Effects of Alpha/Theta Neurofeedback Training for Women with Moderate to Severe Trait Anxiety:

A Randomized, Single-Blind, Clinical Trial

Dissertation

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vorgelegt von
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Declaration

I hereby declare that I have produced the work entitled: "Effects of Alpha/Theta Neurofeedback Training for Women with Moderate to Severe Trait Anxiety: A Randomized, Single-Blind, Clinical Trial", submitted for the award of a doctorate, on my own (without external help), have used only the sources and aids indicated and have marked passages included from other works, as such, whether verbatim or in content. I swear upon oath that these statements are true and that I have not concealed anything. I am aware that making a false declaration under oath is punishable by a term of imprisonment of up to three years or by a fine.

Signed,

Tübingen, 14.6.2018 _____

Date

Bettina Viereck

Abstract

Introduction: Alpha/Theta neurofeedback treatment (A/T NFT) has been administered to adults with anxiety disorders since the late 1960s, yet the efficacy of this treatment remains unclear. The present, single-blind study, for the first time, uses an active placebo NFT control group to test the A/T NFT protocol for trait anxiety on prodromal and clinical adult female participants. The effects this treatment has on activation and arousal states, self-perceived anxiety levels, neural oscillations, and other parameters were assessed.

Methods: Twenty-seven women ranging in age from 19 through 69 who had scored higher than the 66th percentile in the STAI trait anxiety sub-scale (75% of whom had previously been diagnosed with an anxiety disorder) were randomly assigned to either the experimental (EG) or the control group (CG). The EG (n = 14) received ten sessions of A/T NFT in which alpha and theta EEG amplitudes were uptrained at Pz. The CG (n = 13) received ten sessions of active placebo NFT at Pz. During successive sessions beta- (15–19 Hz) and high beta amplitudes (20- 24 Hz) were uptrained or downtrained. Growth curve modeling (GCM) and traditional 2x5 repeated measures ANOVA were performed on the NFT sessions data to model individual and average group learning curves. Cognitive variables, such as treatment outcome expectancy, personal attribution styles, use, types, and efficacy of cognitive strategies in NFT, and correlations between NFT learning performance, time of day the NFT sessions were held, and a participant's best or worst time to learn, were also investigated.

Results: The analysis of individual learning curves, GCM, and ANOVA all confirmed that the majority of participants of the EG up-regulated absolute and relative A+T amplitudes within a NFT session, but so did the participants of the CG. However, a non-significant trend for the EG to have steeper learning curves was observed. Participants of both the EG and the CG felt significantly more *deactivated* by the end of a NFT session and reduced their self-perceived

anxiety on all anxiety measures (STAI, BAI, GAD-7) by the end of the NFT trial. Although a trend could be observed that the EG reduced anxiety scores more than the CG, these differences did not rise to statistical significance. Lastly, no significant changes in the pre-post trial QEEG were found, although a trend of higher combined relative A+T power at the end of the trial was observed in the EG. In the EG the *use of mental strategies* was correlated with lower T/A ratio difference scores between the beginning and the end of the NFT trial but not with increased relative and absolute T+A amplitudes. The *Time-of-day participants prefer or avoid learning* did not correlate significantly with alpha or theta NFT amplitudes, i.e., NFT sessions being held during sub-optimal times of day were not associated with poorer learning performance.

Conclusions: For both EG and CG absolute and relative T+A amplitudes increased *within sessions* and absolute and relative alpha increased *across sessions* although the CG protocol had not included an uptraining of alpha or theta amplitudes, nor low beta amplitudes (below 15 Hz) which may have represented upper alpha peak frequency in some of the younger participants. Thus, upregulation of beta and upper beta in NFT may be associated with alpha frequency uptraining due to functional coupling of alpha and beta EEG frequencies or it may be due to placebo and other non-specific effects such as EEG frequency drifts, alpha's idling mode and inhibitory role during task performance, or perhaps simply that some frequency bands (alpha) are more susceptible to change and easier to train. Especially the inhibition of flanking bands in the NFT protocol, i.e., beta bands in A+T training, to prevent frequency drifts, will be necessary along with detailed GCM modeling of all frequency bands to see if and how the bands change over time and how those processes relate to NFT learning curves.

Keywords: neurofeedback, EEG biofeedback, quantitative EEG, trait / state anxiety, anxiety disorders, active placebo control, alpha/theta protocol, growth curve modeling.

Zusammenfassung

Einleitung: Alpha/Theta-Neurofeedback-Behandlung (A/T-NFT) wird seit Ende der 1960er Jahre zur Behandlung Angststörungen bei Erwachsenen verwendet, doch es ist nicht klar, ob diese Therapie wirksam ist. In der vorliegenden Single-Blind-Studie wird zum ersten Mal eine aktive Plazebo-Kontrollgruppe verwendet, um das A/T-NFT-Protokoll an Frauen mit prodromalen und klinischen Trait-Angst zu testen. Die Auswirkungen dieser Behandlung auf Aktivierung, das empfundene Angstniveau, neuronale Oszillationen und andere Faktoren wurden erhoben.

Methoden: Siebenundzwanzig Frauen im Alter von 19 bis 69, die höher als 66 Prozent im STAI-Trait-Angst-Test abgeschnitten hatten (75% waren zuvor mit einer Angststörung diagnostiziert worden), wurden zufällig auf Experimental- (EG) oder Kontrollgruppe (KG) verteilt. Die EG (n = 14) erhielt zehn Sitzungen A/T NFT, in denen Alpha- und Theta-Amplituden an der Pz-Elektrode verstärkt wurden. Die KG (n = 13) bekam zehn Sitzungen aktives Placebo-Training an der Pz-Elektrode, in denen in aufeinanderfolgenden NFT-Sitzungen jeweils Beta- (15–19 Hz) und High-Beta-Amplituden (20- 24 Hz) verstärkt oder vermindert wurden. Wachstumskurvenmodellierung (WKM) und traditionelle 2x5 ANOVA mit wiederholter Messung wurden mit den Daten der NFT-Sitzungen durchgeführt, um individuelle und durchschnittliche Gruppenlernkurven zu modellieren. Kognitive Variablen wie Behandlungerwartung, persönliche Attributionsstile, Verwendung, Typen und Wirksamkeit kognitiver Strategien in der NFT und Korrelationen zwischen der NFT-Lernleistung, Tageszeit der NFT-Sitzungen und bester oder schlechtester Lernzeit der Probandinnen wurden auch untersucht.

Ergebnisse: Die Analysen der individuellen Lernkurven, WKM und ANOVA bestätigten, dass nicht nur die Mehrheit der Teilnehmerinnen der EG gelernt hatten, die absoluten und relativen A + T-Amplituden innerhalb einer NFT-Sitzung hochzuregulieren, sondern

auch die Probandinnen der KG. Jedoch hatte die EG nicht-signifikante tendenziell steilere Lernkurven. Die Teilnehmerinnen, sowohl der EG als auch der CG, fühlten sich am Ende einer NFT-Sitzung signifikant mehr deaktiviert und hatten am Ende der Studie signifikant verringerte Angstwerte in allen Angstfragebögen (STAI, BAI, GAD-7). Obwohl die EG Angstwerte tendenziell stärker reduzierten als die CG, waren diese Unterschiede nicht statistisch signifikant. Auch wurden keine signifikanten Veränderungen im EEG zwischen Anfang und Ende der Studie gefunden, obwohl ein Trend zu höherer kombinierter relativer A+T-Amplituden am Ende der Studie in der EG beobachtet wurde. In der EG waren die *Verwendung mentaler Strategien* mit niedrigeren T/A-Differenzwerten zwischen Anfang und Ende der NFT-Studie korreliert, jedoch nicht mit erhöhten relativen und absoluten T+A-Amplituden. Außerdem waren die *Tageszeiten, die Probandinnen zum Lernen bevorzugen oder vermeiden*, nicht signifikant mit Alpha- oder Theta-NFT-Amplituden assoziiert, d.h. NFT-Sitzungen, die während suboptimaler Tageszeiten stattfanden, waren nicht mit einer schlechteren Lernleistung verbunden.

Schlussfolgerungen: Sowohl für die EG, als auch für die KG, stiegen die absoluten und relativen T+A-Amplituden *innerhalb* der Sitzungen an und das absolute und relative Alpha nahm *über die Sitzungen hinweg* zu, obwohl das KG-Protokoll keine Verstärkung der Alpha- und Theta-Amplituden beinhaltete. Auch wurden Low-Beta-Amplituden (unter 15 Hz) nicht verstärkt, die bei den jüngeren Teilnehmerinnen die obere Alpha-Peak-Frequenz repräsentiert haben könnte. Daher kann die Hochregulation von Beta- und High-Beta-Amplituden in NFT mit einer Alpha-Frequenzhochregulierung aufgrund funktioneller Kopplung von Alpha- und Betafrequenzen assoziiert sein oder aber die Folge eines Plazebo- und anderen unspezifischen Effekten, wie z.B. EEG-Frequenzdrift, Alpha-Leerlaufmodus, Alphas hemmende Rolle während Aufgabenbewältigungen, oder vielleicht einfach, dass einige Frequenzbänder (Alpha) anfälliger für Veränderungen und einfacher zu trainieren sind. Besonders die Hemmung flankierender

Frequenzbänder im NFT-Protokoll, d.h. Betabänder im A+T-Training, um Frequenzdrift zu verhindern, werden zusammen mit detaillierten WKM-Modellen aller Frequenzbänder benötigt, um herauszufinden, ob und wie diese sich mit voranschreitenden Sitzungen verändern und wie diese Prozesse mit NFT Lernkurven zusammenhängen.

Schlüsselwörter: Neurofeedback, EEG-Biofeedback, quantitatives EEG, Trait / State Angst, Angststörungen, aktive Placebo-Kontrolle, Alpha/Theta-Protokoll, Wachstumskurven-modellierung.

This dissertation is dedicated to my parents,

Irmtraud (1933 –) and Peter (1934 – 1976) Viereck.

Metamorphosis

Referent Atlantis, metaphor. Metamorphosis.

Shards and lavender footpaths in sea salted winds
spiraling utterance

chambered nautilus pulling
its buoyant, gas-filled shell upright
on top of the coral sea

swims in those easy lights, turns, faces greater
blacknesses beneath possibilities of absence – and

gradually descends with the day into that unknowable,
its inside mother of pearl brighter than ever

by Donna M. Fleischer

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My biggest thanks, though, go to Donna Fleischer, my spouse. She put up with several years of my 70-hour work weeks, 'picked up the slack' at home, offered support and generosity when I needed it most, proofread multiple versions of this dissertation, and granted permission to include her poem "Metamorphosis" in this manuscript. Donna, I couldn't have done it without you!

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List of Abbreviations

A %	Relative Alpha Amplitude
ACE	Adverse Childhood Event
AD	Anxiety Disorders
AD-ACL	Thayer's Activity-Deactivity Adjective Checklist
ADHD	Attention Deficit Hyperactivity Disorder
ANI	Applied Neuroscience, Inc.: A Proprietary Normative QEEG Database
ANS	Autonomic Nervous System
APF	Alpha Peak Frequency
A/T	Alpha/Theta NFT (Experimental Group)
B u/d	Alternate Beta Up- and Down-NFT (Control Treatment)
BAI	Beck Anxiety Inventory
BDI-II	Beck Depression Inventory, Version II
CBT	Cognitive Behavioral Therapy
CEN	Central Executive Network
CO	Control NFT Treatment: Beta Up- and Down-Training
ACC dACC rACC	Anterior Cingulate Cortex, Dorsal ACC, Rostral ACC
ACE	Adverse Childhood Event
DMN	Default Mode Network
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorder, fourth edition, Text Revision (2000)
DSM-5	Diagnostic and Statistical Manual of Mental Disorder, fifth edition (2013)
EBT	Empirically-Based Treatment
EEG	Quantitative Electroencephalography
ESEMed	European Study of the Epidemiology of Mental Disorders (2004)
ERD	Event-Related Desynchronization
ERS	Event-Related Synchronization
fMRI	Functional Magnetic Resonance Imaging; rt-fMRI: real-time fMRI
Fm-theta	Frontal-Midline Theta
GAD	Generalized Anxiety Disorder
GAD-7	General Anxiety Disorder 7-Item Inventory
H	Research Hypothesis (e.g., H 1 = hypothesis 1)
HEG	Hemoencephalography

HRV	Heart Rate Variability
IAF	Individualized Alpha Frequency
ICD-10	International Statistical Classification of Diseases and Related Health Problems; 10th revision (1992); in the U.S. currently: ICD-10-CM (2010)
LTP	Long-Term Potentiation
LE	Linked Ears Reference in EEG and NFT
LENS	Low Energy Neurofeedback System
Mini-Q	Mini-Quantitative Electroencephalography, Proprietary Program of *BrainMaster, Inc.* Recording of the10-20 EEG Sites (five times four channels)
NCS-R	U. S. National Comorbity Survey-Replication (2004)
NFT	Neurofeedback Training
OCD	Obsessive Compulsive Disorder
PFC	Prefrontal Cortex
mPFC	Medial PFC
dlPFC	Dorsolateral PFC
vlPFC	Ventrolateral PFC
PD	Panic Disorder
PSD	Power Spectrum Density
PTSD	Post-Traumatic Stress Disorder
PHQ-9	Patient Health Questionnaire-9 Depression Scale
QEEG	Quantitative Electroencephalography
RCT	Randomized Controlled Trial
SAD	Social Anxiety Disorder
SETS	Stanford Expectation of Treatment Scale
SD	Standard Deviation
SN	Salience Network
SNS	Sympathetic Nervous System
SSRI	Selective Serotonin Reuptake Inhibitors
STAI	Spielberger State-Trait Anxiety Inventory
STAI-S	20-item, STAI Sub-scale for State Anxiety
STAI-T	20-item, STAI Sub-scale for Trait Anxiety
T %	Relative Theta Amplitude
T+A %	Summation of Theta Plus Relative Alpha Amplitudes
WM	Working Memory

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1. Introduction

Anxiety disorders (AD) rank as the most common of mental health disorders in the United States, have a high prevalence globally, and are one of the leading causes of disability in western countries (Craske et al., 2017; Wittchen et al., 2010). They tend to be under-recognized, particularly in primary care settings, and under-treated (Sartorius, Üstün, Lecrubier, & Wittchen, 1996; Vermani, Marcus, & Katzman, 2011). In the European Study of the Epidemiology of Mental Disorders (ESEMed; Alonso et al., 2004) only 21% of those interviewed who had an anxiety disorder sought medical help for their disorder. Anxiety disorders are often chronic, in part due to dysregulated neurocircuits of stress response (Teicher, Samson, Anderson, & Ohashi, 2016), fear avoidance, lack of affordable access to treatment, and / or associated stigma (Andrade et al., 2014). Other psychiatric disorders, such as depression, substance use disorder, and schizophrenia often include a significant anxiety component or are comorbid with AD. Furthermore, between 50-67% of patients with AD show a clinically significant improvement after the most commonly used treatments of Cognitive Behavioral Therapy (CBT) and / or medication (SSRIs) are applied (Taylor, Abromowitz, & McKay, 2012). Hence, it is important to find efficacious, non-invasive, evidence-based treatments (EBTs) with little or no side effects to lower anxiety levels for clinical and sub-clinical populations, especially for women, who are twice as likely to experience an anxiety disorder in their lifetime (Bandelow & Michaelis, 2015).

Extraordinary advances in the field of neuroscience in the past ten years have led to a shift toward a new paradigm. No longer are mental disorders seen only as disorders of abnormal neurotransmitters, genetic vulnerabilities, defense mechanisms, and learned cognitive and behavioral responses. Rather, medical and psychological mechanisms are unified in a model of the nervous system as a neuronal network organized into nodes, hubs, and networks that can be partially mapped onto anatomical and functional parts of the brain, or what Kirk (2015) calls a

paradigm shift from a neurochemical to a neuroelectrical model. Neurofeedback treatment (NFT) is uniquely suited within this new model to potentially effect long-term changes in neurocircuits of the brain.

NFT has been used since the late 1960s for a variety of conditions, including anxiety disorders. The efficacy of NFT for some conditions, such as Attention-Deficit / Hyperactivity Disorder (ADHD), has been well-researched (Arns, de Ridder, Strehl, Breteler, & Coenen, 2009; Cortese, et al., 2016; Monastra, Lynn, & Linden, 2005). However, not only have there been only few well-designed research studies on the efficacy of NFT for anxiety conditions, the results of these studies have been mixed, and the U.S. National Institutes of Health's National Center for Complementary and Integrative Health (NCCIH) at this time does not endorse NFT as an efficacious treatment for anxiety problems. A real need exists for rigorously controlled clinical trials with clinical samples for the NFT treatment of AD. This dissertation is an attempt to bridge that gap.

1. 1 Trait Anxiety and Anxiety Disorders

1.1.1 Definition of trait anxiety and anxiety disorders.

Anxiety per se is a normal and evolutionarily adaptive emotion that all humans experience from time to time in response to dangerous events. It alerts a person to a perceived, ambiguous threat via diffuse nervousness and unease which prepare the individual for a potentially adverse future situation. It is accompanied by autonomic nervous system arousal, variously presenting as perspiration, tachycardia, syncope, tremors, upset stomach, and restlessness (Nebel-Schwalm & Davis, 2013; Saddock, Saddock, & Ruiz, 2015). However, if anxiety persists over an extended period—over six months—according to the DSM-5, it is disproportionate to the threat presented and is perceived as "excessive and unreasonable" (ICD-10) by the individual and a diagnosis of AD is likely.

The concepts of state and trait anxiety developed by Spielberger in 1961 were updated in 2015. A personality trait is defined as a "disposition to behave consistently in a particular way" across situations and time (Feist & Feist, 2008). Since the mid-1990s a broad consensus exists that personality can be hypothesized as a hierarchical framework of personality traits. The "Big Five" traits of neuroticism, extraversion, conscientiousness, agreeableness, and openness are higher order traits and a larger number of lower order traits (Digman, 1997) include trait anxiety. Individuals with lower order traits such as trait anxiety, rumination, self-criticism, and negative evaluation, are particularly vulnerable to certain anxiety and depressive disorders (Mahaffey, Watson, Clark, & Kotov, 2016).

Spielberger defines trait anxiety (T-Anxiety) and its relationship to state anxiety (S-Anxiety) as:

> "… relatively stable individual differences in anxiety-proneness, that is, to differences between people in the tendency to perceive stressful situation [sic] as dangerous or threatening and to respond to such situations with elevations in the intensity of their state anxiety (S-Anxiety) reactions. T-Anxiety may also reflect individual differences in the frequency and intensity with which anxiety have been manifested in the past, and in the probability that S-Anxiety will be experienced in the future. The stronger the anxiety trait, the more probable that the individual will experience more intense elevations in S-Anxiety in a threatening situation" (Spielberger, 2015, p. 5).

However, the concept of trait anxiety is often imprecisely defined and operationalized in clinical psychology and neuroscience research, especially in relation to trait fear, which is often used interchangeably with trait anxiety. Sylvers, Lilienfeld, and LaPrairie (2011) characterize trait anxiety as the disposition to react with "persistent hyper-vigilance and prolonged hyper-arousal" (p.128), apprehension, and rumination to ambiguous situations. The threat potential of a

situation tends to be overestimated due in large part to a hypersensitive appraisal circuit. In contrast, trait fear is characterized by avoidance responses such as flight, fight or freeze. Craske et al. (2009) delineate the difference between anxiety and fear, aligning themselves with Barlow's (2004) definition by which fear is defined as an alarm response to a real or perceived concrete threat whereas anxiety "is a future-oriented mood state associated with preparation for possible, upcoming negative events" (Craske, p. 1067). However, they do admit that there exists an overlap of symptoms between anxiety and fear.

Clinically, anxiety disorders are most commonly categorized according to the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-5, 2013) as mental disorders in which fear and anxiety deemed as persistent and out of proportion to the norm are caused by a variety of different situations or objects, depending on the type of anxiety disorder a person has. As anxiety is very likely to be comorbid, a person often has several anxiety disorders that developed during childhood, and if not treated early, remain throughout adulthood. The DSM-5 clearly distinguishes between fear and anxiety:

> *"Fear* is the emotional response to real or perceived imminent threat, whereas *anxiety* is anticipation of future threat. Obviously, these two states overlap, but they also differ, with fear more often associated with surges of autonomic arousal necessary for fight or flight, thoughts of immediate danger, and escape behaviors, and anxiety more often associated with muscle tension and vigilance in preparation for future danger and cautious or avoidant behaviors" (DSM-5, American Psychiatric Association, 2013, p. 189).

If the attribution of excessively anxious or fearful thinking and behaviors are consequences of medication or other substances, or could be better explained by another disorder, such as Alzheimer Disease, AD will not be diagnosed. The DSM-5 (2013) defines the

following disorders under the category of anxiety disorders: *separation anxiety disorder, selective mutism, special phobia, social anxiety disorder (SAD), panic disorder (PD), agoraphobia, generalized anxiety disorder (GAD), substance / medication-induced anxiety disorder, anxiety disorder due to another medical condition, other specified anxiety disorder,* and *unspecified anxiety disorder*. In contrast to the fourth edition of the DSM (DSM-IV-TR, 2000), in use for clinical research and practice up to late 2013, the DSM-5 no longer classifies *obsessive compulsive disorder* (OCD), *post-traumatic stress disorder* (PTSD), or *acute stress disorders* as AD, but rather newly created categories of *obsessive-compulsive and related disorders* and *trauma- and stressor-related disorders*, respectively. Furthermore, *separation anxiety disorder* and *selective mutism* are moved from the category of *disorders usually first diagnosed in infancy, childhood, or adolescence* to the category of anxiety disorders in the DSM-5. Due to this recent DSM re-classification some of the conditions for which NFT was studied as potential evidence-based treatment (EBT) are no longer classified as AD. Nevertheless, these are evaluated in the literature review of this dissertation because there is a large anxiety component present, especially in PTSD and OCD, that is extremely relevant in addressing the potential efficacy of NFT treatment to alleviate the anxiety-related symptoms of these disorders.

As 75% of participants in this clinical trial had a self-reported medical diagnosis of AD, (the majority of whom had a GAD diagnosis, followed by anxiety disorder diagnosed but not specified / remembered, SAD, and specific phobia), the cardinal DSM-5 (2013) diagnostic distinguishing characteristics for AD of adulthood are briefly described below. All AD include the presence of persistent symptoms for six months or more (but one month for PD) and cause the individual "clinically significant distress or impairment" (pp.189). The criterion that the AD cannot be explained better by another medical condition must also be present:

1. *GAD:* Excessive anxiety and worry in multiple areas (such as work, school and social

environment) that are difficult to control and at least three out of six symptoms that are present most days: restlessness, easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension, and sleep disturbance;

2. *SAD (formerly social phobia):* anxiety and / or avoidance of social situations, especially those that involve judgment and scrutiny by others, such as speaking and performing; fear of embarrassing oneself, being humiliated or rejected;
3. *Specific phobias*: excessive fear or anxiety and avoidance of specific objects or situations, such as specific animals, natural environment, blood-injection-injury-related, or situational;
4. *Agoraphobia*: excessive anxiety and / or avoidance of places or situations in which "escape might be difficult, or help might not be available in the event of …. incapacitating or embarrassing symptoms" (p. 218), such as panic or falling; or
5. *PD:* recurring unexpected panic attacks, i.e., "an abrupt surge of intense fear or intense discomfort" (pp. 208) which reach their peak within minutes and involve at least four of the following 13 symptoms: heart palpitations, perspiration, trembling or shaking, sensations of shortness of breath, feeling of choking, chest pain, nausea or abdominal distress, feeling dizzy, chills or heat sensations, paresthesias, derealization, and depersonalization.

Trait anxiety is a construct stemming from the fields of personality and differential psychology whereas the constructs of anxiety disorders are classifications from the fields of psychiatry and clinical psychology. Consequently, different frameworks and interests inform the constructs of trait anxiety and anxiety disorders and while there is a significant correlation between high trait anxiety and an anxiety disorder they are not synonymous. However, for the purposes of this study, trait anxiety as a selection criterion is the more useful concept for the

following reasons:

1. The number of individuals with moderate to high trait anxiety is likely much higher than those diagnosed with an anxiety disorder. This includes possible participants who have a less severe form of anxiety symptoms, such as people with a prodromal anxiety disorder as well as those who have an anxious personality trait and are less likely to have comorbid non-AD-related mental disorders, which is an exclusionary criterion for this study;
2. Having moderate to high trait anxiety is not as stigmatizing for people to admit than an actual mental disorder diagnosis. Consequently, people might be less hesitant to volunteer for a NFT trial; and
3. Using a DSM-IV-TR or DSM-5 definition of anxiety disorder, would likely require a further breakdown for which of the five major anxiety disorders NFT will be evaluated in the clinical trial, to avoid having confounding variables of different, dissimilar anxiety disorders in the study. One could include the difference in anxiety disorder in the statistical analysis as a variable. In order for the statistical analysis to be meaningful, all three groups would have to include a much larger number of participants and preferably a similar number of participants with each anxiety disorder, which would be beyond the scope of this study.

1.1.2 Epidemiology of anxiety disorders.

It is estimated that the lifetime prevalence of anxiety disorders in the United States is 33.7% and in Europe 14.5% according to the latest available large-scale studies, the National Comorbidity Survey in the U.S. (NCS-R; Kessler et al., 2005) and the European Study of the Epidemiology of Mental Disorders (ESEMed; Alonso et al., 2004), respectively. The Mental Health Surveillance Study of the Substance Abuse and Mental Health Services Administration

(SAMHSA, U.S.) found the annual prevalence for that anxiety disorder in 5.7% of the U.S. population (Karg et al., 2015), which makes it the third largest mental disorder following substance use disorder (7.8%) and mood disorders (7.4%). However, looking at the rates for adults ranging in age from 18 to 64, the annual prevalence is much higher at 24.9% in the NCS-R study since children are often not diagnosed with most AD, except separation anxiety disorder and selective mutism, until early adolescence and AD decrease in older age. With the exclusion of PTSD and OCD from the AD classification in the DSM-5 these percentages will go down in future studies.

In the latest available large epidemiological studies, ESEMed (Alonso et al., 2004) and NCS-R (Kessler et al, 2005) the lifetime prevalence female to male ratio is 1.5 and 1.8, respectively, for all anxiety disorders and are the highest ratio for specific phobias. Specific phobias are 1.8 and 2.1 times more likely in females than in males.

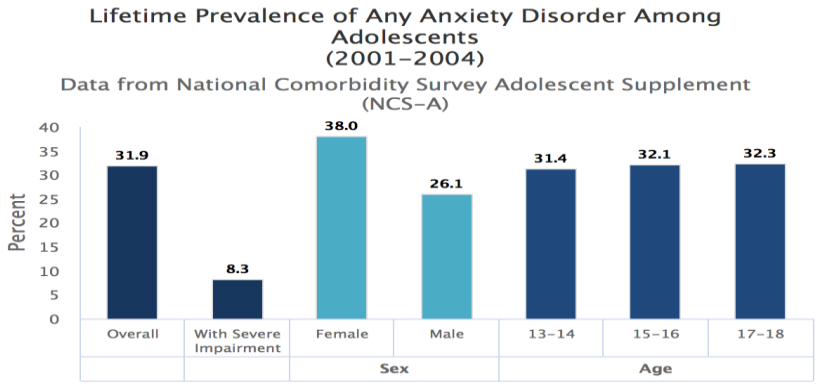

Figure 1.1: Demographics of life time prevalence of AD by age group.
SOURCE: https://www.nimh.nih.gov/health/statistics/any-anxiety-disorder.shtml

According to Bandelow and Michaelis (2015), who compared data from the latest and largest epidemiological studies (NCS, NCS-R, ESEMed, and ECA), the median onset for an anxiety disorder is age 11, but is vastly dependent on the kind of anxiety disorder: Separation anxiety and specific phobias are on average diagnosed at age 7 and social anxiety disorder (SAD) at age 13. The median onset of the other DSM-5 categories for anxiety disorders that

begin in adulthood, are agoraphobia at age 20, panic disorder (PD) at age 24, and Generalized Anxiety Disorder (GAD) at age 31.

Furthermore, moderate to large cross-cultural differences in prevalence rates of anxiety disorders were found by Wittchen and Jacobi (2005) who compared 27 studies from 16 European countries with highly heterogeneous rates. For instance, annual prevalence of GAD ranged between 0.2% and 4.3%, depending on the country and could only be partially explained by different sample collections and methodology.

Moreover, there is a high comorbidity among different AD and between AD and other mental disorders, particularly between SAD and agoraphobia (r = 0.68), PD and agoraphobia (r = 0.64), GAD and SAD (r = .55), and GAD and major depression (r = 0.62), GAD and dysthymia (r = .55) (Bandelow & Michaels, 2015a). Kessler et al. (2005) found that 27% of the respondents from the NCS-R had three or more of the DSM-IV-TR classified mental disorders. Data from large epidemiological studies and long-term longitudinal studies indicate that AD "are quite persistent throughout the life course ... and [the persistence] is usually due to a recurrent-intermittent course that often features waxing and waning of episodes of different comorbid anxiety disorders" (Kessler, Ruscio, Shear, & Wittchen, 2009, pp. 25-26).

1.1.3 Etiology.

Neurofeedback is based on the principles of learning theory (see section 1.2.1). Consequently, it is important to look at a comprehensive learning theory model that can be used in the explanation of the etiology of AD. To date, Mineka and Zinbarg (2006) have proposed the most elaborate learning theory model for anxiety disorders. They postulate *a five-domains model* with two domains of vulnerability—one that is genetic or temperament-based and the other one based on previous learning experiences (such as a person's history with mastery and control over one's circumstances)—as well as three contextual domains: (1) direct or vicarious conditioning,

(2) properties of the unconditioned stimulus (*US*), and (3) perceptions of the predictability and controllability of a learning situation. In this study, the personality trait of perceived control over anxiety-related events is measured with the Rotter (1966) Locus of Control scale (LOC) and the Stanford Expectancy of Treatment Scale (SETS). One strength of Mineka and Zinbarg's theory is that it incorporates post-conditioning factors that influence learning, such as re-evaluation of the *US* and possible inflation of the *US*, as well as the presence of excitatory or inhibitory conditioned stimuli. For instance, they describe the occurrence of an *inflation effect* that can occur when a person initially experiences a minor trauma that does not cause a phobia (e.g., being bitten by a dog), yet later a more severe trauma (e.g., traumatic car accident) which does not necessarily relate to the previous minor trauma may lead to a dog phobia (Mineka & Zinbarg, 2006).

Barlow's *triple vulnerability model* (Barlow, 2000) is a more general model of the etiology of mental disorders that combines factors from the bio-psycho-social sphere, including genetics and physiological, personality, developmental, and cognitive psychology. It consists of three major vulnerabilities that contribute in varying degrees to the etiology of AD:

(1) a general biological vulnerability that includes a genetically-based disposition (high in personality trait of neuroticism) and reactivity to negative emotions;
(2) a general psychological vulnerability shaped by early childhood adverse events and parenting styles, such as overprotective parents, for some anxiety disorders, and may lead to constantly elevated arousal of the sympathetic nervous system (SNS) and an experience of life events as unpredictable and uncontrollable; and
(3) a disorder-specific psychological vulnerability linked to learning experiences, especially of parents and caretakers modeling anxious or fearful behavior incommensurate with the actual

danger of the situation or object and for the child receiving disproportionate attention to experienced somatic sensations.

As this study is concerned primarily with the EEG-based NFT to improve trait anxiety or clinical anxiety symptoms, I will focus my review of current research on those findings that relate directly to brain structure and functionality, namely, neural circuits, neuroendocrinology, structural and functional abnormality of specific brain structures, and autonomic nervous system (ANS)-regulated physiological processes influenced by A/T NFT. These outcomes may be used in the discussion section to further elucidate this study's findings.

The AD, a heterogeneous group of disorders, have shown distinct neural circuits in recent studies, dependent on whether the disorder is more fear- or anxiety-based. Duval, Javanbakht, and Liberzon (2015) thoroughly review recent randomized controlled trials (RCTs). They classify PD, SAD, and phobias as primarily fear-based disorders, and GAD and PTSD as primarily anxiety-based (see section 1.1.1). Lueken et al. (2016) analyzed 60 out of 4,787 reviewed RCTs, 27 of which included genetic markers, 17 neuroimaging, and 16 markers associated with autonomic functioning. This review was to identify biomarkers that could predict risk for anxiety disorder and differential clinical treatment outcome for AD. Both meta-analyses took publication bias into consideration when analyzing the effect size for biomarkers across studies. In both, fear- and anxiety-based circuits, the thalamus receives and integrates input from the primary sensory cortices and sends output to the amygdala, the anterior cingulate cortex (ACC), and the hippocampus. Most functional imaging studies show that, in general, amygdala, hippocampus, and dorsal anterior cingulate cortex (dACC) appear to be hyper-activated, whereas the sub-genual and rostral ACC (sg and rACC) and the mPFC are hypo-activated in most AD. Connectivity across neurocircuits, between the regions responsible for emotion processing, such as the amygdala and insula, and regions of emotion modulation, such as the mPFC and the rostral

ACC (rACC), appear to be decreased. Hypo-activation of the sgACC and rACC and the mPFC may be translated as a possible failure to adequately inhibit the threat response in AD (Duval et al., 2015). The evidence on this concept is mixed at best. A hyper-activated hypothalamic-pituitary adrenal axis (HPA) can be observed in AD in most studies, but particularly in PTSD, which leads to a reduced plasma concentration of cortisol among other effects coupled with the pituitary gland being hypersensitive to glucocorticoids, such as cortisol.

Williams (2016) proposed an interesting taxonomy regarding anxiety and depressive disorders after evaluating a multitude of experimental studies on neural circuit dysfunctions and progress in the *Human Connectome Project* (http://www.humanconnectomeproject.org/). She then related the circuit dysfunctions with typical symptoms for anxiety (and depressive) disorders and suggested specific types of therapeutic interventions depending on which brain circuits are most affected, an *individualized precision-psychiatry*. For instance, she suggests that anxious avoidance was associated primarily with circuit abnormalities of the salience network (SN), specifically with the hypoconnectivity between left and right anterior insula and the sublenticular extended amygdala, and the hyperactivation of the amPFC. These SN network abnormalities according to recent research reviewed by Williams respond particularly well to Deep Brain Stimulation and Selective Serotonin Reuptake Inhibitors (SSRIs). Hyperactivation of the default mode network (DMN) associated with rumination common in GAD and depressive disorders on the other hand, may respond better to transcranial magnetic stimulation, mindfulness and self-context therapies. This dissertation proposes that NFT may be another treatment alternative used to target and normalize the afore-mentioned areas in the SN and DMN.

The review of possible physiological markers that might predict AD proved especially interesting; the autonomic regulation of the heart rate by the vagus nerve and its variability (HRV), beat to beat changes in the heart rhythm, has been extensively researched and led to the *Polyvagal Theory* by Porges (1995, 2009) and the *neurovisceral model of cardiac and emotion regulation* by Friedman (2007). Porges postulated that a cardiopulmonary oscillator is controlled by the dorsal motor nucleus of the vagus nerve in the medulla oblongata and and proposed "a neural process that evaluates risk and modulates vagal output via higher brain structures" (Porges, 2007, p. 6); primary emotions directly interact with autonomic functions when the physiological state is fed back to brain structures via afferent nerves in reaction to environmental stimuli. A reduced HRV and higher heart rate were associated with less flexibility and adaptability to environmental stimuli (Lyonfields, Borkovec, & Thayer, 1995). Lueken et al. (2017), for instance, analyzed several RCTs and found that patients with AD who had high heart rates and low HRV, had better treatment outcomes after CBT psychotherapy compared to psychopharmaceutical treatment or placebo.

Lastly, there is accumulating evidence that the number and intensity of adverse childhood events (ACEs), as well as the time of the exposure to ACEs during sensitive periods of brain development in areas associated with the anxiety and fear circuits can predict the development, severity, and treatment response to various pharmacological, psychotherapeutic, and other adjunctive therapies, such as NFT, EMNDR (Teicher et al., 2016; Fonzo et al., 2016; Hein & Monk, 2017). Hence, ACEs should be assessed, for instance, with the Maltreatment and Abuse Chronology of Exposure (MACE) scale (Teicher & Parigger, 2015) as potential mediators of therapy outcomes in research and prior to treatment planning.

1.1.4 Treatment.

The most researched and empirically supported psychotherapy treatment (EBT**)** for AD is

cognitive-behavioral therapy (CBT), compared to psychodynamic, client-centered, or acceptance and commitment therapy. CBT includes a multitude of different techniques that are used according to the symptomatology of the AD (Bandelow et al., 2015b; Craske, et al. 2015; Schneider, Arch, & Wolitzky-Taylor, 2015). For example, systematically and repeatedly exposing a client to a phobic stimulus is a particularly fruitful technique for fear-based AD, such as phobias or PD (i.e., graduated exposure or other repeated techniques to produce habituation). Cognitive restructuring techniques are especially useful for anxiety-based AD, such as GAD and SAD. Self-monitoring physical manifestations of feelings, thoughts and behaviors and exercises targeting the ANS, such as breathing and relaxation, are useful for most AD. A/T NFT targets the ANS indirectly via increasing alpha and theta oscillations in the brain at Pz, and inhibition of high beta oscillations potentially leads to relaxed calmness, which would make a potentially excellent adjunctive therapy with CBT.

However, a meta-analysis by Hofmann, Asnaani, Vonk, Sawyer, and Fang (2012) revealed that even CBT, in comparison to other psychotherapy techniques, whether placebo or control, was only approximately 50% successful for most investigated AD. A thorough meta-analysis of 234 RCTs on the efficacy of diverse medication treatments, psychotherapy, and combined treatments for anxiety was conducted by Bandelow et al. (2015) and revealed a more differentiated picture. In general, most psychological interventions (CBT, mindfulness therapies, psychodynamic, internet-based therapies, group CBT, and relaxation types), all the tested medication classes (SSRIs, SNRIs, benzodiazepines, tricyclic depressants), as well as the combination of pharmacological and psychotherapeutic interventions were associated with significant improvement of anxiety, in comparison to psychological placebos and waitlist. But SNRIs, SSRIs, benzodiazepines, and combined CBT / medications treatments were associated with the highest effect sizes. However, long-term data of treatment effectiveness were not

available for most studies which poses a serious limitation because AD have high reoccurrence rates, especially the AD associated with the fear-circuit, where extinguished responses can be reversed by excessive stress or traumatic events (see section 1.1.3).

1.2 Neurofeedback

1.2.1 Basis for EEG-based NFT: EEG, brain oscillations, and associated states.

Different distinct rhythms of brain oscillations can be found and attributed to different mental states (Hermann, Strueber, Helfrich, & Engel, 2016). The following major frequency bands have been identified and are distinguished by their sinusoidal rhythms (oscillation frequency) in cycles per second (Hz). The frequency bands have slightly different ranges depending on the author. The ranges used in this study are congruent with the ones Collura (2013) uses in his *Brainmaster Avatar* and *MiniQ* software systems since those systems were used in this study for EEG and NFT recording:

- delta waves (0.5-4 Hz),
- theta waves (4-8 Hz),
- alpha waves (8-12 Hz),
- beta waves (12-30 Hz); which are commonly divided into two or three subdivisions:
    - beta 1 [13-20 Hz] and beta 2 [21-30 Hz], (Kropotov, 2016),
    - low beta [12-16 Hz], beta [16- 20 Hz], and high beta [20 – 30 Hz)], (Collura, 2013) which will be used in this study.
- gamma waves (30-100 Hz).

Delta waves are the dominant wave form during NREM sleep (deep sleep), whereas a mix of theta and delta waves may be observed during drowsiness and early NREM sleep. Delta waves may also play a role as inhibiting oscillations during attention tasks, as attention is shifted

to one stimulus while other stimuli are inhibited (Hermann et al., 2016). Furthermore, dominant delta oscillations and, especially slow wave activity around 1 Hz are associated with memory consolidation and may "represent the cyclical variations in the excitability of the neuronal pool represented by multiple unit activity and the network state and might amplify (in case of high-excitability phase) or suppress (in case of low-excitability phase) the input signals" (Cheron et al., 2016, p. 6).

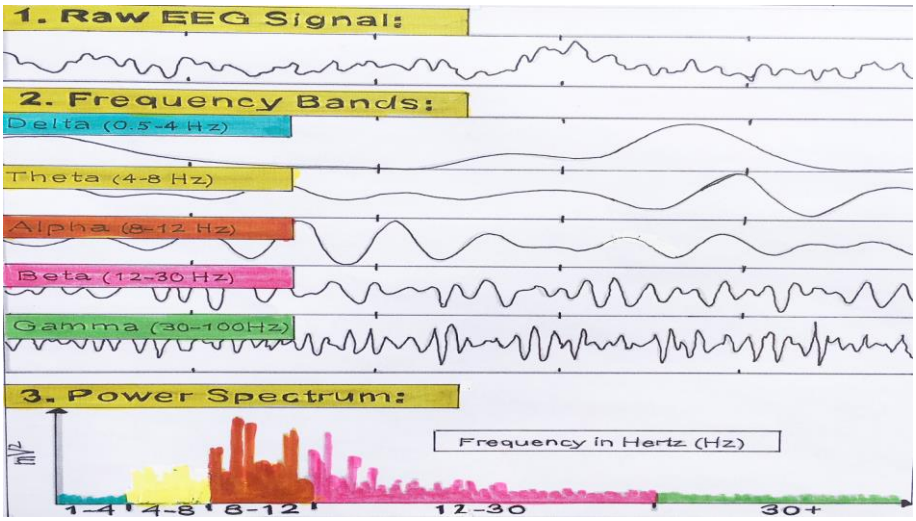

Figure 1.2: Raw signal processing into wavebands by frequency (Hz) and the associated power of the wavebands (μV^2) over 5 seconds of time. (Adapted by B. Viereck from Park, Fairweather, and Donaldson, 2015).

Theta waves, prominent during memory functions of the hippocampus, regulate activity in other structures of the brain with inhibitory processes (Hermann et al., 2016) and are also associated with the recall of pleasant memories in the frontal midline area (Sammler et al., 2007, as cited in Cheron, 2016). According to Horschig et al. (2014) predominant theta oscillations may indicate internal orientation, and encoding, and retrieval of memory in the temporal lobes; it is also related to increased drowsiness before stage 1 NREM sleep. According to Arns et al. (2015) two forms of theta need to be distinguished: phasic frontal midline (fm) theta, likely to stem from the r-ACC areas, and a "tonic drowsiness theta" (p. 1191), which originates in a large variety of cortical areas. Enriquez-Geppert et al. (2014) elaborates that functionally fm-theta is associated with mental tasks responsible for communication of large functional brain networks whereas tonic

theta is not task-related but rather related to general drowsiness before stage 1 NREM sleep.

Dominant *alpha waves* are associated with relaxed wakefulness and with the idling mode of the default mode network (see section 1.1.3). Klimesch, Sauseng, and Hanslmayer (1999) describe that alpha rhythm hinders simultaneous processes that are unnecessary for a present task via increasing the signal-to-noise ratio. Klimesch et al. (2012) posits that increased alpha-band amplitudes represent event-related synchronization (ERS) associated with inhibition of areas not relevant to the task at hand, while decreased alpha-band amplitudes represent event-related desynchronization (ERD) associated with release from inhibition toward a focused attention to the task. In other words, areas of the brain that are activated in a task experience higher beta amplitudes and desynchronized alpha oscillations. Moreover, Cheron et al. (2016) report that alpha rhythm of spindle-shaped episodes around 10 Hz is the predominant spontaneous brain rhythm for a relaxed individual in an eyes-closed state, whereas a relaxed eyes-open state is associated with faster alpha oscillations of smaller amplitudes.

Beta waves, especially high beta waves, are dominant during concentrated cognitive or motor task performance and outward focus. Enhanced high beta waves can also be found during rumination in individuals with AD and depressive disorders.

Gamma oscillations have been observed as a dominant frequency during meditation in a famous study of Tibetan monks (Lutz, Greischar, Rawlings, & Davidson (2004); and these are especially pronounced during concentrated information-processing (Hermann et al., 2016), especially tying together information from different areas of the brain (Horschig, 2014).

Furthermore, several local cortical oscillations are not considered frequency bands of their own; for instance, the mu rhythm, also called wicket or comb rhythm (8-13 Hz), is only generated over the sensorimotor cortex and is related to voluntary motor activity. Sensory motor rhythm (SMR, 12-15 Hz) is most pronounced over the sensorimotor cortex during quiet alert

wakefulness and during light NREM sleep, and synchronized when motor behavior is inhibited (Sterman, 1981). Slow cortical potentials (SCP; < 1 Hz) are event-related changes in direct electrical current, from negative to positive polarization and can be observed in anticipation of a mental or motor task (Walter, Cooper, Aldridge, McCallum, & Winter, 1964).

Lastly, it is important to point out the complexity of interactions in the various EEG oscillation parameters (amplitude, frequency, phase, and coherence) involved in cognition and mental processes. Particularly, *neuronal oscillators* must be taken into consideration*;* these are systems of neurons which generate spontaneous rhythmic brain wave patterns that are stable against minor disturbances (Cheron et al., 2016) and consist not only of one waveband. Furthermore, Hermann et al. (2016) emphasize that there is no 1:1 congruence between a specific kind of waveband and the various cognitive processes of the brain:

> "It is more likely that EEG oscillations contribute to different cognitive functions depending on where in the brain and with what parameters (amplitude, frequency, phase, coherence) they occur. Four important assumptions support this notion:
>
> 1. Different brain regions may perform different but specific functions … .
> 2. EEG oscillations of slow frequency may represent the cooperative activity of large-scale neuronal networks in the brain whereas high-frequency oscillations may predominantly reflect the activity of local neuronal populations … .
> 3. Coherent EEG oscillations in two distant brain regions may reflect the functional cooperation of these two regions … .
> 4. Combining assumptions 2 and 3, it has been suggested that cooperation between nearby cortical regions may be reflected by coherent high-frequency oscillations, whereas cooperation by distant brain regions may require coherent low-frequency oscillations" (Hermann et al., 2016, pp. 12-13).

1.2.2 Neurofeedback definition and general principles.

In Neurofeedback treatment (NFT) individuals are fed back measures of brain activity — such as neuroelectrical activity (EEG), oxygenation levels (rt-fMRI; NIRS), or low energy electromagnetic pulses (LENS)—to learn how to modulate brain activity. Principles of classical and instrumental conditioning are used for the person to up- or down-regulate their own non-perceivable brain oscillation amplitudes or other functional patterns of the brain via auditory and / or visual feedback. The premise of the use of this behavioral technique for psychological and certain neurological disorders is that brain oscillations in certain areas of the brain—or in certain structural or functional networks of the brain (see section 1.1.3) for anxiety disorders —are abnormal or dysregulated and that normalizing brain waves patterns in these areas will lead to an improvement in the symptoms of the disorder (Berger & Davelaar, 2017; Budzynski, Budzynski, & Abarbanel, 2009; Chow, Javan, Ros, & Frewen, 2017; Murphy & Bassett, 2017; Schabus et al., 2017; Thibault, Lifshitz, & Raz, 2016). Several general neurocircuits for anxiety and fear have been identified (see section 1.1.3 and Ledoux, 2011), but the search for general EEG endophenotypes of brain structure and activity distinguishing mental disorders has been less fruitful (Gunkelman, 2008; Johnstone, Gunkelman, & Lunt, 2005; Murphy & Bassett, 2017; Olbrich, van Dinteren, & Arns, 2015). As this study uses EEG-based NFT, also called EEG-biofeedback, the review of physiological and technical principles is limited to EEG-NFT.

In EEG-based NFT the individual's electrophysiological brain oscillations are recorded via EEG, amplified, and processed so that the brain activity bands of interest can be continuously fed back to the person in real time. While the individual tries to influence the amplitude or desired brain oscillations ratio, a feedback signal will be given. The goal for the individual is to learn to up- or down-regulate the oscillation parameters continuously with the help of feedback and positive reinforcement (rewards).

The NFT research to modulate electrical brain activity via EEG goes back to the 1930s but has been more systematically studied since 1941 (Arns et al., 2017) when Jasper and Shagass used classical conditioning with an auditory stimulus to change occipital alpha rhythm. It was not until the 1960s, when Kamiya trained people to control their EEG alpha frequency (1966) and Wyrwicka and Sterman (Wyrwicka & Sterman, 1968; Sterman, 1970) were able to train cats to increase their SMR oscillations, that clinically applied research in this area began. There is evidence and meta-analyses of RCTs for the efficacy of NFT for some disorders, such as ADHD (Arns et al., 2009; Sonuga-Barke et al., 2013; Micoulaud-Franchi et al., 2014; Cortese et al., 2016); epilepsy (Tan et al., 2009); some evidence for Autism Spectrum Disorder (Holtmann, Steiner, Hohmann, et al., 2011; Kouijzer, van Schie, de Moor, et al., 2010; Pineda, Brang, Hecht, et al., 2008); and depression (Johnston, Linden, Healy, et al., 2010; Young, Misaki, Harmer, et al., 2017). The evidence for the efficacy of NFT for AD or high trait anxiety in general is sparse and is reviewed next.

1.2.3 Mechanisms of neurofeedback learning.

To both create an effective, efficient NFT protocol, and predict who may or may not respond to NFT, it is vital to understand what mechanisms are responsible for successful learning of brain regulation patterns. Until the early 1990s mechanisms of NFT were almost exclusively explained by *classical conditioning* (Pavlov,1960; Watson, 1920), and more importantly, by *operant conditioning*, which relied on the research of Thorndike (1911) and Skinner (1948, 1992). During *operant conditioning*, the individual learns to associate an immediate consequence of an action (here: NFT feedback signal) with a behavior (here: regulated brain activity) and this behavior becomes more likely if it is perceived as rewarding (positive reinforcement) and less likely if the the action does not reach the predefined goal (threshold). The closer the temporal proximity of the feedback signal after the successful regulation of brain activity, the stronger the

association learning will be. The individual learns to regulate specific brain activity, the fastest if every correct response is reinforced.

Transfer trials are sometimes integrated into NFTs to generalize newly learned brain regulation from experimental (or therapy setting) to other contexts so that a reduction in anxiety symptoms can be achieved in everyday life. During transfer trials feedback is not given; only at the end of a trial is feedback given at to whether the regulation of brain activity was successful. In relation to the conditioning of EEG parameters, Jasper & Shagass' (1941) study is vital. The authors demonstrated that an unconditioned visual stimulus of a light signal (unconditioned stimulus) in a dark room leads to a suppression of occipital alpha rhythm (unconditioned reaction) during the eyes-open condition. They then paired the light signal with a sound stimulus and thus *classically conditioned* that the quasi-reflexive reaction of alpha-blocking would take place (conditioned reaction) when participants heard the sound (conditioned stimulus).

The other two prominent models or mechanisms of NFT learning are the *dual process theory* (LaCroix, 1981; Smith & DeCoster, 2000) and skill learning (Yin, Mulcare, Hilario, et al., 2009). The dual-process theory divides mental activity into automatic unconscious *(capacity-free processes; type I)* and more controlled conscious processes *(capacity-limited processes; type II).* Wood (2014) states that

> "… type I processes are usually unconscious and difficult to control by self-instruction. Type II processes reflect the activity of a supervisory attention system, specialized in monitoring and regulating the activity in other cognitive systems …, [and] are usually in the center of our focus of attention … are regulated mainly by self-instruction and are fundamental for executive functions and metacognitive abilities ... both automatic and controlled processes have control of behavior as well as of different aspects of cognition … but both learn from and react to different aspects of the task at hand. Automatic

systems learn only through cumulative reward while controlled systems are more flexible, context-oriented and learn fast from instructions" (Wood, 2014, p. 2).

By contrast, the skill learning model involves two distinct phases of learning. During the early phase, changes in performance are rapid, whereas in the late phase learning is marked by the consolidation of the skill and a more gradual improvement of the skill until the skill is learned and changes are minute. Structural and functional changes in the dorsomedial striatum can be observed in the initial phase of learning while changes in the dorsolateral striatum were found during the late phase of skill acquisition (Sitaram, Ros, Stoeckel, et al., 2017).

1.2.4 EEG-based neurofeedback protocols.

A number of different NFT protocols are available. They may be differentiated by what brain frequency bands (gamma, beta, alpha, theta, delta), specialty frequencies (SMR, SCP, mu, or infraslow), or brain frequency ratios (e.g., alpha/theta, theta/beta) are being trained and how many and which electrode locations on the scalp are used to measure the electrophysiological activity. The most common protocols will be briefly described. To treat AD, or anxiety in general, alpha, alpha/theta, alpha symmetry, and QEEG-based individualized NFT have primarily been used.

In alpha and alpha/theta protocols alpha power, alpha and theta power, or theta/alpha ratio are up-regulated to counter hyperarousal, associated with PTSD, PD, and phobias. These protocols may also enhance creativity (Niv, 2013).

Alpha asymmetry protocols (ALAY), introduced by Baehr, Rosenfeld, and Baehr in 1997, focus on increasing alpha power symmetry between the left and right PFC as alpha asymmetry in the PFC correlates highly with approach / withdrawal motivation and internalizing negative emotions of AD and depression (Mennella, 2017).

Beta / SMR NFT uptrains beta and SMR power are associated with alertness, active

concentration, sustained attention, and semantic processing. SMR training is linked to heightened thalamic inhibition and as such is especially efficacious for individuals with ADHD and epilepsy (Niv, 2013). Beta and Beta / SMR protocols are also combined with Theta down-training in order to increase attention.

In slow cortical potential (SCP) protocols individuals are trained to regulate their negative and positive SCP shifts. Originally developed for patients with epilepsy to decrease the probability of seizures (Rockstroh et al., 1993; Kotchoubey et al., 1999 and 2001) they are now effectively used to treat individuals with ADHD as well (Strehl et al., 2017).

The individualized QEEG-based NFT compares a client's average resting EEG oscillations for all 19-24 electrode sites to measurements of the same sites from a normative EEG database (from the *Applied Neuroscience Institute* or from New York University). The databases include EEGs of 600-3000 "normal" individuals and are stored by sex and age group. The client's EEG parameters, such as individual waveband powers for each electrode location, connectivity, and coherence between different electrodes, are compared with the normed results according to the client's sex and age range. The NFT protocol is individualized to normalize the client's wavebands, connectivity, or coherence that are at least three standard deviations from the norm (z-scores). The validity and reliability of the databases have been called into question because the EEGs collected in the database are not a representative sample of the U. S. population and the ideal of the "QEEG normalized brain" has not yet been adequately addressed.

A fairly new protocol is the infra-slow frequency protocol that uses 0.01-1 Hz oscillations to "re-normalize the functional connectivity of our resting state networks" (Othmer et al., 2013, p. 246) and is a promising treatment for PTSD and performance optimization (Smith, Collura, Ferrera, et al., 2014). Randomized controlled studies have yet to be published.

1.2.5 Neurofeedback treatments for anxiety.

As detailed more fully in the next section, a comprehensive review of the relevant literature found that very few randomized single- or double-blind studies have been conducted. Moreover, most used sample sizes of ten participants or less per experimental or control group and results have been mixed. Orne and Paskewitz (1974) and Watson and Herder (1980) found no significant effects for anxiety symptom reduction and Egner, Strawson, and Gruzelier (2002) did not find a significant difference in subjective activation level between alpha/theta NFT and the sham group. On the other hand, a number of studies, such as Hardt and Kamiya (1978), Plotkin and Rice (1981), Sargunaraj, Kumaraiah, Mishra, and Kumar (1987), Rice, Blanchard, and Purcell (1993), Vanathy, Sharma, and Kumar (1998), Sarkar, Rathee, and Neera (1999), Eismont, Lutsyuk, and Pavlenko (2011), and Gruzelier, Thompson, Redding, Brandt and Steffert (2013) did find a significant anxiety symptom reduction through NFT.

Most of the reviewed NFT studies used an Alpha/Theta (or alpha) NFT protocol, during which increasing alpha and theta amplitudes or increasing the theta/alpha ratio or alpha amplitudes at parietal electrode locations (Pz), at occipital locations (O1 and O2, or Oz), and central locations (Cz) were most often used.

1.2.5.1 Critical literature review of neurofeedback for anxiety disorders.

Since the late 1960s NFT has been used to treat adult individuals with AD; yet, most studies were conducted between the mid-1970s and mid-2000s. To investigate the quality of the experimental design and statistical analysis of NFT for AD, an exhaustive literature search of peer-reviewed articles on MEDLINE (1850-2017), PsycINFO (1894-2017), PsycARTICLES, Google Scholar (up to October 2017), as well as hand searches through the “Journal of Biofeedback and Self-Regulation” (from 1976- 2004) and its successor “Applied Psychophysiology and Biofeedback” (2005-2015) were performed.

In most NFT studies an alpha and theta up-training protocol was used (Peniston and Saxby, 1995; Dadashi et al., 2015; Glueck & Strobel, 1975; Sadjadi & Hashemian, 2014; Cheon Koo, & Choi, 2015; Green, 1974; Peniston & Kulkosky, 1991) alpha, theta and beta up-training or a theta/alpha ratio uptraining (Eismont et al., 2011; Egner et al., 2002; Raymond et al., 2005; Egner & Gruzelier, 2003; Gruzelier et al., 2009, 2013, 2014 a and b). Almost equally frequently an alpha uptraining protocol was used (Bhat, 2012; Agnihotri, Sandhu, & Paul, 2007; Rice et al., 1993; Sarkar & Rathee, 1999; Vanathy et al., 1998; Plotkin & Rice, 1981; Hardt & Kamiya, 1978; Walker, 2009; Garrett & Silver, 1976; Dekker, Van den Berg, Denissen, Sitskoorn, & Van Boxtel, 2014). Some researchers preferred a theta uptraining protocol to reduce anxiety (Sittenfeld et al., 1976; Vernon et al., 2002) and two studies downtrained alpha (Kluetsch et al., 2013, Orne and Paskewitz, 1974), (See Table 1.1).

In the past 50 years only six studies were conducted with a clinical population and control group (i.e., not with healthy volunteers): Dadashi et al. (2015), Sadjadi and Hashemian (2014), Vanathy et al. (1998), Rice et al. (1993), Peniston and Kulkosky (1991), Glueck and Strobel (1975); out of those six studies only Vanathy et al. (1998) used a pre- and post EEG to measure if significant changes in brain oscillations could be found. While all authors except Dadashi et al. (2015) used an active control group, only Vanathy et al. (1998) and Rice et al. (1993) used a NFT-based active placebo group. The following three studies with control groups were conducted with healthy adults regarding reduction of anxiety: Garrett and Silver (1974), Plotkin and Rice (1981), and Kluetsch et al. (2013). Kluetsch's study was a one session proof of principle studies, and Garrett and Silver (1974), and Plotkin and Rice (1981) did not use pre-post trial EEG measurements.

The results vary widely (see above), depending on what parameters were used to measure changes in anxiety symptoms. Some studies exclusively used subjective self-report measures for

general anxiety symptoms, such as the Spielberger State Trait Anxiety Inventory (STAI), the Beck Anxiety Inventory (BAI), and the Hamilton Anxiety Rating List (HARS), or specialized questionnaires for specific anxiety disorders, such as the Social Phobia Scale (SPS). These will not be reviewed here due to poor operationalization. However, most studies used multiple instruments to assess changes in anxiety. These included the aforementioned self-report inventories and self-report relaxation measures (e.g., Thayer's Activation-Deactivation Adjective Checklist [AD-ACL]), physiological measures such as heart rate, galvanic skin response, pre- and post-trial QEEG results, NFT EEG T/A ratio, absolute or relative theta, alpha, and /or T+A amplitude changes between the beginning and at the end of the NFT trial — sometimes for 1-3 additional measurements in the middle of the study. Nevertheless, none of the reviewed studies used a general linear mixed effects Growth Curve Model (GCM) – a type of advanced regression model that calculates a regression for each participant (random effect) and uses all NFT data points within and across NFT sessions to compare how the EEG parameters change for each participant within each session and across sessions and comparing them to experimental and control groups. A few studies that were administered in a hospital setting also included a report measure filled out by the clinicians or family members – pre- and post-trial, and during follow-up – for example in Glueck and Strobel, 1975 and Saxby and Peniston, 1995.

Authors	Sample Type	NFT protocol	N sessions /weeks	CG?	Significant Results	Random?	Groups: EG /CG (N of group)	Biolog. Sex	Age	Follow-up?
RCTs										
Agnihotri et al., 2007	adults with anxiety DO (GAD)	A up	12 sessions / 2 weeks	Y, wait list	reduced GSR; reduced self-report trait anxiety	Y	EG I (15): NFT; EG II (15): EMG BFT ; CG (15): wait list	F (24); M (21)	18-30 years	Y, after 4 & 8 weeks
Bhat et al., 2012	adults with anxiety & depressive DOs	A up	40 sessions / 8 weeks	Y, anxiolytic	reduced self-report anxiety scales for both groups	Y	EG (50): NFB + psychopharm (no anxiolytics); EG (50): anxiolytic	F (50); M (50)	M= 30 years	N
Chisholm, 1977	healthy adults	A up	40 sessions / 8 weeks	Y, listening to music	enhanced alpha	Y	EG I (12): contingent NFT; EG II (12): non-contingent NFT; CG (12): listening to music	F (18); M (18)	undergrad. students (18-22 years?)	N
Dadashi et al., 2015	GAD	A+T up	15 sessions / 5-7 weeks	Y, wait list	reduced self-report anxiety questionnaires; reduced anxiety psychiatrist evaluation; enhanced alpha and theta modulation	Y	Group I (14): NFT ; group II (14): wait list	F (14); M (14)	18-50 years	N
Egner et al., 2002	healthy adult students	T/A ratio up	5 sessions / 2 weeks	Y, mock NFT	less activated in ADACL scales; T/A ratio increase within session (no T/A ratio change across sessions)	Y	EG (9): NFT ; CG (9): mock NFT	F (6); M (12)	undergrad. students (18-22 years?)	N
Egner et al., 2003	healthy adult students	T/A ratio up; SMR	10 sessions/ 5 weeks	Y, Alexander Technique	enhanced musical performance; evaluated by blinded experts	Y	Experiment I: EG I (18): A/T NFT ; EG II 18): SMR; Experiment II: EG I (30): NFT ; CG II (31): Alexander relaxation technique	EG (22F/14M); CG (43F/18M)	undergrad. students (18-22 years?)	N
Eismont et al., 2011	healthy children	T/A ratio up	10-12 sessions/	Y, no intervention	increased T/A ratio; increased SMR; decreased anxiety in tests	Y	EG (7): NFT ; CG (10): mock NFT	F(8) / M(9)	10-14 years	N
Faridnia et al., 2012	performance anxiety in elite swimmers	beta & SMR up; T & high beta down	12 sessions/ 4 weeks	Y, mock NFT	reduced anxiety self-report measures; no pre-post EEG used.	Y	EG (10): NFT ; CG (10): mock NFT	F (20), M (0)	young adults	N
Garrett & Silver, 1978	adult students with test anxiety	A up; A up + EMG	6 sess. /10 sess.	Y, no intervention	alpha increase; anxiety reduction on tests (for EMG and NFT groups)	Y	Experiment I: EG 1 (18): NFT alpha up, EG II (18): EMG; CG (18): no intervention; Experiement II: EG II (16): NFT alpha up; CG 1 (16): no intervention; CG II (18) relaxation	not specified	undergrad students (18-22 years?)	N
Gruzelier et al., 2013	healthy adult dance students	T/A ratio up	up to 10 sessions	Y, no intervention	increased creativity on some measures; no anxiety reduction for A/T only for HRV condition	Y	EG (16): NFT; EG 2 (16); HRV BFT ; CG I (16): choreography instructions; CG II (16): no intervent.	F (42); M (12)	18-22 years	N
Gruzelier et al., 2014	healthy adult dance students	EG I: T/A ratio up; EG II: SMR	10 sessions	Y, no intervention	increased T/A ratio within and between sessions; impaired performance due to drowsiness/hypnogic state, except for improvisation; SMR better performance / less performance	Y	EG (7): NFT; EG 2 (6):SMR; CG I (6): no intervention	F (7); M (12)	undergrad. students (18-22 years?)	N
Gruzelier, Hirst et al., 2014	healthy adult dance students	T/A ratio up	10 sessions	Y, no intervention	similiar results than study above (Gruzelier, 2014); replication	Y	EG (8): NFT; EG 2 (8):SMR; CG I (8): no intervention	F (10); M (14)	undergrad. students (18-22 years?)	N
Lu et al., 2017	adults with PD	A up	20 sessions/ 7 weeeks	Y; standard treatment	A up improved; reduction of anxiety on self-report questionnaires	Y	EG (10): NFT; CG (8): standard treatment (anxiolytics)	18	M= 33 years	N
Plotkin & Rice, 1981	healthy adult students	A up; A down	5-7 sessions	Y, opposite NFT	reduction in trait & state anxiety. highly correlated with ratings of perceived success at feedback but unrelated to either direction or magnitude of changes in alpha activity => reduction of anxiety likely placebo/ perceived success effect.	Y	EG (5): NFT alpha up; CG (5): NFT alpha down	10	18-29 years	N
Raymond et al., 2005	healthy adult students	A+T up	9 sessions	Y; mock NFT	both of EG & CG improved moods, more energetic (POMS); but no change in personality traits	Y	EG (6): NFT ; CG (6): mock NFT	12	M= 27 years	N
Rice et al., 1993	anxiety: GAD A up; A down	A up; A down	8 sessions	Y, pseudo meditat.	alpha enhance, alpha reduct, EMG groups: all reduction in anxiety; alpha enhancement: sig. HR reduction.	Y	EG 1 (11): NFT alpha up; EG II (11): NFT alpha down; EG III (11): frontal EMG; CG (11): pseudomeditiation	F (23); M (22)		Y; 4 weeks
Sargunaraj et al. 1987	anxiety neurosis; A up	A up	20 sessions	Y; EMG, no inter-vention	**no reduction in anxiety with alpha FB only for EMG.**	Y	EG (8): NFT; CG 1(8): EMG; CG (5): no treatment.	21	No info	N
Sarkar et al., 1999	anxiety: GAD; A up?	no info on protocol used	40 sessions / 8 weeks	Y, anxiolytic	pharmaco-therapy and NFB therapy improvement on HARS behavior rated by doctor and inkblot tests.	Y	EG I (25): NFT; EG II (25): anxiolytic	50	M=32 years	N
Sittenfeld et al., 1976	healthy subjects, high or low EMG; T up	T up	8 sessions	Y, EMG, no inter-vention	enhanced theta, lower EMG and lower HR. group with high frontal EMG increased theta only when first having EMG training. Low EMG groups did better with theta training only (without EMG training).	Y	EG 1 (5): up T NFT; EG 2 (5): high EMG; E; CG (5): low EMG	20	no info	N
Vanathy, et al., 1998	anxiety: GAD; A up	A up; Theta up	15 sessions/ 4 weeks	Y, wait list	decrease in self-reported, observer-rated anxiety measures, increase in quality of life measure for alpha and theta EGs. No EEG changes.	Y	EG I (6): alpha NFT; EG II (6): theta NFT; CG (6): wait list	(14 M/4 W)	no info	N
Watson & Herder, 1980	psychiatric multiple conditions;	A up	10 sessions	Y; sham NFT; no intervent.	**no significant differences between groups**	Y	EG I (25): alpha NFT; EG(25): sham NFT; CG (25): no treatment	75	no info	N

Figure 1.3 a: RCTs: Research design, sample, and results of NFT for anxiety-related disorders. Light green high light= studies with clinical population. Bue print = significant results of self –report anxiety measures; red print= significant results in EEG-based NFT measures; green print = significant results in de/activation scales.

Authors	Sample Type	NFT protocol	N of sessions /weeks of NFT	CG?	Significant Results	Randomized	Groups: EG /CG (N of group)	Biolog. Sex	Age	Follow-up?
With control group but not randomized										
Glueck & Stroebel, 1975	psychiatric adult inpatient adults with multiple conditions	A+T up	20 sessions / 4 weeks	Y, transcend. meditation; autogenic training	alpha increase within and between sessions, but not outside lab; high attrition and enhanced anxiety for non-responders, stopped after 3/4 weeks	N	EG (32): NFT ; CG I (32): transcendatal meditaton; CG II (32): autogenic training	96	not specified	4-8 weeks after discharge
Kerson et al., 2009	GAD	A down, + A symmetry	8-32 sesssions	Y; first ETB, then NFT	enhancement in alpha asymmetry; reduction of anxiety on self-report questionnaires at 6 months follow-up	N	EG (12): A suppression + A symmetry CG (12): all subjects went though 6 sessions of ear lobe temperature feedback (ETB) first, then went on to EG training	(5 W/3M) + 4 drop-outs	32-55 years	Y, after 6 months
Peeters et al., 2014	healthy adults	A symmetry	1 session proof of prcinciple	Y, opposite NFT	alpha up -and down training improvements; but no associated mood changes (using opposite NFT directions results in more robsut contrast btw. conditions rather than more random sham results?)	N	EG (20): NFT alpha up; CG (20): NFT alpha down	F (40); M (0)	students	N
Peniston & Kulkosky, 1989	psychiat. Patients w/alcohol abuse & depression	A+T up	40 sessions / 8 weeks	Y; tradit alcohol abuse tx	reductions in self-assessed depression & anxiety related items; no other types of assessments given	N	EG I (10): NFT non-alcoholic; EG II (10): NFT alcoholic; CG (10): traditional alcohol treatment	30	M= 49 years	Y, 13 months
Peniston & Kulkosky, 1991	psychiatric inpatient adults (PTSD)	A+T+B up	30 sessions / 6 weeks	Y; tradit psychiatric tx	less psychotropic medication; lower MMPI scores; less relapse.	N	EG I (10): NFT ; CG (10): traditional psychiatric treatment	20	M= 36 years	once a month for 30 months
Sadjadi et al., 2014	children w/ separation anxiety	A/T	20 sessions	Y, mock NFT	lower in separation anxiety in NFT	N	EG (12): NFT; CG (12): sham NFT		7-12 years	N
Walker, 2009	anxiety: PTSD; A up, hiB down	individualized (A up, hiB down;	5-7 sessions	Y	decrease in excessive high beta; increase 10 Hz activity; improvement in chronic anxiety; reduction in anxiety stable 1 month post-test.	N	EG (19): NFT; CG (4): no treatment	(10M/13F)	18-64 years	Y; 4 weeks
White, et al., 2017	adults with anxiety & depressive DOs	inhibit high beta /SMR ratio + HRV	30 sessions	Y	decrease in high beta / SMR ratio; decrease in self-report anxiety measure, higher HRV	N, retros pect. study	EG: anxiety (12) anxiety & depression (19), CG (55)	EG (31), CG (55)	no info	N

Figure 1.3 b: Studies with CG but no randomization: Research design, sample, and results of NFT for anxiety-related disorders. Light green high light= studies with clinical population. Bue print = significant results of self –report anxiety measures; red print= significant results in EEG-based NFT measures.

Authors	Sample Type	NFT protocol	N of sessions /weeks of NFT	CG?	Significant Results	Randomized	Groups: EG /CG (N of group)	Biolog. Sex	Age	Follow-up?
No Control Group										
Cheon et al., 2015	adult psychiatric patients	individualized	variable N of sessions	N	reduced anxiety on Clinical Global Impression Scale; reduced self-report anxiety on questionnaires	N	EG (77): Individualized retrospective analysis	77	variable	N	
Dekker et al., 2014	healthy adult students	A up	10 sessions	N	**no significant changes in any measures**	N	EG (6): NFT	6 students	15-22 years	N	
Dreis et al, 2015	adults with anxiety DO, not specified	indiviualized QEEG based	7-28 sesions	N	reduced self-report anxiety on questionnaires; no changes on pre-post test QEEGs	N, retros pect.	EG (14): NFT	F (9); M (5)	M=32 years, (SD= 16)	N	
Green, 1974	psychiatric adult inpatients	A+T up	80 sessions /16 weeks	N	increasing alpha and theta but no statistical analysis method given	N	EG (?): NFT	not specified	not specified	not specified	
Gurnee, 2003	adults with anxiety DO, not specified	individualized	variable session amounts	N	normalized QEEG; no other measures used	N	100 individual retrospective case studies	100	not specified	N	
Hammond, 2003	anxiety: OCD	individualized	40 sessions / 8 weeks	N	reduction of rumination but only in lab	N	2 (1 male, 1 female)	F (1); M (1)		Y ; after 15 and 30 months	
Hardt & Kamiya, 1978	healthy adults	A suppression	7 sessions / 1 week	N	anxiety changes in high anxiety but not in low anxiety subjects; reduction in frontalis muscle EMG tension; low trait anxiety subjects superior in alpha control	N	EG I (8) NFT, high anxiety; EG II (8) NFT, low anxiety	F (0); M (16)	undergrad. students (18-22 years?)	N	
Kirschbaum & Gistl, 1973	healthy adult students	A% up	1 session	N	higher anxiety score subjects showed lower alpha base rate & lower alpha increase	N	EG (20): NFT	20	20-30 years	N	
Kluetsch et al., 2013	adults with PTSD	A down	1 session proof of prcinciple	N	alpha desynchronization associated with decreased alpha amplitude during NFT followed by increase (rebound) in resting-state alpha synchronization => rebound linked to increased calmness, greater SN connecticivity with r. insula and enhanced DMN connectivity with bilateral posterior cingulate, r. mf gyrus and l. mPFC	N	EG (21): NFT	21	26-52 years	N	
Mills & Solyom, 1974	adults with anxiety DO (OCD)	A up	variable session amounts	N	no reduction of rumniation outside lab; only 3/5 patients improved	N	EG (5): NFT	F (3); M (2)	M= 33 years	N	
Orne & Paskewitz, 1974	healthy adult students	A down	3 sessions	N	anticipation of electric shock did not reduce alpha, but associated with higher: reported anxiety, HR, physiolog arousal, GSR	N	EG (22): NFT	22	undergrad. students (18-22 years?)	N	
Saxby & Peniston, 1995	anxiety: alcoholism with depression; A+T up	A+T up	20 session	N	reduction of anxiety associated with alcoholism	N	EG (14): NFT	14	M=48 years	Y; 21 months	
Singer, 2004	anxiety: performance, dancers	no information on protocol	7-20 sessions	N	reduced anxiety self-report measures; no pe-post EEG used.	N	EG (5): NFT	5	no info	N	
Vernon et al. 2002	healthy subjects, students; T up, inhibit A+D; SMR up, T+B down	T up, inhibit A+D; SMR up, T+B down	8 sessions	N	**no increase in mean theta/delta ratios**	Y	EG 1 (15): T up, inhibit A+D; EG 2 (15): SMR up, inhibit alpha, inhibit beta	(12F/18M)	20-28 years		

Table 1.3 c: Studies without control and no randomization: Research design, sample, and results of NFT for anxiety-related disorders.

Differences in the significant versus non-significant results in these studies are partially due to different participant populations. Many studies with non-significant results had used healthy college students only (Hardt & Kamiya, 1978; Orne & Paskewitz, 1974; Egner et al., 2002). As these participants had no AD, a reduction of already normal anxiety symptoms would have been less likely than in a clinical population. Furthermore, differences in the measures administered pre- and post-NFT might be responsible for differing results. Most studies administered only one to several self-report anxiety scales which were more or less reliable, such as the STAI, Taylor's Manifest Anxiety Scale, Welsh Anxiety Scale, and the GAD-7; whereas some used exclusively clinical observer measures, such as the Hamilton Anxiety Rating List, and less objective unstructured and semi-structured clinical interviews. Moreover, different feedback and reward criteria, NFT electrode locations, and most importantly studies differed regarding the use of CG – from no use of CG, wait-list CG, other treatment CG, to pseudo-NFT were used. Studies that did not use a CG or had a wait-list CG had been very likely to show significant effects.

Many studies did not have any kind of control group (Baehr & Rosenfeld, 2001; Gurnee, 2003; Kluetsch et al., 2013; Mills & Solyom, 1974; Saxby & Peniston, 1995), and quite a few that did not have a NFT control group did have a wait-list or a relaxation group, or a group with another treatment modality such as medication (e.g., Bhat, 2012; Dadashi, Birashk, Taremian, et al., 2015; Peniston & Kulkosky, 1989; Sarkar, Rathee, & Neera, 1999). Other studies had not been controlled for combination of NFT with other treatments, such as psychotherapy, medications, meditation, and breathing and hand warming exercises (e.g., Bhat, 2010; Glueck & Stroebel, 1975; Green, 1974; Peniston and Kulkosky, 1991; Saxby and Peniston, 1995); and some studies with a control group did not have a randomization procedure (Cheon, Koo, Seo, et al., 2015; Green, 1976; Gurnee, 2003; Sargunaraj, Kumaraiah, Mishra, et al., 1987; Saxby & Peniston, 1995). Only two studies had a single- or double-blind research design (Dekker et al.,

2014; Egner & Gruzelier, 2003, respectively). Other studies were an accumulation of a limited number of case studies with individualized NFT treatment (e.g., Hammond, 2003; Moradi et al., 2011; Singer, 2004).

Furthermore, studies had a limited amount of treatment sessions – one to six sessions – (for instance, Chisholm, DeGood, & Hartz, 1977; Egner et al., 2002; Hardt & Kamiya, 1978; Kirschbaum & Gistl, 1973; Orne & Paskewitz, 1974;) or were one session proof-of-principle studies (Kluetsch et al., 2013; Peeters, Bodar, Ronner, van Os, & Lousberg, 2014).

Participant characteristics such as age, education, ethnicity / race range, and socio-economic status were homogeneous; many studies had 18- to 25-year old Caucasian under-graduate students as participants, such as Chisholm et al. (1977), Egner et al. (2002), Gruzelier, Thompson, Redding, et al. (2013) Gruzelier et al. (2014), and Kirschbaum & Gistl, 1973. Furthermore, while generalizations were made about mechanisms of anxiety reduction for people with anxiety disorders, all study subjects were healthy individuals without anxiety diagnoses (e.g., Kirschbaum & Gistl, 1973; Eismont, Lutsyuk, & Pavlenko, 2011; Orne & Paskewitz, 1974; Peeters et al., 2014; and Raymond, Varney, Parkinson, & Gruzelier, 2005). Other mental disorders or chronic diseases that might have influenced the NFT results were not addressed, assessed, or used as an exclusion criterion.

Problems with the statistical analysis of the study data were prevalent. The sample size for many studies of less than 10 for control or experimental groups, respectively, can lead to large confidence intervals. Consequently, incorrect inferences of a population from the sample may occur which would seriously impede the statistical power of the study (e.g., Eismont et al., 2011; Egner, Strawson, & Gruzelier, 2002; Raymond et al., 2005; Gruzelier, Hirst, Holmes, & Leach, 2014; Sargunaraj et al., 1987; Vanathy et al., 1998). Also, traditional averaging of multiple NFT sessions data leads to excessive loss of information, especially in the studies where

only pre-and post- of NFT data, such as alpha and theta amplitudes, were analyzed (e.g., Dadashi, Birashk, Taremian, et al., 2015; Plotkin & Rice, 1981; Vanathy et al., 1998). Moreover, many studies did not address and appropriately factor out the experimenter effect on the results of the study, such as the studies of Sadjadi & Hashemian (2014) and Sargunaraj et al. (1987).

1.3 Considerations Regarding the Study Planning

1.3.1 Neurofeedback protocol.

After reviewing the studies, especially those whose results showed a significant decrease in anxiety symptoms in self-report measure and a significant change in EEG- and NFT-related parameters (see sections 1.2.5.1 and 1.2.4), the NFT protocol that was most efficacious for AD and trait anxiety was the alpha/theta protocol.

Unfortunately, many of the reviewed studies, especially studies before 2010, failed to divulge details of electrode placements, as well as details about how reward criteria were operationalized. For studies that did provide electrode placement locations, Pz or Cz were the most common placements for electrodes. However, the rationale for why an electrode location was chosen often remained unclear in all of the reviewed studies, except for Gruzelier et al. (2009). The Pz electrode placement corresponds most closely to Brodmann area 7. Neuroanatomically, this area corresponds to the caudal superior parietal lobule Gruzelier and colleagues (2009) describe that the A/T training at the Pz location is connected with enhanced hippocampal activity involving the following mechanisms:

> "The ascending mescencephalic-cortical arousal system, and limbic circuits subserving cognitive as well as affective/motivational functions, and including coupling between frontal and posterior cortices, exemplifying a role for theta and alpha waves in mediating the interaction between distal and widely distributed connections. It is theorized that the long-distance connections, afforded by slow rhythms in the brain during a state of deep

> relaxation facilitates associative connections in memory and subsequent retrieval in performance" (p. 108).

Hippocampal activity is integrally involved in memory consolidation and retrieval, (Sauseng, Klimisch, Schabus, et al., 2005; Reiner, Rozengurt, & Barnea, 2014), including memory with associated emotions. Furthermore, Angel, Oviedo, Paloutzian, Runehov, & Seitz (2017) describe that, among other functions, the central parietal area below Pz seems to be involved in self-related functions

> "in mismatch between actual and predicted feedback of actions, (ii) in the parietofrontal network active in conscious access and exocognitation, (iii) in the autobiographical self, underpinned by PMC, as well as (iv) in the default network (and its probable self-related function)" (p. 258).

Consequently, Pz-LE appeared to be a beneficial location for the active NFT electrode, particularly in combination with an A/T NFT protocol for subjects with high anxiety; it might potentially produce enhanced memory consolidation and retrieval and activation of self-related functions that can be used to achieve a relaxed calmness, and down-regulation of the HPA axis, and in combination with CBT or other psychotherapy methods retrieve and restructure maladaptive thought patterns, and effectively encode more adaptive ones (Sections 1.1.1 and 1.1.4).

Regarding visual and auditory feedback conditions for alpha and A/T NFT, Vernon et al. (2005) concluded that the most common ways to create an alpha or A/T feedback protocol by utilizing alpha (and theta) amplitude, percent, or T/A ratio measurements, mostly via auto-thresholding, i.e., as long as the alpha measurements (or T/A ratio) was above a threshold for 60-80% (depending on the study) for a pre-defined time segment an auditory, visual, or combined visual and auditory feedback was given. However, many A/T studies did not report if manual or

automatic thresholding was used in their study protocol (Agnihotri, et al., 2007; Bhat et al., 2012; Eismont et al., 2011; Faridnia et al., 2012), some used automatic thresholding (Lu et al., 2017; Peeters et al., 2014) while the group at the Gruzelier lab used manual thresholding (Egner et al., 2002 and 2003; Gruzelier et al., 2013; Raymond et al., 2005). In the area of NFT research several research groups had used autothresholding as well, such as Gevensleben et al. (2012), van Dongen-Boomsma et al. (2013), and Schoenenberg et al. (2017) mainly to minimize variability of reinforcement protocol by more or less accurate timing to manually change the threshold by the individual experimenters (reliability) and to maximize the replicability of the study. However, a distinct disadvantage of any automatic thresholding protocol is that while it reinforces any upregulation of alpha and theta from the baseline it may also lead to *positive punishment* — "the addition of a stimulus to decrease the probability that a behavior will recur" (Grison, Heatherton, & Gazzaniga, 2017; p. 214) — in other words, in cases where alpha and theta oscillations are up from the past minute measurements but still below the baseline a feedback signal may actually decrease alpha and theta oscillations even more. This study used alpha and theta amplitude changes from baseline and 65% thresholding for the reward criteria was used.

The session lengths in reviewed NFT studies targeting AD in adults showed average sessions of 30 minutes in length, divided into 2 -10 training segments (Ghaziri et al., 2013; Hammond, 2003; Vanathi, Sharma, & Kumar, 1998). After reviewing NFT studies Vernon (2009) comes to the conclusion that a temporary change in EEG wave bands can be successfully achieved by a 20 to 30-minute session of NFT but that those changes are likely transient unless more sessions solidify the learning.

Vernon (2009) adds that evidence regarding the spacing of NFT sessions—from a high frequency of sessions within a short amount of time, over double-sessions within the same day,

to spaced-out sessions over the course of days or weeks— is mixed. In the area of A/T NFT 2-3 sessions per week seemed be most successful (Agnihotri et al., 2007; Egner et al. 2003; Gruzelier et al., 2009).

The number of NFT sessions among all NFT for trait anxiety or AD varied widely, from one session for proof of principle studies (Kluetsch et al., 2013; Peeters et al., 2014) to 40 sessions (Deng et al., 2014). Most studies with significant results used between 5 and 12 session protocols and 2-3 sessions per week within a + / – two-hour timeframe of sessions (Agnihotri et al., 2007; Egner et al., 2003; Gruzelier et al., 2009; Hardt & Kamiya, 1978; Rice et al., 1993; Watson & Herder, 1980) and had a combined audiovisual feedback signal with eyes-open condition. Hence, ten NFT sessions with a combined audiovisual feedback signal, each with three training segments of eight minutes each and with two short, 1-2 minute breaks (30 minutes total), and 2-3 NFT sessions per week were scheduled within the same time of day (+ / – 1.5 hours) were deemed adequate to reach significant results in this study.

1.3.2 Control for non-specific effects.

To differentiate if effects of the NFT were specific to the experimental condition or resulted from the non-specific general environment of the study and participants' expectations, it is vital to create an active CG that mimics the experience of the EG as closely as possible. According to Geuter, Koban, and Wager (2017), a placebo is "a sham medical or therapeutic treatment that appears similar to an actual treatment and evokes expectations of benefit" (p. 168). Consequently, any effects that an individual who receives a placebo treatment in a RCT trial shows can only be due to an individual's "beliefs and expectations, perceptions of the social and physical environment, and generalization from past experiences" (p. 168). In addition, Finniss, Kaptchuk, Miller, and Benedetti (2010) emphasize that the placebo effect is attributable to the "overall therapeutic context" (p. 2) which includes the patient-treatment provider relationship.

Placebo effects are powerful effects responsible for between 66% - 80% of a treatment effect (Roberts, Kewman, Mercier, et al., 1993; Wager & Atlas, 2015), but vary depending on disorders and outcome treatment measures. For instance, a meta-analysis of 114 medical and psychotherapeutical studies by Hrøbjartsson and Gøtzsche, (2001, as quoted in Stewart-Williams & Podd, 2004) showed that not only were placebo effects less widespread and smaller than previously reported but were found only in studies that used subjective self-reports and continuous assessment of improvement.

Learning theory and cognitive expectancy theory explain the two major mechanisms involved with placebo effects. Geuter and colleagues (2017) use learning theory to define the placebo effect as "a form of classical conditioning, which can influence pain, hormone release, and other behaviors …a treatment's reinforcement history… Pairing treatment cues (e.g., an intravenous injection) with a real drug induces associations between the cues and drug effects that can be elicited by the cues alone" (p. 171). Moreover, they describe how cognitive expectancy influences perception, which in turn leads to a placebo effect.

Consequently, to test if effects of the treatment are specific to the active experimental treatment in this study (A/T NFT), the reduction in subjective measures (i.e., self-reported anxiety scores and AD-ACL scores) and objective measures (i.e., EEG-based learning curves and pre-and post-trial QEEGs), would have to be significantly higher for the EG than for the placebo CG. The experimental design called for a control condition that was as closely related as possible to the experimental condition in, invested time, mode of application, treatment expectancy, and learning activity, i.e., actual NFT learning, because the non-specific factors in this placebo NFT would be equal to the unspecific factors in the experimental A/T condition and ensure at least a single-blind study, in which the participants do not know throughout the trial if they are in the experimental or the placebo NFT condition.

Arns and colleagues (2013) define three types of CG conditions: semi-active, active, and placebo control conditions. Active CGs compare two different active conditions regarding the study's parameter of interest. For instance, infraslow frequency training and anxiolytic medication could be used as active CGs for a study concerned with the reduction of anxiety symptoms. However, a control for unspecific effects is not possible when comparing such dissimilar treatment modalities. In a semi-active CG, non-specific treatment effects, such as time, type of energy spent, and amount of interaction with the study personnel, are very similar to the NFT EG. But instead of training brain waves via feedback, participants train muscle activity via EMG biofeedback, or interact with a computer. A placebo CG is identical to the EG in number of sessions, set-up, and reward signals, except that the placebo CG brain oscillations (or other parameters) that are trained are not related to the brain oscillations of interest for the study. It is believed that this CG design will ensure blinding of the CG participant and therefore adequately control non-specific treatment expectancy effects.

There are different approaches to create a successful placebo-controlled CG. Arns and colleagues (2013) state that "some recent neurofeedback studies (mainly pilot and feasibility studies) have employed a placebo-controlled design and failed to provide clear evidence for the superiority of 'real' neurofeedback compared to sham-neurofeedback" (p. 4). The studies which Arns and colleagues quote to back up their claim used NFT protocols that randomly gave children feedback independent of the child's brain oscillations (Arnold, Lofthouse, Hersch, et al., 2013), gave feedback based either on a simulated EEG and not the individual's EEG recording (Lansbergen et al., 2011), or based on a pre-recorded EEG of one of the authors (Perreau-Linck, Lessard, Levesque, & Beauregard, 2010); one study failed to mention what kind of CG protocol was used (Dongen-Boomsma et al., 2013). A variation of the Perreau-Linck protocol, for instance, matches each EG member with a CG group member and plays the NFT feedback from

an individual in the EG group to the CG group member. However, these fake NFT CGs are problematic because self-regulation learning does not occur during the NFT sessions. This will lead to motivational problems and frustration quickly, especially after no changes can be observed by the participant over the course of several sessions. In the case of inactive electrodes being attached to subjects' scalp, participants will likely learn very quickly that no matter what they do it will not cause any artifacts in the EEG, which would be especially suspicious after they had the experience of being instructed to sit still during the pre-trial EEG for good signal receptivity and that eye blink, teeth clenching, slight movements in the chair, or even greasy hair, or scalp perspiration cause observable changes in the EEG. The realization that one is part of the placebo group will have consequences, such as frustration and anger, learned helplessness, negative treatment expectations, worsening of symptoms (nocebo effect) and potentially dropping out of the study, as well as a skewing of any study results in regard to group comparison for non-specific effects (Benedetti, Lopiano, & Colloca, 2007). This would be especially detrimental when working with a clinical population.

Doppelmayr and Weber (2011) found a novel approach to set up a placebo NFT training in their SMR and Theta / Beta NFT study alternately using the same inhibit bands of the EG but up-and down-training of specific and differing beta frequency bins, hence allowing the participants of the CG to learn how to actively regulate frequencies that did not interfere with the training frequencies of the EG and alternating up-and down-regulating randomly changing frequency bins each session—a condition they named randomized broadband feedback—that minimized the probability of learning and NFT training effects to occur in the CG.

Another important aspect of any RCT research study is to use at least a single-blinded protocol, ideally a triple-blinded protocol in which not only the participant does not know if s/he is part of the control or experimental group (single-blind design) but the clinician and personnel

involved with participant contact (double-blind design) and the person analyzing the data (triple-blind design) are not aware of the assignment to which treatment or protocol. A triple-blind design is impossible for a study like this one, whereby all functions—from randomization to performing NFT sessions to the analysis of the data—are conducted by the same person. Triple- and even double-blind studies require a multi-person team with separate and specialized roles, such as one person who randomizes participants not involved with the NFT or the data analysis of study data. Consequently, this study could only be a single-blinded study in which the participants were not informed if they were in the EG or CG until the end of the study.

Participant response to the NFT may certainly be influenced by the expectation of treatment outcome. This might be particularly true for treatments involving technology that is perceived as cutting edge. The Stanford Expectations of Treatment Scale (SETS; Younger, Gandhi, Hubbard, & Mackey, 2012) measures participant outcome expectancy in clinical trials, thereby allowing the researcher to factor out individual differences in this measure. Related to this issue is a person's belief as to how much they can influence the outcome of events. One locus of control scale used in a few NFT studies, such as in Kotchoubey et al. (2001), is Levenson's Locus of Control Scale (1981). However, most NFT studies including the current one utilized Rotter's (1966) Locus of Control scale (LOC). It can be used to measure this construct in which individuals with internal LOC attribute results of their own actions to internal sources, whereas individuals with an external LOC link results of their own actions to external sources, such as luck, chance, or unpredicTable circumstances.

As humans are social beings who develop relationships over the ten NFT sessions, and react to subtle emotional cues, interactions with the NFT technicians will certainly have an effect, especially on anxious participants' general levels of comfortability, trust, motivation, and level of focus on the NFT treatment. A standard protocol of procedures and scripts on how to

explain possible questions, as well as recording any unusual circumstances during each individual NFT session is prudent (see Appendix D: Neurofeedback Session Checklist). The data may be statistically analyzed to exclude the non-specific effect of varying experimenter personalities, varying degrees of professionalism, and potential experimenter bias.

Lastly, it is important to randomize the sample to ensure that EG and CG have participants that are as similar as possible and evenly distributed, regarding sex, age, education, SES, and in the characteristics to be analyzed in the study (here: trait anxiety scores and AD diagnosis). In this study the term *active placebo* will be used to classify the CG based on the understanding of Rief, Hofmann, and Nesturioc (2008). These authors described in the context of acupuncture research where, like in the EG, acupuncture needles in the sham CG were placed. However, the locations of the needles in the sham group were not placed along the course of the meridian, as in the EG. Rief et al. (2008) explain that the CG in the aforementioned acupuncture study "is not an example of a pure placebo condition, but an example of an active placebo condition, because the placebo conditions induced the same side effects and the same expectations than the verum group". (p. 5) Similarily, the present study uses exactly the same procedures for EG and CG — an active NFT training protocol at Pz with the same two auditory and visual feedback signals for the same amount of time. The only difference in the EG and CG protocols is that in the EG alpha and theta amplitudes are uptrained in all ten NFT sessions whereas in the CG two wavebands, beta and high beta, are successively up- and downtrained each session. Thus, while learning beta and upper beta regulation within one NFT session can take place in the next NFT the opposite learning takes place via downregulating beta and upper beta.

2. Objectives and Hypotheses

Due to rapid advances in neurotechnology and neuroscience new mechanisms underlying AD have been discovered (see section 1.1.3). Of particular interest is the way the neuronal system transmits, prioritizes, analyzes electrophysiological signals, and organizes information in nodes, hubs, and networks that can in turn be mapped onto anatomical and functional parts of the brain. Because NFT may cause long-term changes in neurocircuits of the brain via LTP and LTD (see section 1.1.3) it is uniquely suited to become an EBT method for individuals with high trait anxiety or AD. However, there is a paucity of placebo-condition-controlled trials for clinical populations of various ages regarding NFT in general, and for AD in particular. Furthermore, statistical analysis methods of most clinical trials in the field of NFT are fraught with insufficient statistical analysis methods that do not take individual NFT learning curves within and between sessions into account and measure NFT outcome by session means between two to five time points, thereby reducing the wealth of data.

2.1 Study Objectives

The primary objective of this study was to create a rigorous, placebo-controlled, clinical trial with a (sub)clinical sample of women for the NFT treatment of AD to investigate if A/T NFT at Pz is an efficacious method for anxiety symptom reduction. A secondary objective of this study was to search for and implement better statistical analyses methods for NFT trials in general and to investigate cognitive variables involved in NFT, yet often not assessed, such as treatment outcome expectancy, personal attribution styles, the use, types, and efficaciousness of cognitive strategies in NFT.

2.2 Hypotheses

2.2.1 Primary hypotheses.

Hypothesis 1 (H 1a and b): A ten-session NFT protocol of up-training alpha (8-11 Hz) and theta (5-7.5 Hz) frequency bands at Pz will significantly elevate mean absolute and relative theta and alpha amplitudes and absolute and relative theta + alpha (T+A) amplitudes **within (H 1a)** and ***across (H 1b)*** NFT sessions. NFT. These measures will not change significantly in the placebo group.

Hypothesis 2 (H 2): A ten-session NFT protocol of up-training alpha (8-11 Hz) and theta (5-7.5 Hz) frequency bands at Pz will significantly lower the subjective experience of trait anxiety. These measures will not change significantly in the placebo group.

2.2.2 Secondary hypotheses (Treatment effect hypotheses).

Hypotheses 3 (H 3a and 3b): The treatment group will feel significantly more deactivated (as assessed by Thayer's AD-ACL check list) **within** a NFT session (**H 3a**) and will subjectively become significantly more deactivated **across** NFT sessions (**H 3b**) while the placebo group will not.

Hypothesis 4 (H 4): The treatment group will show significant increase in absolute and relative theta and alpha amplitudes and absolute and relative theta + alpha (T+A) amplitudes across sessions which will correlate with higher deactivation and lower activation scores of the AD-ACL, while the placebo group will not.

Hypothesis 5 (H 5): The treatment group will show a significant increase in absolute and relative theta and alpha amplitudes and absolute and relative theta + alpha (T+A) amplitudes across sessions which will correlate with a decrease in trait anxiety as measured by the STAI-T inventory.

Hypothesis 6 (H 6): The treatment group will have a significant increase in absolute and relative theta and alpha amplitudes and absolute and relative theta + alpha (T+A) amplitudes on the mini-QEEG in the Pz region while the placebo control group will not.

Hypothesis 7 (H 7): Self-perceived successful cognitive strategies to modulate brain waves will be significantly correlated with learning as specified by the A/T NFT protocol.

2.2.3 Control for treatment expectations and self-efficacy.

Hypothesis 8 (H 8): No significant differences between the treatment and the placebo group in treatment expectations / self-efficacy as measured by the Stanford Expectations of Treatment Scale (SETS) and the Rotter Locus of Control Scale (LOC) will be observed in the study. There will not be significant differences between the treatment and the placebo group's pre-and post-treatment satisfaction as measured by the SETS modified outcome scale.

Hypothesis 9 (H 9): Participants' NFT learning will be significantly correlated with each participant's self-identified time-of day best, worst or neutral period for learning.

3. Methods

3.1 Procedure

To determine the number of required participants for this study with the adequate power to detect moderate effects between EG and CG a power analysis was performed. The overall design of the study called for a mixed ANOVA where treatment condition (A/T vs. B u/d control) serves as the between-subjects, and pre/post levels of anxiety, as the within-subjects factor. Treatment effectiveness (across both groups) would be reflected in a significant within-subjects effect and the efficacy of NFT specifically would be reflected in an interaction whereby significantly more improvement (i.e., lowered trait anxiety) would be found in the A/T NFT in contrast to the B u/d control condition. A power analysis using *G*Power, version 3.1 for Mac* (Faul, Erdfelder, Lang, & Buchner, 2007; http://www.psycho.uni-duesseldorf.de/abteilungen/aap/gpower3) using the partial eta squared from prior A/T NFT studies with significant results revealed that in a respeated measures 2x2 ANOVA a total of 27 participants (N = 27) was required to detect moderate sized (f = .25) interaction effects and within-subject's effects with adequate power (.80), and was subsequently recruited for this study.

This study was designed to have an experimental and an active placebo group. While I would have gladly offered the placebo group participants the experimental treatment after the end of the trial this was not done due to time and budget constraints. This study was completely self-financed, apart from the office space, NFT, and EEG equipment which Dr. John Saksa graciously supplied me with for free. Furthermore, La Vaque and Rossiter (2001) reported that most participants who initially were in the CG were not interested in receiving the active NFT after the end of the trial.

3.1.1 Recruitment of participants.

The participants were recruited from the greater Hartford, CT area through the publication of the study protocol in *ClinicalTrial.gov*, the National Institutes of Health online trial database (Appendix C). Participants were further recruited via word of mouth and repeated articles in 16 local online publications of *The PatchUSA* (patch.com) for 16 towns within a 20-mile driving radius to the site of this study, as well as in *U-Notes*, the University of Hartford's daily publication for faculty, staff, students, and alumni. Flyers were posted on approved bulletin boards at two universities' student psychological counseling centers, in a local public library, on event boards, at a psychotherapy practice, a local coffee house, and two grocery stores with communal gathering areas. A list with venues, locations and exact dates may be found in Appendix B. The information flyer and online news articles were checked and edited by the Word for Windows reading level analysis until the document was congruent with the 8th grade reading level required by the University of Hartford's Institutional Review Board, the Human Subjects Committee. To recruit people via word of mouth a response template was used to standardize the way information was given.

Potential participants were asked to read and sign a pre-screening consent form informing them of the study, including a description of the procedures, risks and inconveniences, benefits, confidentiality, voluntary participation, and potential questions. They were then given the link to fill out the encrypted *surveymonkey* screening questionnaire (Appendix C). Interested individuals were given further information about the study: one general interest article from the *Scientific American* magazine (Kraft, 2006) and one scientific review article from the *Journal of Neurotherapy* (Hammond, 2011) were emailed to them.

Participants of the study received $5 cash at the beginning of each of the ten NFT

sessions to offset the costs of travel. In addition, they received a $100 gift card of their choice from a local grocery store, restaurant, or any one of various online stores, for their time and expense once they completed all ten NFT sessions, QEEG, and other post-trial questionnaires.

3.1.2 Screening criteria.

Participants were included in the study if they scored in the moderate to severe anxiety range on the State-Trait Anxiety Inventory (STAI-T; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 2015), the Beck Anxiety Inventory (BAI), and the GAD-7. Furthermore, their scores on the Beck Depression Inventory (BDI-II, Beck, Steer, & Brown, 1996) and the PHQ-9 had to indicate either no or mild depression, and they could not have self-reported severe psychiatric or neurological disorders (such as schizophrenia, major depression, substance use disorder, Parkinson's disease, epilepsy, or ALS) as assessed by the *Demographic and Medical Screening Questionnaire* (Appendix C). They may or may not have been diagnosed with an anxiety disorder.

The cut-off score for trait anxiety of above the 66^{th} percentile of the respective normative group was defined as moderate to high trait anxiety and was used to determine if the subject should be included in the study. For the general population of females ages 19-39, scores of > 39, ages 40-49 scores of > 37, and ages 50-69, scores of > 43 were considered accepTable. Traditionally-aged female undergraduate students with a total score of > 43 were included. For the BAI and the GAD-7 the cut-off scores were >15 and >11, respectively, which corresponded with a score of at least moderate anxiety.

To avoid the confounding factor of the frequently observed comorbid condition of depression with anxiety, the BDI-II and the PHQ-9, two reliable depression inventories, were

administered to exclude potential participants whose scores indicated a moderate, moderately severe, or severe depression. Participants with scores of > 19 on the BDI-II and scores of > 9 for the PHQ-9 were screened out.

The use of prescription medications is ubiquitous in the United States; the most recent U.S. Center of Disease Control and Prevention (www.cdc.gov/nchs/data/hus/hus15.pdf#079) Study (2015) reports that 65% of U.S. adults have taken prescription medication within the past 30 days. Moore and Mattison (2017) write that in the 2013 Medical Expenditure Panel Survey 17% of U.S. adults report that they currently take psychotropic medications, with higher percentages for women and Caucasians. For this reason, the customary exclusionary criterion of prescription drugs was not enforced in this study, but a less restrictive parameter was used: prescription medication use had to remain the same for the duration of the study so that difference scores for NFT between sessions and pre- and post-treatment scores on the QEEG and the psychometric measures could be calculated without confounding variable. However, illicit drug and excessive alcohol consumption remained exclusionary criterion for this study.

The initial screening was done through the online platform *surveymonkey* after converting the demographic and medical questionnaire, the GAD-7, and the STAI into online format for potential participants to take whenever they wanted. The two depression measures were taken in the presence of the experimenter and with Dr. John Saksa, an APA-licensed clinical psychologist, in case of any adverse reactions to questions in the depression inventories, such as expressing a desire to commit suicide.

3.1.3 Participants.

All subjects provided both written consent before taking part in the screening and a more detailed written consent form before participating in the experiment (Appendix B). In the consent

form the study procedures, risks and inconveniences, benefits, economic considerations, confidentiality, and voluntary participation were described. Any identifiable information about participants, collected in this study remained confidential and was not stored with personal identifiers, but rather with the subject number. The master list connecting subject number with name was stored a a paper copy in the primary investigator's office in a locked cabinet.

This study was conducted in accordance with Title 45 of the United States Code of Federal Regulation (CFR 46) and the Declaration of Helsinki. It was approved by the Human Subjects Committee (IRB) of the University of Hartford, CT, USA (study number PRO 15070009).

3.1.4 Randomization.

The study participants were randomly assigned to one of two groups: either the experimental group of alpha/theta frequency band uptraining (A/T; n = 15) or the control group of alternating beta/high beta up- and down-training (B u/d; n = 13) without stratification. The randomization was created in *Matlab 9.0* (*MathWorks*, R 2016a). Seven random four-integer zero-one vectors, defined as 2 zeros and 2 ones in random order were created and matched in numerical order with participant numbers 001 to 028. Participants matched with the number zero were assigned to the control group; participants matched with the number one were assigned to the experimental group (see Appendix E 1).

3.1.5 Trial schedule and progression.

After filling out the study consent form participants were scheduled to come in for their initial appointment. At the end of the appointment the schedule for the remaining nine appointments was set up for two to three appointments per week with one day between two consecutive NFT sessions at approximately the same time of day (+/– 1.5 hours). Appointments

were available between 7:00 a.m. and 8:00 p.m., Mondays through Fridays, between 7:00 a.m. and 4:00 p.m., on Saturdays and in rare cases on Sundays. All participants worked or studied full-time or worked part-time, and only one NFT amplifier and computer with NFT software was available. Consequently, it was not always possible to accommodate two to three appointments at the same time per week if participants cancelled appointments after the initial schedule was set up and during the Thanksgiving holidays. In some cases, participants came in only once a week or on rare occasions not at all during one week then resumed their regular schedule; participants 008, 017, 021, and 022 all did not attend any NFT sessions for one week. The mean total days of participation was 32.2 days with a mean participation of 5.6 weeks per participant and a median of 2 sessions of NFT per week.

Participant no.	Days per week	Number of weeks	Total days
001	2,1,1,2,2,2	6	47
002	2,2,2,2,2	5	31
003	2,2,2,2,2	5	26
004	2,2,2,2,2	5	28
006*	1,2,2,2,2,1	6	33
007	1,1,1,2,1,2,1,1	8	44
008	2,1,0,1,1,2,1,1	8	51
009	2,1,3,2,2	5	33
010	1,2,2,2,2,1	6	34
011	2,2,2,2,2	5	31
012	2,2,2,2,2	5	30
013	1,1,3,2,3	5	30
014	2,2,3,2,1	5	30
015	1,2,1,2,3,1	6	27
016	1,1,1,2,1,4	6	30
017	2,0,2,2,2,1,1	7	37
018	1,3,3,2,1	5	27
019	1,3,2,3,1	5	24
020	2,3,2,3	4	24
021	1,2,0,1,3,1,1,1	8	47
022	2,2,2,0,1,1,0,2	8	46
023	1,2,2,2,2,1	6	38
024	1,2,1,1	19 days/5 sessions)	
025	2,1,4,3	4	21
026	4,3,2,1	4	21
027	1,2	10 days/3 sessions	
028	1,4,5	3	15
MEAN		**5.6**	**32.2**

*005 was taken out of statistical calculations because he was the only male in the study.

Table 3.1: NFT sessions per week, number of days and weeks of total NFT.

A *Neurofeedback Session Checklist* (Appendix C) was developed for this study to keep

the preparation for and process of each NFT session as standardized as possible, as well as to record date, time and name of the NFT technician who administered the respective session, observations and potential interferences for each NFT session. The information from all individual Checklists was entered into a master spread sheet (Appendix E). The principal investigator administered 68% percent of the NFT sessions, including all but two of the initial sessions (session 1 with pre-treatment QEEGs) and all last sessions (session 10 with post-treatment QEEGs). The remaining 32% of sessions were administered by two trained graduate assistants, for 14% and 18% of the sessions, respectively.

Forty-six individuals, 38 women and 8 men filled out the initial study consent form and the initial screening questionnaires: Demographic and Medical Questionnaire, STAI, and an abbreviated version of the PHQ-9 on *surveymonkey*, an online survey tool. The PHQ-9 depression screening was administered to screen out individuals that had high depression scores on a short depression measure before they came in for an appointment to take the BDI-II and additional tests. While three men qualified for the study, two decided not to participate after the screening. By the time the first 17 participants had been recruited and started the trial only one male was included. It was decided to continue recruiting women only for the remaining ten participants, allow the only male to finish the trial but replace his data with data from a 28th female participant. Participants were randomly assigned to either the experimental (1) or control group (0) by random 0-1 vector creation in Matlab (Appendix E). All fourteen participants from the EG finished the trial and two participants from the CG dropped out, one after three sessions of NFT and one after five sessions of NFT.

All trial procedures were the same for participants from the EG and CG, except that the EG received an A/T protocol for all ten NFT sessions, whereas the CG received alternating beta

up- and down-training (see 3.4.2).

Pre-Screening: **Total time:** **30 minutes**	Fill out **Screening Questionnaire** (demographic, medical, STAI, and abbreviated PHQ-9) on *surveymonkey*.	20 minutes
	IF qualified, THEN fill out BDI-II and PHQ-9 in person.	10 minutes
	IF BDI-II scores were below cut-off, THEN invite to participate in study.	
	↓	
	Assign participant a three-digit number (001-028) and randomly assign her to either A/T or control NFT group.	
Session 1: **Total time:** **90 minutes**	Welcome, explain procedures, and answer broad questions.	10 minutes*
	Fill out the following questionnaires on *surveymonkey*: 1. Pre-treatment **Stanford Expectations of Treatment Scale (SETS)**, 2. Pre-treatment **BAI**, 3. Pre-treatment **GAD-7**.	10 minutes*
	Pre-treatment **mini-QEEG**: 5x4 channels for 2 minutes each.	30 minutes*
	1. Fill out pre-session **AD-ACL Questionnaire** on *surveymonkey*, 2. **A/T or control NFT** on Pz for 3 x 8 minutes with two 30-60 second breaks in between sets, 3. Fill out post-session **AD-ACL Questionnaire** on *surveymonkey*.	40 minutes*
Sessions 2-9: **Total time:** 8 x 40 minutes = **320 minutes**	1. Fill out pre-session **AD-ACL Questionnaire**, 2. **A/T or control NFT** on Pz for 3 x 8 minutes with two 30-60 second, breaks in between sets, 3. Fill out post-session **AD-ACL Questionnaire**.	40 minutes*
Session 10: **Total time:** **100 minutes**	1. Fill out pres-session **AD-ACL Questionnaire**, 2. **A/T OR control NFT** on Pz for 3 x 8 minutes with two 30-60 second breaks in between sets, 3. Fill out post-session **AD-ACL Questionnaire**.	40 minutes*
	Post-treatment **mini-QEEG**: 5x4 channels for 2 minutes each.	30 minutes*
	Fill out the following questionnaires on *surveymonkey* (in stacked order): • post-treatment **STAI**, • Post-treatment **BAI**, • Post treatment **GAD-7**, • Post-Treatment **SETS**, • **NFT Strategies and Feedback Questionnaire**, • **Rotter LOC Questionnaire**.	25 minutes
	Debriefing	5 minutes
Total Time investment per participant for clinical trial: **510 minutes = 8 .5 hours =** 1 x 90 minutes + 8 x 40 minutes + 1 x 100 minutes. *All times were tested on three healthy adult volunteers before the start of the study and averaged.		

Figure 3.1: Overview of all assessment and treatment sessions of the study.

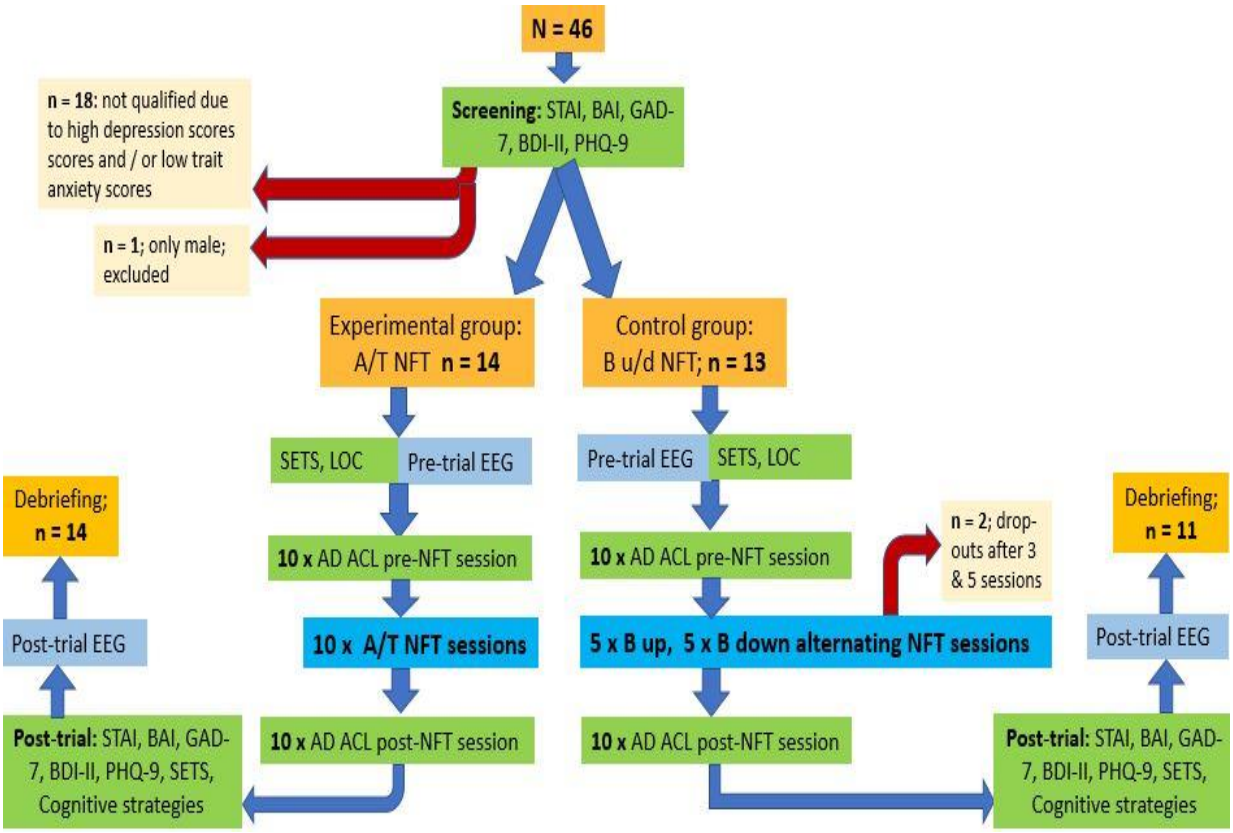

Figure 3.2: Flow chart of trial progression.

3.2 Psychometric Assessments

3.2.1 Demographic and medical questionnaire.

The Demographic and Medical Questionnaire was partially adapted and translated from Mayer (2013, 2016) but also incorporated items from other standard biomedical and demographic questionnaires.

3.2.2 Patient Health Questionnaire Depression Scale (PHQ-9).

The PHQ-9 Depression Scale (Spitzer, Williams, Kroenke, et al., 1992) is a valid and reliable brief instrument to detect severity of depression. The scale was tested by Kroenke et al. (2001) on a sample of 3,000 primary care patients and possesses high internal reliability (Cronbach's $\alpha = .89$), and very good criterion validity (88% sensitivity and specificity, respectively) when comparing depression diagnoses of 580 adults with scores of the PHQ-9 scale. The scale consists of

nine items with four-point Likert–type questions: (0) *not at all*, (1) *several days*, (2) *more than half the days*, (3) *nearly every day*. The total scores for the items range from 0 to 27 with higher scores indicating a higher depression severity: Scores of 1-4 (*no depression*), 5-9 (*mild depression*), 10-14 (*moderate depression*), 15-19 (*moderately severe depression*), and 20-27 (*severe depression*).

3.2.3 Beck's Depression Inventory (BDI-II).

The BDI-II (Beck et al., 1997) contains 21 Likert scale self-report items to assess depression and its severity during the current week. As with the PHQ-9, the scale ranges from *almost never* to *almost always*, with higher scores indicating more severe depressive symptoms: *minimal depression* (0-13 points); *mild depression* (14-19); *moderate depression* (20-28); and *severe depression* (29-63). According to Beck (2015) the BDI-II has a high internal reliability; it was tested on a sample of 500 psychiatric outpatients and sample of 120 college students with Cronbach α of .92 and .93, respectively. The convergent and discriminant validity of the BDI-II was assessed by correlating it with other depression and anxiety scales and showed a high correlation (r =.71) with the Revised Hamilton Psychiatric Rating Scale for Depression (HRSD-R).

3.2.4 Beck's Anxiety Inventory (BAI).

The BAI is a "measure of dispositional anxiety not contaminated by dispositional depression" (Kohn et al., 2008, p. 499). This self-report questionnaire contains 21 Likert-scale questions representing symptoms frequently associated with anxiety, such as being able to relax, being terrified, and fear of losing control. For each symptom, the respondent decides how much it has bothered him or her within the last week on a 4-point rating scale: *Not at all*; *Mildly, it did not bother me much*; *Moderately, it was very unpleasant, but I could stand it*; and *Severely, I*

could barely stand it. The scores are added up from zero points for *Not at all* to three points for *severly* with higher scores indicating more sever anxiety: *minimal anxiety* (scores of 0-7), *mild anxiety* (scores of 8-15), *moderate anxiety* (scores of 16-25), and *severe anxiety* (scores of 26-63).

3.2.5 Spielberger's State Trait Anxiety Inventory (STAI).

The State-Trait Anxiety Inventory (2015) consists of two scales of 20 self-rated Likert–type items each, for assessing trait (STAI-T) and state anxiety (STAI-S). Each item is rated between one and four in intensity. STAI-S items include: *I am tense; I am worried; I feel calm*; and *I feel secure*. Participants choose the number that best describes the intensity of their feelings: *not at all* (1), *somewhat* (2), *moderately so* (3), or *very much so* (4). STAI-T include: *I worry too much over something that really doesn't matter*; *I am content*; and *I am a steady person* and subjects choose how they generally feel by rating the frequency of their feelings of anxiety: *almost never* (1), *sometimes* (2), *often* (3), or *almost always* (4).

The scales are normed for the general and student populations by biological sex and age range. For this study, cut-off scores for inclusion in the study were scores of > 66.9th percentile or trait anxiety for the respective normed group —which equals moderate to high trait anxiety. For the general population of females age 19-39, scores of 40 or higher were considered, for females, ages 40-49 a score of 38 or higher was sufficient, and for females ages 50-69 a score of 44 or higher was considered accepTable. Average-aged female undergraduate students with a total score of 44 or higher were included.

3.2.6 Generalized Anxiety Disorder questionnaire (GAD-7).

The GAD-7 is a seven item self-report scale that was developed and validated on a sample of 2,740 primary care patients by Spitzer, Williams, Kroenke, et al. in 1992 to screen for GAD (89% sensitivity), but according to its manual has good sensitivity to diagnose PD, SAD, and

PTSD (82% sensitivity). The four-point Likert–type response scale has the following anchors: (0) *not at all*, (1) *several days*, (2) *more than half the days*, (3*) nearly every day* and total scores range from 0 to 21, with the following anxiety severities: *No anxiety* (scores of 0-5), *mild anxiety* (6-10), *moderate anxiety* (11-15), and *severe anxiety* (16-21). When screening for anxiety disorders, a recommended cut-off point for further evaluation is a score of 10 or greater (Löwe, Decker, Müller et al., 2008).

3.2.7 Stanford Expectation of Treatment Scale (SETS).

The Stanford Expectation of Treatment Scale (SETS) was developed by Younger, Gandhi, Hubbard, and Mackey in 2012 as a measurement instrument for clinical trials to quantify participants' positive or negative treatment outcome expectancies, which are influenced by the participants preconceived opinions, information from the experimenters, mass media coverage, etc. The SETS is a six-item scale with a seven-point Likert–type response with the following anchors (1) *strongly disagree*, (2) *moderately disagree*, (3) *slightly disagree*, (4) *neither agree nor disagree*, (5) *slightly agree*, (6) *moderately agree*, and (7) *strongly agree*. Items 1, 3, and 5 are averaged for positive expectancy, and items 2, 4, and 6 for negative expectancy.

3.2.8 Thayer's Activation Deactivation Checklist (AD-ACL).

The Activation Deactivation Checklist (AD-ACL) was devised by Thayer (1986, 1989) and is a valid and reliable 20-item Likert–type scale that uses adjectives to describe feelings or mood and activated or deactivated state (energy) levels. Each item is rated on a four-point scale ranging from zero to three: *Definitely do not feel* (0), *cannot decide* (1), *feel slightly* (2), and *definitely feel* (3). The twenty adjectives are divided into four sub-scales: (1) *energy (General Activation)* represented by the adjectives: active, energetic, vigorous, lively, full of pep; (2) *tiredness (Deactivation-Sleep)* depicted by the adjectives sleepy, tired, drowsy, wide-awake,

wakeful; (3) *tension (High Activation)* represented by the adjectives jittery, intense, fearful, clutched-up, tense); and (4) *calmness (General Deactivation)*, depicted by the adjectives placid, calm, at rest, still, quiet. The factors *Energy* and *Tension* can be combined into the higher order factor, *Activation* and the factors *Tiredness* and *Calmness* into the higher order factor, *Deactivation*.

3.2.9 Neurofeedback Session Coding List.

Motivation and mood are two powerful factors that influence learning, especially in the NFT and BCI domains (Nijboer, 2008). Consequently, assessing participants motivation and their positive and negative affect before and after NFT sessions and asking them how they thought they performed could have been a useful tool to check for lacking challenge (Mirifar, Beckmann, & Ehrlenspiel, 2017), frustration and even learned helplessness that may mediate NFT learning performance. In this study any unusual circumstances, such as participants reporting lack of sleep, headache, or frustration with no perceived NFT improvement was recorded on the *NFT Session Coding List* (see Appendix D).

3.2.10 Rotter's Locus of Control Questionnaire (LOC).

The Locus of Control Questionnaire by Rotter (1966) is a 29-item forced-choice scale where a participant must choose between two value statements and six filler forced choice items that are not counted toward a test score. Each item scores as one or zero. The scale measures whether a person attributes a positive or negative outcome as contingent upon her own behavior, such as skill or due to external circumstances, like chance or luck. Related to this attribution a subject may also differ in generalized expectancies for internal versus external control. A high score on the LOC represents an external locus of control. A low score represents an internal locus of control, the mean score across several general populations is 8.19 (SD = 3.47).

3.2.11 Neurofeedback Strategies and Treatment Satisfaction questionnaire.

In every NFT study there are individuals, so-called non-learners, who, even after many sessions, are not able to learn how to modulate their brain waves. This issue has been attracting much research interest of late. It is estimated that between 33% and 50% participants of NFT studies are non-learners, depending on the calculations of change parameters, NFT protocol, and target group of participants (Alkoby, Abu-Rmileh, Shriki, & Todder, 2017). Non-learning of neuromodulation via NFT has various reasons, such as complexity or type of the feedback signal, differences in trainability of certain brain wave amplitudes, poor EEG signal processing (Jeunet, Jahanpour, & Lotte, 2016), but also using cognitive strategies (Hardman, Gruzelier, Cheesman, et al., 1997; Kober, Witte, Ninaus, et al., 2013). Kober and colleagues (2013) hypothesize that the use of strategies might actually "hinder the implicit learning of neuromodulation due to overburdening limited cognitive resources" (p. 7).

Therefore, a questionnaire (Appendix D) was administered after completion of the ten NFT sessions that asked about which mental strategies if any were used during the NFT training and how effective these strategies had been for the respective participants. Furthermore, participants were asked what specific changes (if any) in thoughts, feelings and behavior in everyday life they perceived, and as a measure to control treatment expectancies subjects were asked what group they believed they were part of, EG or CG. Lastly, cognitive tasks, even unconscious ones, such as NFT, involve attention, learning, and memory; they are dependent on the degree of wakefulness of the participant (Knight & Mather, 2013). Hence, questions regarding times-of-day for optimal learning, worst learning and "neutral times" were included.

3.3 Pre- and Post-Treatment QEEG

An EEG was recorded before and after the completion of ten NFT sessions. Participants had been instructed before the start of the study to wash their hair before EEG and NFT sessions and not to use any hair products, such as crème rinse, spray or gel in their hair, as sweat, sebum, and hair products alter the EG signal acquisition. Electro-Cap™ with 19 pure tin electrodes, were positioned on the scalp according to the international 10-20 electrode EEG system and linked ear sensors were used for the recording. The scalp and forehead were prepared with Weaver's *Nuprep* skin prep gel to remove any dead skin cells and other products that might interfere with the EEG signal and ECI's *Electro-Gel* was inserted into each electrode with a syringe.

The *Brainmaster Atlantis I, 4×4 Module ® 3.0* amplifier and *Brain Avatar miniQ* software (Brainmaster Technologies, Inc.; http://www.brainmaster.com/) were used to record EEG brain oscillations (in Hz) for 120 seconds during standardized condition (relaxed, eyes closed, chin lightly placed on a chin and forehead rest) with linked ears as the reference. The raw electrical potential and wave frequency bands (in Hz) were amplified, fed digitally into the Brainmaster software, and transformed. Artifacts, such as movements, eye blinks, heart rate, respiration, and other corrupting factors were removed during the software calibration process. The sampling rate was 250 datapoints/second at 256 Hz. To filter out artifacts from the standard 120 Hz AC/DC electricity in the United States a 60 Hz notch filter was used. Furthermore, an IIR Butterworth filter with a high pass filter at 1 Hz and a low pass filter at 40 Hz with a filter order of 6 was used and the artifact removal was set at 200 microV.

Before statistical analysis, the raw EEG data were fast-fourier transformed (FFT) in *Neuroguide* which allowed an analysis of the data from the 19 channels in term of relative and absolute power of delta, theta, alpha, and beta (Beta 1-3) waves, as well as all combinations of

wave ratios, including T/A ratios. The EEG data were examined with a 2x2 ANOVA, comparing the variable TIME (pre- and post-treatment) and the variable GROUP for each, the changes in relative power for alpha, theta, and the theta/alpha ratio at the Pz location. Since the study hypothesis did not specify directionality of the comparison variance a non-directional, two-tailed significance test was performed with the p-value set at $p < .05$. Eta square was computed to analyze effect size.

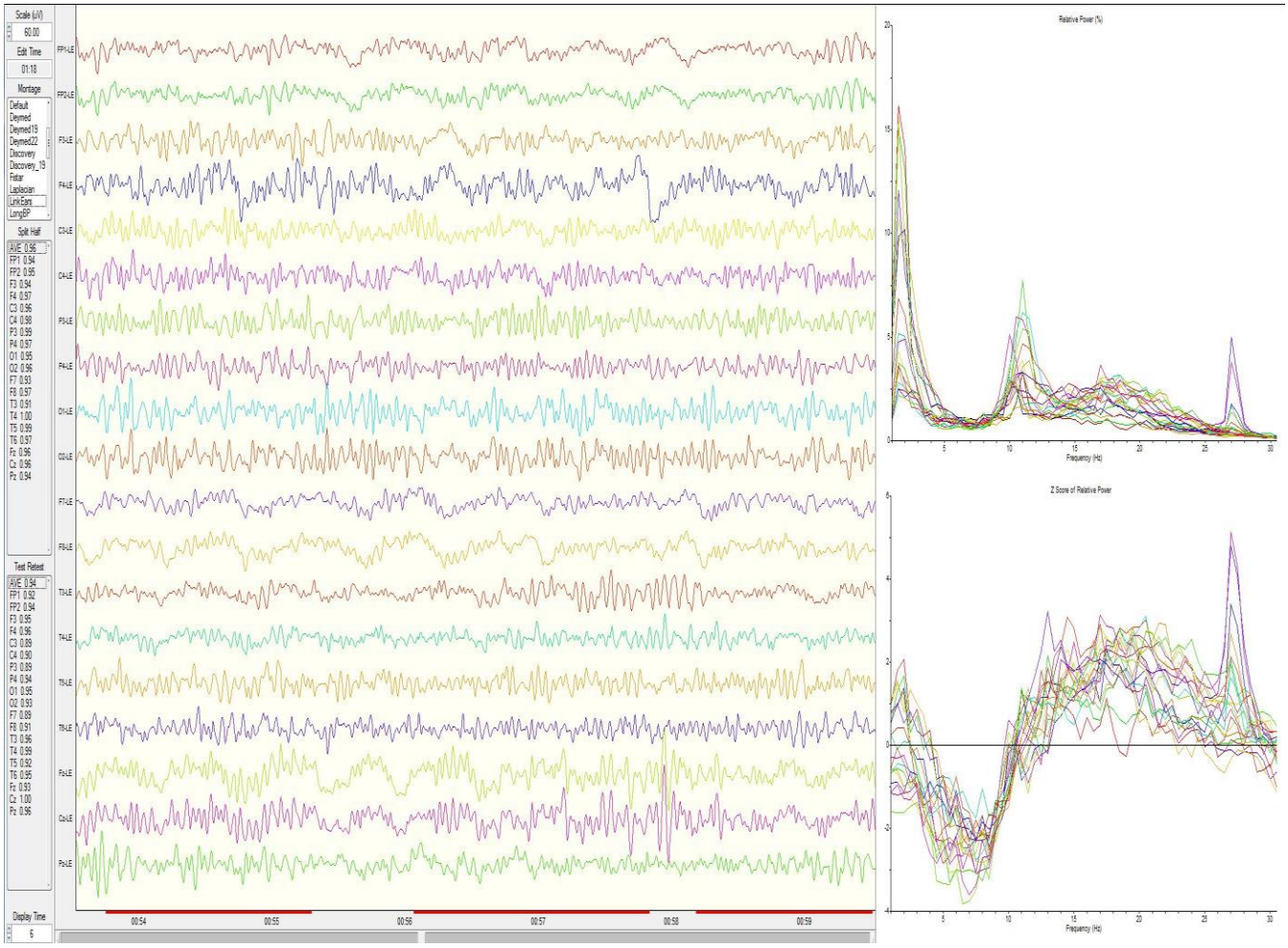

Figure 3.3: Post-trial EEG from a study participant after concatenation of *Brainmaster* data in the *Neuroguide* software with four time-locked channels at a time (from top to bottom, first four channels, time-locked; next four channels time-locked, etc.). On the left: split half and test-retest reliability for all 19 channels; right top: relative power; bottom right: z score of relative power.

3.4 Neurofeedback Training

The BrainAvatar® 4.0 software from Brainmaster Technologies, Inc. was used for all NFT sessions, connected to the *BrainMaster Atlantic I*, 4 × 4 Module (*Brainmaster*

Technologies, Inc.; http://www.brainmaster.com/). The Pz location from 10-20 international EEG location system was selected as the active EEG recording site for both, A/T (EG) and B u/d (CG) training with a reference electrode on the right earlobe and a ground electrode on the left earlobe. The rationale for the respective NFT protocol and the Pz electrode site are described in Section 1.3.1. The ongoing EEG recording at Pz was sampled at 256 Hz per second at a resolution of <0.01 Hz, and 10,000 amplification. Impedance was maintained below 7 kOhm. Band pass filter (80 Hz high and 60 Hz low pass) and an A/D low pass filter (allowing 0.1-30 Hz activity) were used. Global smoothing time was set at 500 ms at 3 dB with a text damping factor at 100 ms and frequency band changes on the fly at .005. The artifact rejection threshold was set at 200 microV to control for eye and muscle artifacts. Amplitude values for delta, theta, alpha and beta bands were extracted from the raw EEG and then Fast Fourier transformed (FFT).

Each NFT session used a standardized Neurofeedback Session Checklist (Appendix D) and lasted for approximately 45 minutes including, filling out the AD-ACL questionnaire pre- and post- NFT session, connecting and disconnecting the EEG leads to the participant, recording of a one- minute baseline EEG at the Pz location and three eight-minute NFT blocks with two, one to two- minute breaks between the blocks. The lengths of the breaks depended on each participant's preference. Participants were seated in a comforTable chair, approximately three feet from the computer monitor giving audio-visual feedback during the NFT sessions. The room in which all QEEG and NFT sessions were administered was windowless, and shortly before the start of the EEG and NFT recording the lights were dimmed to keep distraction to a minimum. The experimenter sat quietly at a second computer screen perpendicular and approximately five feet away from the participants, so as not to distract the subject from the NFT tasks and to monitor artifacts and record participant behaviors and concerns.

After the placement of the electrodes the participant was instructed to relax with eyes open for approximately 60 seconds, allowing the experimenter to check for appropriate signal transmission, impedance, and artifact control. Afterwards the EEG initial baseline was recorded for 30 seconds and used to calculate the reward criteria for the two audiovisual feedback signals. As described above, the Brainmaster Avatar software extracted the component amplitude band width from the continuous data stream, using third order Butterworth filters. The results of the band width filtering were almost instantaneously displayed on the experimenter's computer screen in both raw and extracted amplitude bands. The value of the band amplitude was transformed online into audiovisual feedback which was displayed to the participant on the 22-inch computer monitor. The actual operant reward criteria differed depending on the NFT protocol of the EG and CG will be discussed in the next two Sections (3.4.1 and 3.4.2). Feedback thresholds were kept constant during each of the three eight-minute segments.

Instantaneous visual feedback was given via the *Flying Vulcan* video on the *Brainmaster* multi-media player for EG and CG groups. The video showed a non-threatening dragon slowly flying toward and by the viewer in a continuous eight-second loop. The video brightened (Figure 3.6, left) when the to-be-trained waveband reward thresholds were reached and became successively brighter, the longer the participant's oscillations (alpha and theta for the EG and two Beta bins for the CG) remained above threshold and darkened (Figure 3.3, right graphic) when the oscillations dropped. The *Flying Vulcan* video was only able to generate one feedback signal. Therefore, the visual feedback was programmed by summing the thresholds for feedback conditions 1 and 2 and dividing them by two, creating an average that would be used as input signal for the visual feedback.

Figure 3.4: Computer screen shot for NFT: Visual feedback was given via *Flying Vulcan* video (adapted by B. Viereck from the video from the *Brainmaster* multi-media player). The video brightened (left graphic) when the alpha and theta reward threshold was reached became successively brighter the longer the participant's alpha and theta oscillations remained above threshold and darkened (right graphic) when the oscillations dropped and remained dark as long as the reward threshold was not crossed.

In addition, two auditory feedback sounds were given when the same sustained feedback criteria and refractory time between feedbacks were achieved. Each sound was louder proportionally to the power of the to be trained waveband (i.e., higher the power of the to be trained waveband the louder the sound) and more frequent the more time the participant was able to keep the trained wavelength over the threshold. The two feedback reward sounds were a steel drum sound (MIDI note 52 at 1046.5 Hz) and a pan flute sound (MIDI note 61 at 1760.0 Hz). Loudness starting level was set at 50 with a loudness change rate of 10. Both visual and audio feedback were set for an autothresholding so that reinforcement was provided for 65% of the time and was autoupdated after each 60-second epoch. In each session before the first eight-minute training block a 30-second baseline was taken and for the second and third training block 10-second baselines were taken.

3.4.1 Experimental group: Alpha/theta neurofeedback training.

For participants of the EG, a relative increase in theta amplitude (5-7.9 Hz) for a sustained time of over 250 ms was rewarded with a MIDI steel drum sound. The refractory time between successive rewards was set at 200 ms. A relative rise in alpha amplitude (8-11 Hz) was

rewarded with a MIDI pan flute sound. The visual reward was given when the activity for both alpha and theta was above the supra-threshold at approximately 65% of the time (A+T)/2. Beta (15-30 Hz) and delta (2-4 Hz, inhibited for eye blink artifacts) were inhibited which meant that if relative beta or delta increased no reward would be given, even if alpha or theta amplitudes improved.

3.4.2 Placebo control group: Successive sessions beta up- and down-training.

Participants from the placebo CG received successive sessions of beta and high beta bands up- and down-training. In all uneven NFT (protocol a: sessions 1, 3, 5, 7, and 9) an **increase** in beta (15-19 Hz) and high beta (20-24 Hz) amplitudes over the supra-threshold of 650 ms and 130 ms with a refractory period of 200 ms between feedback sounds were rewarded with a steel drum and pan flute sound, respectively. In all even NFT sessions (protocol b: sessions 2, 4, 6, 8, 10) a **decrease** in beta (15-19 Hz) and high beta (20-24 Hz) amplitudes over the supra-threshold of 350 ms and 750 ms with a refractory of 200 ms between feedback sounds were rewarded with a steel drum and pan flute sound, respectively. Delta at 2-4 Hz was inhibited for eye blink artifacts.

This protocol follows Doppelmayr's (2011) general idea of successively up-and down training different beta bins to allow learning within session but not between sessions. However, in Doppelmayr's so called, randomized broadband placebo feedback randomly selected training frequencies within the beta band changed every session and participants were informed to either increase the amplitudes of 1-Hz broad bands between 6 and 35 Hz for half the blocks during a training session and decrease the same band for the other half of each session. Those bins that interfered with the frequencies of the SMR and theta/beta ratio training of the two experimental groups were inhibited. But Doppelmayr's protocol had technical difficulties with maintaining

appropriate reward levels when switching from increase to decrease of bins and in order to keep participants motivated had to manually change reward thresholds between training blocks. Thus, this researcher made the decision not to switch between up- and down-training of certain beta and high beta bins for half of a session each.

The placebo protocol was used with three healthy volunteers before the start of the clinical trial; the protocol was programmed to have the same sustained time criteria as reward criteria. The trial run showed that beta-up training and high beta down-training received such high reward rate that the reward sounds were almost continuous, and volunteers were easily capable of distinguishing between control conditions a and b due to very high reward rates for beta up training in the uneven sessions and much lower reward rates for the even sessions. This was not a surprising result; high beta band, in this case 20-24 Hz bins, can be easily down-trained just by not thinking too hard and beta band (15-19 Hz) can be fairly easily up-trained according to the instruction that was given to all participants of relaxing and letting yourself be to thinking without much effort. In addition, the almost continuous reward rate was perceived as an unpleasant sound that made volunteers nervous and stressed and might thus artificially inflate the differences in sample between experimental and control groups in de-activation, anxiety level, and treatment satisfaction. To avoid this potential error the reward sound percentage and loudness the placebo protocols a and b were re-programmed to approximately emulate the reward rates of the experimental group. This was achieved by having the three healthy volunteers sit for all three conditions repeatedly and changing the programming for the sustained reward criterion condition met on the Brainavatar software so that volunteers in all three conditions, experimental group and placebo groups a and b, had approximately the same amount of rewards.

3.5 Statistical Data Analysis

Descriptive statistics and inferential statistics for the psychometric instruments were performed in SPSS (version 24.0, IBM Corporation, NY). QEEG data and the regression growth curve modeling for the neurofeedback data was performed in R Studio (version 1.0.136, http://www.R-project.org) with the additionally installed packages (lme4, lmertest, car, ggplot2, lattice).

3.5.1 Demographic and psychometric data analysis.

3.5.1.1 STAI, BAI, and GAD.

A two-factor repeated measure ANOVA was performed with the within-subject factor TIME (pre–post–treatment) and between-subject factor GROUP (A/T, CO) for the STAI-T, the STAI-S, the BAI, and the GAD-7, respectively.

3.5.1.2 AD-ACL.

Thayer's Activation-Deactivation Adjective Checklist (AD-ACL) was administered before and after each NFT session. Four two-factor repeated measure ANOVAs for the AD-ACL sub-scale factors *activated* and *deactivated* were performed with the within-subject factor TIME (pre–post NFT session) and between-subject factor GROUP (A/T, CO).

3.5.2 Correlation of neurofeedback change scores with psychometric measures and neurofeedback strategies and treatment satisfaction.

Pearson correlation calculations were performed to assess the strength of a linear relationship between the change scores of theta and alpha amplitudes, relative theta and alpha and theta/alpha ratio and the change scores of the psychometric measures of activation and deactivation (AD-ACL), treatment expectancy change, trait and state anxiety change, and change scores in the BAI and GAD-7, and Rotter's LOC scores. Additionally, a point-biserial correlation

analysis was performed to establish the strength of relationship between the NFT change scores and the belief in group belonging, time of NFT in relation to optimal learning time-of-day.

The qualitative items from the *NFT Strategies and Treatment Satisfaction Questionnaire* to specify what kind of strategies and changes were experienced due to the NFT were transformed into binary yes-or-no form for the following items:

- Were mental strategies employed?
- Were mental strategies successful?
- Did you experience any changes in feelings in your everyday life due to the NFT?
- Did you experience any changes in thoughts in your everyday life due to the NFT?
- Did you experience any changes behavior in your everyday life due to the NFT?

3.5.3 QEEG analysis.

The *Brainmaster Atlantis I* amplifier was only able to record four EEG channels at once. To obtain a 19-channel EEG the amplifier has a five-position dial that the experimenter switches to record the next set of four channels, and this procedure is repeated four times, until all 19 channels have been recorded, i.e., five recordings of four channels (with no recording on Oz). In other words, after the first four channels were recorded for 120 s the dial was turned, which severs the connection for the first four channels and establishes the connection to the next four channels for the recording. The channel recording sequence was as follows:

- Position #1: **Fz, Cz, F3, F4**
- Position #2: **C3, C4, P3, P4**
- Position #3: **T3, T4, O1, O2**
- Position #4: **F7, F8, T5, T6**

- Position #5: **Fp1, Fp2, Pz** (Oz shows on the screen but there is no electrode on the standard Electro-Cap™ at Oz)

As only four channels each were time-locked (due to the limitations in the Brainmaster EEG recording system) *Neuroguide*'s automatic algorithms for artifact removal for those artifacts that the Brainmaster system had not picked up, could not be used. The *Brainmaster Atlantis I* system did not remove artifacts appropriately, despite correct programming and several consultations with Brainmaster's technical support team.

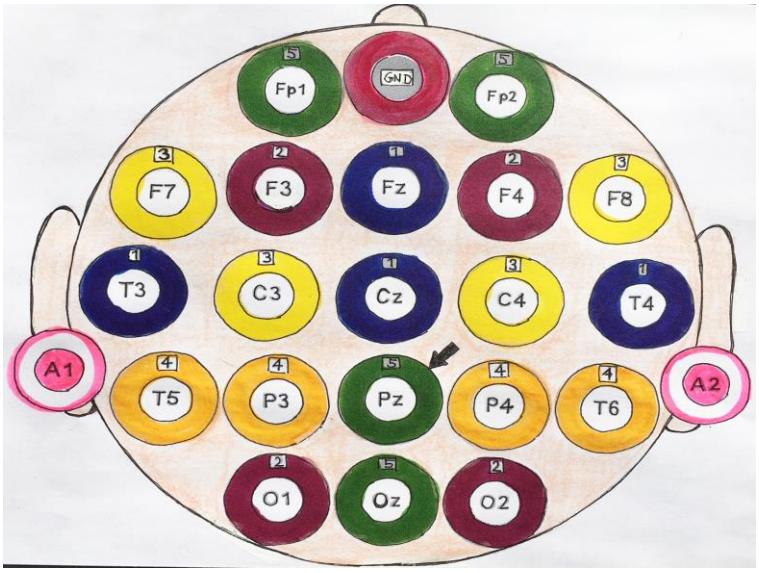

Figure 3.5: Electrode locations and switch positions for the *Brainmaster Atlantis*, 4-channel 5-position MINI-Q 2 EEG (Adapted by B. Viereck from BrainMaster MINIQ II User's Manual, 2007, p. 36; https://brainmaster.com/software/pubs/m-qII.pdf).

Thus, each participant's EEG files had to be imported into the *Neuroguide* software program (*NeuroGuide* 2.8.8, Applied Neuroscience, Inc., USA) and be concatenated into a full 19-channel EEG data set, for additional artifact removal. Since only four channels of each EEG data set were time-locked Neuroguide's automatic artifact removal did not work and artifact removal had to be manually obtained through visual inspection of each of the four time-locked EEG channels at a time. The following textbooks were used to guide the artifact analysis: Ebersole's *Current Practice of Clinical EEG* (2014), Hammond and Gunkelman's *The Art of Artifacting* (2001), and Niedermeyer & Lopes da Silva's (2003, *Electroencephalography—Basic*

Principles, Clinical Applications, and Related Fields (1999). Both split-half and test-retest reliability tests were conducted on the edited, artifact-free EEG segments. The records with > 95% split half reliability, > 90% test-retest reliability, and a total measurement of over 60 seconds were used for further statistical analyses. For all EEG recordings the average measurements split-half and test-retest reliability was > .90. The reliability for individual channels was > .90, except for 29 out of 988 channels recordings (total EEG recordings: 52) where the Brainmaster computer screen showed active oscillations of all channels on the monitor but the ASCII transcript of the channel's EEG had no data recorded. The channels with faulty recordings varied which made it unlikely that there was an electrode malfunction. For seven participants one channel did not record in the pre- and/or post treatment EEG, for three participants two channels, and for two participants three channels did not record correctly under the pre- and/or post-treatment condition.

The raw EEG data were fast-fourier transformed (FFT) which allowed an analysis of the data from the 19 channels in term of relative and absolute power of delta, theta, alpha, and beta (Beta 1-3) waves, as well as all combinations of wave ratios, including T/A ratios. The EEG data were examined with a 2x2 ANOVA, comparing the variable TIME (pre- and post-treatment) and the variable GROUP for the changes in relative power for alpha, theta, and the theta/alpha ratio at Pz. Since the study hypothesis did not specify directionality of the comparison variance a non-directional, a two-tailed significance test was performed with the p-value set at $p < .05$. Eta square was computed to analyze effect sizes.

3.5.4 Neurofeedback data analysis.

The *Brainmaster Atlantis I* provided delta, theta, alpha, low beta, beta, high beta, and gamma amplitude means, mean fraction of EEG energy in each waveform after FFT and the

standard deviation for all values after automatic artifact removal. Mean values were recorded every 15 seconds of the three eight-minute blocks during the NFT training and for a 30 second baseline recording before and after each eight-minute block of NFT. Most artifacts where automatically filtered out by the Brainmaster software algorithms. To capture and remove additional artifacts due to oculomotor, temporalis and frontalis muscles more accurately EMG electrodes at respective muscle sites would have been helpful. Unfortunately, this study had no funding to acquire this additional equipment. According to Goncharova, McFarland, Vaughan, and Wolpaw (2003) the contamination of the EEG by electromyographic artifacts is not very likely at the Pz location as the attachment sites of the temporalis and frontalis muscles, as well as the oculomotor sites are far away from Pz and Oz. Additional artifacts were removed by visually inspecting each NFT session record and excluding all data points for delta, theta, alpha and beta that had a measurement of over 100 Hz, after the initial artifact removal was done by the Brainmaster software. Any recordings over 100 Hz are very likely artifacts, except in epileptic seizures (Ebersole, 2014), which none of participants experienced during the trial. The data were averaged every 15 seconds so that four data points per minute were obtained for the 24 minutes of each NFT session and a 10-second baseline recording without feedback was recorded after minute 24.

The NFT session data were analyzed in *R Studio* with a hierarchical linear mixed model growth curve modeling (GCM) using the R statistical program with the lme4 package (Bates & Sakar, 2013) testing for main effects of within participant change (individual learning curves) and group membership (control or experimental group) and interaction between the two main effects. GCM is particularly well suited to analyze mixed effects time series data and to document learning curves because it can simultaneously analyze within subject effects, as well as between-subjects effects over multiple time points (Mirman, Dixon, & Magnuson, 2008). In comparison to a repeated measures ANOVA or traditional regression analysis for longitudinal

data, GCM regression has the advantage of building a separate regression model for each participant, accounting for individual differences in responding to the NFT, calculated as the random effects in each of the GCM regression models. In contrast, the traditional regression model assumes all participants respond the same to the treatment and the standard error represents differences in treatment response.

A predictor that varies in time (here absolute and relative alpha, theta, and T+A amplitudes, and T/A ratio) is modeled as the weighted sum of main effects between the criterion variables and their interactions with the second predictor being treatment group (A/T) versus control group (B u/d) membership. Predictor variables were added to the initial regression model (model a) in successive steps. In all successive models (b through e) added predictor variables were centered to lessen the collinearity between main effects and interactions. According to Mirman (2014) the strength of the growth curve model in comparison to the traditional multilinear regression model is that the researcher does not have to transform a continuous process arbitrarily into few discrete time bins to do the statistical thresholding. In other words, a lot of information regarding a learning curve is lost by using the mean for each session, or even means for the three eight-minute NFT session averages, instead of all 96 means for each session. Furthermore, GCM is very robust regarding missing data. Data from participants who did not finish the treatment can be included in the GCM. In this study two participants from the control group quit after three and five sessions, respectively.

The equation for the NFT component of this study can be modeled as follows: **T/A ratio (or alpha or theta amplitudes) ~ time effect (run or trial) + participant (within subject effect) + condition effect (experimental or control) + interaction effect (time x condition) + error.**

All analyses modeled were started with a null model (model A): lmer(y~1 +

(1|participant)). This model added the log likelihood (logLik) of the random intercept for each participant, i.e., a different intercept is assumed for each participant. The time variables *time within session* (RUN) and *time across sessions* (TRIAL) were centered, which means that the first-time measurement is defined as point zero, to make the interpretation of the variable coefficients easier. Each model added one of the effect variables seen above into the model and run and an ANOVA was run, comparing the effects of one model with the effects of the new model regarding goodness of fit of the log likelihood (logLik) via the χ^2 test, in other words has the likelihood in the new model increased enough to the predict variable *y* to warrant the addition of the new parameter (for complete R coding script see Appendix E).

4. Results

4.1 Participants

Twenty-seven subjects had been randomly assigned to the treatment condition (A/T NFT, n = 14) or to the control condition (B u/d NFT, n = 13). Two women from the control group dropped out; one after five NFT sessions due to time constraints with work and the other one, a student, after three sessions due to a six-week university holiday break that made the interval between individual sessions too long to be included in the study. Thus, 14 participants from the experimental group and 11 participants from the experimental group completed the study. The existing neurofeedback and AD-ACL data for the two dropouts was included in the study as GCM is very robust regarding missing data.

The participant sample was heterogeneous but normally distributed with a mean age of the women (n = 14) in the control group of 32. 23 years (SD = 12.76 years) with an age range of 19 to 56 years. The mean age of the women in the control group was 36.21 years (SD = 16.62 years) with an age range of 20 to 69 years.

Unfortunately, as Table 4.1a indicates, the participant sample was very homogeneous regarding race / ethnicity and education level: 89% of the participating women were White / Caucasian and 11% Hispanic; no African American, Asian / Pacific Islanders or Native American women participated. In comparison to the U.S. Census Bureau's 2016 data for the United States (https://www.census.gov/quickfacts/fact/table/US/PST045217) 77% of the country identify themselves as white, 18% Hispanic, 13% African American, 6% Asian, 3% multiracial, and 1% as American Indian. The Census further reports that 87% of the population of age 25 and above graduated from high school (or had higher education) and 30% of the population had a bachelor degree (or higher education). All participants had at least a high school diploma; 14.8%

of the participants had some college credits but no degree; 3.7% had an associate degree; 37.0% had a bachelor degree; 29.6% had a master degree; and 14.8% had a doctoral degree.

The 25.9% of women had not been formally diagnosed with any AD. 33.3% of the participants had been diagnosed with GAD, 25.9% with an AD diagnosed but not specified, 11.1% had been diagnosed with SAD, and 3.7% with phobia. There was no option given of marking more than one AD to force participants to choose the AD most prevalent for them. Additional descriptive statistics of the participant sample by group membership (CG or EG) can be found in Table 4.1b.

		N	Percent
Race/Ethnicity			
	White/Caucasian	24	88.9
	Hispanic	3	11.1
	Black	0	0.0
	Asian	0	0.0
	Native American	0	0.0
	Multiple Races	9	0.0
	Total	**27**	**100.0**
Handedness			
	Right-handed	25	92.6
	Left-handed	1	3.7
	ambidexterous	1	3.7
	Total	**27**	**100.0**
Educational level			
	Doctoral degree	4	14.8
	Master degree	8	29.6
	Bachelor degree	10	37.0
	Associate degree	1	3.7
	Some college but no degree	4	14.8
	Total	**27**	**100.0**

		N	Percent
AD diagnosed?			
	No	7	25.9
	Yes*	20	74.1
	Not specified	7	25.9
	GAD	9	33.3
	Phobia	1	3.7
	SAD	3	11.1
	Total	**27**	**100.0**
Taking AD medication?			
	No	20	25.9
	Yes	7	74.1
	Total	**27**	**100.0**
Taking Anti-depressant?			
	No	18	66.7
	Yes	9	33.3
	Total	**27**	**100.0**

Table 4.1 a: Descriptive participant demographics. (*No multiple AD selection was allowed.)

Lastly, Table 4.1 c illustrates that most participants used mental strategies over the course of the NFT trial to regulate their respective brain wave bands (84%) and little difference was

observed between EG and CG (89% of the EG and 82% of the CG). Of the participants who did use strategies, 86 % perceived their mental strategies to be successful (83% of the EG and 89% of the CG). Regarding perceived positive changes in feelings, thinking, and behavior due to the NFT 72% (90% of the EG and 55% of the CG) of participants reported changes in feelings, 48% successful (58% of the EG and 36% of the CG) in thinking, and 40% successful (43% of the EG and 36% of the CG) in behavior, with the participants of the EG reporting positive changes consistently at higher rates than the participants of the CG.

Descriptive Statistics

Experimental condition (AT NFT); Control group (B u/d NFT)		N	Minimum	Maximum	Mean	Std. Deviation
Control group: Bu/d NFT	Age in years	13	19.00	56.00	32.23	12.76
	State anxiety score (pre-NFT trial)	13	28.00	69.00	48.31	12.18
	Trait anxiety score (pre-NFT trial	13	36.00	67.00	50.54	10.10
	Beck anxiety Score (pre-NFT trial)	13	6.00	29.00	18.08	6.69
	GAD-7 anxiety score (pre-NFT trial)	13	4.00	14.00	9.15	3.29
	SETS Expectations of treatment score/ positive items (pre-NFT trial)	13	1.33	6.00	4.05	1.23
	SETS Expectations of treatment score/ negative items (pre-NFT trial)	13	1.00	5.00	2.23	1.56
	BDI Depression scale score (for screening applicants)	13	.00	18.00	7.77	6.51
	PHQ-9 Depression scale score (for screening applicants)	13	.00	10.00	4.08	3.48
	Total of days betw. beginning & end of NFT treatment.	13	10.00	51.00	31.38	11.17
	Mean NFT sessions per week	13	1.37	2.92	2.12	.45
Experimental group: AT NFT	Age in years	14	20.00	69.00	36.21	16.62
	State anxiety score (pre-NFT trial)	14	30.00	62.00	49.93	9.21
	Trait anxiety score (pre-NFT trial	14	40.00	76.00	56.64	10.40
	Beck anxiety Score (pre-NFT trial)	14	5.00	37.00	17.21	10.53
	GAD-7 anxiety score (pre-NFT trial)	14	5.00	18.00	10.86	4.54
	SETS Expectations of treatment score/ positive items (pre-NFT trial)	14	2.00	6.67	4.71	1.28
	SETS Expectations of treatment score/ negative items (pre-NFT trial)	14	1.00	4.67	2.05	1.29
	BDI Depression scale score (for screening applicants)	14	2.00	19.00	12.29	5.99
	PHQ-9 Depression scale score (for screening applicants)	14	2.00	10.00	5.86	2.60
	Total of days betw. beginning & end of NFT treatment.	14	14.00	47.00	30.14	9.46
	Mean NFT sessions per week	14	1.49	5.00	2.57	.92

Table 4.1 b: Descriptive statistics of interval variables of the participant sample by group.

		N	Percent
Race/Ethnicity			
White/Caucasian	EG	13	48.2
	CG	11	40.7
	All	**24**	**88.9**
Hispanic	EG	1	3.7
	CG	2	7.4
	All	**3**	**11.1**
Black	**All**	**0**	**0.0**
Asian	**All**	**0**	**0.0**
Native American	**All**	**0**	**0.0**
Multiple Races	**All**	**0**	**0.0**
	Total	**27**	**100.0**
Handedness			
Right-handed	EG	14	51.9
	CG	11	40.7
	All	**25**	**92.6**
Left-handed	EG	0	0
	CG	1	3.7
	All	**1**	**3.7**
Ambidexterous	EG	0	0
	CG	1	3.7
	All	**1**	**3.7**
Total		**27**	**100.0**
Educational level			
Doctoral degree	EG	3	11.1
	CG	1	3.7
	All	**4**	**14.8**
Master degree	EG	4	14.8
	CG	4	14.8
	All	**8**	**29.6**
Bachelor degree	EG	5	18.5
	CG	5	18.5
	All	**10**	**37.0**
Associate degree	EG	0	0.0
	CG	1	3.7
	All	**1**	**3.7**
Some college but no degree	EG	2	7.4
	CG	2	7.4
	All	**4**	**14.8**
High school diploma / GED	**All**	**0**	**0.0**
Less than high school diploma /	**All**	**0**	**0.0**
Total		**27**	**100.0**

		N	Percent
AD diagnosed?			
No	EG	4	14.8
	CG	3	11.1
	All	**7**	**25.9**
Yes*	EG	11	40.7
	CG	9	33.3
	All	**20**	**74.1**
AD diagnosed, not specified	EG	5	25.9
	CG	2	7.4
	All	**7**	**33.3**
GAD	EG	3	11.1
	CG	6	22.2
	All	**9**	**33.3**
Phobia	EG	1	3.7
	CG	0	0.0
	All	**1**	**3.7**
SAD	EG	2	7.4
	CG	1	3.7
	All	**3**	**11.1**
Total		**27**	**100.0**
Taking AD medication?			
No	EG	9	33.3
	CG	11	40.7
	All	**20**	**74.1**
Yes	EG	5	18.5
	CG	2	7.4
	All	**7**	**25.9**
	Total	**27**	**100.0**
Taking Anti-depressant?			
No	EG	10	37.0
	CG	7	25.7
	All	**18**	**66.7**
Yes	EG	4	14.8
	CG	5	18.5
	All	**9**	**33.3**
	Total	**27**	**100.0**

Table 4.1 c: Descriptive statistics of categorical variables: *Mental strategies used*?, *Mental Strategies successful*?, *Change in feelings, thinking and behavior due to NFT*? of the participant sample by group.

4.2 Psychometric Results

To ensure there were no significant differences at baseline between the participants from the experimental group (A/T NFT) and the control group (B u/d NFT) a Levene's tests for

equality of variances and independent samples t- tests for equality of means were performed for the variables age, education level, pre-trial STAI, BAI, and GAD-7, AD-ACL, and SETS expectations of treatment. All Levene and t-tests had non-significant results which means that experimental and control groups had similar variances and means, respectively, and did not significantly differ from each other for all analyzed variables at baseline.

4.2.1 Anxiety questionnaires: STAI, BAI, and GAD-7.

Two-way mixed model ANOVAs were performed with the within-subject factor TIME (pre–post treatment) and the between-subject factor GROUP (A/T, CO) for the STAI (sub-scales STAI-T and STAI-S), the BAI, and the GAD-7. Assumptions were tested before running each ANOVA. A Shapiro-Wilk test to check for normality of distribution for each cell of the design was performed. The equality of variances and the equality of covariance matrices were tested with the Levene and Box Test, respectively. All tests had non-significant results which means that all necessary statistical assumptions for the 2x2 ANOVA were met.

For the analyses of all self-report anxiety measures the factor time was significantly reducing participants' scores in the various anxiety measures and an associated large effect size as measured by partial η^2. For the STAI, sub-scale state anxiety (STAI-S), the anxiety scores decreased significantly between the beginning (M = 53.70, SD = 10.53) and the end of the trial (M = 46.63, SD = 8.52) for $F(1, 25) = 9.518$, p = .005, partial η^2 = .276; for the STAI, sub-scale trait anxiety (STAI-T), the anxiety scores decreased significantly between the beginning (M = 49.15, SD = 10.56) and the end of the trial (M = 41.63, SD = 9.32) for $F(1, 25) = 22.988$, p = .0001, partial η^2 = .479; for the BAI the anxiety scores decreased significantly between the beginning (M = 17.63, SD = 8.73) and the end of the trial (M = 12.41, SD = 6.59) for $F(1, 25)$ = 11.524, p = .002, partial η^2 = .316; and for the GAD-7 the anxiety scores decreased significantly

between the beginning (M = 10.04, SD = 4.00) and the end of the trial (M = 7.48, SD = 4.52) for $F(1, 25) = 22.988$, p = .0001, partial η^2 = .479. However, none of the interactions between TIME and GROUP were significant: STAI-S ($F(1, 25) = .41$, n.s.); STAI-T ($F(1, 25) = .09$, n.s.); BAI ($F(1, 25) = .15$, n.s.), and GAD-7 ($F(1, 25) = .18$, n.s.), i.e., no differences between scores of the experimental and the control groups regarding the reduction in self-reported anxiety measures were observed.

4.2.2 Stanford Expectation of Treatment scale (SETS).

Repeated measures ANOVA were conducted with the within-subject factor TIME (pre–post-treatment) and between-subject factor GROUP (A/T, CO) for Cronbach's α = .05 for the SETS-positive and the SETS-negative items sub-scales (Figure 4.2). A Shapiro Wilk test to check for normality of distribution for each cell of the design was performed. The equality of variances and the equality of covariance matrices were tested with the Levene and Box Test, respectively. All preliminary tests had non-significant results which means that all necessary statistical assumptions for the 2x2 ANOVA were met.

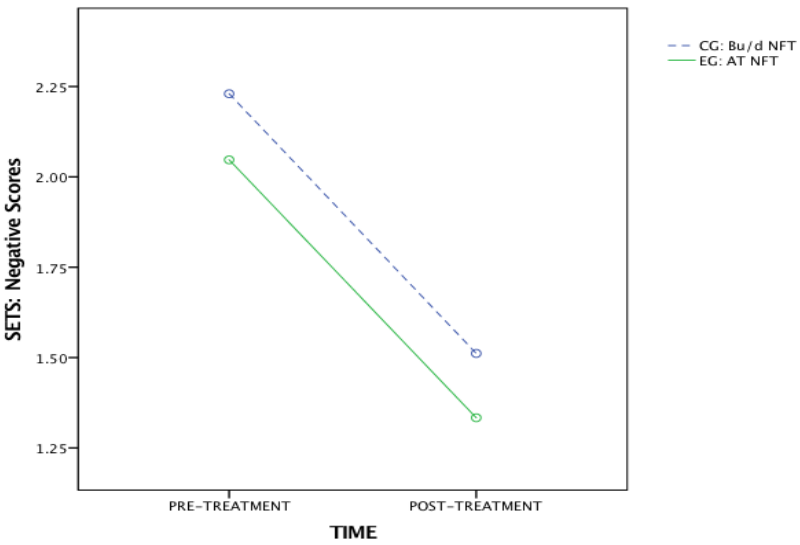

Figure 4.1: Mean SETS negative expectancy test score differences for EG (solid line) and CG (dotted line). Pre- and post-treatment: A significant reduction of scores in the negative treatment expectancy sub-scale were observed between beginning and end of the trial. However, no significant difference between the EG and CG was observed.

While a significant reduction in the SETS-negative sub-scale could be observed between the beginning (M = 2.14, SD = 1.40) and the end of the NFT trial (M = 1.42, SD = .94) for $F(1, 25) = 5.809$, p = .024, partial η^2 = .189), the GROUP x TIME interaction for SETS-negative ($F(1, 25) = .01$, n.s.) was not significant. For the SETS-positive sub-scale, neither factor TIME ($F(1, 25) = .25$, n.s.) nor the TIME x GROUP ($F(1, 25) = 1.09$, n.s.) were significant.

4.2.3 Activation Deacktivation Checklist (AD-ACL).

All preliminary tests had non-significant results which means that all necessary statistical assumptions for the 2x2 ANOVA were met, except for the AD-ACL sub-scale *tension* for the pre-trial measurement; the Box test had a significant result (p = .027) for this sub-scale. As all other assumptions for the ANOVA were met no additional one-way repeated measures ANOVA for each group of the between-subjects factor *tension* were run.

4.2.3.1 Traditional 2x2 and 2x5 ANOVAs for AD-ACL activation and deactivation scales and four sub-scales

Repeated measure 2x2 ANOVAs were conducted with the within-subject factor TIME (pre–post-treatment) and between-subject factor GROUP (A/T, CO) for Cronbach's α = .05 for the *activation* and *deactivation* scales, as well as for each of the four sub-scales (*energy, tension, tiredness, calmess*). *Activation,* comprised of the *tension* and *energy* sub-scales, decreased significantly between the beginning (M = 3.951, SD = 1.126) and the end of a NFT session (M = 3.280, SD = .968), $F(1, 256) = 157.295$, p < .0001, partial η^2 = .381. *Activation* decreased significantly more for the CG (M_{pre} = 4.059, SD_{pre} = .979; M_{post} = 3.263, SD_{post} = .790), p < .034, partial η^2 = .017)) than the EG (M_{pre} = 3.859, SD_{pre} = 1.232; M_{post} = 3.295, SD_{post} = 1.098), $F(1, 256) = 4.539$, p < .034, partial η^2 = .017) between the beginning and the end of a NFT session. *Deactivation,* made up of the *tiredness* and *calmness* sub-scales, increased

significantly between the beginning (M = 4.617, SD = 1.217) and the end of a NFT session (M = 5.623, SD = 1.157), $F(1, 256) = 171.981$, $p < .0001$, partial $\eta^2 = .402$), (Figure 4.3). *Deactivation* scores did not significantly differ between pre- and post-session for the CG and the EG ($F(1, 256) = .339$, n.s.).

Source	*Mean* $_{pre\text{-}session}$	*SD* $_{pre\text{-}session}$	*Mean* $_{post\text{-}session}$	*SD* $_{post\text{-}session}$	*N*
Activation					
EG	3.860	1.213	3.294	1.097	140
CG	4.060	.979	3.263	.790	118
Total	**3.951**	**1.126**	**3.280**	**.968**	**258**
Deactivation					
EG	4.508	1.316	5.554	1.267	140
CG	4.746	1.079	5.705	1.011	118
Total	**4.617**	**1.217**	**5.623**	**1.157**	**258**
Tiredness					
EG	2.257	.918	2.660	.919	140
CG	2.486	.859	3.013	.853	118
Total	**2.362**	**.897**	**2.821**	**.905**	**258**
Energy					
EG	2.119	.820	1.833	.810	140
CG	2.085	.731	1.645	.666	118
Total	**2.104**	**.779**	**1.747**	**.752**	**258**
Calmness					
EG	2.251	.720	2.895	.714	140
CG	2.237	.737	2.699	.651	118
Total	**2.245**	**.726**	**2.805**	**.697**	**258**
Tension					
EG	1.740	.858	1.461	.595	140
CG	1.983	.713	1.605	.570	118
Total	**1.851**	**.802**	**1.527**	**.587**	**258**

Table 4.2 a: Descriptive statistics for the AD-ACL scores: Pre-post-NFT session results for EG and CG.

All four ANOVAs for the sub-scales showed a main effect for the factor TIME (Figure 4.3). On average the participants' *energy* decreased significantly between the beginning (M = 2.10, SD = .78) and the end of a NFT session (M = 1.75, SD = .75), $F(1, 256) = 63.24$, $p < .001$, partial $\eta^2 = .198$; and so did their *tension* between the beginning (M = 1.85, SD = .80) and the end of a NFT session (M = 1.53, SD = .59), $F(1, 255) = 69.63$, $p < .001$, partial $\eta^2 = .214$, as well. In contrast, participants' *calmness* increased significantly on average between the beginning (M = 1.27, SD = .74) and the end of a NFT session (M = 1.77, SD = .70), $F(1, 255) = 103.21$, $p < .001$, partial $\eta^2 = .29$) and so did their *tiredness* between the beginning (M = 1.46,

SD = .66) and the end of a NFT session (*M* = 1.74, *SD* = .58), *F*(1, 255) = 39.01, p < .001, partial η^2 = .13).

Source: Pre-post-NFT session difference scores	***SS***	***df***	***MS***	***F***	***p***	**partial η^2**
Activation						
Time	59.278	1	59.278	157.295	**<.001****	.381
Time* group	1.711	1	1.711	4.539	**.034***	.017
Error	96.476	256	.377			
Deactivation						
Time	128.531	1	128.531	171.981	**<.001****	.402
Time* group	.253	1	.253	.339	.561	.001
Error	191.323	256	.747			
Tiredness						
Time	27.644	1	27.644	67.228	**<.001****	.208
Time* group	.483	1	.483	1.74	.280	.005
Error	105.268	256	.411			
Energy						
Time	16.896	1	16.896	63.239	**<.001****	.198
Time* group	.760	1	.760	2.843	**.093**	.011
Error	68.399	256	.267			
Calmness						
Time	39.087	1	39.087	147.745	**<.001****	.366
Time* group	1.051	1	1.051	3.974	**.047***	.015
Error	67.717	256	.265			
Tension						
Time	13.789	1	13.789	69.628	**<.001****	.214
Time* group	.315	1	.315	1.589	.209	.006
Error	50.699	256	.198			

Table 4.2 b: 2 x 2 ANOVA for AD-ACL Pre-post-NFT session results for EG and CG.

The interaction of group and *calmness* was significant (*F*(1, 256) =3.94, p = .047, partial η^2 = .015) with the EG experiencing significantly larger increase in calmness than the CG, but the effect size is small. The interaction of group and *energy* neared significance (*F*(1, 256) =2.84, p = .093, partial η^2 = .011) with the EG experiencing a not quite significantly larger decrease in energy than the CG. The interactions of group and *tension* (*F*(1, 255) =1.59, n.s.), and group and *tiredness* (*F*(1, 255) =1.174, n.s.) were not significant, indicating that on average no significant differences in the reduction in tension and the increase in tiredness from before to after the NFT sessions between the experimental and control groups were found.

Source: pre-post-NFT session difference scores	***SS***	***df***	***MS***	***F***	***p***	**partial η^2**
Activation (Scale)						
Time (within-subjects effect)	1.273	4	.318	.607	.659	.024
Time* group (within-subjects effect)	.085	4	.021	.041	.997	.002
Group (between-subjects effect)	.093	1	.093	.038	.847	.002
Deactivation (Scale)						
Time (within-subjects effect)	.667	4	.167	.513	.726	.020
Time* group (within-subjects effect)	2.479	4	.620	2.909	.115	.071
Group (between-subjects effect)	2.834	1	2.834	3.499	**.073**	.123
Tiredness (Sub-scale)						
Time (within-subjects effect)	2.112	4	.528	1.883	.119	.070
Time* group (within-subjects effect)	.598	4	.150	.533	.712	.021
Group (between-subjects effect)	.475	1	.475	.347	.561	.014
Energy [1](Sub-scale)						
Time (within-subjects effect)	1.030	3.125	.329	1.264	.293	.048
Time* group (within-subjects effect)	.671	3.125	.215	.823	.489	.032
Group (between-subjects effect)	.638	1	.638	1.080	.309	.041
Calmness (Sub-scale)						
Time (within-subjects effect)	1.031	4	.258	1.304	.274	.050
Time* group (within-subjects effect)	.383	4	.096	.484	.747	.019
Group (between-subjects effect)	1.259	1	1.259	1.501	.232	.057
Tension (Sub-scale)						
Time (within-subjects effect)	.245	4	.061	.479	.751	.019
Time* group (within-subjects effect)	.946	4	.236	1.848	.126	.069
Group (between-subjects effect)	.474	1	.474	.622	.438	.024

[1] Greenhouse –Geiser adjustment used.

Table 4.3: 2 x 5 AD-ACL NFT session difference scores for sessions 1+2, 3+4, 5+6, 7+8, and 9+10 for EG and CG.

Repeated measures 2x5 ANOVAs with the within-subject factor TIME, for the averages of sessions 1-2, 3-4, 5-6, 7-8, and 9-10, and the between-subjects factor GROUP (EG or CG) were performed for all AD-ACL scales (Table 4.3 and Figure 4.2). No significant changes in difference scores were observed across the course of the NFT sessions for the any of the AD-ACL scales or sub-scales: *Activation* ($F(4, 100) = .726$, n.s.), *Deactivation* ($F(4, 100) = .607$, n.s.), *Tension* ($F(4, 100) = .479$, n.s.), *Calmness* ($F(4, 100) = 1.304$, n.s.), *Tiredness* ($F(4, 100) = 1.883$, n.s.), and *Energy* ($F(4, 78.134) = 1.264$, n.s.). Furthermore, the EG and CG did not differ significantly in their results of AD-ACL scales and sub-scales throughout the course of the NFT trial as no interactions between factors TIME and GROUP were found for any of the scales and sub-scales: *Activation* ($F(4, 100) = .041$, n.s.), *Deactivation* ($F(4, 100) = 1.909$, n.s.), *Tension* ($F(4, 100) = 1.848$, n.s.), *Calmness* ($F(4, 100) = .484$, n.s.), *Tiredness* ($F(4, 100) = .533$, n.s.),

and *Energy* ($F(4, 78.134) = .823$, n.s.).

For the between-subjects factor GROUP the results of the *Deactivation* scale were near significance ($F(1, 25) = 3.499$, $p = .073$, partial $\eta^2 = .0123$), whereas the results of the other scales and sub-scales were not significant: *Activation* ($F(1, 25) = .0381$, n.s.), *Tension* ($F(1, 25) = .438$, n.s.), *Calmness* ($F(1, 25) = .232$, n.s.), *Tiredness* ($F(1, 25) = .347$, n.s.), and *Energy* ($F(1, 25) = 1.080$, n.s.). Additional figures modeling difference scores per session for all ten NFT sessions with confidence intervals are attached in Appendix E.

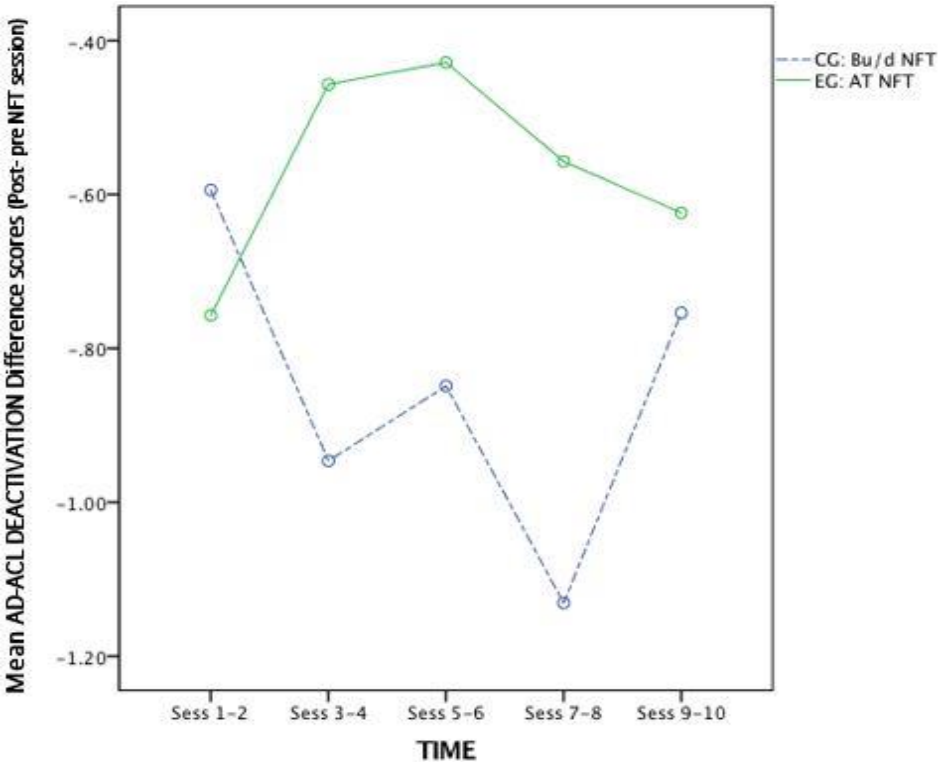

Figure 4.2: **AD-ACL deactivation pre–post session difference score changes for EG (solid line) and CG (dotted line) over the course of the NFT trial**, averaging scores from sessions 1 & 2, 3 & 4, 5 & 6, 7 & 8, and 9 & 10. Deactivation approached significance (p = .073) in decreasing more across sessions for the CG than for the EG.

4.2.3.2 Growth curve modeling for AD-ACL activation and deactivation scales, and four sub-scales

In addition to the traditional 2x5 ANOVAs (see section 4.2.3.1) a growth curve modeling (GCM) analysis was performed in R Studio, version 1.0.136. The GCM theory and principles will be explained in detail in the next section (4.3.1). The GCM considers pre- and post-NFT

AD-ACL session difference scores of all ten sessions instead of combining pre-post session difference results of two sessions each and therefore offers a more nuanced statistical analysis than ANOVAs.

The GCM confirmed the results from the 2x5 ANOVAs of AD-ACL scales and sub-scales in that across NFT sessions there was no significant change in scores in any of the scales or sub-scales, except for the activation scale (Table 4.4 a) which neared significance (β = 0.280, *SE* = 0.149, p = .071) with participants of the CG getting nearly significantly less activated as they progressed throughout the NFT sessions. As an interaction effect between factors TIME and GROUP was detected as well in this scale (β = 0.054, *SE* = 0.026), p < .05) a difference in patterns of activation across sessions is suggested. This makes an interpretation of the GROUP factor results difficult. Visually inspecting Figure 4.5 elucidates that while EG and CG have relatively similar difference scores in the activation scale in the first and last 2 sessions, in the in between 6 sessions members of the CG group were far less activated than in beginning or end of the 10 NFT sessions whereas EG group members were more activated remaining in those 6 sessions.

Predictor for AD-ACL Activation scale	**β (*SE*)**	***p***
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	-0.006 (0.019)	.742
Intercept	**-0.676 (0.109)**	**< .001*** **
MODEL D: GROUP: group across sessions	0.280 (0.149)	.071
MODEL E: TIME ACROSS SESSIONS x GROUP	**0.054 (0.026)**	**< .0.5***

Table 4.4 a: Results from GCM regression analyses predicting AD-ACL Activation from across sessions, and group (EG, CG). Note: Standard errors are given in parentheses. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for AD-ACL Deactivation scale	**β (*SE*)**	***p***
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.004 (0.022)	.853
Intercept	**-0.986 (0.175)**	**< .001*** **
MODEL D: GROUP: group across sessions	0.064 (0.260)	.808
MODEL E: TIME ACROSS SESSIONS x GROUP	-0.009 (0.032)	.788

Table 4.4 b: Results from GCM regression analyses predicting AD-ACL Activation from across sessions, and group (EG, CG). Note: Standard errors are given in parentheses. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for AD-ACL Energy sub-scale	β (*SE*)	*p*
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	-0.0192 (0.018)	.288
Intercept	**-0.266 (0.112)**	**< .0.5***
MODEL D: GROUP: group across sessions	0.149 (0.124)	.240
MODEL E: TIME ACROSS SESSIONS x GROUP	0.023 (0.020)	.249

Table 4.4 c: Results from GCM regression analyses predicting AD-ACL energy sub-scale from across sessions, and group (EG, CG). Note: Standard errors are given in parentheses. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for AD-ACL Tired sub-scale	β (*SE*)	*p*
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.027 (0.019)	.182
Intercept	**0.328 (0.146)**	**< .0.5***
MODEL D: GROUP: group across sessions	0.130 (0.191)	.504
MODEL E: TIME ACROSS SESSIONS x GROUP	-0.025 (0.025)	0.341

Table 4.4 d: Results from GCM regression analyses predicting AD-ACL Tired sub-scale from across sessions, and group (EG, CG). Note: Standard errors are given in parentheses. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for AD-ACL Calm sub-scale	β (*SE*)	*p*
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	-0.0.028 (0.018)	.132
Intercept	**0.674 (0.094)**	**< .001*** **
MODEL D: GROUP: group across sessions	0.179 (0.154)	.255
MODEL E: TIME ACROSS SESSIONS x GROUP	0.028 (0.030)	.349

Table 4.4 e: Results from GCM regression analyses predicting AD-ACL Calm sub-scale from across sessions, and group (EG, CG). Note: Standard errors are given in parentheses. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for AD-ACL Tense sub-scale	β (*SE*)	*p*
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	-0.014 (0.012)	.255
Intercept	**-0.410 (0.081)**	**< .001*** **
MODEL D: GROUP: group across sessions	0.013 (0.146)	.485
MODEL E: TIME ACROSS SESSIONS x GROUP	0.029 (0.030)	.349

Table 4.4 f: Results from GCM regression analyses predicting AD-ACL Tense sub-scale from across sessions, and group (EG, CG). Note: Standard errors are given in parentheses. Intercept information is only shown for significant models. Significant results are shown in bold red.

4.3 Neurofeedback Training Results

Descriptive statistics run on the NFT session data set in SPSS revealed a limited amount of missing data due to alpha and theta amplitude artifacts that had not been automatically removed by the *BrainAvatar® 4.0* software, such as any amplitudes over 100 Hz that had not been removed although appropriate band pass filters had been programmed into the Brainmaster program. The data were replaced by averaging the amplitudes for all waves (delta, theta, alpha, beta, and gamma) of the minute before and the minute after the recorded artifact. 1.28%

(83/6480 minutes) of recorded NFT session minutes had to be replaced by the averaging method. Participant 011 was the only person who was consistently an outlier throughout the trial with extremely high alpha and theta amplitudes and corresponding alpha and relative theta amplitudes but average T/A ratio. The participant was taken out of the statistical calculations which reduced the standard error (SE) of the measurements slightly but did not change any of the statistical analysis results. Consequently, 011 was left in the final report of statistical results as this study had a small sample size and a reduction in sample would lead to a reduction in power.

4.3.1 Growth curve modeling with absolute and relative alpha, theta, T+A, and T/A ratio.

The NFT data were analyzed by modeling absolute and relative alpha, theta, and T+A, and T/A ratio. Due to some large standard error values in comparison to the unstandardized beta values additional analyses of all variables using the growth curve modeling approach. As discussed in chapter 3.5.1, a logit mixed effects GCM was programmed into R-Studio and p values were obtained by lmerMod.

A χ^2 test for each of the criterion variables was administered regarding factor TIME WITHIN SESSIONS (RUN) and showed significant likelihood of fit for model C, with the added assumption that the intercept is different for each participant (center_t | participant), represented the best model fit for the regression equation for all tested criterion variables— with absolute and relative alpha, theta, T+A, and T/A ratio (run: χ^2 test: $p < .0001$) | trial: χ^2 test; $p < .0001$). Additionally, model E, the interaction between TIME WITHIN SESSION and GROUP, represented an equally good fit with the χ^2 test result of $p < .0001$ for all criterion variables. The χ^2 test for the factor TIME ACROSS SESSIONS (TRIAL) was significant ($p < .0001$) for models C and E only for absolute alpha and theta amplitude, and relative T+A amplitude (Table

4.3 a, e, d). For relative alpha and theta amplitude, and T/A amplitude ratio (Table 4.5 b, f, c) only model C presented the best fit, i.e., the χ^2 test was only significant for model C and not for model for the factor TIME ACROSS SESSIONS. Interestingly, model E represented an alternative best fit model for prediction of all criterion variable scores within sessions (run) and most of the criterion variables between sessions although none of the interactions showed significant fixed effects in any of the criterion variables. The only criterion variable where the interaction between TIME x GROUP is at least remotely approaching significance is for TIME WITHIN SESSIONS for the T/A amplitude ratio ($p = .114$). All other p values are between .231 and .918. The Bayesian Information Criteria (BIC) values for model C were slightly lower for all variables than for model E. The BIC is an estimate of how probable each of a number of finite models is of being true, with a lower BIC value representing a better fit model. Consequently, model C represents a better fit and the best model to predict NFT alpha and theta amplitudes, as well as for the Relative T+A amplitude.

TIME WITHIN SESSIONS was a significant predictor for all tested criterion variables, which means that on average over the course of a session a significant increase in absolute alpha amplitude ($\beta = 0.066$, $SE = 0.012$, $p < .0001$), T/A amplitude ratio ($\beta = -0.004$, $SE = 0.001$, $p = .002$), relative alpha amplitude ($\beta = 0.067$, $SE = 0.010$, $p < .0001$), relative theta amplitude ($\beta = 0.007$, $SE = 0.0003$, $p < .001$), and relative A+T amplitude ($\beta = 0.074$, $SE = 0.0017$, $p < .0001$) could be observed within NFT sessions and nearing significance for absolute theta amplitude ($\beta = 0.026$, $SE = 0.015$, $p < .094$). The analysis of TIME ACROSS SESSIONS revealed that as time passed between sessions absolute alpha amplitude ($\beta = 0.134$, $SE = 0.048$, $p = .011$) and relative alpha amplitude ($\beta = 0.121$, $SE = 0.013$, $p < .0001$) increased significantly on average. But no such significant trend could be observed for T/A ratio ($\beta = -0.006$, $SE = 0.004$, $p = .109$, n.s.),

absolute theta amplitude (β =0.029, *SE* = 0.053, p = .589, n.s.), relative theta amplitude (β =0.013, *SE* = 0.036, p = .735, n.s.), or relative T+A amplitude (β =0.019, *SE* = 0.014, p = .171, n.s.). The analysis of the GROUP factor did not reveal any significant change for the factor TIME WITHIN SESSION, nor for TIME ACROSS SESSIONS for T/A amplitude ratio.

Predictor for ABSOLUTE alpha amplitude (in µV)	**β (*SE*)**	***p***
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	**0.066 (0.012)**	**< .0001 *** **
Intercept	**9.442 (0.739)**	**< .0001 *** **
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	**0.134 (0.048)**	**.011 ***
Intercept	**9.691 (0.755)**	**< .0001 *** **
MODEL D: GROUP: within session	0.165 (1.172)	.889
MODEL D: GROUP: group across sessions	0.439 (1.464)	.767
MODEL E: TIME WITHIN SESSIONS x GROUP	0.012 (0.019)	.556
MODEL E: TIME ACROSS SESSIONS x GROUP	0.055 (0.093)	.560

Table 4.5 a: Results from GCM regression analyses predicting absolute alpha amplitude from run (within session), trial (across sessions), and group (EG, CG). Note: Standard errors are given in parentheses. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for RELATIVE alpha amplitude (in %)	**β (*SE*)**	***p***
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	**0.067 (0.010)**	**< .0001 *** **
Intercept	**17.585 (0.613)**	**< .0001 *** **
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	**0.121 (0.013)**	**< .0001 *** **
Intercept	**17.709 (0.589)**	**< .0001 *** **
MODEL D: GROUP: within session	-0.065 (1.149)	.955
MODEL D: GROUP: group across sessions	0.376 (1.164)	.749
MODEL E: TIME WITHIN SESSIONS x GROUP	0.022 (0.018)	.244
MODEL E: TIME ACROSS SESSIONS x GROUP	0.014 (0.115)	.901

Table 4.5 b: Results from GCM regression analyses predicting relative alpha amplitude from run (within session), trial (across sessions), and group (EG, CG). Note: Standard errors are given in parentheses. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for T/A RATIO	**β (*SE*)**	***p***
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	**-0.004 (0.001)**	**.002 ** **
Intercept	**0.993 (0.037)**	**< .0001 *** **
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	-0.006 (0.004)	.109
MODEL D: GROUP: within session	-0.033 (0.071)	.647
MODEL D: GROUP: group across sessions	-0.023 (0.068)	.739
MODEL E: TIME WITHIN SESSIONS x GROUP	-0.003 (0.002)	.114
MODEL E: TIME ACROSS SESSIONS x GROUP	-0.001 (0.007)	.918

Table 4.5 c. Results from GCM regression analyses by successively adding predictors for T/A amplitude ratio from run (within session), trial (across sessions), and condition (EG, CG). Note: Standard errors are given in parentheses. Intercept information is only shown for significant models. Sigificant results are shown in bold red.

Predictor for RELATIVE A+T amplitudes (in %)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS	**0.074 (0.017)**	**< .0001 *****
(24 one-minute runs per NFT session)		
Intercept	**34.251 (0.664)**	**< .0001 *****
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.019 (0.014)	.171
MODEL D: GROUP: within session	0.483 (1.240)	.700
MODEL D: GROUP: group across sessions	0.456 (0.796)	.572
MODEL E: TIME WITHIN SESSIONS x GROUP	0.039 (0.097)	.690
MODEL E: TIME ACROSS SESSIONS x GROUP	-0.014 (0.033)	.667

Table 4.5 e: Results from GCM regression analyses predicting relative A+T amplitudes from run (within session), trial (across sessions), and group (EG, CG). Note: Standard errors are given in parentheses. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for ABSOLUTE theta amplitude (in µV)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS	0.026 (0.015)	**.094**
(24 one-minute runs per NFT session)		
Intercept	**8.303 (0.443)**	**< .0001 *****
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.029 (0.053)	.589
MODEL D: GROUP: within session	0.418 (0.786)	.600
MODEL D: GROUP: group across sessions	-0.018 (0.859)	.983
MODEL E: TIME WITHIN SESSIONS x GROUP	0.039 (0.097)	.690
MODEL E: TIME ACROSS SESSIONS x GROUP	0.030 (0.100)	.768

Table 4.5 f: Results from GCM regression analyses predicting theta amplitude from run (within session), trial (across sessions), and group (EG, CG). Note: Standard errors are given in parentheses. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for RELATIVE theta amplitude (in %)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS	0.007 (0.014)	.690
(24 one-minute runs per NFT session)		
Intercept	**8.594 (0.348)**	**< .0001 *****
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.013 (0.036)	.735
MODEL D: GROUP: within session	-0.147 (0.682)	.710
MODEL D: GROUP: group across sessions	-0.592 (0.717)	.416
MODEL E: TIME WITHIN SESSIONS x GROUP	-0.034 (0.028)	.231
MODEL E: TIME ACROSS SESSIONS x GROUP	-0.015 (0.072)	.842

Table 4.5 g: Results from GCM regression analyses by successively adding predictors for relative theta amplitude from run (within session), trial (across sessions), and group (EG, CG). Note: Standard errors are given in parentheses. Intercept information is only shown for significant models. Significant results are shown in bold red.

To summarize the results from Table 4.5 a-f, regarding the factor TIME over the course of a session on average, there was a significant increase in absolute alpha amplitude (β = 0.066, *SE* = 0.012, p < .0001), absolute T/A amplitude ratio (β = -0.004, *SE* = 0.001, p = .002), relative alpha amplitude (β = 0.067, *SE* = 0.010, p < .0001), relative theta amplitude (β = 0.007, *SE* = 0.0003, p < .001), and relative A+T amplitude (β = 0.074, *SE* = 0.0017, p < .0001). Relative theta amplitude neared significance (β = 0.026, *SE* = 0.015, p < .094). Regarding the factor TIME across sessions there was on average a significant increase in absolute alpha amplitude (β =0.134, *SE* = 0.048, p = .011) and relative alpha amplitude (β =0.121, *SE* = 0.013, p < .0001). But no significant change could be observed for the T/A amplitude ratio (β = -0.006, *SE* = 0.004, p = .109, n.s.), absolute theta amplitude (β =0.029, *SE* = 0.053, p = .589, n.s.), relative theta amplitude (β =0.013, *SE* = 0.036, p = .735, n.s.), and relative T+A amplitude (β =0.019, *SE* = 0.014, p = .171, n.s.). No significant differences for the factor GROUP were observed between the treatment (A/T NFT) and control group (B u/d NFT), neither over course of treatment, nor within course of session for T/A amplitude ratio.

4.3.2 Traditional 2x5 ANOVAs for with absolute and relative alpha, theta, T+A, and T/A ratio.

Because the original protocol for this study included the traditional statistical data analysis of the NFT data via a 2x5 Repeated Measures ANOVA these analyses were performed as well. The average of absolute and relative alpha, theta, and T+A amplitudes in µV, as well as and to the T/A amplitude ratio were calculated for two sessions, for the aggregated data of sessions 1+2, 3+4, 5+6, 7+8, and 9+10, respectively.

A visual analysis of the Normal Q-Q plots was performed and revealed a fairly linear distribution of the values. This attests that the observed values are normally distributed.

Additionally, a Shapiro-Wilk test of normality was run on the studentized residuals of all variables. Values for the T/A ratios, relative theta, relative alpha amplitude, and A+T amplitudes were normally distributed ($p > .05$) for both, experimental and control groups, except for the relative alpha of the experimental group in session 1-2 ($p = .026$).

For absolute theta amplitude most values were normally distributed ($p > .05$) except for mean absolute theta for the CG in combined sessions 1-2 ($p = .015$), session 7-8 ($p = .015$) and session 9-10, ($p = .011$) and for the experimental group in sessions 1-2 ($p = .001$). For absolute alpha amplitude all values were normally distributed ($p > .05$) for the CG but not for the values in the EG, session 1-2 ($p = .001$), session 3-4 ($p = .003$), session 5-6 ($p = .001$), session 7-8 ($p = .004$), and session 9-10, ($p = .004$) and for the EG in sessions 1-2 ($p = .004$) due to consistent extreme outlier values for participant 011. Participant 011 was removed from the analysis but because results of the 2x5 ANOVA were similar in both analyses, the normal Q-Q plot revealed a normal distribution except for subject 011, she remained in further statistical analysis and no data transformation was performed. Mauchly's test of sphericity indicated that the assumption of sphericity was violated for theta amplitude ($p = .002$) χ^2 (9) = 26.479, $p = .002$. A Greenhouse-Geiser correction had to be applied to changes in absolute and relative alpha, theta, and T+A amplitudes, as well as and to the T/A amplitude ratio.

The factor TIME was significant for absolute alpha amplitude $F(2.643, 66.076) = 4.881$, p = .006, partial $\eta^2 = .163$), T/A ratio $F(4, 100) = 2.843$, p = .044, partial $\eta^2 = .102$), relative alpha amplitude $F(2.355, 58.875) = 6.951$, p = .001, partial $\eta^2 = .218$), and relative T+A amplitude $F(2.540, 63.512) = 5.376$, p = .004, partial $\eta^2 = .177$). Absolute T+A amplitude was nearing significance with $F(2.785, 69.619) = 2.332$, p = .086, partial $\eta^2 = .085$). Absolute theta $F(2.773, 69.336) = .739$, n.s.), and relative theta amplitudes $F(2.643, 68.285) = .739$, n.s.) did not

change significantly over the course of the NFT sessions. To determine which combination of time points were changing significantly over the course of treatment, post-hoc ANOVAs were conducted. A significant interaction effect was found for absolute theta (F(2.773, 69.336) = 2.843, p = .043, partial η^2 = .105), and relative theta amplitudes (F(2.771, 68.285) = 3.398, p = .026, partial η^2 = .120) which makes further interpretation of time effects ambiguous.

Source: Pre-post-NFT session difference scores	***SS***	***df***	***MS***	***F***	***p***	**partial η^2**
Absolute alpha amplitude (in µV) [1]						
Time (within-subjects effect)	35.674	2.643	13.497	4.881	**.006****	.163
Time * group (within-subjects effect)	13.003	2.643	4.920	1.779	.166	.066
Group (between-subjects effect)	40.320	1	40.320	.403	.532	.016
Relative alpha amplitude (in %) [1]						
Time (within-subjects effect)	52.926	2.355	22.474	6.951	**.001****	.218
Time * group (within-subjects effect)	8.084	2.355	3.433	1.062	.361	.041
Group (between-subjects effect)	14.204	1	14.204	.217	.645	.009
Absolute theta amplitude (in µV) [1]						
Time (within-subjects effect)	4.887	2.773	1.762	.739	.523	.029
Time * group (within-subjects effect)	19.446	2.773	7.012	2.940	**.043***	.105
Group (between-subjects effect)	.353	1	.353	.012	.914	.000
Relative theta amplitude (in %) [1]						
Time (within-subjects effect)	.285	2.731	.104	.082	.961	.003
Time* group (within-subjects effect)	11.767	2.731	4.308	3.398	**.026***	.120
Group (between-subjects effect)	8.351	1	8.351	.397	.534	.016
T/A ratio						
Time (within-subjects effect)	.084	4	.021	2.843	**.028***	.102
Time* group (within-subjects effect)	.053	4	.013	1.777	.139	.066
Group (between-subjects effect)	.036	1	.036	.191	.666	.008
Absolute alpha+theta amplitudes (in µV) [1]						
Time (within-subjects effect)	47.478	2.785	17.049	2.332	**.086**	.085
Time * group (within-subjects effect)	53.276	2.785	19.131	2.616	.062	.095
Group (between-subjects effect)	36.262	1	36.262	.172	.682	.007
Relative alpha+theta amplitudes (in µV) [1]						
Time (within-subjects effect)	49.842	2.540	16.619	5.376	**.004****	.177
Time * group (within-subjects effect)	10.521	2.540	4.141	1.135	.337	.043
Group (between-subjects effect)	.773	1	.773	.009	.927	.000

[1] Greenhouse –Geiser adjustment used.

Table 4.6: 2 x 5 EEG parameter NFT session difference scores (pre-post session scores)

Consequently, post-hoc ANOVAs were only conducted for absolute and relative alpha amplitude, T/A ratio, and relative T+A amplitude to find out which pairwise time comparisons were significant. To reduce the family-wise error I Bonferroni adjustments for the four time

comparisons were run. Absolute alpha amplitude increased significantly between sessions 1+2 and 5+6, as well as between sessions 1+2 and 7+8, with adjusted p = .024 in both cases. Relative alpha amplitude decreased significantly between sessions 1+2 and 3+4 (adjusted p = .012), sessions 1+2 and 5+6 (adjusted p = .001), and sessions 1+2 and 7+8 (adjusted p = .008); sessions 1+2 and 9+10 approached significance (adjusted p = .064). T/A ratio decreased significantly between sessions 1+2 and 3+4 (adjusted p = .012),but was not significant for the other three session comparisons. Relative T+A amplitude increased significantly between sessions 1+2 and 5+6 (adjusted p = .001), sessions 1+2 and 7+8 (adjusted p = .001; sessions 1+2 and 9+10 approached significance (adjusted p = .068) and the comparison between sessions 1+2 and 3+4 was not significant (p = .116), (Figure 4.6).

No differences between the EG and CG regarding changes in absolute alpha amplitude $F(1, 25) = .403$, n.s.), relative alpha amplitude ($F(1, 25) = .217$, n.s.), absolute theta amplitude $F(1, 25) = .012$, n.s.), relative theta amplitude $F(1, 25) = .397$, n.s.), T/A ratio $F(1, 25) = .191$, n.s.), absolute T+A amplitudes ($F(1, 25) = .172$, n.s.), and relative T+A amplitude $F(1, 25) = .009$, n.s.) were observed.

4.4 QEEG Results

A 2x2 repeated-measures ANOVA with the within-subjects factor TIME and factor GROUP were performed for theta, alpha, T+A absolute and relative power, and T/A ratio at Pz. A visual analysis of the Normal Q-Q plots was performed for all variables which revealed a fairly linear distribution of the values which attests that the observed values are normally distributed. Only one extreme outlier (SD > 2.5) was found for the T/A ratio (participant 025) and few other outliers (SD > 1.0): for relative theta power (participants 012 and 025), for absolute theta (participants 021 and 023), absolute alpha (participant 007), and for T/A ratio

(participant 23). None of the variables showed a statistically significant change between pre- and post-treatment and no differences between EG and CG was observed for any of the variables, either.

4.4.1 Theta and alpha absolute power.

The 2x2 ANOVA for absolute theta power revealed that the factor TIME was not statistically significant, indicating that no significant change in theta power was observed at Pz between the beginning and the end of the trial (pre-trial (M = 19.169, SD = 16.626); post-trial (M = 19.178, SD = 14.292); $F(1, 25) = 0.000$, $p = .985$, partial $\eta^2 = .000$; n.s.). The TIME*GROUP interaction exhibited no statistically significant difference between the EG and CG for absolute theta power at Pz between pre- and post-trial ($F(1, 25) = 0.426$, $p = .520$, partial $\eta^2 = .066$; n.s.) which suggests that no differential treatment effect for the A/T NFT (or for the placebo NFT) was observed for absolute theta.

The 2x2 ANOVA uncovered no statistically significant change for absolute alpha power in the EEG at Pz between pre- and post-trial ($F(1, 25) = 0.179$, $p = .676$, partial $\eta^2 = .007$; n.s.). Moreover, no statistically significant difference between the EG and CG for absolute alpha power at Pz between pre- and post-trial was observed ($F(1, 25) = 0.004$, $p = .953$, partial $\eta^2 = .000$; n.s.).

4.4.2 Theta and alpha relative power.

The 2x2 ANOVA indicated that no statistically significant change in relative theta power in the EEG at Pz between pre-and post-treatment ($F(1, 25) = 0.705$, $p = .409$, partial $\eta^2 = .027$; n.s.) and no statistically significant difference in relative theta power between the EG and CG and time of the EEG was found ($F(1, 25) = 1.763$, $p = .196$, partial $\eta^2 = .066$; n.s.).

The 2x2 ANOVA revealed no significant change for relative alpha power in the EEG at

Pz between the pre- and post-trial ($F(1, 25) = 0.224$, $p = .640$, partial $\eta^2 = .009$; n.s.) and no statistically significant difference between the EG and CG and time of the EEG was observed ($F(1, 25) = 0.435$, $p = .515$, partial $\eta^2 = .017$; n.s.).

4.4.3 Theta / alpha power ratio.

The 2x2 ANOVA showed no significant change for the theta / alpha power ratio in the EEG at Pz between pre-and post-treatment ($F(1, 25) = 0.916$, $p = .348$, partial $\eta^2 = .035$; n.s.) and no significant interaction between the EG and CG and time of the EEG could be observed ($F(1, 25) = 0.172$, $p = .682$, partial $\eta^2 = .007$; n.s.).

4.4.4 Theta + alpha absolute power.

The 2x2 ANOVA revealed no statistically significant change in (T+A) absolute power in the EEG at Pz between pre-and post-treatment ($F(1, 25) = 0.151$, $p = .701$, partial $\eta^2 = .006$; n.s.) and no significant difference between the EG and CG and time of the EEG ($F(1, 25) = 1.944$, $p = .317$, partial $\eta^2 = .040$; n.s.) µV

4.4.5 Theta + alpha relative power.

The 2x2 ANOVA did not indicate a statistically significant change for the (T+A) relative power in the EEG at Pz between pre-and post-treatment ($F(1, 25) = 1.117$, $p = .330$, partial $\eta^2 = .043$; n.s.). The TIME*GROUP interaction was not significant, either, which suggests that no difference in treatment effect between the EG and CG could be observed ($F(1, 25) = 2.442$, $p = .131$, partial $\eta^2 = .089$; n.s.). However, relative T+A power between groups shows a slight trend toward significance ($p = .131$) with a medium effect size.

4.5 Correlations

Quantitative variables of the study were analyzed via Pearson correlation matrix (Tables 4.7 to 4.9). For any measure that was assessed pre-and post- trial (i.e., BAI, STAI-T, STAI-S, GAD-7, and QEEG measures) difference scores were calculated by subtracting the post-session score from the pre-session score. For measures that were gaged before and after each NFT session (i.e., NFT EEG measures and ADACL scores) mean difference scores of sessions 1 and 2 and sessions 9 and 10 were subtracted from each other, i.e., (sessions 9+10) / 2 – (sessions 1+2) / 2 = difference score. Hence, the higher the difference score was the higher the post treatment score was. The examination of the bivariate relationships showed, as was expected, higher correlations within groups of related variables, such as between the different anxiety instruments and between EEG alpha and NFT alpha measurements.

	1. EG /CG	2. NFT x prefer learning time	3. Belief in EG?	4. Total days trial	5. Sessions/ week	6. Mental strats	7. Mental strats success	8. Change think	9. Change feel?	10. Change behavior?	11. Age	12. LOC score	13. STAI-T diff	14. STAI-S diff	15. BAI diff	16. GAD diff	17. SETS pos. diff	18. SETS neg diff	19. Alpha diff	20. A% diff	21. Theta diff	22. T% diff	23. T+A diff	24. T+A % diff	25. T/A ratio diff	26. ADACL Activ diff	27. ADACL Deactiv diff	28. ADACL Energy diff	29. ADACL Tired diff	30. ADACL Tense diff	31. ADACL Calm diff
1. EG/CG	1																														
2. NFT x preferred learning time	.048	1																													
3. Belief in EG of CG	.186	-.230	1																												
4. Total days pre-post trial	-.062	.031	.040	1																											
5. sessions / week	.306	-.149	.074	-.730**	1																										
6. Mental strategies used in NFT	.053	.025	.010	-.022	.082	1																									
7. Mental strategies success: y/n	.042	-.241	.008	-.208	.247	.556**	1																								
8. NFT=> change think: y/n	.206	-.053	.540**	-.013	-.044	.201	.159	1																							
9. NF => change in feel: y/n	.256	-.230	.418*	-.035	.113	.168	-.052	.316	1																						
10 NFT=> change in behavior: y/n	.066	.077	.459*	.113	-.156	.134	.106	.523**	.385	1																					
11. Age	.138	-.103	.451*	.088	.024	.116	-.049	.257	.229	.441*	1																				
12. Rotter LOC score	.019	-.478*	-.001	-.021	.120	-.241	-.243	-.258	-.072	-.171	-.204	1																			
13. STAI-T_post-pre-trial diff	-.060	.007	-.007	.036	-.277	.066	-.218	.127	-.129	.226	.417*	-.021	1																		
14. STAI-S diff	-.126	.012	-.254	.164	-.269	.031	-.301	-.016	-.144	.126	.428*	.035	.715**	1																	
15. BAI post-pre-trial diff	.078	.088	-.134	.236	-.381	-.022	-.159	.058	-.099	-.203	-.291	.198	.057	.127	1																
16. GAD post-pre-trial diff	-.084	-.336	-.021	-.137	.211	.289	.474*	-.169	-.184	-.035	.187	.125	-.073	-.122	-.271	1															
17. SETS pos, post-pre-trial diff	-.204	.257	.161	.182	-.290	.100	.080	.430*	-.075	.393	-.270	-.028	.010	-.088	.299	-.283	1														
18. SETS neg, diff	.002	-.127	-.331	-.261	.360	.160	.240	.050	-.066	-.281	-.094	.236	.052	.168	.231	.168	-.247	1													
19. Alpha amp sess. 910_12 diff	.122	.210	-.381	.016	-.074	.042	-.040	-.095	-.221	-.040	-.239	-.009	.298	.217	.011	-.296	-.107	.098	1												
20. A % diff	.103	-.097	.012	.174	-.311	.188	.134	.350	-.048	.133	-.280	-.163	.110	-.015	.185	.029	.111	-.128	.371	1											
21. Theta amp, diff	-.061	-.123	.014	-.432*	.307	-.297	-.374	-.162	-.051	-.229	.052	.145	.336	.009	-.146	-.267	-.135	.054	.011	-.395*	1										
22. T %, diff	-.204	.028	-.187	-.301	.255	-.260	.004	.043	-.038	.068	-.099	.017	-.193	.000	.019	-.285	.125	.390*	-.158	-.292	.317	1									
23. T+A, diff	-.067	-.137	-.137	-.463*	.226	-.137	-.332	-.095	-.169	-.335	-.188	.126	.420*	.069	-.019	-.191	-.164	.125	.332	.120	.807**	.088	1							
24. (T+A) %, diff	-.027	-.092	-.105	-.018	-.147	.021	.138	.381	-.073	.178	-.337	-.150	-.012	-.015	.195	-.150	.187	.117	.267	.802**	-.190	.338	.174	1							
25. T/A ratio, diff	-.224	.095	-.095	-.186	.168	-.432*	-.180	-.288	.077	.061	.121	.106	-.124	-.053	-.219	-.271	-.006	.023	-.238	-.784**	.459*	.636**	-.037	-.374	1						
26. ADACL-activ, sess. 910_12 diff	.159	.131	.047	-.153	.194	.044	-.103	-.277	-.196	-.348	-.145	.300	-.335	-.295	.010	.044	.049	-.189	-.317	-.339	.228	.030	.077	-.314	.158	1					
27. ADACL deactiv, diff	-.010	-.047	.000	.199	-.085	.123	.201	.269	.061	.012	-.090	-.467*	-.163	.074	-.042	.000	-.033	.060	.094	.501**	-.477*	-.032	-.274	.474*	-.438*	-.586**	1				
28. ADACL energetic, diff	.055	.412	-.117	-.226	.151	-.015	-.119	-.155	-.332	-.294	-.365	.314	-.264	-.347	.176	-.037	.196	.065	-.166	-.281	.220	.110	.167	-.208	.182	.784**	-.613**	1			
29. ADACL tired, diff	-.170	-.277	.362	.088	.018	.292	.297	.437*	.210	.354	.196	-.289	.119	.197	-.340	-.030	.261	-.159	.026	.286	-.263	-.063	-.210	.242	-.243	-.372	.575**	-.602**	1		
30. ADACL tense, diff	.139	-.335	.201	-.071	.182	.050	-.053	-.326	.079	-.255	.176	.168	-.245	-.055	-.181	.120	-.221	-.299	-.380	-.324	.165	-.011	-.069	-.325	.119	.664**	-.196	.099	.055	1	
31. ADACL calm diff	.034	.189	-.255	.296	-.163	.001	.092	.026	-.167	-.086	-.272	-.296	-.302	-.033	.286	-.026	.057	.127	.050	.337	-.469*	.017	-.277	.343	-.293	-.401*	.669**	-.175	-.016	-.445*	1

Table 4.7a: EG & CG: Pearson Point-Biserial and Bivariate Correlations between Demographic, Qualitative, Psychometric and EEG-Based Post-Pre-Difference Scores. Significant correlations are marked in bright orange. Muted colors mark related items. Qualitative items (items 6-10) have been transformed into quantified version. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

4.5.1 Participant demographic correlations.

The participants age in years correlated significantly with the STAI-T ($r = .417$; $p = .030$) and STAI-S ($r = .428$; $p = .026$) difference scores (Table 4.7 a); higher age was significantly related to higher post-treatment scores in state and trait anxiety; in other words, the older participants did not exhibit as high of a reduction in anxiety by the end of the NFT as younger participants. Related to this finding is that older individuals were not able to reduce their level of calmness, as evidenced by the AD-ACL calmness sub-scale, as much as younger individuals between start and end of NFT sessions ($r = -.434$, $p = .024$). Age was also significantly correlated with lower learning rates of alpha and theta, as signified by lower theta ($r = -.426$, $p = .027$) and alpha ($r = -.531$, $p = .004$) amplitude differences from the beginning to the end of a NFT trial, but not significantly correlated with T/A ($r = -.103$, $p > .05$, n.s.), and (T+A) relative amplitude differences ($r = -.338$, $p > .05$, n.s.). However, higher age did significantly relate to higher relative alpha measurements in the QEEG between pre- and post-trial ($r = -.432$, $p = .024$).

Education level correlated positively with GAD-7 difference scores ($r = .409$, $p = .034$) pre- and post-treatment; in other words, the higher the education level was the greater the reduction in anxiety, as measured by the GAD-7. However, the other anxiety measures, STAI-T ($r = .261$, $p > .05$, n.s.), STAI-S ($r = .153$, $p > .05$, n.s.), and BAI ($r = -.030$, $p > .05$, n.s.) did not show a significant correlation between perceived anxiety and education level.

4.5.2 Duration of treatment and sessions per week correlations.

The *duration of treatment* for ten NFT sessions significantly correlated negatively with

theta amplitude difference (r = -.426, p = .027) and *T/A ratio difference* (r = -.482, p = .011) from beginning to end of a NFT session; i.e., more days between NFT sessions were associated with poorer learning of *theta amplitudes up-regulation* and less change *in T/A ratio difference* between beginning and end of the trial (Table 4.7 a). Confirming these results was, *sessions of NFT per week* was only related to *T/A ratio difference* (r = .443, p = .021), i.e., the *less sessions per week* (the longer the duration of the NFT trial) the lower their *T/A ratio difference score* between the beginning and the end of the NFT trial. However, number of sessions per week did not significantly relate to theta amplitude differences.

4.5.3 Anxiety questionnaires correlations.

Age significantly correlated with both the STAI-S (r = .417, p < .05) pre-post difference scores and the STAI-T (r = .428, p < .05): The younger participants were the more state and trait anxiety was reduced after the ten NFT sessions (Table 4.3). Furthermore, GAD-7 pre-post difference scores were significantly related to the perceived success of mental strategies used to elevate the EEG parameters of the NFT protocols (r = .474, p < .05): The more successful the mental strategies were perceived the lowerwas the reduction in perceived anxiety at the end of the NFT trial. Lastly, STAI-T difference scores were significantly associated with absolute T+A amplitude increases between the means of sessions 1 and 2 in comparison to the mean of sessions 9 and 10 (r = .420, p < .05). All other parameters of the matrix did not significantly correlate with any of the study's anxiety parameters.

4.5.4 Activation and deactivation (AD-ACL) correlations.

The AD-ACL mean difference scores of sessions 9 +10 subtracted from sessions 1 + 2 for *deactivation* and *activation* scales and the *tiredness, calmness, tenseness,* and *energy* sub-scales did not significantly correlate with any other measure, except for the AD-ACL *calmness*

sub-scale which significantly related to age (see above), including all anxiety self-report questionnaires and the participant perceiving their mental strategies as success ($r = .437$, $p = .031$), i.e., the more tired participants felt across sessions the more successful they perceived their mental strategies (Table 4.7 a).

Furthermore, a correlation matrix was calculated that simply used the pre-post difference score of all sessions in its relationship to the other study parameters. No significant correlations were observed between the AD-ACL scales and sub-scales and any of the anxiety scales. But most of the AD-ACL scales and sub-scales significantly correlated to the item whether any change of behavior was observed in everyday life due to the NFT training; a change in behavior (positive change regarding anxiety symptomology in all cases) was significantly associated with lower perceived *deactivation* ($r = -.565$, $p > .01$), lower *tension* ($r = -.467$, $p > .05$), less *tiredness* ($r = -.661$, $p > .01$), and higher *energy* ($r = .642$, $p > .01$) post-NFT session; and a perceived change in thinking was associated with less perceived *tiredness* ($r = -.462$, $p > .05$) post-NFT session.

As the CG protocol did not uptrain alpha and theta amplitudes, a bivariate correlation matrix was calculated for the EG only. The results of this new matrix were then compared to the correlation matrix for all study participants and (Table 4.7 b). Higher significant correlations for the AD-ACL deactivation scale for relative alpha differences between sessions 1+2 and last sessions 9+10 ($r = .676$, $p < .01$, instead of $r = .501$, $p < .01$), absolute theta ($r = -.613$, $p < .05$, instead of $r = -.474$, $p < .05$), relative T+A ($r = .714$, $p < .01$, instead of $r = .474$, $p < .05$) and T/A ratio ($r = -.591$, $p < .05$, instead of $r = -.438$, $p < .05$) were observed. Thus, the higher the relative alpha and relative T+A amplitudes were in sessions 9+10 in comparison to the sessions 1+2 (larger difference score) the more deactivated participants felt. The higher the absolute theta

amplitudes and T/A ratio difference scores between sessions 1+2 and 9+10 were the less deactivated subjects felt. These trends were significant for both EG and CG but even more pronounced for participants of the the EG. However, no significant correlations were observed between AD-ACL deactivation and absolute alpha, absolute T+A, and relative theta, neither for the correlation matrix for the EG only nor for all participants.

	Alpha amplit. diff	Perc Alpha diff	Theta amplit. diff	Perc. Theta diff	(T+A) diff	Perc. (T+A) diff	TA ratio diff
ADACL activ_diff	-0.408	-0.496	0.463	0.312	0.303	-0.346	0.322
ADACL deactiv_diff	-0.008	.676**	-.613*	-0.018	-0.385	.714**	-.591*
ADACL energy_diff	-0.052	-0.327	0.405	0.241	0.445	-0.207	0.181
ADACL tired_diff	0.015	.553*	-0.407	-0.023	-0.298	.578*	-0.405
ADACL tense_diff	-.686**	-.539*	0.333	0.351	-0.018	-0.369	0.416
ADACL calm_diff	0.007	.543*	-.631*	-0.095	-0.411	0.525	-.566*

Table 4.7 b: EG only: Pearson bivariate significant correlations between AD-ACL measures and EEG-based NFT pre-post-difference scores between session 1 & 2 and 9 & 10. Significant correlations are marked in orange or red: orange = are significant for both, EG & CG, red = only significant when looking at EG only. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

Analyzing the correlation between the AD-ACL mean difference scores (of sessions 9 + 10 subtracted from sessions 1 + 2) for scales and sub-scales and EEG-based measures revealed a more nuanced picture on deactivation and activation. While the AD-ACL difference scores in *energy* did not significantly correlate with any of the NFT measures, the other AD-ACL sub-scales did: *tired* ($r = .553$, $p < .05$), *tense* ($r = -.539$, $p < .05$), and *calm* ($r = .543$, $p < .05$), sub-scales significantly correlated with relative alpha. The AD-ACL *tired* significantly correlated with relative T+A ($r = .578$, $p < .05$) and absolute theta ($r = -.631$, $p < .05$); and T/A ratio ($r = -.566$, $p < .05$) correlated with the AD-ACL *calm* sub-scale (Table 4.4). All but the absolute theta correlations were significant for the EG only (not for EG and CG combined), i.e., for the EG the higher the relative and absolute alpha amplitude became over the course of the ten-session NFT trial, the less tense they felt; the higher the relative alpha amplitude became the more tired and calm participants felt; the lower the T/A ratio became the calmer EG participants felt.

4.5.5 QEEG-related correlations.

Several QEEG pre- and post-treatment differences correlated with psychometric difference scores and demographic participant characteristics. The theta relative power difference between pre- and post-treatment correlated with two of the anxiety measures but in opposite ways: BAI (r = .417, p = .031) and GAD-7 (r = -.449, p = .019) (Table 4.9); for the BAI an increase in relative theta amplitude was associated with an increase in perceived BAI anxiety scores post treatment, whereas an increase in relative theta amplitude post treatment was associated with a decrease in post-treatment perceived anxiety scores on the GAD-7 (Table 4.5). Higher absolute theta power was associated with higher perceived anxiety scores in the BAI (r = .564, p = .002) and higher education level was associated with higher post-treatment absolute alpha power (r = .410, p = .034). Alpha relative power was positively related to age and education level (Section 4.5.1) and T/A ratio was not significantly correlated with any measure, except, like expected, with other EEG-related measures.

	1. Total Days	2. Sessions / Week	3. Age in Years	4. Educ. Level	8. BAI	9. GAD	16. EEG T Rel. Power	17. EEG A Rel. Power	19. EEG T Abs. Power	20. EEG A Abs. Power	21. TA Ratio
1. Total Days	1										
Sig (2-tailed)											
2. Sessions / Week	**-.730****	1									
Sig (2-tailed)	(.000)										
3. Age in Years	.088	.024	1								
Sig (2-tailed)	(.662)	(.907)									
4. Education Level	-.245	.176	.399*	1							
Sig (2-tailed)	(.219)	(.380)	(.039)								
8. BAI	.236	-.381	-.291	-.030	1						
Sig (2-tailed)	(.236)	(.050)	(.140)	(.884)							
9. GAD-7	-.137	.211	.187	.409*	-.271	1					
Sig (2-tailed)	(.497)	(.291)	(.350)	(.034)	(.172)						
16. EEG T Rel. Power	.069	-.044	-.186	-.370	.417*	-.449*	1				
Sig (2-tailed)	(.731)	(.827)	(.352)	(.057)	(.031)	(.019)					
17. EEG A Rel. Power	-.115	.177	.432*	.395*	-.314	.242	-.545**	1			
Sig (2-tailed)	(.569)	(.377)	(.024)	(.042)	(.111)	(.224)	(.003)				
19. EEG T Abs. Power	.255	-.214	-.074	-.189	.564**	-.187	.613**	-.181	1		
Sig (2-tailed)	(.200)	(.284)	(.713)	(.345)	(.002)	(.350)	(.001)	(.365)			
20. EEG A Abs. Power	-.003	.013	.316	.410*	-.059	.211	-.497**	.702**	.148	1	
Sig (2-tailed)	(.989)	(.950)	(.109)	(.034)	(.771)	(.290)	(.008)	(.000)	(.462)		
21. EEG TA Ratio	-.482*	.443*	-.103	-.150	-.065	-.290	.105	.098	-.079	-.183	
Sig (2-tailed)	(.011)	(.021)	(.609)	(.457)	(.747)	(.143)	(.603)	(.626)	(.695)	(.361)	

Table 4.8: Pearson bivariate significant correlations between psychometric and EEG-based pre-post-difference scores and participant characteristics. Significant correlations are marked in grey. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

The only two correlations that proved to be significant in the QEEG and NFT pre-post-difference scores (between session 1 & 2 and 9 & 10) correlation matrix were the correlations between NFT relative theta and QEEG absolute alpha difference scores ($r = -.398$, $p < .05$) and between NFT relative theta and QEEG absolute T+A difference scores ($r = -.432$, $p < .05$); i.e., the higher the mean post-trial absolute QEEG theta amplitude was the less was the change of absolute alpha and absolute T+A amplitudes between sessions 1+2 and 9+10 (Table 4.9).

CG&EG	EEG A abs diff	EEG A rel diff	EEG T abs diff	EEG T rel diff	EEG T+A abs	EEG T+A rel	EEG_T/A diff
Abs A 910-1 diff	.159	-.011	-.167	-.182	.091	-.115	.017
Perc A diff	.143	-.229	-.055	-.132	.112	-.346	.294
Abs T diff	-.244	-.037	-.029	.275	-.230	.109	-.073
Perc T diff	-.398*	-.017	-.229	.115	-.432*	.044	-.007
Abs T+A diff	-.129	-.196	-.055	.156	-.134	-.146	.132
Perc T+A diff	-.108	-.236	-.198	-.058	-.160	-.313	.285
T/A ratio	-.190	.244	-.054	.127	-.189	.361	-.350

Table 4.9: Pearson bivariate significant correlations between QEEG-based pre-post-difference scores and NFT pre-post-difference Scores between session 1 & 2 and 9 & 10. Significant correlations are marked in grey. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

4.5.6 Cognitive strategies and time-of-day of neurofeedback.

The use of mental strategies ($r = .010$, n.s.) and the perceived success of mental strategies ($r = .008$, n.s.) did not correlate with the belief that the participant belonged to the EG. As expected, perceived changes in everyday thinking ($r = .540$, $p < .01$), feeling ($r = .418$, $p < .05$), and behavior ($r = .459$, $p < .05$) highly correlated with the belief in EG, in other words, participants who believed in being part of the EG reported changes in thinking, feelings, and behavior due to the NFT in higher numbers than the participants who believed they were part of the CG (Table 4.7 a).

Neither absolute alpha, theta, and A+T amplitudes, A/T ratio, nor relative alpha, theta, and A+T, were significantly correlated on the correlation matrix that included both, EG and CG (Table 4.7 a). However, looking at the correlation matrix for the EG (Appendix E) a significant

negative correlation was observed between the T/A ratio and the use of mental strategies ($r = -.556$, $p < .05$); i.e., mental strategies use in the EG was associated with lower T/A ratios in sessions 9+10 in comparison to sessions 1+2. Furthermore, relative alpha ($r = .546$, $p < .05$), and relative T+A ($r = .609$, $p < .05$), amplitudes were positively correlated, meaning that a reduction in anxious thinking after the NFT trial was associated with higher relative alpha and T+A amplitudes by the end of the trial.

As detailed in section 4.5.5, GAD-7 pre-post-difference scores were significantly related to the perceived success of mental strategies improving NFT reward rate ($r = .474$, $p < .05$): The more successful that mental strategies were perceived by the participant the greater the reduction in perceived anxiety at the end of the NFT trial.

The correspondence of the time-of-day of the NFT sessions (Appendix D: *Neurofeedback Session Checklist*) with the *times-of-day of best learning* did not correlate significantly with the difference scores between session 1+2 and 9+10 differences in absolute alpha ($r = .210$, n.s.) or theta ($r = -.123$, n.s.) amplitudes, nor relative alpha ($r = -.097$, n.s.) or theta ($r = .028$, n.s.), T/A ratio ($r = .095$, n.s.), nor relative ($r = -.137$, n.s.), or absolute T+A ratio ($r = -.092$, n.s.), meaning NFT sessions being held during a time of worst or preferred learning was not associated with a significant improvement in regulation of the parameters in the EG, nor was it associated significantly with any of the AD-ACL pre–post session difference scores, except for a difference in energy ($r = .412$, $p < .10$) and tension ($r = -.335$, $p < .10$) which were approaching significance. In other words, participants who had NFT sessions during their “worst time for learning” (which can be seen as a measure of tiredness, inattentiveness, and exhaustion) reported less energy and more tension throughout the NFT sessions in comparison to participants who had their NFT sessions scheduled during a neutral or best time for learning. The only other item preferred

learning time correlated with significantly was Rotter's Locus of Control scale (r = -.478, p <.05); worst time of learning highly correlated with participants who had a more internal locus of control (higher LOC score), which may be a spurious correlation.

4.6 Treatment Satisfaction and Self-Efficacy (SETS, LOC, Belief in Treatment)

The SETS negative and positive expectations of treatment analyses were performed with a 2x2 ANOVA. A significant decrease in negative treatment expectations was observed between the beginning of the NFT trial and the end of the trial (pre-trial (M = 2.047, SD = 16.626); post-trial (M = 1.419, SD = .937); $F(1, 25) = 5.809$, p = .024, partial $\eta^2 = .189$) with a large effect size. The TIME*GROUP interaction exhibited no statistically significant difference between the groups for both negative ($F(1, 25) = 0.001$, p = .993, partial $\eta^2 = .001$; n.s.) and positive ($F(1, 25) = 1.090$, p = .306, partial $\eta^2 = .042$; n.s.) treatment expectations between pre- and post-trial. Change in treatment expectancy as a measure of treatment satisfaction shows that both, EG and CG participants, who had moderately high treatment expectancy (4.6 /7.0) at the beginning of the trial (EG: M = 4.714, SD = 1.280; CG: M = 4.501, SD = 1.280) experienced no significant drop in treatment expectations over the course of the treatment.

The Rotter Locus of Control Scale was administered at the end of the NFT trial to gauge the participants' self-efficacy. On average, study participants had an above the mean LOC score (EG: M = 12.429, SD = 3.502; CG: M = 12.308, SD = 3.172). In fact, only three or the 27 participants had a score below the mean for women of the Rotter scale (M = 8.42 = 58th percentile; SD = 4.06) and 11 participants scored at least one SD higher than the mean (> 12.48 = 88th percentile). A low score represents an internal locus of control. Hence, participants of this study tended to have an external locus of control on average, which means that they tended to attribute successes or failures to external circumstances rather than their own efforts. However,

the standardization scores for the LOC have not been updated in more than fifty years and results need to be interpreted with caution. A one-way ANOVA was performed to investigate if differences in means could be detected between participants from the EG in comparison to members of the CG. No significant differences between the two groups were found ($F(1, 25) = 0.009$, $p = .926$; n.s.). Point-biserial correlations were performed between the LOC score and all QEEG measures (e.g., Alpha and theta absolute and relative power and NFT measures (e.g., theta and alpha amplitudes and relative amplitudes /percent), as well as for the various anxiety measures (BAI, STAI, and GAD) and no correlation was significant (see correlation matrix in Appendix E).

Belief in EG participation is another variable closely aligned with treatment satisfaction; 19/27 participants (70.4%) believed that they were in the EG and were receiving an active treatment (11/14 members of the EG (78.6%) and 8/13 members of the CG (61.5%). Conversely, no *belief in EG participation* aligns with treatment dissatisfaction; 8/27 participants (29.6%) believed that they were part of the placebo group (5/13 participants from the CG (38.5%) and 3/14 participants of the EG (21.4%). While differences in *Belief in EG participation* could be observed between the EG and CG with more participants from the EG believing in EG participation these differences were neither significantly associated with any of the QEEG and NFT EEG-related parameters, nor with any of the anxiety measure differences or AD-ACL measures.

A point-biserial correlation was performed for the *Belief in EG participation*. All participants were asked at the end of the trial if they believed they had been part of the experimental or control group. *Belief in EG participation* was significantly correlated with participants reporting a change in thinking ($r = .540$, $p < .01$), change in feelings ($r = .418$,

$p < .05$), and change in behaviors ($r = .459$, $p < .05$) due to the NFT trial. It comes as no surprise that participants who reported that they believed to be part of the EG reported change in thinking, feelings, and behaviors significantly more often than participants who did not believe that they had been part of the EG. Furthermore, *Belief in EG participation* was associated with age ($r = .451$, $p < .05$), i.e., the older the participants were the more they believed that they had been part of the EG, although no significant differences in the age distribution between EG and CG had been observed after the initial randomization of participants.

4.7 Successful A+T Amplitude Learner Analysis

According to a position paper by Uryniak, Chan, Fedorov, et al. (2011) the main purpose of a clinical trial is not only to demonstrate that a treatment effect is statistically significant but more importantly that this effect reveals a clinically relevant improvement of the primary outcome measure, i.e., a clinically relevant reduction in disease symptoms. A common way to show that there is a significant clinical improvement is to dichotomize the continuous primary outcome measure of a study into responders and non-responders and re-analyze the data; statistically significant data is likely to achieve a larger effect size and the associated improvement in effect size after re-analysis. One frequently used method is to define a clinically relevant change from baseline in the primary outcome variable apriori; participants are henceforth considered responders if they exceed this threshold. Some clinical societies and regulatory boards even require this method (Lin, 2016; Uryiak et al., 2011). Furthermore, a responder analysis is often used in a post-hoc analysis after statistical significance of the primary outcome measure has been established; it is in fact recommended by the European Medicines Agency (2002, as cited by Uryniak et al., 2011).

However, a responder analysis “cannot rescue otherwise disappointing results in the

primary variables" (Uryniak et al., 2011, p. 478). It is important to point out that responders in the above discussed medical literature are defined as clinical responders, trial participants who experience a significant improvement of reduction in illness symptoms. In NFT literature the term "responder" is in some studies used interchangeably with the term "learner" or "regulator". In this study "responder" is understood as a participant who shows improvements of anxious cognitive emotional and behavioral components of anxiety as well as a reduction in tension (higher deactivation). In comparison, "learners" are those participants who significantly enhance their A+T brain wave amplitudes at Pz.

Learner analyses are used in some NFT studies after the primary outcome measures were not significant, for instance by median split (e.g., Studer et al., 2014). However, when a learner threshold value is chosen post-hoc without a valid reason this might constitute a potentially "inappropriate manipulation of the data" (Lin, 2016, p. 66). There seems to be no consensus of a definition on what exactly constitutes a responder to treatment; definitions depend on the area of disease and more careful research is needed to define a responder in NFT. Zuberer et al. (2015), for instance, elucidate in their meta-analysis of ADHD-related NFT studies of how each of the respective 15 research teams define the criterion of a learner differently regarding successful regulation of brain activity. In general, three approaches are used. A "good performer" might be defined by a predefined criterion, such percentage cut-off (where learners are classified as such if they reached the learning goal in a predetermined percentage of sessions). Another approach is to define participants as learners if the wave bands they trained were significantly improved in the last NFT session in comparison to the first session or when they increased across all or most sessions. The last type of approach was the median split which divides participants into halves depending on the improvement on the training parameter which, in the case of uneven

distribution of learners and non-learners, leads to a mis-classification of participants.

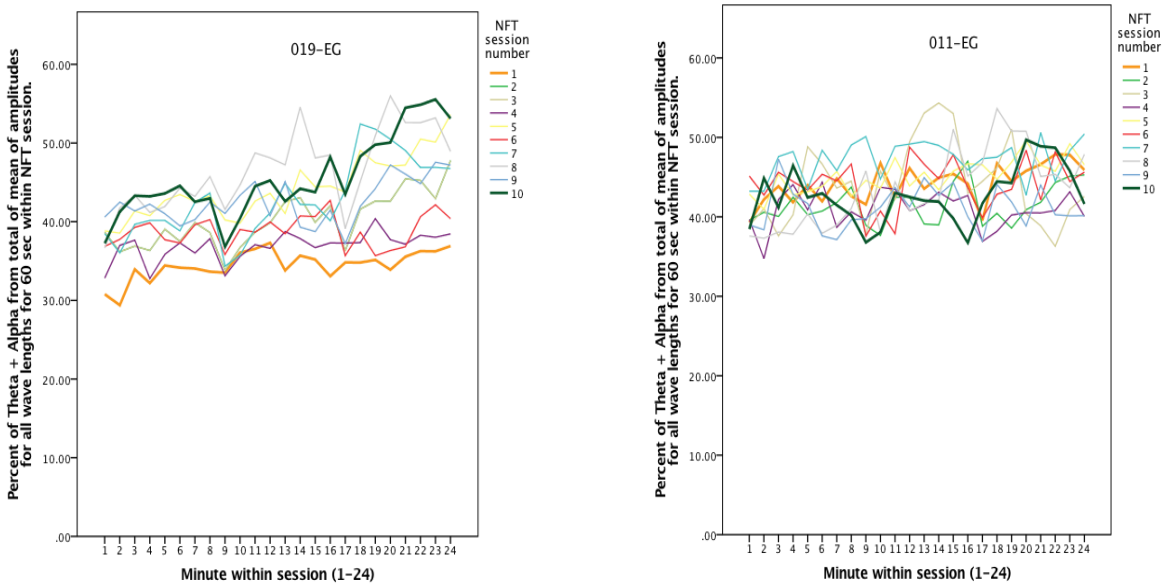

Figure 4.3: **Learning curve for single participant for relative A+T amplitude per minute (24 minutes) for ten NFT sessions.** The bold orange line represents the first session learning curve, the bold dark green line, the last / tenth session learning curve**. Left:** Participant 019 of the EG is a learner: learning curves within and between sessions mostly improve from first to last session**. Right:** Participant 011 of the EG is a non-learner; learning curves between first and last session remain flat.

One goal of the current study was to review commonly used methods of operationalization and statistical analysis in NFT studies and find alternatives that might potentially help with NFT data analysis but more importantly to start a conversation about methodological considerations in this field. However, the current study revealed neither traditional statistical analysis with ANOVAs nor growth curve modeling, significantly better accounted for learning results in up-regulating alpha and theta for the EG than for the CG. Consequently, it would be inappropriate to use the method of learner analysis for a study in which general results are not significant. A learner (or responder) analysis, as explained above, should only be used to make an already statistically significant trial result more clinically significant by re-running the analysis with participants from the EG in comparison to the CG who had a (sufficiently) positive response to the treatment. The learner analysis in the current paper is included as a general example of how to define learners in NFT research, apart from the

commonly used median split. Furthermore, this thesis demonstrates that depending on which NFT parameter is used to determine a learner (alpha and theta absolute amplitude, alpha and theta relative amplitude, or T/A ratio) the subsequent analysis has quite different results.

The method of median split was not used in this study to avoid labeling participants learners who might not have been able to up-regulate their alpha and theta amplitudes. Instead, a linear regression line with the associated regression equation was calculated using mean alpha+theta amplitudes per minute, 240 data points per participant, over the course of ten sessions at Pz. For the EG, participants were considered learner if they exhibited a positive slope b of the regression line (Figures 4.5 and Table 4.10). The EG learner were then compared to all participants from the placebo group in all statistical analyses performed and described earlier (see sections 4.1 to 4.8).

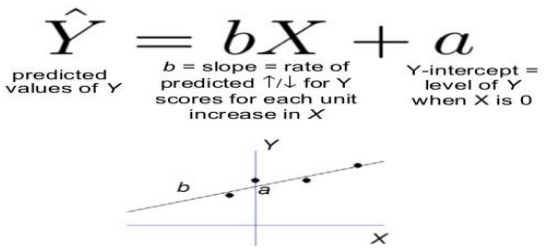

Figure 4.4: Regression equation (without error term). In this study, a learner was defined as any participant whose regression line over the course of 10 sessions had a positive slope b.

The following participants from the EG had positive regression slopes and were therefore entered into statistical re-analysis:

Learner analysis 1: EG Absolute (A+T) amplitude leaners of EG vs. all CG participants

EG: 003, 011, 012, 014, 017, 019, 022, 023, 025, 028 (n = 10).

CG: All CG participants (n = 13).

Learner analysis 2: EG Relative (A+T) amplitude learners vs. all CG participants

EG: 001, 006, 012, 014, 017, 019, 022, 025, 028 (n = 9)

CG: All CG participants (n = 13).

Unfortunately, the further reduction of an already small sample size, reduced the statistical power of results and test sensitivity considerably which made it more difficult to detect any but large effects, for the relative (N = 23) and absolute (N = 22) A+T amplitudes learner analyses, respectively. Detailed results of both learner analyses can be found in Appendix E. A brief comparison of the GCM significant results of all participants and the two learner analyses can be found in Table 4.6 below.

Comparing the results from the original GCM with the two learner GCM analyses reveals, as expected, that more of the EEG-based parameters of the factor TIME were significant after reducing the EG group to participants who were able (on average) to up-regulate A+T across sessions. This was especially true for the absolute A+T learner analysis (learner analysis 1), an analysis that used the summation of absolute alpha and theta amplitudes as a criterion to determine learners.

In the original GCM absolute and relative alpha amplitudes within and across sessions and absolute and relative A+T amplitude, and T/A ratio within sessions had been significant. Absolute theta amplitudes had not been significant neither within sessions nor across sessions and T/A ratio, and relative and absolute A+T amplitudes had not been across sessions. Furthermore, absolute and relative T+A became significant across sessions. By comparison, the relative A+T learner analysis showed only an added significance for the T/A ratio across sessions and all other EEG-based parameters remained non-significant.

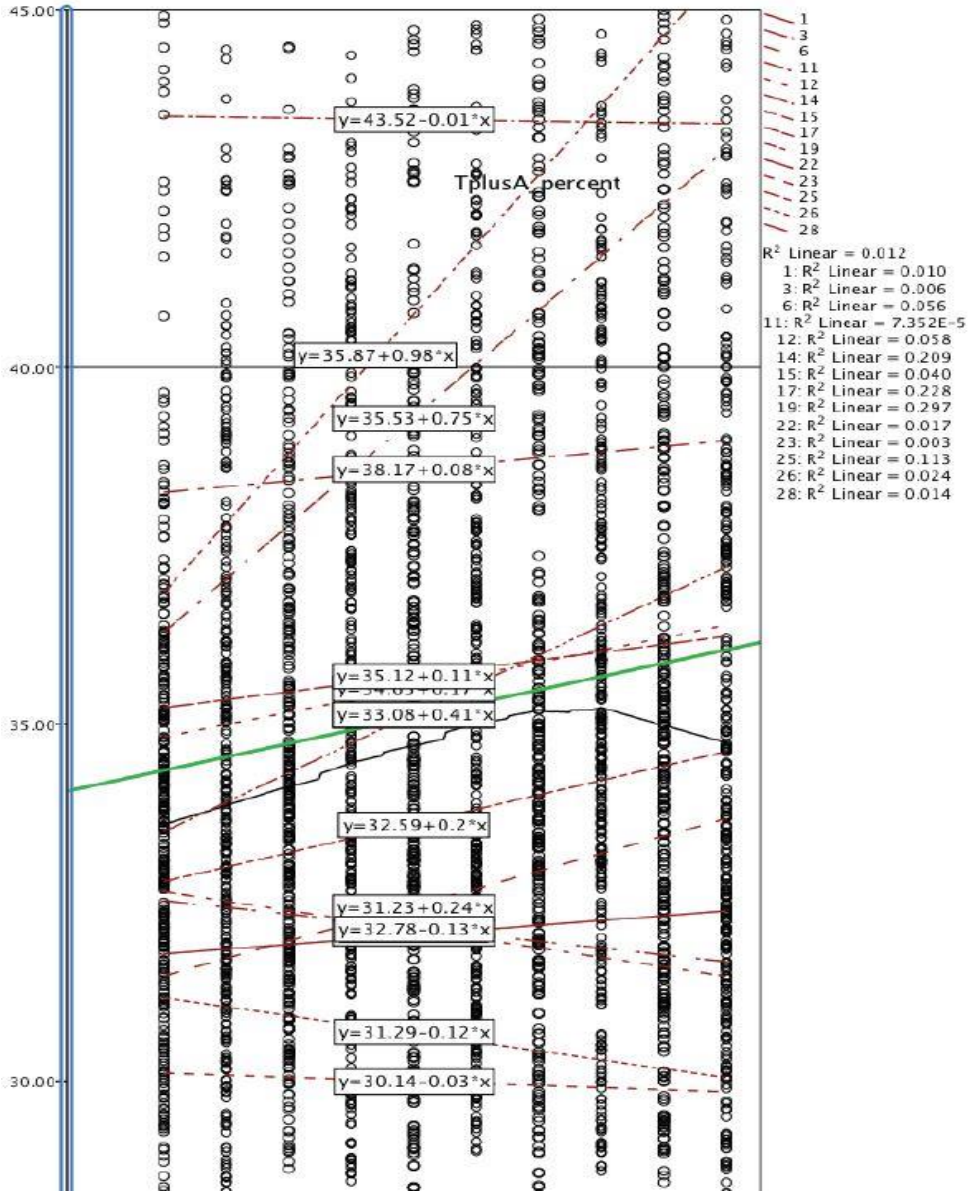

Figure 4.5: Individual EG participants' linear regression lines with associated individual regression equations for mean alpha + relative theta amplitude in percent for the course of the ten NFT (240 data points per participant). Green thick line represents the mean learning regression line across sessions. R^2 represents how close each participants' data points are to the mean regression line.

In learner analysis 1, absolute theta amplitude neared significance within sessions (β = 0.031, *SE* = 0.017, p = .076), and absolute A+T amplitude (β = 0.249, *SE* = 0.086, p < .01), and relative A+T amplitude (β = 0.210, *SE* = 0.072, p < .01**), became significant across sessions in comparison to the original statistical analysis. In learner analysis 2, absolute A+T amplitude

(β = -.009, *SE* = 0.003, p < .01), and T/A ratio (β = 0.210, *SE* = 0.072, p < .01), became significant across sessions in comparison to the original statistical analysis.

All participants (n_{EG} = 14; n_{CG} = 13)

Predictor for ABSOLUTE alpha amplitude (in μV)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS	0.066 (0.012)	< .0001 ***
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.134 (0.048)	< .05*
Predictor for RELATIVE alpha amplitude (in %)		
MODEL C: TIME WITHIN SESSIONS	0.067 (0.010)	< .0001 ***
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.121 (0.013)	< .0001 ***
Predictor for T/A RATIO		
MODEL C: TIME WITHIN SESSIONS	-0.004 (0.001)	< .01**
Predictor for RELATIVE A+T amplitudes (in %)		
MODEL C: TIME WITHIN SESSIONS	0.074 (0.017)	< .0001 ***
Predictor for ABSOLUTE A+T amplitudes (in %)		
MODEL C: TIME WITHIN SESSIONS	0.074 (0.017)	< .0001 ***

Not significant within sessions: absolute and relative theta.
Not significant across sessions: absolute and relative theta, absolute and relative T+A, T/A ratio.

EG Absolute A+T amplitude responders vs. all CG participants (n_{EG} = 10; n_{CG} = 13)

Predictor for ABSOLUTE alpha amplitude (in μV)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS	0.070 (0.847)	< .0001 ***
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.177 (0.050)	< .01**
Predictor for RELATIVE alpha amplitude (in %)		
MODEL C: TIME WITHIN SESSIONS	0.068 (0.011)	< .0001 ***
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.188 (0.067)	< .01**
Predictor for T/A ratio		
MODEL C: TIME WITHIN SESSIONS	-0.003(0.001)	< .01**
Predictor for ABSOLUTE A+T amplitude (in μV)		
MODEL C: TIME WITHIN SESSIONS	0.100 (0.028)	< .01**
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.249 (0.086)	< .01**
MODEL E: TIME ACROSS SESSIONS x GROUP	0.347 (0.148)	< .05*
Predictor for RELATIVE A+T amplitude (in %)		
MODEL C: TIME WITHIN SESSIONS	0.081 (0.020)	< .0001 ***
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.210 (0.072)	< .01 **
Predictor for ABSOLUTE theta amplitude (in μV)		
MODEL C: TIME WITHIN SESSIONS	0.031 (0.017)	.076

Not significant within sessions: relative theta.
Not significant across sessions: absolute and relative theta; T/A ratio.

EG relative A+T amplitude responders vs. all CG participants (n_{EG} = 9; n_{CG} = 13)

Predictor for ABSOLUTE amplitude (in μV)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS	0.061 (0.011)	< .0001 ***
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.141 (0.547)	< .05 *
Predictor for RELATIVE alpha amplitude (in %)		
MODEL C: TIME WITHIN SESSIONS	0.065 (0.010)	< .0001 ***
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.218 (0.062)	< .01 **
Predictor for T/A RATIO		
MODEL C: TIME WITHIN SESSIONS	-0.003 (0.001)	< .01 **
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	-0.009 (0.003)	< .01 **
Predictor for RELATIVE A+T amplitude (in %)		
MODEL C: TIME WITHIN SESSIONS	0.093 (0.025)	< .01 **
Predictor for ABSOLUTE A+T amplitude (in μV)		
MODEL C: TIME WITHIN SESSIONS	0.083 (0.024)	< .01**

Not significant within sessions: absolute and relative theta.
Not significant across sessions: absolute and relative theta, relative T+A.

Table 4.10: **Results from GCM regression analyses from run (within session), trial (across sessions), and group (EG, CG).**

Unexpectedly, all statistical results regarding the factor GROUP remained non-significant in both learner analyses. In other words, the NFT protocol was not associated with a significantly better regulation of alpha and theta up-regulation. One significant interaction effect was observed in absolute A+T up-regulation ($\beta = 0.347$, $SE = 0.148$, $p < .05$), in comparison to the original analysis (see section 4.3.1), which indicates that while there are no differences overall between the EG and CG regarding up-regulation of theta and alpha there are significant differences in how the up-regulation took place over the ten NFT sessions. This result relates well to the 2x5 ANOVA performed in Section 4.3.1 which confirms the differences in learning curves across NFT sessions.

5. Discussion

The primary objective of this study was to create a rigorous, placebo-controlled, clinical trial with a (sub)clinical sample of variously aged adults for the NFT treatment of AD in order to investigate if A/T NFT at Pz is an efficacious method for anxiety symptom reduction in women, as shown by neurophysiological changes in the EEG, changes in NFT learning curves, and changes in subjectively experienced anxiety symptoms. A secondary objective was to search for potentially better analyses methods for NFT trials in general that would not limit the aggregate amount of NFT EEG data to 2 to 5 time points, but, instead use GCM modeling to analyze individual learning curves. A variety of parameters are used in A/T and alpha NFT protocols (i.e., alpha and theta amplitudes, T/A ratio, relative alpha and theta values) to investigate how diverse types of statistical analyses with varying study parameters may influence the outcome of a study. The GCM analysis of each participant's learning curve was then used to separate learners and non-learners. Models different from linear regression, specifically quadratic and cubic regression curves, were investigated as well. This type of analysis is, to the best of my knowledge, a novel application of statistical methodology in the field of NFT research. The third and last last objective of this study was to investigate cognitive variables involved in NFT, such as treatment outcome expectancy, personal attribution styles, use, types, and efficacy of cognitive strategies in NFT, which are rarely assessed in NFT trials. Also new to this investigation into whether there is a significant correlation between NFT learning performance, time of day the NFT sessions were held, and a participant's best or worst time to learn.

The present study, to my knowledge, was the first single-blind trial to test the A/T NFT protocol for trait anxiety in a clinical adult population with a placebo NFT control group, instead of a waitlist CG, other treatment modality CG (e.g., anxiolytics, EMG, meditation), or fake NFT

EG. Moreover, this trial was one of the first studies to use growth curve modeling for NFT data analysis and to define individual learners by positive regression curve slope.

5.1 Primary Outcomes (H 1- H 2)

5.1.1. Up-training of alpha and theta amplitudes within session (H 1a) and across sessions (H 1b).

Hypothesis 1 (H 1a and H 1b): *A ten-session NFT protocol of up-training alpha (8-11 Hz) and theta (5-7.5 Hz) frequency bands at Pz will significantly elevate mean absolute and relative theta and alpha amplitudes and absolute and relative theta + alpha (T+A) amplitudes* ***within (H 1a)*** *and* ***across (H 1b)*** *NFT sessions of the NFT. These measures will not change significantly in the placebo group.*

H 1 was only partially confirmed. Contrary to expectations, both, A/T NFT training at Pz (EG) and active placebo B u/d NFT training improved the participants' absolute and relative alpha amplitudes, absolute and relative T+A measures, and absolute theta amplitude neared significance **within sessions** (while absolute alpha, theta and T+A amplitudes did not change substantially). **Across sessions** only absolute and relative alpha amplitudes increased (and not absolute and relative theta, absolute and relative T+A, nor the T/A ratio), i.e., there was no significant difference on average between the EG and CG when increasing the alpha- and theta-related parameters. Significant learning curves for the relative values within sessions were found for the EG as well as the CG, i.e., while there was a trend for the EG to have steeper learning curves there was no significant difference between the EG and CG in increasing the alpha and theta related parameters.

This result is especially surprising because the CG protocol neither included feedback within the theta or in the alpha frequency range. Nor did it include feedback from the low beta

frequencies below 15 Hz that might have been upper alpha peak frequency in some of the younger participants. A fair amount of research indicates large interindividual differences in alpha peak frequency (APF) depending on biological trait and age (Niedermeyer & Lopes da Silva, 1999; Klimesch, 1999) and intraindividual differences depending on tasks (Klimesch, 1999; Mierau, Klimesch, and Lefebvre, 2017) with younger age routinely being associated with higher individual APF.

After the GCM a re-analysis of the data regarding time **across NFT sessions (H 1b)** with the traditional repeated measures 2x5 ANOVA was performed because this had been the method of choice for all previous NFT studies investigating ADs with post-hoc one-way ANOVAs for significant results. In the analyses for the current study EEG training data from only five data points per participant are used by aggregating data for each EEG parameter from two NFT sessions into one measurement point: sessions 1 + 2 (**measurement 1**), sessions 3 + 4 **(2),** sessions 5 + 6 **(3),** sessions 7 + 8 **(4),** and sessions 9 + 10 **(5).** Alpha amplitude, relative alpha amplitude, and relative T+A amplitude all increased significantly between most measurement points with large effect sizes for absolute and relative alpha amplitude and medium effect sizes for relative T+A. Absolute T+A amplitude was nearing significance *(*p = .086; medium effect size) but absolute and relative theta amplitude did not change significantly over the course of the NFT sessions. Furthermore, a significant interaction effect was found for absolute and relative theta amplitude (medium effect size) which made further interpretation of time effects ambiguous. Post-hoc one-way ANOVAs were only conducted for absolute and relative alpha amplitude, T/A ratio, and relative T+A to find out which pairs of time comparisons were significant. A significant increase of relative alpha amplitude in three of four measurement comparisons (measurements 1 and 2, 1 and 3, 1 and 4) and the last comparison nearing

significance (measurement 1 and 5) was observed. Absolute alpha amplitude increased in two of the four comparisons (measurements 1 and 3, 1 and 4). A+T across two of the four comparisons (measurements 1 and 3, 1 and 4, and 1 and 5 nearing significance). It also showed an interaction effect between TIME and GROUP for absolute and relative theta that had not been observed in the GCM, i.e., no overall difference between the EG and CG regarding changes in absolute and relative theta over the course of the ten-session NFT trial was observed but the time course of theta changes was significantly different between EG and CG (see Appendix E). Generally, interaction effects are either due to different baseline values of the groups or due to a genuine effect of the treatment. Initial t-tests between EG and CG of absolute and relative alpha, theta, and T+A, as well as for T/A ratio proved no significant differences at baseline (4.3.2) leaving a treatment effect as a possibility, but as this result could not be confirmed by the more detailed GCM analysis, skewed artificial significance due to data point aggregation may be assumed. Consequently, GCM may be the approach of choice to keep spurious results to a minimum. Another possible explanation for the difference in time course of the change between EG and CG is that this might have been due to successive sessions of beta up-and down-training. However, aggregating data of subsequent sessions averages the results of one beta up-training session with the results of one beta-down-training session.

Reducing the EG group to the 10 out of 14 participants who were able to (on average) up-regulate A+T **across sessions (H 1b)** showed a more nuanced picture. In this learner analysis, in comparison to the previous analysis which had included all EG participants, revealed that absolute theta amplitude neared significance within sessions, and that on average, absolute and relative alpha increased significantly over the course of the ten NFT sessions and so did the summation of relative and absolute alpha and theta amplitudes. Unexpectedly, all statistical

results regarding the factor GROUP remained non-significant in both learner analyses: i.e., the A/T-NFT protocol was not associated with a significant better regulation of alpha and theta.

The A+T learner analysis showed a significant interaction effect in absolute A+T up-regulation in comparison to the original analysis which indicates that while there are no differences overall between the EG and CG regarding up-regulation of A+T there are significant differences in *how* the up-regulation took place over the course of the ten NFT sessions. This result is similar to those of the 2x5 ANOVA performed in Section 4.3.1 which confirm the differences in learning curves across NFT sessions. As explained in 5.1.2, the difference in the course of the changes between EG and CG for the aggregation of two successive sessions of beta up-and down-training for the 2x5 ANOVA should have eradicated any gains, i.e., the results of a session of uptrained beta which may have been associated uptraining of interdependent alpha waves should have been negated by downtraining beta and interdependent beta in the next session. Unfortunately, the GCM analysis models the 60 second aggregations of all 240 time points over the ten NFT sessions (24 minutes for 10 sessions) and as such does not offer CG and EG means per session to be compared for significant differences between EG and CG per session.

As the 30-second baseline reading was confounded with the first minute of NFT training, it could not be used for further analysis. While the missing baseline values were of concern to pre- post-difference measurements of alpha and theta analyzed by ANOVAs, it had negligible effect on the statistics as GCM is a continuous model of alpha and theta band changes within and across all sessions.

Similar results to the current study were found by Egner et al. (2002 and 2003) for healthy adults, although Egner and colleagues (2002) reported that EG and CG differed in T/A

ratio increase within sessions but not across sessions. Unfortunately, in a few studies which used active placebo NFT in the CG, the EEG amplitudes of participants from the CG were not recorded nor included in the later analysis (e.g., Raymond et al., 2005). These analyses did not take into consideration the effect that mock NFT may have on brain wave modulation and calculated only whether there was a significant improvement of alpha and theta amplitudes. This method is rather questionable, particularly considering the results of my study: if I had only analyzed the EG's improvement in A/T regulation within and across sessions the result would have been that participants learn to successfully up-regulate their absolute and relative alpha, and T/A ratio within and across sessions and theta brain waves within sessions with a clinically relevant large effect size. Yet, comparing the NFT results to a placebo NFT group shows that although the EG is better at up-regulating alpha and theta than the CG, but not significantly. Consequently, it is possible that the observed NFT effects are non-specific in nature rather than the product of a specific NFT protocol.

The only way to assure that there is a causal relationship between the particular NFT protocol and participants' modulation of brain waves is to use an active placebo NFT protocol for the CG, which is as similar as possible in all parameters (i.e., reward frequency, reward sounds and visuals, length of each training session and number of sessions) to the EG protocol. Furthermore, the frequency bands to be trained in the CG cannot interfere with the target frequency bands of the EG. There is a lack of such study protocols in NFT for AD. Of course, there are some experimental studies that report significant changes in EEG parameters for individuals with AD throughout the NFT trial (Dadashi et al., 2012; Garrett & Silver, 1978; Glueck & Strobel, 1975; Lu et al., 2017) but all are questionable because they the lack the kind of analysis described above. The same can be said for studies regarding anxiety in healthy

participants (mostly university students), such as Chisholm (1977), Eismont et al. (2011), Gruzelier et al. (2014a, b), and Sittenfeld (1976).

Some critics assert that NFT active placebo CG are not necessary or cannot be successfully performed (Hammond, 2011 b), partially due to changes in some frequency bands in the control condition that may lead to other unintended consequences for the frequency bands trained in the experimental condition. Ros and colleagues (2013), for instance, observed in an fMRI study that used an alpha amplitude downregulation NFT protocol that the "within-subject amplitude correlations between theta, alpha, and beta bands during NFB were consistently positive within a statistically significant range of 0.5 to 0.7 suggesting a broader effect of NFB training on [non-trained] flanking frequency bands" (Ros et al., 2013, p. 328). More research is needed to understand what kind and how much of an effect specific NFT protocols may have on neighboring frequency bands. Moreover, Rogala (2016) states that there might be differences in the trainability of certain frequencies, as was evident in research with macaque monkeys (Carmina, 2003).

The most plausible explanation for the surprising result regarding H1 is that uptraining beta and upper beta in NFT may lead to alpha frequency uptraining due to interdependency of alpha and beta bands, a concept that was not commonly known during the design and study protocol phase of this study (2015-2016). Only few researchers in the NFT realm, such as Ros et al. (2013), acknowledged that uptraining of certain beta bins may possibly lead to an increase in certain alpha bins. But not until very recently in a study by Jurewicz, Paluch, Kublik, Rogala, Mikicin, and Wróbel (2018) was this issue in my study were better at up-regulating alpha amplitudes within sessions they were also nearing significance of up-regulate theta within sessions. Furthermore, Rogala et al. (2016) report that especially changes in *upper* alpha

amplitudes were observed when subjects were told they were in the alpha inducing group. The individual learning curves (Figure 4.5) show that ten of fourteen participants in the EG learned how to increase their A+T amplitudes which corresponds to a 71.43% success rate. However, looking at individual alpha and theta amplitudes one of the ten successful A+T regulator actually did not upregulate their theta amplitude but instead had a real large increase in alpha, so only nine out of fourteen participants were able to increase their theta and alpha amplitudes across the NFT sessions (64.29%). Yet, while the EG's amplitudes improved generally more, no statistically significant difference was found between the EG and the CG.

In addition, the effectiveness of both groups heightening T and A amplitude **within a session** could be caused by participants' fatigue which lead to decreased beta activity and increased alpha, theta, and delta activity rather than by learning. This explains individual learning curves in some sessions for some participants. However, the majority of women did not follow this pattern but significantly increased their absolute and relative alpha and T+A amplitudes across sessions, which would be unlikely if little or no learning took place within sessions. Tiredness could definitely be a contributing factor to why the CG up-regulated their absolute and relative alpha, and T+A amplitudes with no active feedback since alpha and especially theta amplitudes increase when people get tired (see section 1 2.1). While tiredness was qualitatively tracked with the *NFT Session Coding List*, the AD-ACL pre-and post-session questionnaire, and participants' best and worst time of day for learning, it would have been helpful to ask participants directly before each NFT session how many hours they slept the night before and how sleepy they currently felt.

The decrease in energy over the course of a NFT session may be explained by mental fatigue, especially in conjunction with specific changes in alpha and theta band power in the

mid-parietal region. Mental fatigue in this context can be defined as subjective feelings of low energy, motivation, and drowsiness with additional difficulties of difficulties of performing continuous mental tasks (Trejo, Kubitz, Rosipal, Kochavi, & Montgomery, 2015). Trejo et al. (2015) analyzed spontaneous EEG power spectrum densities (PSD; obtained by decomposing an EEG time series into a voltage/frequency graph via FFT (Niedermeyer & Lopes da Silva, 1999) of continuous simple mental arithmetic tasks of 22 healthy volunteers until they felt fatigued. They investigated the occurrence of fatigue and its EEG correlates, as well as subjectively experienced moods and energy levels assessed by the AD-ACL and other measures. The authors discovered that in as little as 15 - 30 minutes of continuous performance mental fatigue occurred and "produced decreased general activation (i.e., self-reported energy) and preparatory arousal (i.e., self-reported calmness) and increased general deactivation (i.e., self-reported tiredness) but did not significantly influence other moods" (Trejo et al., 2015; p. 582). Lengthening response times and decreasing alertness were also reported but but did not lead to changes in the response accuracy of the mental tasks.

The NFT sessions in the current study also involved a continuous rather complex mental task of learning to regulate EEG frequencies via feedback may be comparable to the Trejo study and shows that even a relatively short amount of time, such as the 25-minutes of the NFT session can cause mental fatigue. But even more interesting are the changes in PSD Trejo and colleagues (2015) found associated with mental fatigue. A significant and distinctive increase of alpha+theta PSD across subjects during fatigued states was observed, especially in frontal midline theta (Fz) and midline parietal (Pz) alpha activity, which increased as a function of time on task, without changes in other frequency bands. These results had previously been observed in extended performances of air traffic controllers (Krishnan, Dasari, & Ding, 2014; as quoted in Trejo et al.,

2015). Trejo and colleagues relate these decreases in performance and increases in alpha activity during mental fatigue to Pfurtscheller's (1999) model how coherent (increase in) alpha band activity likely indicates decreased cognitive processing of the neuronal populations underlying the area (Lim et al., 2010; as quoted in Trejo et al., 2015). Furthermore, Trejo asserts "spatially diffuse theta rhythms associated with sleepiness, spatially focused, theta rhythms associated with cognitive effort and WM (working memory) load, lower alpha rhythms (8 - 10 Hz) associated with relaxed wakefulness, and focused higher alpha rhythm (10 - 12 Hz) suppression associated with spatial and non-spatial shifts of attention." (Trejo et al., 2015; p. 585). In general, these research results seem to point to mental fatigue being associated with a shift toward the DMN which is accompanied by a low alpha idling mode (8-10 Hz) and lowered activities in the executive and attention networks. Both, EG and CG experienced mental fatigue and an upregulation of theta and especially alpha at Pz as each NFT progressed, as evidenced by the AD-ACL changes between beginning and end of the NFT session. Consequently, it is not clear if any learning had actually taken place, especially in light of the fact that the CG upregulated A+T without being trained for it, or if upregulating A+T is the result of mental fatigue alone.

The EG and CG being able to uptrain relative and absolute alpha **within and across sessions** could be a sign that A/T NFT is an elaborate placebo and that sitting in front of a computer in a relaxed position while attempting to not think of anything in a quiet room with dim lighting has the unspecific effect causing alpha waves and even theta waves to increase. This might be especially true when one looks at the participants' busy lives trying to balance work, family, and study. NFT sessions provide a refuge from the noisy stressful environment outside the lab.

Unfortunately, due to financial limitations and because this trial was essentially a one-researcher and time-limited operation the scheduling of at least one or several follow-up appointments to re-assess QEEG and self-report anxiety scales and qualitative questions about changes in thinking, feeling and behavior was not feasible. Additional follow-up appointments would have allowed to analyze if and which long-term changes resulted after the NFT concludes, as well as if any differences between the EG and CG could be observed. Especially in NFT studies, which had used transfer trials, participants in the area of ADHD and epilepsy maintained the gains through the NFT in follow-up appointments (Strehl et al., 2014; Gevensleben et al., 2009 and 2010; Leins et al., 2007). Furthermore, Engelbregt (2016) studied the short- and long-term effects of frontal beta NFT on healthy adults by re-testing all subjects 36 months after the end of the NFT and showed that the gained increase in beta oscillations was maintained for the EG even after three years although the cognitive improvement originally observed right after the completion of the NFT were no longer observed.

Lastly, as discussed in chapter 1.3.1, EG and CG were both trained at the Pz-LE locations which (beside Cz-LE) were the most used often used electrode placements in A/T NFT for ADs. The Pz electrode placement corresponds to the caudal superior parietal lobule which is connected with enhanced hippocampal activity which may be especially beneficial for enhanced memory consolidation and retrieval and activation of self-related functions that can be used to achieve a relaxed calmness, and down-regulation of the HPA axis according to Gruzelier et al. (2009). Yet, Olejarczyk, Bogucki, and Sobieszek (2017) in their study on the underlying mechanisms of split alpha peaks found that, depending on the choice of reference electrodes, alpha rhythm generators were not just found at the regular occipital (O1 and O2) and frontal locations but were also found at Pz (10 Hz) in some healthy participants. While Olejarczyk and colleagues were more

interested in finding out how alpha generators outside the occipital and frontal areas may influence the creation of overlapping double alpha peaks (split alpha) due to frequency differences between two alpha generator locations, the result of their study may offer another possible explanation why in the current study alpha amplitudes were raised even in the CG that did not uptrain alpha. If Olejarczyk and collegues' (2017) results are replicable in a majority of individuals it may mean that independent of the NFT protocol, as long as the active electrode is placed at Pz rising alpha amplitudes are to be expected in cases of heightened attention which enhances alpha rhythm production (Klimesch, 1999). Thus, in future research it may be beneficial to consider different electrode locations, especially for the CG.

5.1.2 Reduction of trait and other anxiety measures (H 2).

Hypothesis 2 (H 2): *A ten-session NFT protocol of up-training alpha (8-11 Hz) and theta (5-7.5 Hz) frequency bands at Pz will significantly lower the subjective experience of trait anxiety. These measures will not change significantly in the placebo group.*

H 2 was partially confirmed. Contrary to expectations, both, A/T NFT training at Pz (EG) and active placebo B u/d NFT training (CG) led to a significant reduction in anxiety in all self-report anxiety scales anxiety (STAI-T and STAI-S, BAI, and GAD-7), including trait with large effect size. Yet a trend was observed that the A/T NFT protocol reduced anxiety measures more than the active placebo protocol of the CG.

The most plausible explanation for EG and CG showing significantly decreased scores in trait anxiety as well as in all other anxiety measurements is that both groups increased relative A+T amplitudes. Increasing alpha and theta oscillations targets the ANS indirectly and potentially leads to relaxed calmness and reduced anxiety symptoms (see chapter 1.1.4). Predominant theta oscillations may indicate internal orientation and increase drowsiness among

others (Horschig et al., 2014) whereas dominant alpha waves are associated with relaxed wakefulness and reduction of simultaneous processes that are unnecessary for a present task via increasing the signal-to-noise ratio (Klimesch et al., 2012).

Furthermore, this study had an active placebo group which made sure that all parameters were exactly the same for CG and EG except for the frequency bins trained. Consequently, a placebo effect may have been observed that caused both groups to feel less anxious, as elaborated above. Participants developed relationships with the experimenter and NFT technicians which most certainly influenced the individual's general level of comfortability, trust, motivation, and level of focus on the NFT treatment. This may be especially relevant for research with individuals with GAD and SAD as they often are uncomforTable with social situations. Also, having 45 minutes twice a week for ten sessions in a quiet pleasant room where participants are welcomed and receive undivided attention by the NFT trainer from the often busy often stressful lives trying to balance work, family, and study may serve as refuge and lessen anxiety.

A possible explanation of the results is offered by social psychologist Leon Festinger's *theory of cognitive dissonance* (Festinger, 1962). Festinger postulated that having conflicting cognitions cause an aversive arousal, the so-called dissonance, which a person attempts to reduce by choosing one of the inconsistent cognitions and devaluing and rejecting the other. Redelmeyer and Dickinson (2011) apply Festinger's theory to the medical field by hypothesizing that when patients choose and endure a lengthy and /or unpleasant medical procedure they may reduce their dissonance by exaggerating the benefits of the treatment and downplay the negative parts of the procedure. Similarly, to participate in a ten session NFT clinical trial, with associated EEG sessions, and a multitude of self-report measures constitutes a lengthy time commitment,

especially for working women. Enhancing the positive effects of the NFT and downplay negative parts of the trial may be the result, specifically thoughts that such lengthy time investment might not have led to the reduction in anxiety symptoms that participants had hoped for.

In addition, the participants' reduced self-perceived anxiety scores may certainly have been influenced by the expectation of treatment outcome and by a person's belief as to how much they can influence the outcomes of events in general. This might be particularly true for treatments involving technology that is perceived as cutting edge (Beier; 1999 and 2004*)*

The studies of Bhat et al. (2012), Garrett & Silver (1978), and Rice et al. (1993) were the only three that had an active CG; Bhat compared NFT to pharmacological treatment, whereas Garrett & Silver (1978) and Rice used a semi-active control as they compared alpha NFT and frontal EMG-Feedback. In contrast, Agnihotri et al. (2007), Dadashi et al. (2015), and Vanathy et al. (1988) used wait-list participants. Only Lu et al. (2017) reported that even though an active treatment of anxiolytics was used for the CG the EG that received A/T NFT decreased anxiety symptoms significantly more than the CG. However, the sample size of this study was very small (N = 18).

Another reason for the current study not significantly differentiating between EG and CG regarding the reduction in self-perceived anxiety may be the small sample size in this study (N = 27) as a larger sample size would have been more sensitive to differences between groups. However, Lu (2017; EG: n = 10, CG: n = 8), Faridnia (2012; EG: n = 10, CG: n = 10), and Vanathy (1998; EG 1: n = 6, EG 2: n = 6, CG: n = 8) all had even smaller sample sizes and were still able to show significant differences in reduction of anxiety between EG and CG. Other studies found no significant difference between EG and CG reduction of anxiety for EG and CG after NFT: Bhat et al. (2012) with a larger sample of participants (N = 100) who had been

diagnosed with anxiety and depressive disorders, Rice et al. (1993) for participants with GAD, and Watson and Herder (1980) for psychiatric patients with multiple Disorders. While Bhat et al. (2012) used standard anxiolytic treatment as CG, Watson and Herder (1980) used a sham NFT, and Rice et al. (1993) used active opposite NFT protocols. Raymond et al. (2005) came to the same conclusion in a study with healthy adults. In contrast, other RCTs reported that the EG had a significantly larger drop in self-reported anxiety scores than the CG, such as Lu et al. (2017), Faridnia et al. (2012), Garrett and Silver (1978), and Vanathy et al. (1998), for participants with PD, athletic performance anxiety, test anxiety, and GAD, respectively. None of the above studies used an active placebo group; one used mock NFT, while the others used wait list, no intervention, or treatment as usual (anxiolytics).

Most NFT studies discovered significantly decreased anxiety scores on self-report tests for the EG for adults with AD (Agnihotri et al., 2007; Dadashi et al., 2015; Faridnia et al., 2012; Lu et al., 2017; Vanathy et al., 1998) and for a non-clinical population (Eismont et al, 2011; and Plotkin & Rice, 1981). Yet, only Bhat et al., (2012), Garrett & Silver (1978), and Rice et al., (1993) reported decreased anxiety symptoms for both, the EG and CG, as was the result in this study.

5.2 Other Treatment Effects (H 3– H 8)

5.2.1 Activation and deactivation within session (H 3a) and across sessions (H 3b).

Hypothesis 3 (H 3a and 3b): *The treatment group will feel significantly more deactivated (as assessed by Thayer's AD-ACL check list)* ***within*** *a NFT session (****H 3a****) and will subjectively become significantly more deactivated* ***across*** *NFT sessions (H 3b) while the placebo group will not.*

H 3a was partially confirmed. A repeated measure 2x2 ANOVAs to test pre-and post-

NFT session differences in AD-ACL scores revealed that *general activation* (consisting of sub-scales *energy* and *tension*) decreased significantly between the **beginning and the end of a NFT session** (large effect size) and decreased significantly more for the CG than the EG (large effect size). *General deactivation* (composed of sub-scales *calmness* and *tiredness*) increased for both, EG and CG, significantly between the beginning and the end of a NFT session (large effect size) but no significant differences between EG and CG were observed. An analysis of the four AD-ACL sub-scales showed that in both groups, EG and CG, participants' *energy* and *tension* decreased significantly between the beginning and the end of a NFT session (large effect sizes) and their *calmness* and *tiredness* increased significantly (large and medium effect sizes, respectively). However, the EG experienced a significantly larger increase in *calmness* than the CG (small effect size) and an almost significant larger decrease in *energy* ($p = .093$; small effect size). No differences between groups were observed for the sub-scales *energy* and *tension*. Thus, to summarize the results, participants in EG and CG experienced significant changes in the activation and deactivation scales and all four sub-scales of the AD-ACL pre-to post NFT session. The CG additionally experienced a significantly larger decrease in general activation than the EG and the EG felt a significantly larger decrease in energy and increase in calmness than the CG.

H 3b was not confirmed. A 2x5 repeated measures ANOVA that aggregated two pre- and post-session AD-ACL difference scores into one measurement point: sessions 1 + 2 (**measurement 1**), sessions 3 + 4 **(2),** sessions 5 + 6 **(3),** sessions 7 + 8 **(4),** and sessions 9 + 10 **(5)** were performed. Differences between the EG and CG were detected for the *activation* scale where results approached significance with the CG being less activated than the EG ($p = .073$, medium effect size), i.e., across sessions the CG became more deactivated than the EG. No

significant changes across the five time-point comparisons were observed for the AD-ACL scales *activation* and *deactivation* and the individual sub-scales *calmness, tiredness, tension*, and *energy*. To summarize the results, neither EG nor CG experienced any significant changes in any of the scales and sub-scales of the of AD-ACL across sessions, but the CG was almost more *deactivated* than the EG across sessions.

The GCM confirmed the results from the 2x5 ANOVAs of AD-ACL scales and sub-scales. However, an interaction effect between factors TIME and GROUP was detected in this scale which suggests a difference in patterns of activation across sessions and makes an interpretation of the GROUP factor difficult. Visually inspecting Figure 4.5 elucidates that while EG and CG have relatively similar difference scores in the *activation* scale in the first two sessions of the NFT and in the last two sessions in the remaining six sessions members of the CG group are far less activated than in beginning or end of the ten NFT sessions whereas EG group members are more activated in the remaining six sessions.

The results of the current trial were not surprising as they had been observed in a number of other studies regarding within session change (H 3a), such as by Egner et al. (2002; A/T NFT study) and by Gruzelier et al. (2014; SMR study) who showed that *activation* (as measured by the AD-ACL) decreased significantly between the beginning and the end of a NFT session and *deactivation* increased significantly although not differentiated analyses of the sub-scales were performed, which in the current study showed differences between EG and CG. Thus, no comparison to other studies regarding these additional parameters were possible. Additionally, the current study analyzed pre-and post- AD ADCL difference scores across sessions in which no significant changes over the course of the 10 sessions were observed and neither were group differences (although a reduction of activation in the CG approached significance). None of the

reviewed NFT studies had performed an across sessions statistical analysis of the AD-ACL scores. NFT studies in the realm of anxiety and emotion regulation that had utilized a mood and energy scale comparable to the AD-ACL were also reviewed, such as Raymond et al. (2005) and Chow et al. (2017), who had used the Profile of Mood States (POMS). The POMS has sub-scales for *tension, depression, anger, vigor, fatigue,* and *confusion* (McNair, Lorr, and Droppleman, 1971) is very similar to the AD-ACL. The tension, vigor, and fatigue sub-scales correspond to some degree with the *tense, energy*, and *tired* sub-scales of the AD-ACL, respectively. But in these studies no across sessions comparisons had been performed, either.

As described in chapter 5.1.1, the decrease in activation over the course of a NFT session may be explained by mental fatigue, Trejo et al. (2015) found that already 15 - 30 minutes of continuous performance, such as in a NFT session, could cause mental fatigue in a participant associated with decreased energy and increased calmness and tiredness as measured by the AD-ACL. Especially the increase of alpha+theta amplitudes associated with mental fatigue serve as a likely explanation why both EG and CG experienced a significant reduction in general activation and a significant increase in general deactivation over the course of the NFT.

However, why the CG experienced significantly higher decrease in general activation than the EG over the course of a NFT session may not be explained by the mental fatigue model and remains unclear. Perhaps, not being able to continuously learn a protocol over the course of the NFT sessions but subsequent up-and down-training of beta and high beta is frustrating to participants, causes tension, and questions their self-efficacy which in turn may lead to disen-gagement from any kind of conscious techniques in trying to regulate their brain oscillations which reduces tension more than the continuous reinforcement of the same oscillation bands in the EG. Clearly, more research in this area is needed.

Furthermore, the EG showed a significantly larger increase in calmness between the beginning and the end of a NFT session which could be explained by the intended A/T NFT working as intended, as enhanced A+T amplitudes were supposed to cause a decrease in participants' anxiety levels via increase in calmness (and decrease in general tension which the protocol did not do in the current study).

Across NFT sessions none of the AD-ACL scales had reached significance which was expected (if one assumes that an increase in A+T amplitudes is associated with a reduction in general activation and an increase in general deactivation) because absolute and relative A+T did not significantly increase across sessions, only absolute and relative alpha amplitudes did.

5.2.2 Correlations: NFT measures and activation / deactivation difference scores (H 4).

Hypothesis 4 (H 4): *The treatment group will show significant increase in absolute and relative theta and alpha amplitudes and absolute and relative theta + alpha (T+A) amplitudes across sessions which will correlate with higher deactivation and lower activation scores of the AD-ACL, while the placebo group will not.*

H 4 was partially confirmed. The bivariate EG-CG correlation matrix revealed that higher relative alpha and relative T+A amplitudes, signaling more learning between sessions 1+2 and 9+10, were significantly associated with higher *deactivation* scores on the AD-ACL for both, the EG and the CG. The correlations were even more pronounced in the EG-only correlation matrix. However, in contrast to H 3 higher absolute theta amplitudes and T/A ratio were associated with lower *deactivation* scores, and negative correlations were even stronger in the EG-only matrix.

Analyzing the correlation between the AD-ACL sub-scales and NFT measures revealed a more nuanced picture. In the bivariate EG-CG correlation matrix the only AD-ACL sub-scale that showed a significant correlation with any of the NFT parameters was the significant negative correlation of the *calm* scale with the absolute theta amplitude, i.e., the greater the absolute theta

amplitude increase between sessions 1 + 2 and 9 + 10 was, the less *calm* participants felt. This was even more pronounced in the EG-only correlation matrix. However, analysis of the EG-only correlation matrix revealed that AD-ACL *tired, tense,* and *calm* sub-scales significantly correlated with relative alpha amplitudes. A larger increase of the relative alpha amplitude over the course of the NFT study was associated with an increase of *tiredness*, a decrease in *tenseness*, and an increase in *calmness*. In contrast, a reduction in *tenseness* was the only sub-scale dimension that was significantly associated with higher absolute alpha amplitudes. These results indicate that perceived energy and mood changes might not be so much associated with an increase in absolute alpha amplitude but perhaps more with a reduction of other waves such as beta and high beta waves which are traditionally associated with rumination, especially in GAD and SAD (Section 1.2.1).

Furthermore, in comparison to the EG-CG correlation matrix, the *tired* sub-scale of the EG-only matrix significantly correlated with relative T+A, and the *calm* sub-scale significantly correlated with the T/A ratio; i.e., for the EG, an increase of the relative T+A amplitude over the course of the NFT study was associated with an increase in *tiredness*, and an increase of the T/A ratio was correlated with a reduction in *calmness*. Relative theta and relative T+A still were not significantly associated with any of the AD-ACL scales or sub-scales.

While an increase in tiredness over the course of a session was reported in most of the reviewed studies on A/T NFT (Table 1.4 a-c) no statistical analyses regarding differences in tiredness throughout the trial, via AD-ACL, POMS, or other scales, have been analyzed in any of the more than 40 studies. Particularly perplexing in our study is that increased tiredness was not significantly correlated with relative T+A amplitudes in the EG and CG correlation matrix but was significantly related in the EG-only matrix. Both CG and EG had a similar age distribution,

so age-related mental fatigue, associated with higher frontal midline theta for older people (Arnau, Moeckel, Rinkenauer, & Wascher, 2017) could not have played a leading role.

Furthermore, an increase in mental task demand due to longer training periods, or different time of day of training is often associated with mental fatigue and increase of frontal midline theta for people regardless of age (Arnau et al., 2017); yet, in this study the duration of the training remained constant across sessions, so did (for the most part) time of day of the training, and most importantly, the NFT did not increase in difficulty but auditory and visual rewards were given for relative increases in in theta (5-7.9 Hz) and alpha amplitude (8-11 Hz). It would have been helpful to have further information on what dimensions of tiredness participants felt; mental or physical fatigue and fatigue due to reduced motivation potentially differ in origin and associated physiological parameters, with mental fatigue being directly related to the concentration on the NFT task, whereas physical tiredness may be only tangentially related to the task and more related to time of day, amount of sleep the night before, stress and amount of work during the work day and other unspecific effects. Age, *belief of being part of the EG*, and preferred learning time, factors that are routinely related to mental tiredness, did not significantly correlate with the AD-ACL *tired* sub-scale, neither in the CG-EG nor for the EG-only correlation matrices. Reduced motivation on the other hand is likely related to participants' perceptions of not improving and associated frustration. In future studies the *Multidimensional Fatigue Inventory* by Smets, Garssen, Bonke, & De Haes (1995) can further illuminate this issue. Lastly, age, *belief of being part of the EG*, and preferred learning time, factors that are routinely related to mental tiredness, did not significantly correlate with the AD-ACL *tired* sub-scale, neither in the CG-EG nor for the EG-only correlation matrices.

5.2.3 Correlations: NFT measures and anxiety measures difference scores (H 5).

Hypothesis 5 (H 5): *The treatment group will show a significant increase in absolute and relative theta and alpha amplitudes and absolute and relative theta + alpha (T+A) amplitudes across sessions which will correlate with a decrease in trait anxiety as measured by the STAI-T inventory.*

H 5 was partially confirmed. The STAI-T difference scores were significantly associated with absolute T+A amplitude increases between the means of sessions 1 and 2 in comparison to the mean of sessions 9 and 10; i.e., an increase in absolute T+A amplitudes was significantly associated with a reduction in trait anxiety. However, as seen in section 5.1.1.2, no significant differences between the EG and CG were observed and all other correlations between NFT EEG parameters and the STAI-T (and STAI-S, BAI, and GAD-7) were not significant. The only RCT study that reviewed NFT parameters and anxiety self-report scales and reported significant correlations was Lu et al. (2017) for patients with PD. Here an improvement of alpha amplitude from beginning to end of a twenty-session NFT trial was associated with a reduction in BAI scores. However, Lu and colleagues did not use an active placebo NFT placebo group but another active treatment modality, anxiolytic medication, as CG. Therefore, their results offer limited comparability with the current study.

5.2.4 Physiological results: Pre–post differences in QEEG (H 6).

Hypothesis 6 (H 6): *The treatment group will have a significant increase in absolute and relative theta and alpha amplitudes and absolute and relative theta + alpha (T+A) amplitudes on the mini-QEEG in the Pz region while the placebo control group will not.*

H 6 was not confirmed. A 2x2 repeated-measures ANOVA with the within-subjects factor TIME and factor GROUP was performed for theta and alpha absolute power, theta and

alpha relative power, theta / alpha ratio, and theta + alpha absolute and relative powers at Pz. None of the variables showed a statistically significant change between pre- and post-treatment and no differences between EG and CG could be observed for any of the variables, except for A+T relative power with a small trend toward significance ($p = .131$) for time and group interaction with the EG having higher combined relative alpha and relative theta amplitudes in comparison to the CG with medium effect size.

Furthermore, the only two correlations that proved to be significant in the QEEG and NFT pre-post-difference score correlation matrix (between session 1 + 2 and 9 + 10) were the associations between NFT relative theta and QEEG absolute alpha difference scores and between NFT relative theta and QEEG absolute T+A difference scores. The larger the mean post-trial absolute QEEG theta amplitude was, the smaller was the change of absolute alpha and absolute T+A amplitudes between sessions 1 + 2 and 9 + 10 (Table 4.6).

Observing non-significant results in QEEG recordings between pre-and post-treatment seems to be common in NFT trials of anxiety DO (e.g., Vanathy et al., 1998; Dreis et al., 2015), and especially the older reviewed RCT studies did not even use pre- and post-treatments QEEG to measure improvements, such as Garrett & Silver (1978), Glueck & Strobel (1975), Peniston & Kulkosky (1991), Egner et al. (2002 and 2003), Gruzelier et al. (2013 and 2014 a, b), and Faridnia et al. (2012). Walker et al. (2009), Dadashi et al. (2015), Dekker et al. (2014), and Dreis et al. (2015) analyzed pre-post EEG but only Dadashi reported significantly increased alpha and theta amplitudes in the EEG recording post-trial in the occipital area for the EG. However, Dadashi et al. (2015) used a waitlist group as their CG which is not able to take a placebo effect into consideration which, as elucidated in chapter 1.3.2, contributes significantly to people's perception of treatment success, as well as to changes in physiological parameters for

participants of a CG. There was no significant correlation in the current study between participants' belief that they were part of the CG and any of the measured anxiety, NFT, pre-post-QEEG measures. This means that the active placebo condition was associated with a large placebo effect that would mitigate the treatment effect of the EG.

5.2.5 Qualitative Results: Behavioral and cognitive effects (H 7).

Hypothesis 7 (H 7): *Self-perceived successful cognitive strategies to modulate brain waves will be significantly correlated with learning as specified by the A/T NFT protocol.*

H 7 was not confirmed. Neither absolute alpha, theta, and A+T amplitudes, nor relative alpha, theta, and A+T, were significantly correlated in the correlation matrix that included only the EG as well as the matrix that included both, EG and CG. However, the correlation matrix for the EG did reveal a significant negative correlation between the T/A ratio and the use of *mental strategies*; i.e., for the EG the use of *mental strategies* was associated with lower T/A ratios in the difference scores of sessions 9+10 and 1+2 but was not correlated significantly with any of the other NFT EEG parameters (increase of absolute and relative alpha, theta, and A +T).

To date, none of the NFT studies for AD has assessed participants' use and type of cognitive strategies and their relation to learning of the NFT protocol. A review of NFT studies regarding other disorders garnered almost no results regarding the influence of mental strategies on NFT performance, either. Only four studies addressing cognitive strategies were found. Hardman et al. (1997) report from a three session NFT trial to improve left and right hemisphere activation across F3 and F4 via slow cortical potentials negativity shifts towards the left or the right hemisphere The group that was given instructions to use positive emotional strategies to improve left hemisphere activation and negative emotional strategies to activate the right hemisphere did not better than the control group that received no instructions. Moreover, *within*

session improvement were larger in the *no strategy* group, particularly in the last third of each session.

Kober and colleagues (2013) came to a similar result in a ten-session NFT study to uptrain either SMR or gamma power. Twenty healthy participants were initially instructed to stay focused on the computer screen and remain relaxed during the NFT. After their first and last NFT session participants were asked to write down the cognitive strategies they had used. These strategies were classified as breathing, conscious relaxation, concentration, visual, auditory, and cheering strategies. The four participants of the SMR group who had reported no specific mental strategies were the only ones who significantly improved their SMR performance. The other six participants in the SMR condition did not, but neither did any of the participants in the gamma condition, even if they had not used any mental strategy. However, only one of the ten participants of the gamma group had reported using no strategies. As the number of participants of this study was small results should be interpreted with caution, though, especially regarding the gamma group. The authors of the study interpret the results as an indication that the use of elaborate strategies to increase SMR may overburden the finite amount of cognitive resources and may lead to no significant learning of SMR over the course of the NFT sessions.

Furthermore, Witte et al. (2013) performed a study with ten NFT sessions in which 10 healthy participants underwent sham NFT whereas the other 10 participants were trained to increase their SMR power. An increase of SMR power over the ten sessions was significantly correlated with lower scores in the expectancy to control technological devices. Witte et al. hypothesized that the expectation of controlling the device may consume additional cognitive resources and lead to pressure or "forced mastery" (p. 1) that is not congruent with the effortless relaxation that may improve SMR power. Thus, Kober et al. (2013) and Witte et al. (2013) agree

in their interpretation that mental strategies may lead to a reduction in available finite resources which in turn may lead to worse learning of NFT parameters.

Lastly, Nan et al. (2012), in a twenty-session NFT trial to improve memory functions with 32 healthy students, found that thinking about positive categories, particularly about friends, love, and family improved the ability to increase relative alpha amplitudes during and across NFT sessions, in comparison to thinking about neutral or negative strategies. All participants of this study had been instructed to use whatever mental strategies worked for them or use no mental strategies, if they so chose, to increase the respective wavebands that were trained. Taking the results of these studies mentioned above into account, the non-significant results of this study are not in line with any of their results, although non-significant results regarding mental strategies were observed in the gamma power group of the Kober et al. (2013) study. However, although the NFT protocol for the EG in this study uptrained both alpha and theta and not the T/A ratio it is interesting to observe that the use of mental strategies lead to significantly lower theta uptraining in comparison to the rise of alpha amplitude which in turn led to a lower T/A ratio. This observation may be in line with the results of the aforementioned three studies; considering that it is more difficult to uptrain theta than alpha, as mentioned above, a lower T/A ratio may point to limited resources not being used as efficiently to uptrain theta in relation to alpha while theta amplitude uptraining on its own had not been significant.

5.3 Control for Unspecific Effects (H 8 - H 9)

Hypothesis 8 (H 8): *No significant differences between the treatment and the placebo group in treatment expectations / self-efficacy as measured by the Stanford Expectations of Treatment Scale (SETS) and the Rotter Locus of Control Scale (LOC) will be observed in the study. There will not be significant differences between the treatment and the placebo group's*

pre-and post-treatment satisfaction as measured by the SETS modified outcome scale.

5.3.1 Control for Experimenter Bias

Humans are complex social beings who react to subtle emotional cues and develop relationships over the course of a ten-session trial. Consequently, interactions with the three NFT technicians certainly may influence the participant's level of comfortability, trust, motivation, and focus. This would be an especially sensitive issue because all the women participating in this trial had moderate to high trait anxiety and 75% of them had a diagnosed AD. An unknown psychotherapeutic / medical environment with an unfamiliar technical procedure may bring up former negative experiences about medical illness. Therefore, the two NFT technicians who administered one third of the NFT sessions had been trained with a standard protocol of procedures and scripts on how to explain possible questions and practiced trial sessions before they administered NFT sessions. Unusual circumstances during each NFT session, such as excessive sleepiness, fidgeting, and unusual artifacts and equipment malfunctions were recorded in the *Session Coding List*. The NFT data was analyzed with t-tests before any other statistical analysis was performed to exclude the non-specific effect of varying experimenter personalities, varying degrees of professionalism, and potential experimenter bias. No significant differences between the three experimenters and the NFT session EEG parameters, as well as the experimenters and the pre-and post session AD-ACL results were found. Consequently, no experimenter bias influenced the results of the NFT sessions significantly.

5.3.2 Control for Treatment Satisfaction and Self-Efficacy (H 8).

No significant differences between the treatment and the placebo group in treatment expectations / self-efficacy as measured by the Stanford Expectations of Treatment Scale (SETS) and the Rotter Locus of Control Scale (LOC) were observed in the study. The use of *mental*

strategies and the *perceived success of mental strategies* did not correlate with the *belief in EG participation*. As expected, perceived changes in everyday thinking, feeling, and behavior highly correlated with the *belief in EG participation.* Participants who believed in being part of the EG were significantly more likely to report changes in thinking, feelings, and behavior due to the NFT than participants who believed they were part of the CG (Table 4.7 a).

A significant decrease in negative treatment expectations was observed between the beginning of the NFT trial and the end of the trial with large effect size. The TIME*GROUP interaction exhibited no statistically significant difference between the EG and CG for both negative treatment expectations between pre- and post-trial which suggests that no significant differences between the EG and CG were observed in the reduction of negative treatment expectations regarding A/T NFT.

Positive treatment expectancy did not significantly change between the beginning and the end of the NFT trial. Change in treatment expectancy as a measure of treatment satisfaction shows that both, EG and CG participants, who had moderately high treatment expectancy, reported no significant drop in treatment satisfaction over the course of the treatment.

The Rotter Locus of Control Scale was administered at the end of the NFT trial to gauge the participants' self-efficacy. Participants of this study tended to have an external locus of control on average, attributing successes or failures to external circumstances rather than their own efforts. A one-way ANOVA was performed to investigate if differences in means could be detected between participants from the EG in comparison to members of the CG. No significant differences between the two groups were found. Point-biserial correlations were performed between the LOC score and all QEEG measures (i.e., absolute and relative alpha, theta, T+A power and T/A ratio) and NFT measures (i.e., absolute and relative theta, alpha, and T+A

amplitudes, and T/A ratio), as well as for the various anxiety measures (BAI, STAI, and GAD) and no correlation was significant (see Table 4.7 a; correlation matrix).

Belief in EG participation is another variable closely aligned with treatment expectation; 19/27 participants (70.4%) believed that they were in the EG and were receiving an active treatment (11/14 members of the EG (78.6%) and 8/13 members of the CG (61.5%). Conversely, *belief in CG participation* empirically aligns with treatment dissatisfaction; 8/27 participants (29.6%) believed that they were part of the placebo group (5/13 participants from the CG (38.5%) and 3/14 participants of the EG (21.4%).

While differences in *Belief in EG participation* were observed between the EG and CG, these differences were neither significantly associated with any of the QEEG and NFT EEG-related parameters, nor with any of the anxiety measure differences or AD-ACL measures, i.e., the *Belief in EG participation* had no impact on any of the measured parameters.

Belief in EG participation was significantly correlated with participants reporting changes in thinking, feelings, and behaviors attributed to the NFT trial. It comes as no surprise, that participants who reported that they believed to be part of the EG reported change in thinking, feelings, and behaviors significantly more often than participants who did not believe that they had been part of the EG. Furthermore, *Belief in EG participation* was associated with age with older participants being more likely to believe that they had been part of the EG, although no significant differences in the age distribution between EG and CG had been observed after the initial randomization of participants.

5.3.3 Time-of-day of NFT (H 9).

Hypothesis 9 (H 9): *Participants' NFT learning will be significantly correlated with each participant's self-identified time-of day best, worst or neutral period for learning.*

The correspondence of the time-of-day of the NFT sessions with the times-of-day of best learning did not correlate significantly with the difference scores between session 1+2 and 9+10 differences in absolute alpha or theta amplitudes, nor relative alpha or theta, T/A ratio, nor relative, or absolute T+A ratio. This means NFT sessions being held during a time of worst or preferred learning were not associated with a significant improvement in regulation of the parameters in the EG, nor was it associated significantly with any of the AD-ACL pre- post-session difference scores, except for a difference in energy and tension which was approaching significance. Participants who had NFT sessions during their *worst time for learning* (which can be seen as a measure of tiredness, inattentiveness, and exhaustion) reported less energy and more tension throughout the NFT sessions in comparison to participants who had their NFT sessions scheduled during a neutral or best time for learning. The variable *worst time for learning* was significantly associated with participants who had a more internal locus of control (higher LOC score), which may be explained by participants with more internal control being more likely to use mental strategies to influence the outcome of a NFT session and the use of mental strategies are more exhausting than not using any strategies. Hence, those participants using mental strategies are prone to be more impacted by less favorable learning times.

As Cheon et al. (2016) point out, there are complex interactions between amplitude, frequency, phase, and coherence in mental processes. Especially neuronal oscillators are of concern which generate spontaneous rhythmic wave patterns that are sTable against minor disturbances and consist of more than one waveband, a continuum of brain oscillatory flux that changes from slow to fast rhythms during the daily cycle. Hence, depending on time of the day there may be different over-arching rhythmic patterns picked up by the EEG at Pz that may skew results between sessions if the time of the NFT session was changed during the trial, which had

to be done on occasion due to changes participants' schedules. For statistical comparison of standardized conditions, testing within the same +/- 1.5 hours throughout the trial should definitely be observed. However, to transfer the newly learned waveband training to other situations, especially during times of day where one is not as alert, may be beneficial in later training sessions. But upregulation of alpha and theta wavebands will have to have been sufficiently learned to apply it to new (time) conditions. A similar concept guides *transfer trials* in later sessions of NFT for ADHD (Drechsler et al., 2007; Mayer et al., 2015; Strehl et al., 2006) as mentioned above.

5.4 Limitations

Many of the hypotheses of this study, most notably the primary hypothesis, were only partially confirmed and some were not confirmed at all. Several weaknesses of the study design may be responsible for this. The study was a single-blind RCT design. The participants did not know if they were part of the CG or EG. However, the experimenters knew which group each participant belonged to because they saw the summary of protocol parameters when the NFT program was opened for each pre-programmed participant session and the person setting up and analyzing the data was this study's prinicipal investigator. Consequently, a double or triple-blind design was impossible for a study like this one, whereby all functions were conducted by the same person. Triple-and double-blind studies require a multi-person team with separate and specialized roles.

Moreover, the number of NFT sessions was limited to ten sessions. There are NFT studies, such as in the area of NFT for ADHD, that used between 20 and 40 NFT sessions and showed significant results (Arns et al., 2009), but in the area of NFT for AD most studies with significant results employed 5 to 12 session protocols (Watson & Herder, 1980; Hardt &

Kamiya, 1978; Rice et al., 1993; Egner et al., 2003; Gruzelier et al., 2009; Agnihotri et al., 2007) and reported significant results in at least some of the examined parameters. After reviewing existing studies in the field of A/T NFT it remains unclear how many sessions might be needed for participants to learn alpha and especially theta wave uptraining to significantly differentiate their absolute relative A+T amplitude up-regulation from the results of the CG.

Definitions for boundaries between various EEG bands are not set in stone and vary slightly amount depending on the research study. A fair amount of research indicates large interindividual differences in alpha peak frequency depending on biological trait and age (Niedermeyer & Lopes da Silva, 1999; Klimesch, 1999) and intraindividual differences depending on tasks (Klimesch, 1999; Mierau, Klimesch, & Lefebvre, 2017). Mierau et al. (2017) had suggested to use individual alpha peak (APF) frequency, i.e., the spectral component of alpha with the largest power estimate (between 6 and 13 Hz) to define an individual's alpha frequency for different scalp locations rather than using fixed frequency bands for all study participants. This procedure would have prevented from participants' being accidently uptrained on a low beta frequency if their APF was on the low end (around 8 Hz) in some of the older participants and the beta frequency starting lower than normal, for instance at around 11 Hz. Unfortunately, this adds a level of complexity to the study design that was beyond this dissertation. Every participant would have had to be reliably tested (more than once as APF is quite sensitive to change) for their APF at rest at Pz via EEG and complex FFT functions in *Matlab* or *Neuroguide* and an individualized NFT protocol for the specific APF would have had to be added.

Furthermore, having a larger number of participants in the study would have been more sensitive to detect differences between EG and CG and thus could have potentially led to

significant results, especially in those analyses where trends toward significance had been observed, such as the self-reported, post-treatment anxiety being more reduced in the STAI-T in the EG and small tendency toward significance ($p = .131$) of the EG having a higher A+T relative power increase in the QEEG at the end of the NFT trial. As specified in chapter 3.1 a power analysis was performed to find out how many participants would be necessary to detect moderate effects between EG and CG. This study enlisted 14 participants for the EG and 13 participants for the CG. A total of 27 participants had been determined by power analysis to be sufficient to detect moderate sized ($f = .25$) interaction effects and within-subject's effects with adequate power (.80). Furthermore, the results of the power analysis were compared with the number of subjects of other clinical NFT trials in AD that found significant effects. Eleven out of the nineteen (58%) RCTs which reported an effect in any variable had considerable less participants (N=5-11) in the EG than the current RTC (Egner et al. 2002, Eismont et al., 2011; Faridnia et al., 2012; Gruzelier et al., 2014a and b; Lu et al., 2017; Plotkin & Rice, 1981; Raymond et al., 2005; Rice et al., 1993; Sittenfeld et al., 1976; and Vanathy et al., 1998). Five (26%) RCTs had 12-16 participants per EG, approximately the same number as the current study ($n_{EG} = 14$); i.e., Agnihotri et al., 2007; Chisholm et al., 1977; Dadashi et al., 2015; and Gruzelier et al., 2013. Only four studies (21%) enlisted significantly more participants (Bhat et al., 2012 [$n_{EG} = 50$]; Egner et al., 2003 [$n_{EG} = 18$]; Sarkar et al., 1999 [$n_{EG} = 25$]; and Garrett and Silver, 1978 [$n_{EG} = 18$). However, the probability that recruiting more than 14 participants in the EG (and 13 for the CG) for this study would have shown significant differences between the EG and CG regarding A+T upregulation and pre- and post-trial QEEG results is small. A power analysis of those NFT RCT with significant results showed that moderate sized interaction effects and within subject effects of adequate power could be detected with a total number of 27 subjects.

Moreover, while larger samples are more sensitive to show significant changes in statistical analyses they may also reduce the power of the results to the point where statistical changes are not clinically relevant (Mertler & Vannatta, 2013; Aron, Coups, & Aron, 2013).

As Engelbregt and colleagues (2016) point out that the short-term versus long-term effects as well as the generalized versus specific effects of A/T NFT for AD need to be addressed better. Long-term effectiveness of treatments is not available for most studies which poses a serious limitation, especially for AD associated with the fear-circuit, where extinction responses can be reversed to excessive stress or traumatic events (see section 1.1.3).

Several limitations regarding the characteristics of study participants were observed. As it was very difficult to recruit a sufficient number of male participants this trial was conducted with women only and thus does not allow generalizations to be made to both biological sexes. However, no significant differences had been found between men and women in any of the reviewed RCT NFT studies for ADs (see chapter 1.2.5.1). Consequently, biological sex had not a significant factor in former studies regarding learning outcomes in NFT and was thus not a likely serious limitation of this study. Furthermore, the participant sample was very homogeneous regarding race/ethnicity and education level. Thus, generalizing results to ethnic minorities and less educated population is questionable. However, the majority of NFT studies to date suffer from these limitations. In many studies 18- to 25-year old (mostly Caucasian) undergraduate students served as participants (Kirschbaum & Gistl, 1973; Chisholm et al., 1977; Egner et al., 2002; Gruzelier, Thompson, Redding, et al., 2013; Gruzelier et al, 2014) whereas this study's age range was heterogeneous and normally distributed (range = 19 to 69 years). Furthermore, participants were included in this study who were taking various prescription medication and caffeine daily but participants were asked not to change their medication and caffeine during the

course of the trial so that difference scores remained same between pre- and post-tests remained the same. Ideally, only participants not taking any medication or caffeine that might change brain oscillations should have been recruited but this would have been an unrealistic aim because caffeine consumption and prescription drug taking is ubiquitous in the United States. According it a recent study by Mitchell et al. (2014) 85% of the U.S. population consume at least one caffeinated beverage per day and 65% of the population have taken at least one prescription drug within the the past 30 days (Kantor et al., 2015).

The most important technical limitation of this study regarding the pre-and post-EEG recordings, though, was that the *Brainmaster Atlantis I, 4×4 Module ® 3.0* amplifier which only allowed the recording of four EEG channels at a time, i.e., 5 x 4 channels had to be recorded which resulted in only 4 channels being time-locked. Consequently, coherence, phase differences between hemispheres and different cortical areas and comodulation of brain waves throughout the brain could not be assessed in the EEG. Furthermore, *Neuroguide'*s automatic algorithms for artifact removal for those artifacts that the Brainmaster system had not picked up, could not be used and artifact removal had to be manually obtained through visual inspection of each of the four time-locked EEG channels at a time and records with >95% split half reliability, >90% test-retest reliability, and a total measurement of over 60 seconds were used for further statistical analyses. An additional technical limitation of this study was that no ocular and temporalis or frontalis EMG sensors to measure eye movement and blinking artifacts or jaw tensing were available. Goncharova et al. (2003) point out that the EMG of temporalis and frontalis muscles can mimic EEG alpha, mu, or beta rhythms over the entire scalp and contaminate the EEG but that contamination of the EEG by EMG is not very likely at the Pz location as the attachment sites of the temporalis and frontalis muscles, as well as the oculomotor sites are far away from Pz

and Oz. Furthermore, the *Brainavatar* software has built in algorithms to detect EMG artifacts, although no studies exist, to my knowledge, on how effective these algorithms are in detecting and removing artifacts.

In addition, the 30-second baseline reading for the beginning segment of each NFT session was included within the first minute of NFT training recording, i.e., half of the first minute was baseline recording and thereafter the feedback began and thus could not be used for further analysis. While the missing baseline values were of concern to pre-post-difference measurements of alpha and theta analyzed by ANOVAs, it had negligible effect on the statistics as GCM is a continuous model of alpha and theta band changes within and across all sessions.

Procedural limitations of this study also need to be addressed. First, participants' responses to NFT may be influenced by the expectation of treatment outcome and by their belief as to how much they can influence the outcomes of events in general. This may be particularly true for treatments involving technology that is perceived as cutting edge. The Stanford Expectations of Treatment Scale (Younger et al., 2012) was used to measure the general outcome expectancy in this trial and the Rotter (1966) Locus of Control scale was assessed to control for participants' general internal or external locus of control beliefs. Both scales revealed no differences between CG and EG and showed no significant correlations to other measures. It would have been helpful to administer the LOC pre- and post-trial to investigate if the A/T NFT treatment caused any changes in participants' belief as to how much they can influence outcomes of events. Second, hours and quality of sleep per night during the course of the NFT trial were not formally assessed, although it was noted on the NFT Session Checklist form for the respective session if a participant mentioned that she was excessively tired. Significant sleep reduction, sleep deprivation, and poor quality of sleep may lead to be irritability, tension, inattentiveness, and

reduced learning due to reduced memory consolidation of dendritic spine formations via LTP during sleep (Yang, Lai, Cichon, Ma, et al., 2014). The lack of so-called *transfer trials* may have made it difficult for study participants to generalize study gains to regular life circumstances. Such trials, while not used in NFT for AD in the past, have been used in NFT studies for children and adults with ADHD (e.g., Drechsler et al., 2007; Mayer et al., 2015; Strehl et al., 2006) and in these studies are correlated with a reduction in reduction in ADHD symptoms.

6. Future Directions

In order to gain a clearer understanding if A/T NFT is an efficacious treatment changes in the operationalization of the research design and the NFT protocol need to be instituted. As mentioned before, few NFT researchers acknowledged that uptraining of certain beta bins may lead to increase in alpha bins (Ros et al., 2013; Jurewicz et al., 2018). Thus, the analysis of CG beta band data in relation to theta and alpha band data will be necessary to evaluate how successful participants were in the upregulation of beta bins and if this upregulation of beta bins is associated with the upregulation of certain alpha and / or theta bins. Similarly, it is important to find out how successful participants were in learning to downtrain beta bins and associated changes in other wave bands or if a slow rise of beta and alpha are observed in both beta up-and downtraining protocols which would indicate non-specific factors, as in Jurewicz et al. (2018) study, and learning did not take place. In future studies inhibits for alpha and theta should be built into the NFT protocols of a CG to prevent the simultaneous rise of alpha and or theta.

Measuring each participant's alpha peak frequency and using it for an individualized A/T NFT protocol instead of the standard fixed EEG frequency ranges used in this study because as Bazanova (2016) points "…low and upper frequency range alpha factors with identical peak frequencies, which relate to different neuronal functions" (p. 1).

Furthermore, integration of a learner analysis using each EG participant's increase (or decrease) in linear regression equation slope before the start of a study could be added. A cut-off value for the slope can be determined below which a study participant is considered a non-learner regarding the study-specific EEG training parameter and would be excluded from the study – although this may have unintended emotional and ethical consequences for participants which needs to be discussed further.

Moreover, using a more homogenous group of study participants based on what type of AD they have may be beneficial. Williams (2016) provided a detailed taxonomy for AD and depression regarding neural circuit dysfunctions and relates them to associated brain networks. Thus, targeting networks associated with a specific AD with an A+T protocol protocols would be helpful. For instance, a future study may recruit only participants with SAD or phobias, two AD that have symptoms of anxious avoidance at their center. Anxious avoidance, according to Williams (2016) is associated primarily with circuit abnormalities of the salience network, specifically the hypoconnectivity between left and right anterior insula and the sublenticular extended amygdala, and the hyperactivation of the amPFC. NFT training electrodes could be placed over the areas of the anterior insulae at the FC5, FT7 and FC6, FT8 electrode locations and A+T could be uptrained in both right and left insula or the less activated insula could be uptrained alternatively. Associated with a more precise NFT electrode locations would be to record to have an electrode cap with 60 leads, including FC5, FT7 and FC6, FT8 available for the EEG. According to Lau, Gwin, and Ferris (2012) the analysis of 35 timelocked EEG channels for pre-and post EEGs for reliably recording EEGs should be sufficient. In addition, ocular and temporalis or frontalis EMG sensors to measure eye movement and blinking artifacts or jaw tensing to limit artifacts during the EEG recordings and during NFT sessions would be helpful.

Another consideration is to change the location of the NFT electrode location from Pz-LE – the location used for EG and CG in this study – to another location. (The Pz-LE and Cz-LE locations had been the most commonly used electrode placement in A/T NFT for AD). Yet, as discussed before, Olejarczyk, Bogucki, and Sobieszek (2017) found that alpha rhythm generators, beside the occipital and frontal locations, were also found at Pz in some healthy

participants which may indicate independence of the NFT protocol, as long as the active electrode is placed at Pz enhanced alpha rhythm production is to be expected in cases of heightened attention. Thus, in future A/T NFT research it may be beneficial to consider different electrode locations, especially for the CG.

Participants developed relationships with the experimenter and NFT technicians which most certainly influenced the individual's general level of comfortability, trust, motivation, and level of focus on the NFT treatment. This may be especially relevant for research with individuals with GAD and SAD as they often are uncomfortable with social situations. Development of a standardized method of recording and description of subject interaction with NFT technicians of interactions would ensure the recording and better factoring out of the NFT trainer / participant interactions. The English translation of the Fragebogen zur Erfassung relevanter Therapiebedingungen (FERT), developed by Vollmann et al. (2009), administered after each NFT session may be helpful to assess this variable and factor out these influences via co-variate analysis. Secondly, standardized structured NFT strategies tools to assess mental strategies used by participants after each session may be helpful.

Lastly, scheduling at least one or several follow-up appointments, for instance after 6 months, 12 months and 24 months to re-assess QEEG and self-report anxiety scales and qualitative questions about changes in thinking, feeling and behavior will be beneficial to analyze if and what long-term changes resulted due to continued practice of A/T self-regulation in vivo after the NFT concludes.

7. Summary and Conclusions

The present study, to my knowledge, is the first single-blind trial to test the A/T NFT protocol for trait anxiety in a highly anxious adult female population with an active placebo NFT control group and was one of the first NFT studies to use GCM for statistical NFT data analysis.

The primary objective of this study was the design and implementation of a rigorous, placebo-controlled clinical trial to investigate if A/T NFT is an efficacious treatment method for women with moderate to high trait anxiety. Twenty-seven women ranging in age from 19 through 69 who had scored higher than the 66th percentile in the STAI trait anxiety sub-scale (75% of which had previously been diagnosed with an anxiety disorder) were randomly distributed to either a ten-session alpha/theta NFT EG (n = 14) in which alpha and theta amplitudes were uptrained at Pz. The rest of the participants (CG) were given a ten-session active placebo training (n = 13) at Pz during which they received successive NFT sessions of up- and downtraining beta and high beta.

Growth curve modeling (and traditional 2x5 repeated measures ANOVA) were performed on the NFT sessions data to model individual and average group learning curves and to separate learners and non-learners. Cognitive variables, such as treatment outcome expectancy, personal attribution styles, use, types, and efficacy of cognitive strategies in NFT, and correlations between NFT learning performance, time of day the NFT sessions were held, and a participant's best or worst time to learn, which are rarely assessed in NFT trials, were also investigated.

The study's primary hypothesis that A/T NFT is an efficacious treatment method for women with moderate to high trait anxiety could only be partially confirmed as for both, EG and CG a significant rise in A+T amplitudes and a reduction in self-perceived anxiety was observed.

An analysis of individual learning curves, GCM, and ANOVA all confirmed that the majority of women of the EG up-regulated absolute and relative A+T amplitudes within a NFT session, but so did the participants of the CG who had not received any A+T uptraining. Participants of the EG and CG felt significantly more *deactivated* at the end of a NFT session in comparison to the beginning; the AD-ACL sub-scales *energy* and *tension* decreased significantly while *calmness* and *tiredness* increased significantly but no significant gains in *deactivation* across NFT sessions were made. In both groups participants' anxiety was significantly reduced on all anxiety measures. Although a trend could be observed that the EG reduced anxiety scores more than the CG these differences did not rise to statistical significance. Lastly, no significant changes in the pre-post trial QEEG were found pre-post, although a trend of higher combined relative A+T power at the end of the trial was observed in the EG.

In the EG the *use of mental strategies* was associated with lower T/A ratio difference scores between the beginning and the end of the NFT trial. However, it was not correlated with the T+A parameter trained in the EG. *Belief in EG group membership*, not surprisingly was highly correlated with reported changes in everyday thinking, feeling, and behavior at the end of the NFT trial. *Time-of-day participants prefer for learn for learning activities in life* and *time-of-day participants avoid for learning activities* did not correlate significantly with alpha or theta NFT parameters, i.e., NFT sessions being held during sub-optimal times of day were not associated with poorer learning performance.

The failure of the A/T protocol to lead to significantly better results than the active placebo group could be due to an elaborate placebo effect: sitting in front of a computer in a relaxed position in a quiet, dimly-lit room while attempting to not think of anything is a refuge from the stressful busy lives of participants. It is an unspecific effect that causes alpha waves and

even theta waves to increase. Regarding the anxiety AD-ACL scales, participants could also have both engaged in the largely unconscious process of reducing cognitive dissonance by enhancing the positive effects of the NFT trial — which constitutes a significant time investment— and downplayed negative parts of the trial. More well-designed RTCs are needed to conclude if A/T NFT is an efficacious treatment method for anxiety disorders or if the effects of this NFT method are largely due to non-specific effects, such as placebo effects, EEG frequency drifts, alpha's idling mode and inhibitory role during task performance, functional coupling of certain EEG frequencies in general, or perhaps simply that some frequency bands (alpha) are more susceptible to change and easier to train. Especially inhibiting flanking non-trained bands in the NFT protocol, i.e., beta bands in A+T training upregulation and alpha and theta bands in beta upregulation, to prevent frequency drifts will be necessary along with larger sample sizes and detailed GCM modeling of all frequency bands, not just the frequency band/s trained via NFT protocol, and how they change over the time of the NFT will be necessary to find an answer to this question.

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9. Appendices

Appendix A: IRB Approval Forms, NIH Protocol Publication, and Recruitment Materials

A.1 Institutional Review Board Approval

UNIVERSITY OF HARTFORD

October 22, 2016

Bettina Viereck
East Hall 117G
viereck@hartford.edu

Dear Professor Viereck,

Proposal ID# PRO15070009

Upon review of your most recent modifications (10/14/2016) by the Human Subjects Committee, your proposal, *"Alpha/Theta Neurofeedback Training as Treatment Method for Individuals with Moderate to Severe Trait Anxiety,"* has been re-approved for one year according to expedited review guidelines established by federal regulation 45 CFR 46.11O (b).

The modifications involve the following:

- Addition of the Rotter locus of control questionnaire (other changes previously approved on 10/12/16)

Approval for this project will expire October 22, 2017.If you plan to continue the project beyond that point please inform the committee at least one month prior to that date.

Please keep in mind that it is your responsibility to notify and seek approval from this Committee of any modifications to your project, and that it is your responsibility to report to this Committee, any adverse events that occur related to this study. Reporting forms are available online at the HSC website, http://www.hartford.edu/hsc.

This institution has an Assurance of Compliance on file with the Office of Human Research Protections (Federalwide Assurance FWA00003578).

Congratulations and good luck with your study.

Sincerely,

Barbara Crane, PhD
Chair, Human Subjects Committee
University of Hartford

A.2 NIH: ClinicalTrials.gov Study Protocol Registration

ClinicalTrials.gov PRS
Protocol Registration and Results System

Contact ClinicalTrials.gov PRS
Org: UHartford User: BViereck

Home > Record Summary > Protocol Section > Contacts/Locations

ID: PRO15070009 EEG Alpha/Theta Neurofeedback to Reduce Trait Anxiety NCT02964520

Contacts/Locations

Protocol Section Help Definitions

Edit **Overall Contacts**

Central Contact: Bettina Viereck, Dipl.-Psych. 860-768-5323
viereck@hartford.edu

Central Contact Backup: John Saksa, Psy.D. 860 404 2040
saksa@behavioralcognitive.com

Overall Study Officials: Principal Investigator Bettina Viereck, Dipl-Psych
University of Hartford, Department of Psychology
Study Chair Ute Strehl, Ph.D.; Dipl.-Psych. University of Tuebingen, Institute for Medical Psychology and Behavioural Neurobiology, Germany
Study Chair Boris Kotchoubey, Ph.D.; M.D. University of Tuebingen, Institute for Medical Psychology and Behavioural Neurobiology, Germany

NOTE: Official Degrees should have no more than 12 characters.

Copy locations... from a master list, extracted from this organization's records.

United States, Connecticut

Edit **Location**

University of Hartford
West Hartford, Connecticut, United States, 06117
Contact: Bettina Viereck, Dipl-Psych 860-768-5323
viereck@hartford.edu
Contact: John Saksa, PsyD 860-404-2040
saksa@behavioralcognitive.com
Sub-Investigator: Ute Strehl, PhD

× Delete Location

Sub-Investigator: Boris Kotchoubey, MD, PhD

A.3 Recruitment Flyer

UNIVERSITY OF HARTFORD

Scientific Study for Fall 2016:

Does EEG Neurofeedback Training Reduce Anxiety Symptoms in Anxious People?

Researchers at the University of Hartford are trying to find out if training people's brain waves with EEG neurofeedback training can make people with anxious personalities less anxious. The few studies done in the past 40 years regarding this topic have been inconclusive.

In neurofeedback training people's brain waves are measured on their scalps and fed back to them on a computer screen. This way people can learn to regulate their own brain waves by enhancing waves that are associated with calm alertness and reducing waves associated with anxiety.

If you qualify to participate in our study, you will be randomly assigned to either the treatment group or the control group. As part of the treatment group, you will receive the anxiety reduction training. As part of the control group you will receive an alternative neurofeedback training. You will not know in which group you participated until the end of this study. Any data we collect from you during the study will not be stored with any personal identifiers, but rather with an assigned number.

During the neurofeedback sessions you will be seated in a comfortable chair in front of a computer screen. We will place three sensors on your scalp with a drop of paste, record the electrical activity in your brain, and feed it back to you. We will train you for 10 half hour sessions (2-3 times per week for 3-5 weeks). This is a very safe procedure; you will not receive any electric shocks.

Our hope is that this neurofeedback training will reduce anxiety symptoms in people with anxious personalities and become another great adjunct treatment option for them.

To participate:

1. You have to be 18 years or older.
2. **You have to consider yourself an anxious individual.**
3. **You do NOT consider yourself an severly depressed individual.**
4. You should have had no prior EEG neurofeedback training experience.
5. You should not suffer from seizure disorders or have co-occuring serious mental health conditions, such as schizophrenia, bipolar disorder, major depressive disorder or substance use disorder.
6. You will have to answer a pre-screening survey on Survey Monkey. This will take about 20-30 minutes to complete. You may or may not be invited to participate in our neurofeedback study depending on your survey results.

Training location: *Behavioral and Cognitive Treatment Associates, LLC* / 270 Farmington Ave (*Farmington Exchange* building), Suite 313 / Farmington, CT (across the street from the UCONN Health Center)

You will receive $5 at each of the ten sessions to off set the travel costs. You will also receive a $100 gift card of your choice for your time and effort when you finish all ten neurofeedback sessions.

Please help us advance scientific knowledge about this important topic!

For further details contact the study's principal investigator, **Dipl.-Psych. Bettina Viereck, MS, MFA** at **viereck@hartford.edu** or at **(860) 768-5323**.

This study has been approved by the University of Hartford *Institutional Review Board* (Study number: PRO15070009) and has been found to be a safe and ethical study design for human participants.

Appendix B: Screening and Trial Participation Consent Forms

B.1 Screening Consent Form

UNIVERSITY OF HARTFORD

DEPARTMENT OF PSYCHOLOGY

CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

SUBJECT CODE:

LAST 2 letters of your LAST name: →

MIDDLE initial **or** underscore if you don't have a middle initial: →

FIRST letter of your first name: →

for example: *"Dora M Smith"* = **TH + M + D** = *THMD/ "Ernesto_ Pirello"* = **LO + _ + E** = *LO_O*

PROJECT TITLE: ***Alpha/Theta Neurofeedback Training as Treatment Method for Individuals with Moderate to Severe Trait Anxiety***

PRINCIPAL INVESTIGATOR: Dipl.-Psych. Bettina Viereck, MS, MFA

INVITATION TO PARTICIPATE IN A PRESCREENING QUESTIONNAIRE AND DESCRIPTION OF THE PROJECT

You are invited to fill out a **pre-screening testing questionnaire** on *SurveyMonkey*® for a research study that will use electroencephalographic (EEG)- based neurofeedback training. We want to find out if and how ten half hour sessions of neurofeedback training improves anxiety symptoms in individuals with an anxious personality, also called trait anxiety. Depending on your scores on two psychological anxiety questionnaires you may, or may not, be invited to participate in our neurofeedback training study.

In the past 40 years few studies have been conducted to find out if EEG-based neurofeedback training can successfully reduce anxiety in people and the studies have been inconclusive so far. We are trying to find out if training people's brain waves with EEG neurofeedback can make people with anxious personalities less anxious. In neurofeedback training the individual's brain wave signals are fed back to the person who can learn to regulate his/her own brain wave patterns by up-training alpha and theta waves while down-training beta and delta waves. Technological advances in neurofeedback software over the past decade offer more effective ways to simultaneously feed back information from multiple types of brain waves to the person, using visual and auditory signals. In our study participants will be randomly assigned to either the neurofeedback group or the control group, which will receive an alternative neurofeedback placebo treatment.

In order to decide whether or not you wish to be a part of this pre-screening testing you should know enough about its risks and benefits to make an informed judgment. This consent form gives you detailed information about the research study. Please feel free to ask a member of the research team at any time if you have any questions or concerns. Once you understand the study, you will be asked if you wish to participate in the screening; if so, you will be asked to sign this form.

Description of Procedures

You will be asked to fill out the following *SurveyMonkey®* questionnaire, https://www.surveymonkey.com/r/University_of_Hartford_Neurofeedback_Study_2016 , which includes a section of demographic and medical questions and the on-line version of the State-Trait Anxiety Inventory. It typically takes about 10-15 minutes to complete the questionnaire.

Risks and Inconveniences

There are no known risks associated with filling out the *SurveyMonkey®* Questionnaire.

Benefits

Filling out the pre-screening *SurveyMonkey®* questionnaire was not designed to benefit you directly. It will allow us to find participants who meet certain research criteria for our study about if and how neurofeedback training may improve anxiety symptoms.

Confidentiality

The *SurveyMonkey®* Questionnaire is SSL(Secure Sockets Layer) encrypted. SSL is a protocol developed for transmitting private information over the internet by creating a secure by encrypting sensitive information through a web pages. Banking and on-line commerce websites use SSL.

Furthermore, any identifiable information that is obtained in connection with this study will remain confidential. Your **subject code** (last two letters of last name + middle initial + first letter of first name) will be assigned a **subject number**. A record associating your subject code and number will be confidentially kept in paper form in a locked file cabinet in a locked office to be seen only by the researchers involved in this study, separately from any other files of this study. Any other data we collect from you during the study (such as your EEG recordings and the results of your questionnaires) will not be stored with any personal identifiers, but rather with your subject number. The University of Hartford Human Subjects Committee (the Committee that reviews, approves and monitors research on human participants in research projects) may inspect the study records. Your name or subject code will not be used in any published reports of this study.

Voluntary Participation

You are free to choose not to participate and if you do become a participant in this pre-screening you are free to withdraw from this pre-screening at any time during its course. If you choose not to participate or if you withdraw it will not adversely affect your relationship with the study researchers from the University of Hartford.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully — as long as you feel it is necessary — before you make a

Authorization:

I, → , (subject code of participant from page 1) have read this form and have decided to fill out the *SurveyMonkey®* Questionnaire described above.

The project's general purposes, the particulars of involvement, possible hazards and inconveniences have been explained to my satisfaction. My initials also indicate that I have received a copy of this consent form by email.

→ →

Subject Code of Participant from page 1 (serves as signature) Date

Signature of Principal Investigator: Date
Dipl.-Psych. Bettina Viereck

Thank you so much for your time and consideration to participate in this pre-screening!

This study has been approved by the University of Hartford Human Subjects Committee (ID: PRO15070009).
If you have questions about your rights as a research subject, please contact the **University of Hartford Human Subjects Committee (HSC)** at **860-768-5371**. The HSC is a group of people that reviews research studies and protects the rights of people involved in research.

B.2 Trial Participation Consent Form

UNIVERSITY OF HARTFORD

DEPARTMENT OF PSYCHOLOGY

CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

SUBJECT CODE:

LAST 2 letters of your LAST name: →

MIDDLE initial **or** underscore if you don't have a middle initial: →

FIRST letter of your first name: →

for example: *"Dora M Smith"* = **TH + M + D** = *THMD/ "Ernesto_ Pirello"* = **LO + _ + E** = *LO_O*

PROJECT TITLE: ***Alpha/Theta Neurofeedback Training as Treatment Method for Individuals with Moderate to Severe Trait Anxiety***

PRINCIPAL INVESTIGATOR: Dipl.-Psych. Bettina Viereck, MS, MFA

Invitation to Participate and Description of Project

You are invited to be a participant in a research study that will use electroencephalographic (EEG)- based neurofeedback training. EEG places small sensors on specific areas of your scalp. It is a very safe procedure. The sensors record electrical brain activity on the scalp of your brain. You will not receive any electric shocks. You have been invited because you scored moderate or high on the two Anxiety Questionnaires you filled out on *SurveyMonkey®*.

In the past 40 years few studies have been conducted to find out if EEG-based neurofeedback training can successfully reduce anxiety in people and the studies have been inconclusive so far. We are trying to find out if training people's brain waves with EEG neurofeedback can make people with anxious personalities less anxious. In neurofeedback training the individual's brain wave signals are fed back to the person who can learn to regulate his/her own brain wave patterns by up-training alpha and theta waves while down-training beta and delta waves. Technological advances in neurofeedback software over the past decade offer more effective ways to simultaneously feed back information from multiple types of brain waves to the person, using visual and auditory signals. In our study participants will be randomly assigned to either the neurofeedback group or the control group, which will receive a an alternative neurofeedback placebo treatment.

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed judgment. This consent form gives you detailed information about the research study. Please feel free to ask a member of the research team at any time if you have any questions or concerns. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

Description of Procedures

Cleaning gel is used on dime-size areas of your scalp and ear lobes. Then a conductive paste will be applied in order to attach the EEG sensors. Both cleaning gel and conductive paste wash out easily. In your first and tenth sessions of this study an elastic cap with sensors will be fitted to your scalp and ears in order to record an EEG. It takes approximately 10 minutes to both install the cap and set up the recording program and 10 minutes for the actual EEG recording. Once recorded, you will be asked to fill out the brief Stanford Expectation of Treatment Scale (SETS).

We will teach the neurofeedback training in sessions one through ten. Each session will consist of three eight-minute periods with a 90-second relaxation interval before and after each eight-minute period. During each session you will sit comfortably in front of a computer screen. Two sensors will be attached to your scalp and two sensors will be attached to your ear lobes. The sensors on the scalp will record your brain activity surrounding the area where the sensors are attached. You will be asked to relax and keep your eyes open. The more frequently your recorded brain activities agree with the brain frequencies that are consistent with less anxiety (or placebo condition), the more frequently a visual cue will appear and a pleasant sound will be emitted. In other words, you will receive positive visual and auditory feedback, when and as long as your brain waves (in the areas of the attached sensors) are at the frequencies that respond to less anxiety (or to the placebo frequency), and in so doing you will learn to control your brain waves. Moreover, you will be required to fill out the brief Activation-Deactivation Checklist (AD-ACL) before and after each neurofeedback session.

You will receive a full debriefing after the data collection phase of the study, in which we will more thoroughly explain the purpose of the study via email and by which you may ask us any questions you wish. You may decide to withdraw from the study at any time.

In summary, you are consenting to participate in the following (**please mark XX on the left of each statement to indicate that you are aware of the different procedures**):

→ __ **EEG** in the first and last sessions of the neurofeedback training;

→ __ Ten sessions of **neurofeedback training**;

→ __ Fill out the Stanford Expectation of Treatment Scale (**SETS**) and two Depression Questionnaires (**BDI-2** and **PHQ-9**) in the first neurofeedback session;

→ __ Fill out two short Anxiety Questionnaires (Beck's Anxiety Questionnaire, State Trait Anxiety Questionnaire) after the last neurofeedback session.

→ __ Fill out short Activation-Deactivation Checklist (**AD-ACL**) before and after each neurofeedback session;

→ __ Fill out two short Anxiety Questionnaires (**BAI** and **STAI**), the **Rotter Locus of Control Questionnaire** and some **qualitative questions about treatments outcome** after the last neurofeedback session.

Risk and Inconvenience

EEGs are considered to be among the safest ways to examine the human body. They record the electrical activity

your brain produces and make those waves visible and recordable on a computer. This study has no painful parts. You will be watched closely throughout the study. Every once in a while, an individual may feel uncomfortable or anxious during the EEG or neurofeedback training. If this happens you may ask to stop the study at any time and we will detach the EEG electrodes. On rare occasions, some individuals might feel dizzy, fatigued, or develop a headache. These sensations usually go away quickly but please tell the research staff if you have them. In rare cases you might have an allergic reaction to the cleaning solution or adhesion paste of the EEG equipment. In that case or if you have more prolonged reactions to the neurofeedback training, a visit to a local urgent care clinic will be facilitated (at UConn Medical School, 250 yards from the site). However, your insurance carrier will be responsible to pay for the treatment.

This neurofeedback study is done for research purposes only and is not in any way a clinical diagnosis of diseases for you. The EEG recordings in this study are not designed for diagnosis.

Benefit

This study was not designed to benefit you directly. It will allow us to study if and how neurofeedback training may improve anxiety symptoms. You will be randomly assigned to the treatment group or a control group, which does not receive active neurofeedback anxiety reduction training, but a harmless alternative neurofeedback training. However, if you are a subject participating in the treatment group, where you attempt to control activity in a specific brain area, you may gain some control over your anxiety symptoms. Once all the study participants have been through their neurofeedback training, if you so choose, you will be informed as to whether you were part of the treatment or the control group.

Economic Consideration

For your participation, you will receive $5 at each of the ten sessions to off-set the costs of travel. In addition, you will receive a $100 gift card of your choice for your time and expenses after you finish all ten neurofeedback sessions. **Please check XX which gift card you prefer**:

→ ___ Amazon
→ ___ Whole Foods
→ ___ Stop & Shop
→ ___ Other (please specify): _____

Confidentiality

Any identifiable information that is obtained in connection with this study will remain confidential. Your **subject code** (last two letters of last name + middle initial + first letter of first name) will be assigned a **subject number**. A record associating your subject code and number will be confidentially kept in paper form in a locked file cabinet in a locked office to be seen only by the researchers involved in this study, separately from any other files of this study. Any other data we collect from you during the study (such as your EEG recordings and the results of your questionnaires) will not be stored with any personal identifiers, but rather with your subject number. The University of Hartford Human Subjects Committee (the Committee that reviews, approves and monitors research on human

participants in research projects) may inspect the study records. Your name or subject code will not be used in any published reports of this study.

Voluntary Participation

You are free to choose not to participate and if you do become a participant in this study you are free to withdraw from this study at any time during its course. If you choose not to participate or if you withdraw it will not adversely affect your relationship with the study researchers from the University of Hartford and *Behavioral and Cognitive Treatment Associates, LLC*.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you do not understand. Consider this research and the consent form carefully and for as long as you feel it is necessary, before you make a decision.

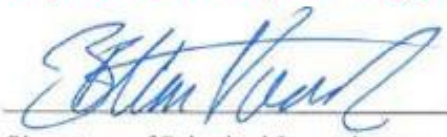
Authorization:

I, → , (subject code of participant from page 1) have read this form and have decided to fill out the *SurveyMonkey®* Questionnaire described above.

The project's general purposes, the particulars of involvement, possible hazards and inconveniences have been explained to my satisfaction. My initials also indicate that I have received a copy of this consent form by email.

→ →

Subject Code of Participant from page 1 (serves as signature) Date



9/9/2016

Signature of Principal Investigator: Date
Dipl.-Psych. Bettina Viereck

Thank you so much for your time and consideration to participate in this pre-screening!

This study has been approved by the University of Hartford Human Subjects Committee (ID: PRO15070009).

Appendix C: Selected Questionnaires

C.1 SETS Pre-trial Questionnaire Sample

Q1

Participant number (in 3 digits, e.g. 001,022)

Q2

Each of the words below describes a feeling or a mood. Please use the rating scale next to each word to describe your feelings at this moment.

This treatment will be completely effective	Moderately Agree
I am worried about my treatment	Strongly Disagree
My condition will be completely resolved after treatment	Neither Agree Nor Disagree
I have fears about this treatment	Strongly Disagree
I have complete confidence in this treatment	Moderately Agree
I am nervous about the negative effects of this treatment	Strongly Disagree

Q3

What treatment are you going to receive?

Neurofeedback Training

Q4

What specific benefits (if any) do you expect to receive from this treatment?

To have a better control under my anxiety, learn how to minimize the negative effects it has in everyday life and decrease my level of stress due to a greater control and decrease in my anxiety.

Q5

What specific harms or negative side-effects (if any) do you think may occur because of this treatment?

N/A

Q6

Have you ever received this treatment before?

No

C.2 SETS Post-Trial Questionnaire Sample

Q1

Participant number (in 3 digits, e.g. 001,022)

Q2

Each of the words below describes a feeling or a mood. Please use the rating scale next to each word to describe your feelings at this moment.

This treatment was completely effective	Moderately Agree
I am worried about this treatment	Strongly Disagree
My condition was completely resolved after treatment	Moderately Agree
I still have fears about this treatment	Strongly Disagree
I have complete confidence in this treatment	Strongly Agree
This treatment had negative effects for me	Strongly Disagree

Q3

What specific benefits (if any) did you receive from this treatment?

I find that I am able to clear my mind to focus on one thing at a time instead of splitting my mind between tasks.

Q4

What specific harms or negative side-effects (if any) did you have from this treatment?

None

C.3 NFT strategies, change in thinking, feeling, behavior, and best & worst times of day for learning (sample answers)

Participant number (in 3 digits, e.g. 001,022)

Q2

What kind of mental strategies (if any) did you use to control your brain waves and improve the reward sounds and visual rewards? Please specify.

Trying to completely relax during the test in order to not increase my stress. Also focusing on one thing such as the screen brightness or a color on the dragon.

Q3

Which mental strategies (if any) worked best?

Listening to music that put me into a calm and peaceful mood definitely improved my results and my ability to have a clear mindset during the test.

Q4

Which mental strategies (if any) did not work?

Overthinking the task, or getting frustrated with the task did not improve the results.

Q5

Did you experience any changes in feelings in your everyday life due to the neurofeedback treatment? If yes, please specify.

Yes, I believe that I am overall better able to de-stress.

Q6

Did you experience any changes in thoughts in your everyday life due to the neurofeedback treatment? If yes, please specify.

Yes, I believe that I have improved my ability to focus on one activity at a time.

Q7

Did you experience any changes in behavior in your everyday life due to the neurofeedback treatment? If yes, please specify.

Yes, I was hoping it would help lower my stress level.

Q8

What is the time period of day that you learn best / are the most productive (in full hours, for example 8-11 a.m. or 2-4 p.m.)?

.

Q9

What is the time period of day that you learn the least well/ are the least productive (in full hours, for example 8-11 a.m. or 2-4 p.m.)?

.

Q10

In this study, which group do you think you were part of?

experimental group (active treatment)

Q11

Are there any recommendations you have for us regarding this research study? If yes, please specify.

No.

Appendix D: Neurofeedback Session Checklist

NEUROFEEDBACK SESSION CHECKLIST

Experimenter Initials:		**Experimenter:** payment received	**Signature:**	**Amount:**	$
Participant number (three digits, e.g. 002)			**Nasion to inion measurement** (with one decimal point)	.	cm
Date			**Pz location**=30% of total measurement (nasion to inion) from inion	.	cm
Time					
Number of appointment (1-10)					

Before participant arrives	**Y or N**	**Comments**
Take out tape measure, alcohol swabs, abrasive paste, *10 Twenty* paste, tissues		
Turn on Computer; hook up NFB *Brainmaster* Avatar box to computer; attach electrodes cable to box		
Open Avatar NFB program (Avatar short cut on desktop) **Open folder to run new NFB session** (for subjects input by BV before session): **Set up > Folder selection > Select folder >** **0XX_NFB, 0XX_NFB_a** or **0XX_NFB_b** **folder a :** uneven session numbers (1,3,5,7,9) **folder b:** even session numbers (2,4,6,8,10) **Select & run**		**To create a folder for a new subject (if BV unavailable)** **Set up >** **Create folder >** 0XX_NFB, 0XX_NFB_a or 0XX_NFB_b **Create & select settings >** **Select**
Open SurveyMonkey link to ADACL Checklist		

After participant arrives	**Y or N**	**Comments**
Pay participant $5 & have participant initial this sheet		**Payment received** (initial with subject ID):
Put office phone on "Do Not Disturb"		
Turn off phone & other electronic devices (including fitbits)		
Comfortable? Need to go to bathroom?		Wearing ear buds for NFB Training?
Adjust chair?		**Yes / NO** (please circle correct choice)
Have subject fill out **pre-session AD-ACL** → on SurveyMonkey		
Measure Pz location		
Preparation of electrode attachment sites: Swab electrode attachment sites with alcohol swab with abrasive paste Dry off with clean tissue		
Attach 3 electrodes: White=Pz / **Red** = right ear lobe (lead behind ear) / **Green=** left ear lobe (lead behind ear)		
Attach three leads to subject's shirt with medical tape Make sure that no pulling on electrode wires when participant moves head		
Turn off overhead lights		
Press GO in NFB program Make sure all leads are attached properly and recording is low in artifact; when the reading is good hit "OK"		
Turn on multimedia player to Vulcan flying file (Home screen>Window> multimedia>Vulcan flying)		
Remind subject to relax, sit still, and let the protocol happen • ***the longer & louder the two reward sounds are*** the more your brain waves correspond to a less anxious state • ***the brighter & clearer the dinosaur film clip is*** the more your brain waves correspond to a less anxious state		
Record three segments of eight minutes of NFB: **Segment 1**		
Segment 2		
Segment 3		
After NFB clean off sensor sites with alcohol pad & clean tissue		
Have subject fill out **post-session AD-ACL** → on SurveyMonkey		
Confirm next appointment: DATE:		**DAY: TIME:**

Appendix E: Additional Tables and Graphs

E1: Randomization Procedure of Study

Vector	Integers within vector	Participant numbers 001-028 (with assigned conditions: 0=control condition; 1=experimental group)
Vector 1	**[1010]**	001 (1), 002 (0), 003 (1), 004 (0)
Vector 2	**[1100]**	005*(1), 006 (1), 007 (0), 008 (0)
Vector 3	**[0011]**	009 (0), 010 (0), 011 (1), 012 (1)
Vector 4	**[0110]**	013 (0), 014 (1), 015 (1), 016 (0)
Vector 5	**[1010]**	017 (1), 018 (0), 019 (1), 020 (0)
Vector 6	**[0110]**	021 (0), 022 (1), 023 (1), 024 (0)
Vector 7	**[1100*]**	025 (1), 026 (1), 027 (0), 028 (*1, replacing 005)

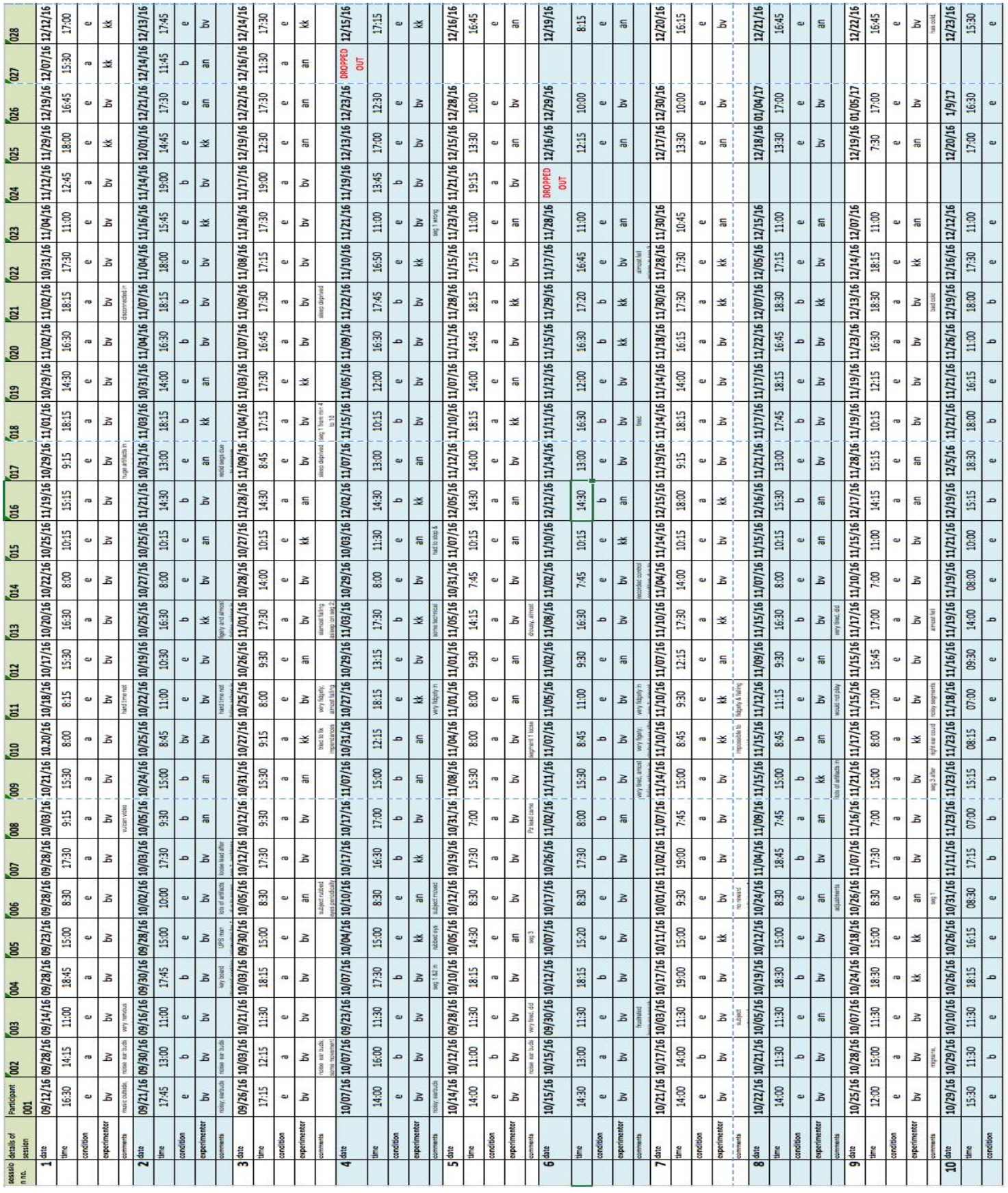
control group participants (n = 13):	002, 004, 007, 008, 009, 010, 013, 016, 018, 020, 021, 024, 027
experimental group participants (n = 15):	001, 003, 005*, 006, 011, 012, 014, 015, 017, 019, 022, 023, 025, 026, 028

(* participant 005 finished the treatment but had to be replaced with participant 028 because he was the only male participant in the study. To control the study for biological sex he had to be replaced by a female participant (028) in the treatment group).

E2: Faulty QEEG recording by participants and channels.

FAULTY QEEG RECORDING BY PARTICIPANTS AND CHANNELS					
participant number	experimental or control group?	pre and/or post treatment?	channel	channel	channel
008	C	pre	F4-LE		
		post			
010	C	pre	P4-LE		
		post			
011	E	pre	P4-LE	O2-LE	
		post	C3-LE	T6-LE	
013	C	pre	PZ-LE		
		post	P3-LE		
014	E	pre	F4-LE		
		post	P4-LE		
015	E	pre	P3-LE		
		post	P3-LE,		
016	C	pre	O1-LE	T3-LE	T5-LE
		post	C4-LE		
017	E	pre	O1-LE		
		post	P4-LE	CZ-LE	
019	E	pre	FP1-LE	F3-LE	
		post			
022	E	pre			
		post	FP1-LE	F8-LE	
025	E	pre			
		post	FP1-LE	P3-LE	CZ-LE
026	C	pre	P3-LE	F8-LE	
		post			
028	E	pre			
		post	T6-LE		

E.3: Session Checklist Results



E.4: GCM: R-Script for GCM Example for Alpha Per Run and Trial Alpha amplitude per Run (within sessions)

```
library(lme4)
library(lmerTest)
library(lattice)
setwd("~/Desktop/FILENAME")
read.csv("FILENAME.csv",h=T)->m.data

xyplot(Alpha~RUN, data=m.data, groups=trial,type = "b",auto.key=T)
m.data$RUN - 1 -> m.data$center_r

lmer(Alpha~1 + (1|participant),data=m.data, REML=FALSE)->modelAr.a
summary(modelAr.a)

lmer(Alpha~1 + center_r + (1|participant),data=m.data, REML=FALSE)->modelAr.b
summary(modelAr.b)
anova(modelAr.a,modelAr.b)

lmer(Alpha~1 + center_r + (center_r|participant),data=m.data, REML=FALSE)->modelAr.c
summary(modelAr.c)
anova(modelAr.b,modelAr.c)

lmer(Alpha~1 + center_r + condition + (center_r|participant),data=m.data, REML=FALSE)->modelAr.d
summary(modelAr.d)
anova(modelAr.c,modelAr.d)

lmer(Alpha~1 + center_r + center_r:condition + (center_r|participant),data=m.data, REML=FALSE)-
>modelAr.e
summary(modelAr.e)
anova(modelAr.d,modelAr.e)
```

Alpha amplitude per Trial (between sessions)

```
library(lme4)
library(lmerTest)
library(lattice)
setwd("~/Desktop/FILENAME")
read.csv("FILENAME.csv",h=T)->m.data

xyplot(Alpha~trial, data=m.data, groups=trial,type = "b",auto.key=T)
m.data$trial - 1 -> m.data$center_t

lmer(Alpha~1 + (1|participant),data=m.data, REML=FALSE)->modelAt.a
summary(modelAt.a)

lmer(Alpha~1 + center_t + (1|participant),data=m.data, REML=FALSE)->modelAt.b
summary(modelAt.b)
anova(modelAt.a,modelAt.b)

lmer(Alpha~1 + center_t + (center_t|participant),data=m.data, REML=FALSE)->modelAt.c
summary(modelAt.c)
anova(modelAt.b,modelAt.c)
```

```
lmer(Alpha~1 + center_t + condition + (center_t|participant),data=m.data, REML=FALSE)->modelAt.d
summary(modelAt.d)
anova(modelAt.c,modelAt.d)

lmer(Alpha~1 + center_t + center_t:condition + (center_t|participant),data=m.data, REML=FALSE)->modelAt.e
summary(modelAt.e)
anova(modelAt.d,modelAt.e)
```

E.5: GCM: EG Absolute A+T amplitude responders vs. all CG participants

Predictor for ABSOLUTE alpha amplitude (in µV)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	**0.070 (0.847)**	**< .0001 *****
Intercept	**9.699 (0.847)**	**< .0001 *****
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	**0.177 (0.050)**	**< .01****
Intercept	**9.812 (0.847)**	**< .0001 *****
MODEL D: GROUP: within session	0.536 (1.367)	0.699
MODEL D: GROUP: group across sessions	0.312 (1.702)	0.856)
MODEL E: TIME WITHIN SESSIONS x GROUP	0.017 (0.023)	0.460
MODEL E: TIME ACROSS SESSIONS x GROUP	0.175 (0.085)	0.055

Table 4.10 a: Results from GCM regression analyses predicting **alpha amplitude** from run, trial, and group. Note: Standard errors are given in parentheses. *p < .05, **p< .01, ***p< .001. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for RELATIVE alpha amplitude (in %)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	**0.068 (0.011)**	**< .0001 *****
Intercept	**17.976 (0.651)**	**< .0001 *****
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	**0.188 (0.067)**	**< .01****
Intercept	**18.043 (0.651)**	**< .0001 *****
MODEL D: GROUP: within session	0.880 (1.280)	0.499
MODEL D: GROUP: group across sessions	1.189 (1.280)	0.366
MODEL E: TIME WITHIN SESSIONS x GROUP	0.025 (0.023)	0.225
MODEL E: TIME ACROSS SESSIONS x GROUP	0.057 (0.133)	0.673

Table 4.10 b: Results from GCM regression analyses predicting **relative alpha amplitude** from run, trial, and group. Note: Standard errors are given in parentheses. *p < .05, **p< .01, ***p< .001. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for ABSOLUTE A+T amplitude (in µV)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	**0.100 (0.028)**	**< .01****
Intercept	**18.560 (1.229)**	**< .0001 *****
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	**0.249 (0.086)**	**< .01****
Intercept	**18.784 (1.324)**	**< .0001 *****
MODEL D: GROUP: within session	1.919 (2.253)	.403
MODEL D: GROUP: group across sessions	0.899 (2.664)	.739
MODEL E: TIME WITHIN SESSIONS x GROUP	0.003 (0.051)	.960
MODEL E: TIME ACROSS SESSIONS x GROUP	**0.347 (0.148)**	**< .05***
Intercept	**18.802 (1.322)**	**< .0001 *****

Table 4.10 c: Results from GCM regression analyses by successively adding predictors for **T/A amplitude ratio** from run, trial, and group. Note: Standard errors are given in parentheses. *p < .05, **p< .01, ***p< .001. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for RELATIVE A+T amplitude (in %)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	**0.081 (0.020)**	**< .0001 *** **
Intercept	**34.736 (0.732)**	**< .0001 *** **
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	**0.210 (0.072)**	**< .01 ** **
Intercept	**34.905 (0.771)**	**< .0001 *** **
MODEL D: GROUP: within session	1.471 (1.364)	0.292
MODEL D: GROUP: group across sessions	0.817 (1.545)	0.602
MODEL E: TIME WITHIN SESSIONS x GROUP	-0.010 (0.037)	0.792
MODEL E: TIME ACROSS SESSIONS x GROUP	0.085 (0.144)	0.536

Table 4.10 d: Results from GCM regression analyses predicting **theta + relative alpha amplitude** from run, trial, and group. Note: Standard errors are given in parentheses. *p < .05, **p< .01, ***p< .001. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for ABSOLUTE theta amplitude (in µV)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	**0.031 (0.017)**	**0.076**
Intercept	**8.864 (0.445)**	**< .0001 *** **
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.074 (0.057)	0.200
MODEL D: GROUP: within session	0.617 (0.898)	0.499
MODEL D: GROUP: group across sessions	0.131 (0.986)	0.886
MODEL E: TIME WITHIN SESSIONS x GROUP	-0.012 (0.033)	0.716
MODEL E: TIME ACROSS SESSIONS x GROUP	0.135 (0.102)	0.201

Table 4.10 e: Results from GCM regression analyses predicting **theta amplitude** from run, trial, and group. Note: Standard errors are given in parentheses. *p < .05, **p< .01, ***p< .001. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for RELATIVE theta amplitude (in %)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	0.0128 (0.016)	0.438
Intercept	**16.766 (0.375)**	**< .0001 *** **
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.022 (0.041)	0.594
MODEL D: GROUP: within session	0.066 (0.757)	0.931
MODEL D: GROUP: group across sessions	-0.371 (0.815)	0.654
MODEL E: TIME WITHIN SESSIONS x GROUP	-0.027 (0.032)	0.411
MODEL E: TIME ACROSS SESSIONS x GROUP	0.007 (0.081)	0.928

Table 4.10 f: Results from GCM regression analyses by successively adding predictors for **relative theta amplitude** from run, trial, and group. Note: Standard errors are given in parentheses. *p < .05, **p< .01, ***p< .001. Intercept information is only shown for significant models. Significant results are shown in bold red.

E.6: GCM: EG relative A+T amplitude responders vs. all CG participants:

Predictor for ABSOLUTE amplitude (in µV)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	**0.061 (0.011)**	**< .0001 *** **
Intercept	**9.013 (0.545)**	**< .0001 *** **
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	**0.141 (0.547)**	**< .05 * **
Intercept	**9.217 (0.547)**	**< .0001 *** **
MODEL D: GROUP: within session	-0.082 (1.057)	.939
MODEL D: GROUP: group across sessions	-0.268 (1.102)	.810
MODEL E: TIME WITHIN SESSIONS x GROUP	0.014 (0.021)	.524
MODEL E: TIME ACROSS SESSIONS x GROUP	0.071 (0.109)	.522

Table 4.11 a: Results from GCM regression analyses predicting **alpha amplitude** from run, trial, and group. Note: Standard errors are given in parentheses. *p < .05, **p< .01, ***p< .001. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for RELATIVE alpha amplitude (in %)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	**0.065 (0.010)**	**< .0001 *****
Intercept	**17.546 (0.567)**	**< .0001 *****
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	**0.218 (0.062)**	**< .01 ****
Intercept	**17.458 (0.483)**	**< .0001 *****
MODEL D: GROUP: within session	0.282 (1.131)	.805
MODEL D: GROUP: group across sessions	-0.389 (0.931)	.680
MODEL E: TIME WITHIN SESSIONS x GROUP	0.024 (0.020)	.231
MODEL E: TIME ACROSS SESSIONS x GROUP	0.134 (0.115)	.259

Table 4.11 b: Results from GCM regression analyses predicting **relative alpha amplitude** from run, trial, and group. Note: Standard errors are given in parentheses. *p < .05, **p< .01, ***p< .001. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for T/A RATIO	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	**-0.003 (0.001)**	**< .01 ****
Intercept	**0.991 (0.035)**	**< .0001 *****
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	**-0.009 (0.003)**	**< .01 ****
Intercept	**0.997 (0.032)**	**< .0001 *****
MODEL D: GROUP: within session	-0.035 (0.067)	.607
MODEL D: GROUP: group across sessions	-0.002 (0.063)	.981
MODEL E: TIME WITHIN SESSIONS x GROUP	-0.002 (0.002)	.187
MODEL E: TIME ACROSS SESSIONS x GROUP	-0.007 (0.006)	.268

Table 4.11 c. Results from GCM regression analyses by successively adding predictors for **T/A amplitude ratio** from run, trial, and group. Note: Standard errors are given in parentheses. *p < .05, **p< .01, ***p< .001. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for RELATIVE A+T amplitude (in %)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	**0.093 (0.025)**	**< .01 ****
Intercept	**17.532 (0.823)**	**< .0001 *****
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.136 (0.090)	.155
MODEL D: GROUP: within session	-0.137 (1.576)	.932
MODEL D: GROUP: group across sessions	-0.430 (1.913)	.825
MODEL E: TIME WITHIN SESSIONS x GROUP	0.006 (0.049)	.896
MODEL E: TIME ACROSS SESSIONS x GROUP	0.025 (0.177)	.888

Table 4.11 d: Results from GCM regression analyses predicting **theta + relative alpha amplitude** from run, trial, and group. Note: Standard errors are given in parentheses. *p < .05, **p< .01, ***p< .001. Intercept information is only shown for significant models. Significant results are shown in bold red.

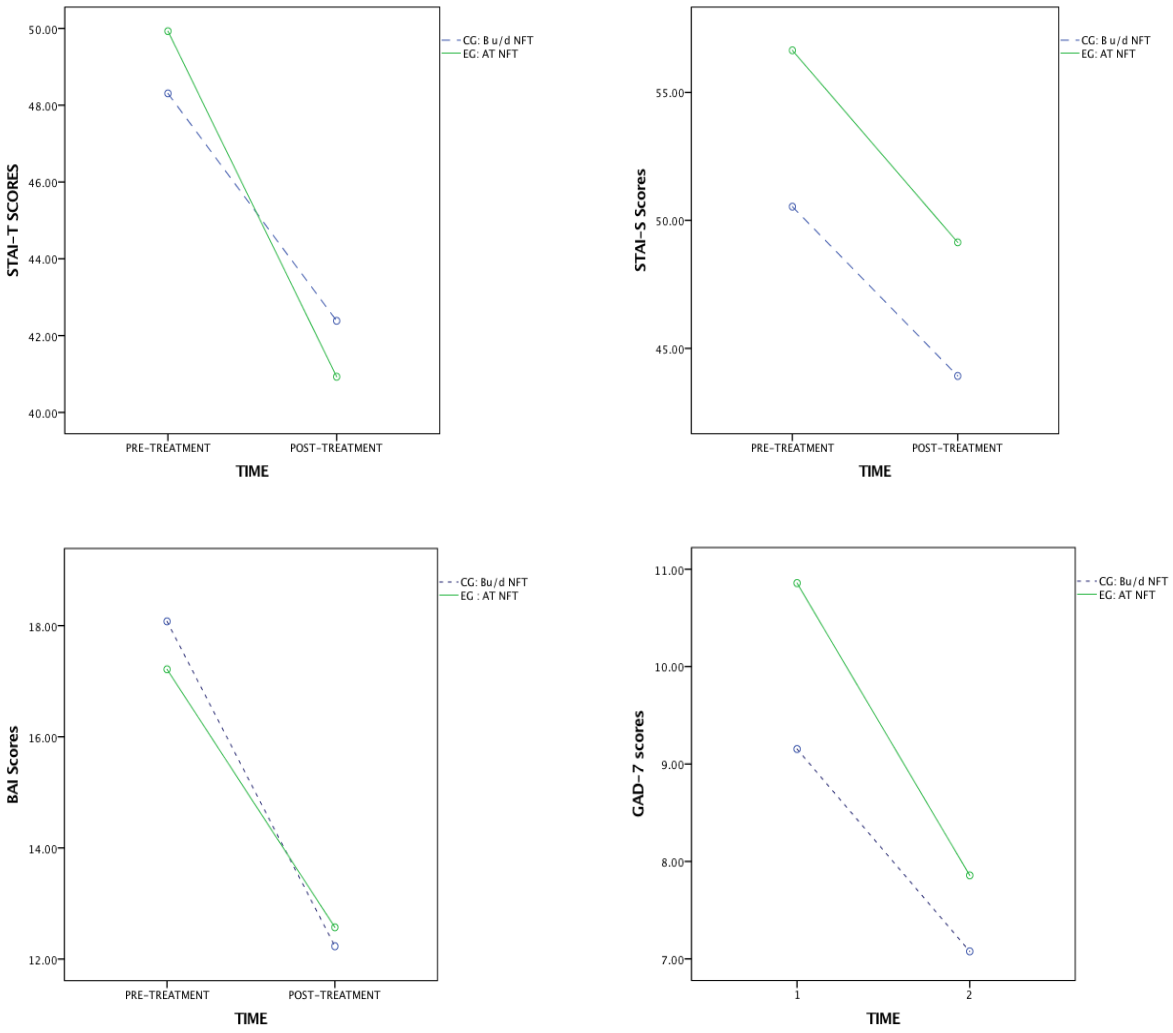
Predictor for ABSOLUTE theta amplitude (in µV)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session)	0.031 (0.016)	.094
Intercept	**8.523 (0.337)**	**< .0001 *****
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	-0.003 (0.051)	.951
MODEL D: GROUP: within session	-0.157 (0.656)	.813
MODEL D: GROUP: group across sessions	-0.454 (0.542)	.593
MODEL E: TIME WITHIN SESSIONS x GROUP	-0.006 (0.031)	.849
MODEL E: TIME ACROSS SESSIONS x GROUP	-0.049 (0.088)	.584

Table 4.11 e: Results from GCM regression analyses predicting **theta amplitude** from run, trial, and group. Note: Standard errors are given in parentheses. *p < .05, **p< .01, ***p< .001. Intercept information is only shown for significant models. Significant results are shown in bold red.

Predictor for RELATIVE theta amplitude (in %)	β (*SE*)	*p*
MODEL C: TIME WITHIN SESSIONS (24 one-minute runs per NFT session) **Intercept**	0.014 (0.016) **16.743 (0.377)**	.401 **< .0001 *****
MODEL C: TIME ACROSS SESSIONS (ten NFT sessions)	0.014 (0.041)	.742
MODEL D: GROUP: within session	0.014 (0.761)	.986
MODEL D: GROUP: group across sessions	-0.346 (0.813)	.674
MODEL E: TIME WITHIN SESSIONS x GROUP	-0.025 (0.032)	.447
MODEL E: TIME ACROSS SESSIONS x GROUP	-0.012 (0.082)	.884

Table 4.11 f: Results from GCM regression analyses by successively adding predictors for **relative theta amplitude** from run, trial, and group Note: Standard errors are given in parentheses. *p < .05, **p< .01, ***p< .001. Intercept information is only shown for significant models. Significant results are shown in bold red.

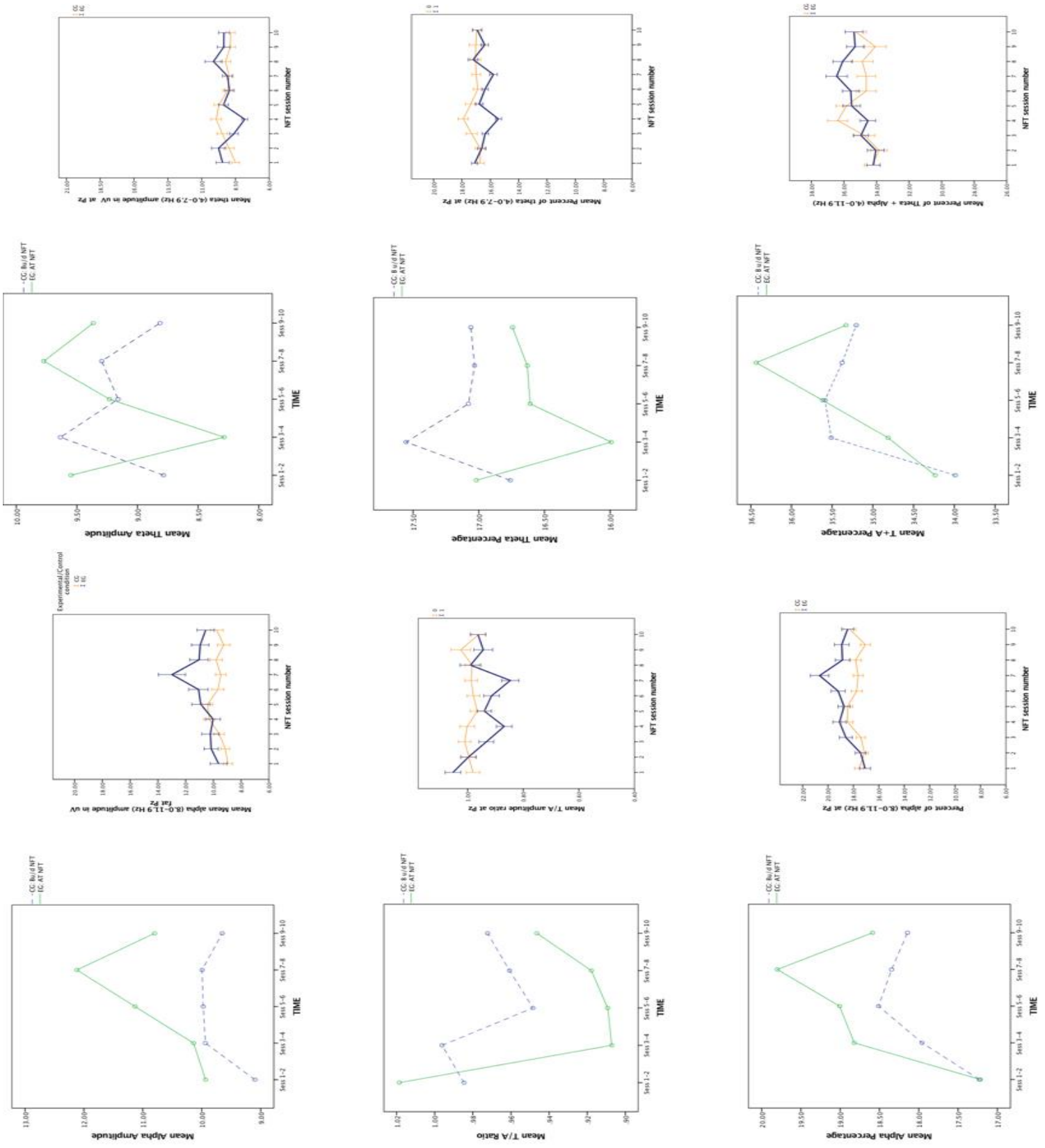
E.7: Mean anxiety test score differences for EG (Solid Line) and CG (Dotted Line) pre- and post-treatment



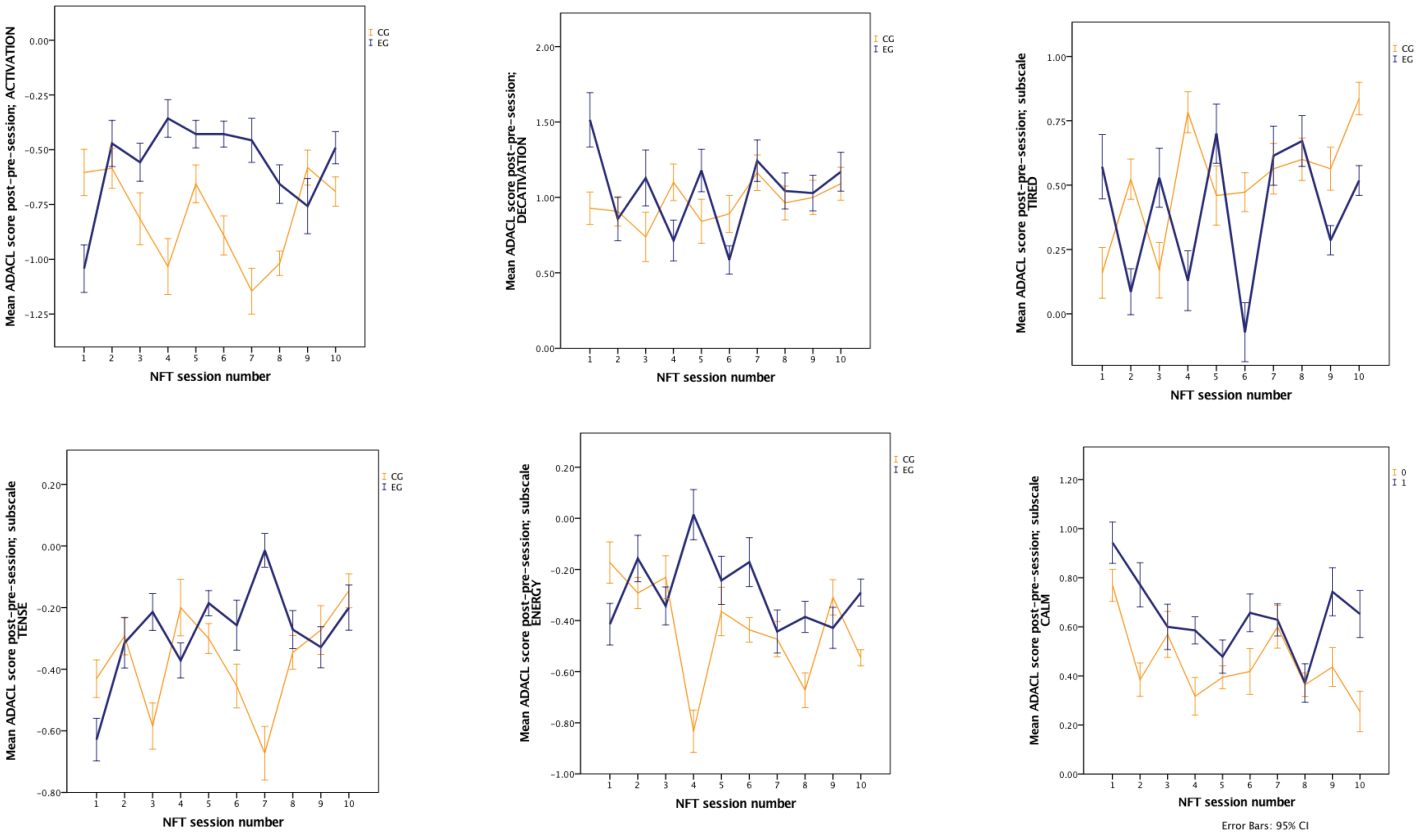
Clockwise from upper right: STAI-T, STAI-S, GAD-7, and BAI. All anxiety test scores decreased significantly between beginning and end of the NFT trial but no significant differences in reduction could be observed between EG and CG.

E.8: Mean NFT measures for EG (Solid Line) and CG (Dotted Line) over the course of the NFT Trial

averaging scores from sessions 1 & 2, 3 & 4, 5 & 6, 7 & 8, and 9 & 10 and corresponding mean NFT measures for EG (dark bold line) and CG (light thin line) over the course of ten sessions with 95% CI bars. **By row from upper left:** alpha amplitude for combined sessions and 10 sessions; theta amplitude for combined sessions and 10 sessions; T/A ratio for combined sessions and 10 sessions; relative theta amplitude for combined sessions and 10 sessions; relative alpha amplitude for combined sessions and 10 sessions; Relative T+A amplitude for combined sessions and 10 sessions.

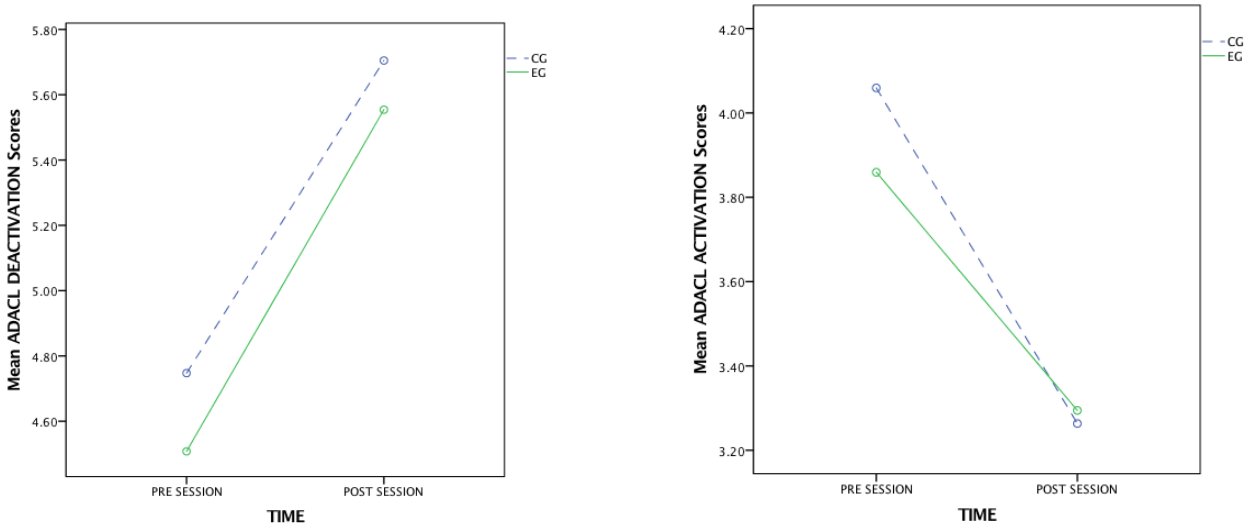


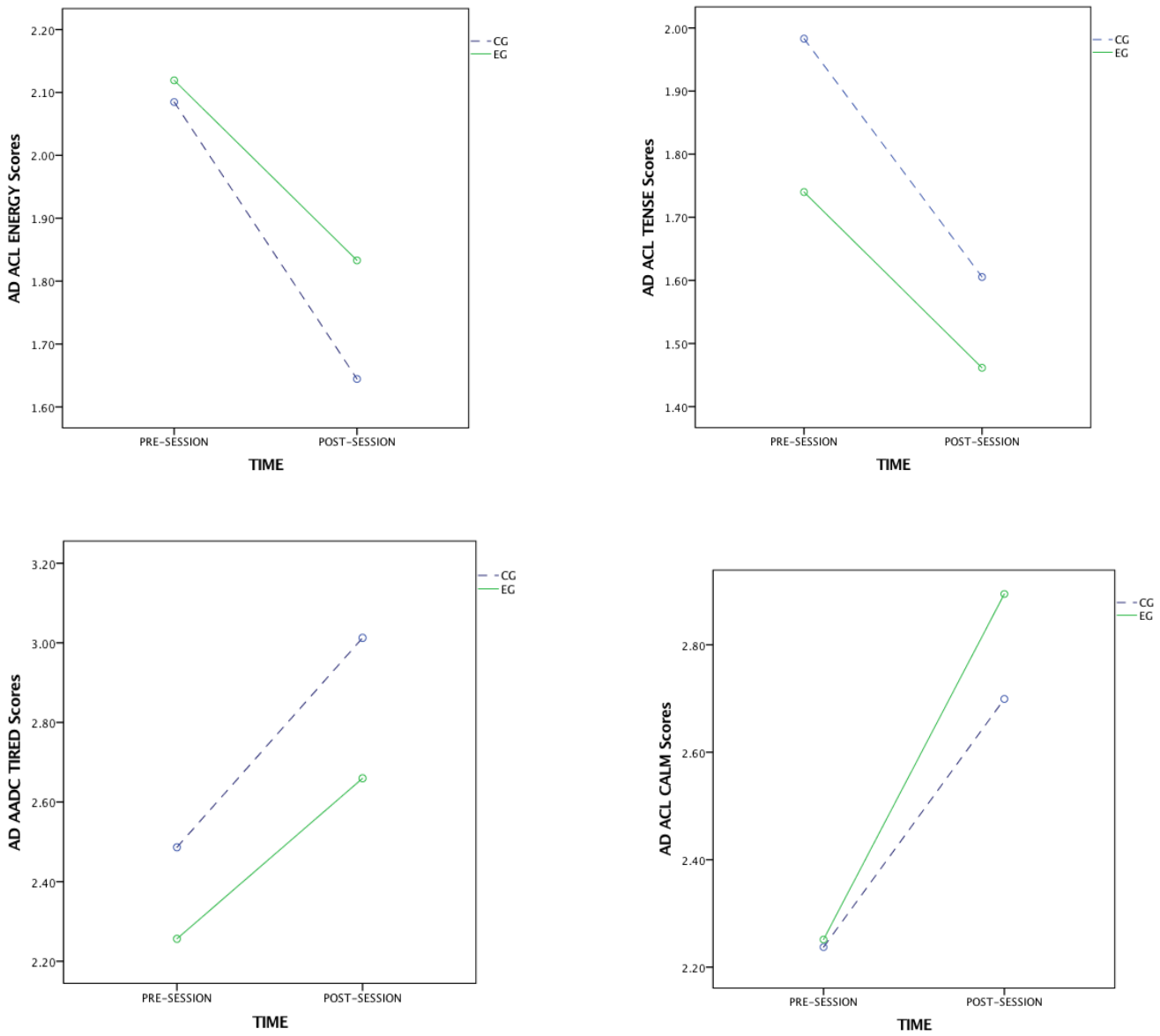
E9: Mean AD-ACL test score differences for EG (dark, bold, purple line) and CG (light, thin, orange line) over the course of ten sessions



Mean AD-ACL test score differences for EG (dark, bold, purple line) and CG (light,t hin, orange line) over the course of ten sessions with 95% confidence interval error bars. Clockwise from upper right: Activation and deactivation scores, and sub scale scores: tension, calmness, energy, and tiredness scores.

E10: Mean AD-ACL test score differences for EG (solid line) and CG (dotted line).





Mean AD-ACL test score differences for EG (solid line) and CG (dotted line). Pre- and post-treatment for clockwise from upper right: Activation, Deactivation, and for Sub-scales: Tension, Calmness, Tiredness, and Energy. Significant differences were observed for the activation and deactivation scales and for all four sub-scales.

E.11 For EG and CG: AD-ACL items pre-Post session Pearson Point-Biserial and Bivariate Correlations between Demographic, Qualitative, Psychometric and EEG-Based Post-Pre-Difference Scores.

CG & EG	Belief in EG	Total days	Sessions / week	Mental strat.?	Strategy success?	Change think?	Change feel?	Change behav.?	Age	LOC	STAI-T diff	STAI-S diff	BAI diff	GAD diff	SETS + diff	SETS - diff	Abs. A diff	Rel. A diff	Abs. T diff	Rel. T diff	Abs. T+A diff	Rel. T+A diff	TA ratio diff	ADACL deact	ADA CLact iv	ADACL energ	ADA CL tense	ADA CL tired	AD ACL Lalm
Time-of-day																													
Belief in EG?	1																												
Total days	.040	1																											
Sessions / week	.074	-.730**	1																										
Mental strat.?	.010	-.022	.082	1																									
Strategy success?	.008	-.208	.247	.556**	1																								
Change think?	.540**	-.013	-.044	.201	.159	1																							
Change feel?	.418*	-.035	.113	.168	-.052	.316	1																						
Change behavior?	.459*	.113	-.156	.134	.106	.523**	.385	1																					
Age	.451*	.088	.024	.116	-.049	.257	.229	.441*	1																				
LOC	-.001	-.021	.120	-.241	-.243	-.258	-.072	-.171	-.204	1																			
STAI-T diff	-.007	.036	-.277	.066	-.218	.127	-.129	.226	.417*	-.021	1																		
STAI-S diff	-.254	.164	-.269	.031	-.301	-.016	-.144	.126	.428*	.035	.715**	1																	
BAI diff	-.134	.236	-.381	-.022	-.159	.058	-.099	-.203	-.291	.198	.057	.127	1																
GAD diff	-.021	-.137	.211	.289	.474*	-.169	-.184	-.035	.187	.125	-.073	-.122	-.271	1															
SETS + diff	.161	.182	-.290	.100	.080	.430*	.075	.393	-.270	-.028	.010	-.088	.299	-.283	1														
SETS - diff	-.331	.261	.360	.160	.240	.050	-.066	-.281	-.094	.236	.052	.168	.231	.168	-.247	1													
Abs. A diff	-.381	.016	-.074	.042	-.040	-.095	-.221	-.040	-.239	-.009	.298	.217	.011	-.296	-.107	.098	1												
Perc. A diff	.012	.174	-.311	.188	.134	.350	-.048	.133	-.280	-.163	.110	-.015	.185	.029	.111	-.128	.371	1											
Abs. T diff	.014	-.432*	.307	-.297	.374	-.162	-.051	-.229	.052	.145	.336	.009	-.146	-.267	-.135	.054	.011	-.395*	1										
Perc. T diff	-.187	.301	.255	-.260	.004	.043	.038	.068	-.099	.017	-.193	.000	.019	-.285	.125	.390*	-.158	-.292	.317	1									
Abs. T+A diff	-.137	-.463*	.226	-.137	-.332	-.095	-.169	-.335	-.188	.126	.420*	.069	-.019	-.191	-.164	.125	.332	.120	.807**	.088	1								
Perc. T+A diff	-.105	.018	-.147	.021	.138	.381	.073	.178	.337	.150	-.012	-.015	.195	-.150	.187	.117	.267	.802**	-.190	.338	.174	1							
T/A diff	-.095	-.186	.168	.432*	-.180	.288	.077	.061	.121	.106	-.124	-.053	.219	-.271	.006	.023	-.238	-.784**	.459*	.636**	-.037	.374	1						
ADACL deact. diff	-.114	-.164	.133	.015	.191	.319	.150	.565**	.164	.158	.033	.046	.311	.130	.093	.107	.067	.035	.204	.202	.267	.161	.152	1					
ADACL active diff	.156	.261	.090	.041	.037	.097	.199	.085	.116	.097	.125	.064	.028	.145	.076	.204	.173	.228	.004	.259	.190	.062	.208	.410*	1				
ADACL energic diff	.028	.377	.205	.102	.106	.278	.197	.642**	.335	.184	.010	.202	.281	.040	.132	.167	.143	.011	.431*	.048	.586**	.041	.152	.603**	.496**	1			
ADACL tense diff	.171	.095	.252	.151	.169	.150	.385	.467*	.174	.295	.084	.062	.245	.138	.022	.390*	.047	.312	.397*	.266	.289	.141	.145	.080	.639**	.314	1		
ADACL tired diff	.152	.262	.320	.115	.221	.462*	.381	.661**	.111	.016	.069	.117	.120	.052	.105	.000	.175	.389*	.524**	.093	.423*	.325	.203	.766**	.093	.666**	.444**	1	
ADACL calm diff	.062	.162	.175	.167	.044	.009	.168	.117	.074	.287	.096	.053	.288	.096	.048	.280	.098	.491**	.323	.475*	.050	.187	.574**	.677**	.503**	.222	.400**	.114	1

EG & CG: AD-ACL items pre-Post session Pearson Point-Biserial and Bivariate Correlations between Demographic, Qualitative, Psychometric and EEG-Based Post-Pre-Difference Scores. Significant correlations are marked in bright orange. Muted colors mark related items. Qualitative items (items 6-10) have been transformed into quantified version. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

E.12 For EG only: AD-ACL items pre-Post session Pearson Point-Biserial and Bivariate Correlations between Demographic, Qualitative, Psychometric and EEG-Based Post-Pre-Difference Scores.

EG only	Belief in EG	Total days	Session s/week	mental strat.	strat success	Change think	Change feel	Change behav.	Age	LOC	STAI-T diff	STAI-S diff	BAI diff	GAD diff	SETS+ diff	SETS - diff	Abs A diff	Perc A diff	Abs T diff	Perc T diff	Abs T+A diff	Perc T+A diff	T/A ratio	Deact. diff	Activ diff	Energ. diff	Tense diff	Tired diff	Calm diff
Belief in EG	1																												
Total days	-.011	1																											
Sessions/ week	-.212	-.920**	1																										
Mental_strat?	-.213	.096	.026	1																									
Strat_success	-.145	-.193	.251	.679**	1																								
Change think?	.603*	.077	-.202	.059	.040	1																							
Change feel?	.576*	-.278	.281	-.213	-.145	.251	1																						
Change behav?	.452	.192	-.258	-.059	-.040	.458	.452	1																					
Age	.322	.215	-.178	-.071	-.195	.093	.322	.538*	1																				
LOC	-.450	-.051	.181	-.069	-.335	-.403	-.140	-.623*	-.328	1																			
STAI_T diff	-.134	.488	-.484	.000	-.156	.081	-.501	.182	.430	-.214	1																		
STAI_S diff	-.395	.528	-.392	-.033	-.337	.035	-.338	.234	.443	.110	.575*	1																	
BAI diff	.050	.475	-.553*	.216	-.025	.003	-.238	.281	-.435	.372	-.185	-.085	1																
GAD diff	-.254	-.063	.289	.595*	.651*	-.280	-.085	-.164	.253	-.058	-.092	.013	.229	1															
SETS + diff	.209	.335	-.416	.021	.014	.599*	-.034	.260	-.284	-.251	.150	.068	.402	-.531	1														
SETS - diff	-.543*	-.524	.615*	.526	.441	-.229	-.261	-.471	-.261	.398	-.262	-.026	-.024	.429	-.272	1													
Abs A diff	-.408	.049	-.105	.073	.084	-.078	-.427	.052	-.358	.186	.340	.159	.130	-.280	.174	.071	1												
Perc A diff	.204	.331	-.344	.367	.284	.546*	-.104	.234	-.360	-.238	.007	-.125	.274	-.041	.405	-.260	.305	1											
Abs T diff	-.002	-.377	.305	-.514	-.393	.259	-.059	-.300	-.035	.221	.192	-.229	-.274	-.384	-.138	.013	-.049	-.520	1										
Perc T diff	.057	-.551*	.499	-.167	-.164	.041	.305	.092	-.117	.065	-.366	-.190	-.148	-.329	.169	.335	-.237	-.393	.481	1									
Abs T+A diff	-.123	-.367	.285	-.313	-.231	-.136	-.290	-.430	-.423	.300	.165	-.334	-.140	-.404	-.072	.085	.289	-.053	.827**	.256	1								
Perc T+A diff	.252	.028	-.073	.315	.207	.609*	.069	.305	-.455	-.217	-.210	-.247	.206	-.239	.534*	-.080	.186	.839**	-.272	.172	.095	1							
T/A diff	.015	-.383	.334	.556*	.449	-.383	.283	.068	.346	.091	.036	.011	.369	.282	-.212	.006	-.190	-.860**	.707**	.615*	.252	.557*	1						
Deactiv diff	-.011	.036	-.004	.002	.034	-.347	.000	-.541*	-.341	.059	-.173	-.466	.197	.022	-.022	-.195	.217	-.012	.091	.253	.132	-.163	-.078	1					
Activ diff	-.377	-.019	.053	.088	.053	.085	.297	.103	.156	.212	.358	.550*	.067	.127	.172	.478	.223	.300	.253	.463	.134	.047	.307	-.717**	1				
Energ diff	-.055	.406	-.265	.060	.097	.218	.099	.771**	.566*	.258	.417	.720**	.246	.051	.190	.229	.185	.100	-.349	-.025	.482	.092	.040	-.620*	.411	1			
Tense diff	-.305	-.346	.261	.004	.017	.105	.386	.544*	.312	.433	.010	.050	.163	.202	.004	.639*	.067	.394	.551*	.475	.539*	.141	.287	-.181	.637*	-.438	1		
Tired diff	-.194	-.311	.331	.178	.195	.549*	.115	.734**	.245	.323	.090	.386	.017	.037	.249	.179	.269	.528	.644*	.201	.512	.446	.438	.726**	.207	.709**	.391	1	
Calm diff	.216	.381	-.346	.174	.148	.089	.149	.002	.213	.274	.167	.277	.277	.086	.222	.489	.090	.535*	.535*	.564*	.351	.239	.567*	.692**	.836**	.169	.689**	.009	1

EG only: Point-Biserial and Bivariate Correlations between Demographic, Qualitative, Psychometric and EEG-Based Post-Pre-Difference Scores. Significant correlations are marked in bright orange. Muted colors mark related items. Qualitative items (items 6-10) have been transformed into quantified version. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).