al, 2017) and in the sequencing and formation of episodic memory representations (Heusser et al., 2016), in addition to episodic memory retrieval (Koster et al., 2014; Mormann et al., 2005). Importantly, de Lara et al. (2018) demonstrated disruption of episodic memory formation by implementing transcranial alternating current stimulation in the form of high gamma (80 Hz) bursts during the trough of a theta wave (5 Hz) cycle during a verbal associative learning task. This highlights the connectedness between gamma and theta and that the simultaneous operation of both frequency bands is crucial for successful encoding of episodic content.

It is currently unclear what is the exact nature of theta-gamma coupling's role in different types of memory, although it is proposed to be a key part of information processing whilst communicating and maintaining task-relevant information across large-scale networks (Canolty & Knight, 2010). Whether this has a direct or indirect role in episodic memory processes is a question that warrants further investigation. However, the study by de Lara et al. (2018) provides a causal link between a precise interdependent theta-gamma relationship and the encoding of new episodic memories. This invites future research which could explore methods for capturing this specific pattern of oscillatory activity to inform the parameters for the neuromodulatory techniques discussed within this thesis, and whether it subsequently enhances episodic memory. Furthermore, individualised neural markers of this theta-gamma coupling activity could be harnessed to tailor the effects of these interventions and optimise the potential beneficial effects on episodic memory.

6.5.3 Naturalistic memory paradigms

Another factor to consider in relation to studies investigating neuromodulatory techniques such as EEG-NF and AVE alike, could be the detached nature of the memory paradigm used to measure memory performance from real-life day-to-day episodic memory processes. The majority of studies in this area use limited laboratory-based stimuli such as word lists and pictures of objects. Whilst such memory paradigms provide widely accepted valid measures of episodic memory processes used in real life, such as our memory for contextual details, more recent studies have incorporated richer stimuli which might better reflect what we experience in everyday life. Thus, to evaluate the true benefit of neuromodulatory techniques on episodic memory, the empirical findings from laboratory-based experiments could lay the foundations for research using more naturalistic paradigms.

A study by Rozengurt et al., 2023 demonstrated a positive consolidatory effect of theta EEG-NF training completed after watching a 15-minute silent movie. Theta EEG-NF group participants were able to successfully recall more basic details of the movie's general content prompted by a 12-item questionnaire, at a one-week timepoint following viewing, and relative to the active (low-beta) and passive (Sudoku) control groups. This paradigm resembles more closely our episodic memory of events experienced in a naturalistic way; however, it could be argued that one crucial element missing from this is the individual's personal involvement, or representation of 'self', in the scene to be remembered. They were not interacting with the event, only experiencing it via their point-of-view simply observing from the 'outside' in an arguably passive way. In the case of individuals experiencing impaired episodic memory and how it manifests in day-to-day activities, some more adaptive techniques are used with older adults, such as 'life stories' which involves the re-experiencing of personal memories through recollection, and the application of classification and labeling strategies using their own photographs (Mendonca et al., 2022). This approach is more interactive and ecologically valid and could serve to target the deficit more specifically.

Given the self-referential basis of episodic memories, which are defined by the involvement of autonoetic consciousness, perhaps a shift towards more personally relevant, ecologically valid measures could be examined in the future. For example, virtual reality paradigms that reflect subjective experience of real-life scenarios where episodic memory processes are engaged could be utilised, and wearable EEG-NF kits used to facilitate flexibility in such real-life paradigms along with day-to-day memory measures. This approach would enable measurement of memory performance in a realistic and controlled setting, removing the lack of generalisability and comparability in autobiographical memory testing. Furthermore, virtual reality-based EEG-NF has been shown to produce a superior response to self-regulation of the alpha frequency band, when directly compared to a standard, 2D feedback display involving increasing the height of a bar (Berger & Davelaar, 2017). By engaging the individual in a more immersive EEG-NF training experience, and including task content that is more relatable to their everyday life, together this could deliver optimal results in enhancing their episodic memory. Ultimately, this could serve to transfer performance in generic laboratory-based tasks following EEG-NF training which do not have the same depth of episodic memory processing as in real life, to the real-life task of interest.

6.5.4 Lessons Learned

6.5.4.1 Study replication and extension

Firstly, in future experiments where one of my aims is to replicate a finding, I would conduct an experiment which is a direct replication. This would require running the experiment using the exact same population type, behavioural paradigms and procedures, and EEG-NF parameters and protocols. It is noted that the key aim in Chapter 3 was to investigate whether theta EEG-NF training could enhance different types of episodic memory, in addition to free recall as evidenced by Rozengurt et al. (2017). The use of word pairs instead of single objects in the memory paradigm therefore allowed for cued recall and source memory to also be probed, meaning this differed from the stimuli used by Rozengurt and colleagues.

However, it is noted that altering certain experimental design features requires acknowledgement of the differences between the studies and the potential impact of these, although this may be speculation if too many changes are introduced into the empirical process. Therefore, a sensible approach would be to directly replicate the previous study and then incorporate any changes into the next study to extend on the original findings.

6.5.4.2 EEG-NF self-regulation success

As previously discussed, a key feature of an EEG-NF intervention study is ‘respondability’ i.e. participants successfully upregulating the target band. This is essential to empirically investigate the effects of theta EEG-NF on episodic memory – the central research question in this thesis. One of the main outcomes of Chapter 3’s

EEG-NF experiment was that for many participants this was unfortunately not the case (48% non-responders in the Theta group and 67% in the Low beta group). Whilst possible explanations for this have been discussed and additional analyses have been performed focused on responders, it is prudent at this stage to summarise what lessons have been learned in this regard which could feed into ways in which EEG-NF respondability can be maximised in future research.

Firstly, given the EEG-NF protocol was taken from a previous study (Rozengurt et al., 2017), this provided proof of concept supporting the use of this protocol for participants to successfully upregulate both theta and low beta frequencies. However, some limitations had been identified in the study e.g. the use of high beta as an artifact inhibit bar possibly, making low beta difficult to upregulate due to it flanking high beta. This actioned subsequent research into alternative effective inhibit bars commonly used in other EEG-NF study designs i.e. delta (0.5 Hz – 2 Hz) and beta2 (22 Hz – 45 Hz) for ocular and body movements, respectively. Whilst piloting of the EEG-NF training protocol was conducted prior to data collection, to fully optimise EEG-NF respondability rates, more substantial and dedicated time could be invested in testing such parameters, including those used for online feature extraction, as discussed in Section 6.4.1.

In terms of measuring and analysing EEG-NF respondability, it is important that online and offline EEG-NF data processing pipelines are identical (e.g. use of the same band pass filter) to ensure that offline measurements more accurately reflect participants' brain activity changes in real time during EEG-NF training. Relative power calculations could better represent target band activity in relation to the full spectrum of activity by reducing the frequency range of the denominator from the default value inbuilt in the BioSemi system to encompass more relevant frequencies (e.g. up to 100 Hz). Finally, whilst line graphs are displayed in Chapter 3, EEG-NF learning trajectories could be explored in more detail, as opposed to using the measure of the average of all active EEG-NF blocks (relative to the resting EEG baseline). This measure could conceal the fact that some participants may not learn to upregulate until they have received more training. For example, it has been shown in some studies that EEG-NF learning success does not occur imminently, but instead after a number of EEG-NF training sessions (Hsueh et al., 2016; Wei et al., 2017). More precise depictions of EEG-NF training patterns and trajectories could qualify understanding of respondability and inform more accurate definitions of EEG-NF responders.

6.5.4.3 Use of additional control measures

An active control has been used in Chapter 3's EEG-NF study, as has been recommended within the EEG-NF literature (Enriquez-Geppart et al., 2017). The rationale for the use of an active control in EEG-NF research is to ensure that control participants have the exact same schedule as the experimental participants during which they are involved in an active task (Ros et al., 2020; Sorger et al., 2019). Therefore, any improvement seen in the experimental group can be attributed to the neurofeedback intervention and not to other non-specific factors, such as: participant-experimenter interaction, motivation, and repetition-related effects.

However, it is acknowledged that intervention studies also benefit from a passive control to ascertain whether any findings are due to the target intervention itself i.e. theta upregulation, or simply whether an effect is present due to the existence of non-specific effects linked to the intervention. For example, a passive control would allow a comparison to be made based on the provision of a baseline where no intervention was performed at all. This is especially important in EEG-NF studies, to rule out that it is simply EEG-NF training that has a neurophysiological effect, rather than the specific and hypothesised target band. It is also noted that the inclusion of a sham control group could have provided a solution to the potential regression to the mean issue. Therefore, an optimal study design could include these additional control measures in a multi-armed study, to isolate the effects of the intervention.

6.6 Conclusion

In summary, this thesis reports on the efficacy of two neuromodulatory techniques: EEG-NF and AVE, involving one 30-minute session implemented during the retention period between encoding and retrieval of new information. The main aim was to determine whether they could enhance episodic memory based on a range of objective and subjective measures.

The findings presented in this thesis provide a detailed overview of the EEG-NF literature and contribute tentative empirical evidence that supports the efficacy of EEG-NF as an intervention for enhancing episodic memory in individuals who respond successfully to this intervention by modulating target oscillatory activity during EEG-NF training. Investigation of an alternative intervention, via audio-visual entrainment, found no evidence for an enhancement in memory. The work completed for this thesis highlights both the overall high degree of variability across EEG-NF studies in terms of study design quality, protocols and parameters, and the complexity of the underlying mechanisms at play driving modulation of individuals' oscillatory activity. A small-size effect of EEG-NF on episodic memory might be insufficient to support the application of EEG-NF in both healthy and clinical populations; however, it may provide encouragement for further quality research which focuses on determining how and for whom EEG-NF works.

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Appendix 1: EEG recordings of the entrainment effects of the DAVID AVE device

Prior to completing the main study outlined in Chapter 5 a pilot experiment was conducted to establish the effectiveness of the AVE intervention i.e. that the DAVID LIVE app and SPECTRUM Eyeset deliver rhythmic auditory and visual entrainment of neural oscillations at the desired frequency.

Method

Participants

Eleven healthy volunteers were randomly recruited from Cardiff University Brain Research Imaging Centre (CUBRIC). The sample size was considered sufficient based on participants undertaking AVE under both the experimental and the control condition. Eligibility criteria for the participants are described in the Participants section of the main study. All participants provided informed consent to participate in the study which was approved by the School of Psychology Ethics Committee for Cardiff University.

Design

Participants engaged in AVE at both theta (5.5 Hz) and low beta (14 Hz) frequencies in a within-subjects experimental design. The order of delivery of AVE frequency condition was counterbalanced across participants and they were not informed which frequency they were being stimulated at in either condition.

Electrophysiological recordings

Participants were prepared for electroencephalography (EEG) recording using a BioSemi Active Two system (BioSemi, Amsterdam, The Netherlands). Thirty-two silver-chloride, pin-type active electrodes were mounted in a fitted elastic cap according to the standard 10-20 system and in a standard memory montage. Conductive gel was used at electrode sites to facilitate a connection between the electrode and the participant's scalp. Electrooculography (EOG) recordings were taken using four flat-type active electrodes placed at the left and the right outer canthus sites (LOC and ROC, respectively) to detect horizontal eye-movements (HEOG), and at the infraorbital and supraorbital sites (1cm below and above the eye, respectively) to detect vertical eye-movements (VEOG). An additional flat-type active electrode was placed on each the left and the right mastoid bone, to which the data were re-referenced both during the online EEG-NF protocol and for offline EEG data analysis. The offset for each active electrode was kept between +/-40 mV to ensure sufficient electrode connection and signal-to-noise ratio. The raw EEG signal was recorded for the full duration of each 15-minute AVE session and stored for offline analysis (see 'Offline EEG-NF analysis'). Participants were instructed to sit comfortably and remain still during all EEG recordings.

AVE procedure

The duration of AVE for each repeated measures condition (i.e. both theta 5.5 Hz and low beta 14 Hz) was 15 minutes. Participants rested for a few minutes between conditions whilst the experimenter adjusted the settings on the AVE application. The AVE procedure was otherwise identical to the main experiment (see '3.3 AVE procedure').

Offline EEG analysis

The raw signal for the 32 EEG data channels was preprocessed using EEGLAB (Delorme & Makeig, 2004) toolbox in MATLAB. The data were downsampled to 1000 Hz and a 55 Hz Blackman windowed sinc FIR filter applied, with transition bandwidth 0.2 Hz and a length of 27,500 points. Next, the data were segmented into 2 second consecutive, non-overlapping epochs, and each epoch de-meaned. The data were then re-referenced to the average of the left and right mastoid reference electrodes, and manually inspected for bad channels. Independent component analysis (ICA) was performed on the data to detect and remove ocular and channel artifacts, which were identified using SASICA plugin for EEGLAB (Chaumon et al., 2015) and visually inspected for validity. The power spectra were calculated using Bartlett's method which involves averaging the non-overlapping periodograms given by each epoch. FFT (Fast Fourier Transform) was used to calculate the spectral power for each epoch between 1 - 20 Hz, in 0.5 Hz steps, which was then normalised using a log transform and averaged over epochs.

Results

AVE absolute power spectra

The EEG data show a clear entrainment effect on neural oscillatory activity for the pilot sample. Strong peaks are depicted at the target frequency for each condition i.e. 5.5 Hz for the theta condition and 14 Hz for the low beta condition. Associated harmonics are visible in the theta condition at 11 Hz, 16.5 Hz and 22 Hz. Both conditions display strong peaks in the delta band at approximately 1 Hz, and the alpha band at approximately 10-11 Hz which is likely attributed to participants closing their eyes during the entrainment.

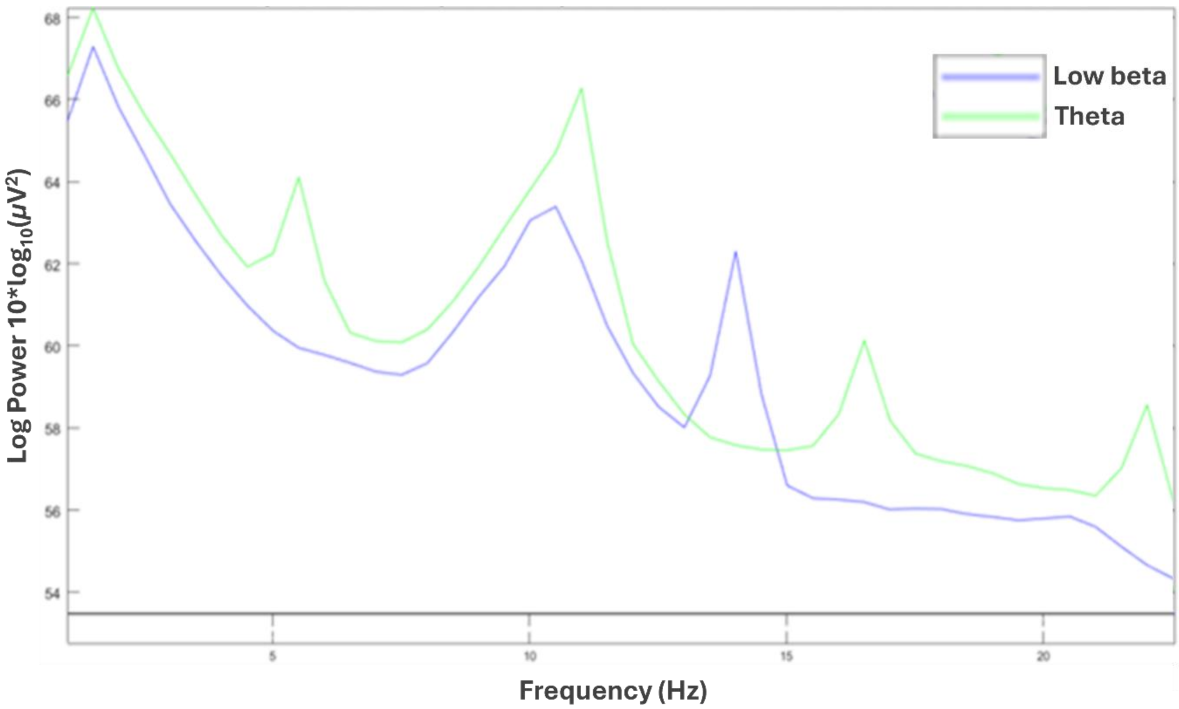

Figure 21. Graphical representation of the absolute power spectra based on the average power calculated across all participants for both the 5.5 Hz (theta) and 14 Hz (beta) groups.