The Potential of Neurofeedback

A Master's Thesis on the potential of neurofeedback for scientific inquiry

and development of novel therapeutic methods

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Abstract

Throughout the centuries, humans have aspired to comprehend and control the inner workings of the mind and brain. Neurofeedback is the process of influencing physiological brain activity by making a person aware of it in real-time, thereby allowing self-regulation. Neurofeedback has been gaining momentum as a viable treatment option for several mental disorders and as a practical methodology for researchers to alter brain function in the attempts to induce particular states of mind.

The purpose of the present master's thesis is to investigate whether neurofeedback holds a potential to inform about mind-brain causal relationships. The thesis assumes the ontology of mind and brain to be the same process seen through different epistemologies and in doing so seeks to investigate whether neurofeedback can trace any causal codetermining mind-brain relationships. In keeping with this focus the thesis delves into the underlying principles of neurofeedback and the two competing theoretical accounts of the "conditioning-and-repair" model and "skill-acquisition" model for the therapeutic causal effects of neurofeedback. Here, the two models explanatory power and competing assumptions about the causal mechanism of neurofeedback in altering brain activity and by extension mental states is discussed. Taking offset in an empirical investigation into the neurophysiological basis of language learning efficiency the thesis generates hypotheses that reflects on the models accounts of causal inference through neurofeedback.

In facing up to the question of what the potential neurofeedback holds for investigating mind-brain causality the thesis suggests several key favorable aspects, such as the it's ability to manipulate brain activity as the independent variable and measure the effect on states of mind. Moreover, neurofeedback provides a method for creating evolving experimental paradigms that can identify unpredicted mind-brain relationships and eliminate competing causal hypotheses. Yet, neurofeedback also has several limitations in inferring causality, in particular strict unidirectional causality and a susceptibility to arguments pointing to a third cause of the mind-brain relationship. Here, it is argued that the advantages and limitations are amplified and attenuated respectively when neurofeedback is coupled with other methodological approaches.

The thesis culminates with a new view on causal inference, one in which scientific investigations enables causal accounts to gradually increase on a continuum of likelihood rather than being either causal or non-causal in an absolutely sense whilst still recognizing the unique potential of neurofeedback to investigate mind-brain causal relationships.

Table of Contents

“The great thing, then, in all education is to make our nervous system our ally instead of our enemy.

It is to fund and capitalize our acquisitions, and live at ease upon the interest of the fund. For this we must make automatic and habitual, as early as possible, as many useful actions as we can, and guard against the growing into ways that are likely to be disadvantageous to us, as we should guard against the plague. The more of the details of our daily life we can hand over to the effortless custody of automatism, the more our higher powers of mind will be set free for their own proper work.“

William James, 1890, Principles of Psychology, p.121

1. Introduction

1.1 Thesis Objective

Throughout history, there have been three major ways of influencing the brain for the treatment of mental disorders, known colloquially as the methods of "the knife, the pill and the therapist couch", or represented by their disciplines as psychosurgery, psychopharmacology and psychotherapy (deCharms, 2008a). Now more than ever, there is need for a fourth alternative that encompasses the objective of applying neuroscience in evidence-based practice to treat mental disorders. Emerging directly from laboratory research, biofeedback and its subcategory neurofeedback measure an underlying physiological signal non-invasively and in real-time (Sulzer et al., 2013,p.1-11; Yucha and Montgomery, 2008,p.8). The signal is then "fed" back to the individual so that they can learn to regulate it, with the intention of improving health and performance. An illustration of a neurofeedback setup is seen in (**Figure 1);** the analysis of psychophysiological measurements keeps pace with data acquisition and is then visualized as a feedback signal to the individual, influencing subsequent data production and acquisition and thereby forming an iterative loop.

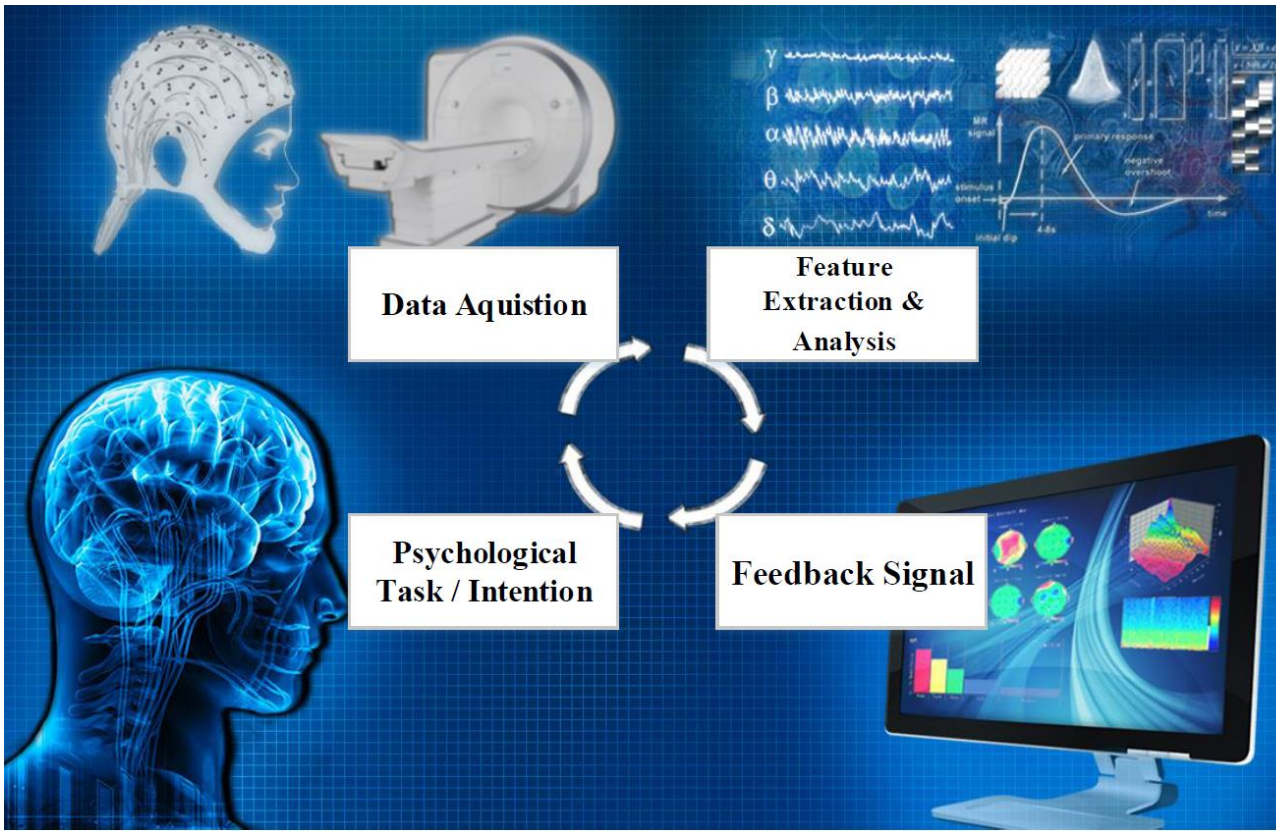

Figure 1. Diagram of the Neurofeedback Loop
Top left: Psychophysiological signals are measured from the scalp or from within the brain. **Top right:** The data is read by a computer where online analysis is performed. **Bottom right:** A feedback signal is presented to the individual in the form of a graphical or sound according to the recorded brain activity. **Bottom Left:** The individual learns control over the feedback signal by influencing brain activity through intentional and subjective experience (Kübler and Kotchoubey, 2007,p.2; Weiskopf et al., 2004,p.6).

The purpose of the present thesis is an investigation of the potential of this fourth alternative of bio/neurofeedback to inform about mind-brain causal relationships. Causality is the inferred necessary relationship between two occurring contiguous events, where one is seen as the cause of the other (the effect) (Kurthen, 2010,p.1-14). Causal relationships between mind and brain are particular hard to infer, as experimental evidence from neuroscience is often limited to showing that a neural correlate of mind exists without knowing its exact neural cause. Moreover, the matter is even more complicated by the fact that cognitive functions such as attention, executive function etc. are psychologically defined constructs that cannot be measured directly, but must be inferred from behaviour (Gazzaniga et al., 2010,p.96-146; Lindeløv, 2015,p.7f).

Humans introspectively experience the content of their minds or mental states by default, yet have little or no way to consciously perceive the concurrent physiological processes taking place in the brain, until now (deCharms, 2008,p.1-8, 2007,p.1-9). The breakthrough of neurofeedback has made it possible to illuminate the functioning of human brain in real time and thereby access both sides of the mind-brain interface simultaneously (ibid.). This approach also has widespread clinical implications regarding the treatment of mental disorders and represents a major paradigm shift from using biomedical devices not only as a diagnostic tools, but also as a therapeutic tool (Cantor and James, 2014, xviii). Moreover, neurofeedback might hold the potential to address questions of causality between brain activity and mental functions rather than mere correlations and thus represents an exciting new frontier for scientific discovery (LaConte, 2011,p.13; Sulzer et al., 2013,p.7).

1.2 Problem Statement

What potential does neurofeedback hold for investigating mind-brain causal relationships

1.3 Metatheoretical standpoint

The matter of the relationship between mind and brain (or mind-body) is often a topic of great debate, a debate that often precludes an easy answer to the question of whether the mind can be reduced to the brain (Chalmers, 2003,p.1-41, 1995,p.1-17; Kurthen, 2010,p.1-4). The present thesis is no exception. While it deals with aspects of the mind-brain issue, in doing so it naturally omits discussing certain dimensions of the larger debate. The present section aims to clearly define its standpoint on the mind-brain debate for the reader and thus circumvent the philosophical questions within the mind-

brain debate, that the thesis provides no adequate evidence to address. The thesis' metatheoretical perspectives are twofold; i) of clearly delineating the types of reductionism uses, ii) distinguishing between different levels of analysis.

The present author will argue that any discussion of mind-brain issue is similarly a discussion on the adequacies of reductionism (i.e., is the higher level of mind reducible to a lower level of neurons) (Franks, 2013,p.108). However, there are many meanings of reductionism, and so, any thorough analysis dealing with matters of the mind-brain issue, necessitates clarification on the types of reductionism(s) one is attempting to perform. According to Murphy (2003), there are at least five separate meanings of reductionism (Murphy, 2003,p.11f).

1) *Methodological* reductionism; is a research strategy that separate complex systems into parts. This is exactly what analysis means and allows one to trace the relationship between interacting parts.
2) *Epistemological* reductionism; holds that theories and laws of higher levels of science should be traced in causal terms to arise from the lower levels' laws.
3) *Logical or Definitional* reductionism; language referring to one type of entity can be translated without loss of the language about another type of entity.
4) *Causal* reductionism: all causation is bottom up. Ultimately herein the parts of subatomic parts of the system determine all the parts on a higher level
5) *Ontological* reductionism: Higher-level entities are seen as nothing but the sum of its part. As a consequence as we go up the levels, we need no new metaphysical entities ("ingredients") added to higher levels from these lower level ones (e.g. no need for an immaterial mind to get consciousness).

The present thesis deals with epistemological reductionism as it's focal point where it discusses the extent of neurofeedback to investigate instances of mind-brain reductions. In during so, it has a special purpose in mind, which is the question of whether we through the extent of neurofeedback research to investigate mind-brain relationships have consequently satisfied a scientific causal account of a codetermining law between mind and brain (James, 1890,p.1-10).

The question of how the mind fits into our universe and whether or not "you are nothing but a pack of neurons" (Crick, 1995,p.3), or whether there is need for an expansion of natural ontology (Chalmers, 1995,p.1-17), is therefore left untouched by the present thesis. Here, the thesis carefully avoids the questions of why mind states have associated conscious experiences or "qualia" (ibid.). The core assumption of the thesis, is thus, that there is scientific value in discovering if one can epistemologically trace the causal relationships between higher levels of mind and lower levels of neural phenomena, even if one remains entirely agnostic about their base ontology. At times, the thesis may entertain questions regarding adequacies of *causal* and *logical* reductionism, however, the heart of the matter is whether epistemological reductionism in certain cases is possible when appealing to neurofeedback research. There are at least two positions regarding epistemological reductionism, that of constitutive reductionism and eliminative reductionism (Lilienfeld, 2007,p.3). Both of these positions acknowledge that higher level mental events are ultimately rooted in the activities of the nervous system (ibid.), i.e., they are "different aspects of the same process" (James, 1890,p.136). Yet constitutive reductionism does not assume that the physiological level of analysis is always superior to and the only inevitable understanding of psychological events (Lilienfeld, 2007,p.3). Dovetailing with this, the present author argues that in order to arrive at a comprehensive understanding of the potential of neurofeedback for addressing mind-brain causal relationships one must distinguish between differing levels of analysis.

One influential framework for addressing the concept of levels of analysis in neuroscience was advanced by David Marr (Marr, 1982,p.1-25). Marr proposed three distinct levels of analysis (see **Table 1**), which he termed the *implementational*, *algorithmic* and the *computational* levels. The implementational level specifies the physical mechanisms which carry out this process, whereas the algorithmic level specifies the procedures by which this is to be carried out, while the higher computational level specifies the overall function that the cognitive system has to perform (Bechtel, 1994,p.1f; Ochsner and Kosslyn, 2013,p.2).

Level of Analysis	Level Definition	Neurofeedback Description
Computational	What is the goal of the computation?	Self-regulation of brain activity.
	Why is it appropriate?	Due to an *a priori* association between the initial brain state and psychopathology or mental state.
	What is the logic of the strategy by which it can be carried out?	An attempt to induce specific mental states or clinically meaningful therapeutical gains
Algorithmic	How can this computational theory be implemented? What is the representation of the input and output? What is the algorithm for the transformation?	Positive reinforcement the perturbations of the psychophysiological measurements that go towards the desired behaviour and negative reinforcement away from the undesired.
Implementational	How can the algorithm be physically realized?	Biomedical devices measuring the psychophysiological processes.

Table 1: Marr's three levels at which any cognitive system's information processing must be understood in relation to an explanatory account of neurofeedback. Adapted from Marr (1982), p.25. The description of neurofeedback is meant as a tentative working definition of the cognitive process based on the following authors; (Fultz, 2002,p.1-3; Gevensleben et al., 2014,p.1-2; Ros et al., 2014,p.1; Strehl, 2014,p1-6; Sulzer et al., 2013,p.9)

Critical for the present matter, is that for any cognitive process or mental state, be it neurofeedback itself or a mind-brain relationships that neurofeedback aims to investigate, the higher computational level affords a psychological interpretation (Lilienfeld, 2007,p.3-4). The appeal to a computational level of analysis is justified by the fact that the neurophysiological nomenclature gets one nowhere near the psychological phenomena to which an explanation is sought (Gavazzi, 2014). The levels are of course intimately linked, yet an analysis (or description) at one level does not satisfy as an explanation for another level (Marr, 1982,p.1-25; Overgaard and Mogensen, 2014,p.1-11). In other words, trying to understand a cognitive process while studying only neurons is by analogy like trying to understand bird flight by studying only feathers (i.e. highly unpractical) (Marr, 1982,p.25). Although, as argued by eliminative reductionism, such "epistemic gaps" may one day close (Chalmers, 2003,p.9; Lilienfeld, 2007,p.3-4). To summarize, the main cause of action for the thesis is to discuss what potential neurofeedback holds for identifying mind-brain causal relationships and as such. Lastly, the thesis is constrained in its scope on the matter at hand and therefore shows *aspects* of neurofeedback and the mind-brain causality debate in order to answer the problem statement. Accordingly, the reader should be aware, that many other examples and perspectives have carefully been deselected, due to the limiting scope of the thesis.

1.4 Structure of the Thesis

The thesis is divided into chapters beginning subsequent to this introductory chapter. In chapter two, several key principles underlying bio/neurofeedback is brought forth providing a necessary background for later discussions. The third chapter titled "Mind Over Chatter", describes foremost the neurophysiological basis of electroencephalography (EEG) neurofeedback, along with its wide applied use for mental disorders and functions. Next, the chapter discusses two competing theoretical models of how neurofeedback exerts a causal effect on mind-brain relationships which is used to generate hypotheses within an empirical investigation of the neurophysiological underpinnings of language learning. Chapter four comprise a review of the several key features of the neurofeedback modality of real-time functional magnetic resonance imaging (rtfMRI) used in the subsequent chapter. In chapter five on "The Causal Explanatory Potential of Neurofeedback" the criteria required for causal inference in neuroscience are outlined. In facing up to the question of the explanatory potential of neurofeedback, this chapter presents several key advantages as well as limitations to inferring mind-brain causality through neurofeedback research in addition to discussing a new view on the potential of neurofeedback for causal inference. Chapter six integrates the points brought forth by the thesis and reflects on them in the light of the problem statement in order to conclude on the thesis.

2. Principles of Biofeedback

2.1 Historical antecedents of Biofeedback

There are most likely multiple historical trends that converged into the formation of bio/neurofeedback as a scientific discipline. However, one of the crucial factors was that of the meeting between western science and eastern philosophy (Walsh and Shapiro, 2006,p.1-7). The burst of excitement in the 1960s and 1970s for altered states of consciousness led researcher Elmer Green to bring the first portable electroencephalography (EEG) to India to measure a Buddhist yogi while he was meditating (Green & Green, 1977,p.197-207). It is estimated that expert meditators use more than 10.000-50.000 hours of meditation practice in order to achieve what contemplatives term ”being in the moment” or “one-pointed concentration” (Brewer et al., 2011,p.1; Brefczynski-Lewis et al., 2007,p.1f), which is an amount of dedication that may seem daunting to most Westerners. If it was possible, through neurofeedback, to learn to induce this altered state of consciousness by inducing the corresponding neurophysiological state at will, the method could serve as a pragmatic “short-cut” (Brandmeyer and Delorme, 2013,p.1-4). The obvious question at this point, and one that is central to the thesis, is whether the neurophysiological state and the co-occurring state of consciousness is a bi-product or epiphenomenon of each other (Chalmers, 2003,p.32-35).

Concurrently Joseph Kamiya attempted to investigate the induction of a neurophysiological state and the associated mental state in his seminal papers on EEG operant conditioning, which would later be known as EEG biofeedback, Neurofeedback or Neurotherapy (Kamiya, 1962,p.6; Kamiya, 1969,p.1-11; Frederick, 2012,p.1f). Kamiya asked whether participants could learn to discriminate when a particular frequency of brain waves called “alpha” was above a given threshold. He found that not only could participants learn to be aware of whether alpha power was high or low, but also to control alpha brain waves upon instruction (ibid.).

A similar line of scientific inquiry that paved the way for the emergence of neurofeedback was Barry Sterman's NASA funded research into the toxicity of rocket fuel (Arns and Lyle, 2011,p.1; Sterman, 2000,p.1-6). Rocket fuel contains toxic compounds that absorb essential co-enzymes for the synthesis of inhibitory neurotransmitters in the nervous system. Exposure of rocket fuel to an organism will therefore cause disinhibited movements and seizures. Using cats as subjects, Sterman found a clear dose-response relationship between the amount of administered rocket fuel and seizure symptomology, except for a subset of the cats that seemed to resist the propensity for seizures. By serendipity, Sterman had, in another study, conditioned this subset of cats by administering and

withholding milk each time they increased or decreased the power of the sensory motor rhythm (SMR) of the EEG spectrum. What Sterman came to realize was that, through this blunder of standard scientific protocol, he had created an experimental model of cats that were highly resistant to seizures (ibid.). In the following years, Sterman translated this finding into a therapeutic setting by upregulating the SMR frequency band of a women suffering from epilepsy. The results were a reduction in epileptic seizures, providing the first evidence that neurofeedback could have therapeutic potential (Sterman and Friar, 1972,p.1-6; Sterman, 2000,p.1-6). The examples of Kamiya and Sterman are meant to illustrate the potential of bio/neurofeedback techniques for scientific inquiry and the development of novel therapeutic methods. What Kamiya set in motion is mirrored today in the current research into the neural correlates of consciousness and the use of neurofeedback in as a research tool in this context, something the thesis will deal more thoroughly with in the final chapter. Similarly, Sterman's clinical approach also has widespread implications for future treatment, diagnosis and prevention of mental disorders, something that later chapters will explore.

2.2 Zeitgeist of Neurofeedback

To fully understand the scope of neurofeedback in its current form, one must appreciate the "zeitgeist" or the defining spirit that presently pervades the modern conception of mental health. For more than three decades, the biomedical model of mental health has been dominant within the western health care systems (Engel, 1977,p.1-7; Deacon, 2013,p.1ff). The biomedical model trivializes the influence of psychosocial factors and holds that mental disorders should be conceptualized as brain diseases or chemical imbalances (ibid.). It assumes an eliminative reductionist position to the relationship between mind and body which posits that psychological *understandings* are suboptimal momentary placeholders for a physiological understanding (Lilienfeld, 2007,p.2f).

In the recent decade, the biomedical model has been challenged, most notably by the biopsychosocial model and its method of behavioral medicine, also known as integrative medicine or mind-body medicine (Engel, 1977,p.1-7; Kabat-Zinn, 1990,p.171-175; Simonsen and Mohl, 2010,p.36-45). This model expands beyond the biomedical to address the mind in addition to the body, behaviors, beliefs, thought and emotion, in addition to purely biological signs and symptoms. It shifts the orientation of the etiology of mental disorder from chemical imbalances in the brain to include the patients' own perceptions and representations of the world around them. As an example of the contrast between the two models, the biopsychosocial model was able to explain how, given an exposure to the same disease agents and environmental conditions, some individuals would get sick and others not. The

model proposed that socio-psychological factors such as personal beliefs, attitudes and health behaviors plays a vital role in the person's susceptibility to illnesses and mental disorders. Prima facie neurofeedback seems to support a biomedical model, it places emphasis on the role of biology in understanding and influencing mental disorders, and on the idea that treatment of brain processes yield psychological benefit (Gevensleben et al., 2014a,p.2). Yet, there are also authors who argue that neurofeedback can be subsumed under the paradigm of behavioral medicine and sustain that it is an inherently interdisciplinary field, attempting to bridge the gap between neurobiology and the cognitive sciences of the mind (Kirlangic and Ivanova, 2003,p.1-3; Nash, 2005,p.1-5). Similar to other behavioral medicine approaches such as cognitive behavioral therapy (CBT) and meditation based treatments, neurofeedback attributes a crucial role to human self-agency (Brenninkmeijer, 2013,p.1-18; Kabat-Zinn, 1990,p.171; Ninaus et al., 2013,p.5-9; Yucha and Montgomery, 2008,p.1-58). Neurofeedback highlights one of the core tenets of behavioral medicine: that humans indeed are more in control over their physiology than previously assumed (deCharms et al., 2005,p.1-5), and that this ability itself can be strengthened through training.

2.3 Neuroplasticity

The conventional approach among most early neuroscientists has been to adhere to the idea of "localizationism", meaning that specific psychological functions correspond rigidly to a "hardwired" location in the brain, analogously to a computer (Doidge, 2007,p.6-116). However, a core theme emerged during the latest decades of neuroscientific research has been that the brain is not a preassembled and hardwired network of neurons, but instead changeable throughout life (Doidge, 2007,p.1-10; Pinel, 2011,p.3; Giedd et al., 1999,p.1f; Mogensen, 2011,p.1-9) The term for this feature is "neuroplasticity", meaning characteristics of the nervous system to be weak enough to yield to an influence, but strong enough not to yield all at once (Doidge, 2007,p.1-10; James, 1890,p.105). In the neuroscientific literature; "plasticity", has become an umbrella-term to explain several facets of brains functioning such as learning and memory (Pinel, 2011,p.269-296). The brain's potential of dynamically rearranging itself also goes beyond everyday mental functioning and pays dividends as a crucial component of successful neurorehabilitation after brain injury (Mogensen, 2011,p.1-3). Neurofeedback taps into the malleable nature of the brain. Neurofeedback measures the neurophysiological processes and strives to change them towards a desired state and through neuroplasticity strengthens the ability of the system that mediated that change (Ros et al., 2010,p.1-8). Moreover, the concept of transfer is deeply embedded into the aim of neurofeedback training.

Transfer, in this context, means that the successful regulation through neurofeedback resulted in a therapeutic effect that is maintained in the absence of feedback or in a different setting or non-trained task (Sulzer et al., 2013,p.3).

2.4 Natural Born Cyborgs

A similar underlying principle of neurofeedback stems from the brain's extraordinary ability to autocorrect its responses to signals in the environment. One of the first indications that a hardwired view of the brain was incomplete came from Bach-y-Rita, a scientist and rehabilitation physician (Bach-Y-Rita et al., 1969,p.1f). In his article which appeared in the highly prestigious journal, Nature, Bach-Y-Rita described a device that would allow congenitally blind individuals to see. The device was a chair with a vibrating back that would relay electrical signals from a camera attached to the chair.

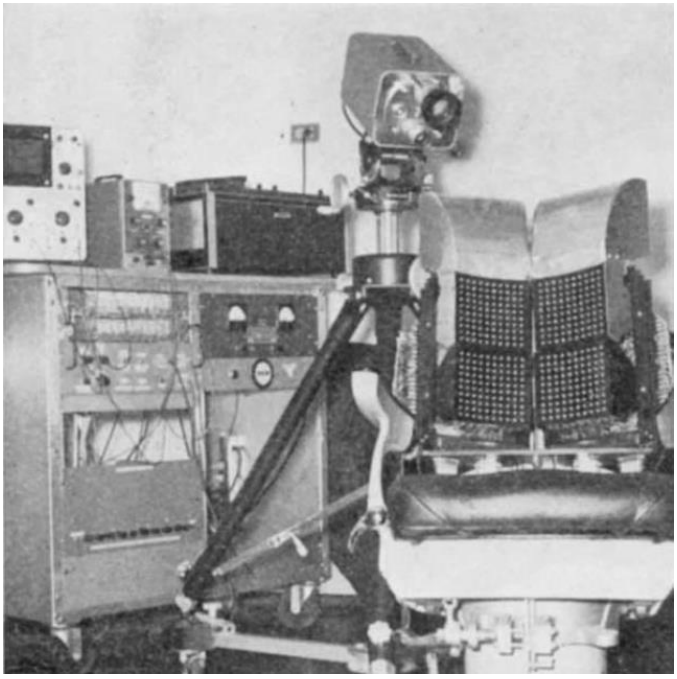

Figure 2. Tactile television hardware constituting the vision substitution system. Adapted from (Bach-Y-Rita et al., 1969,p.1f).

This meant that the visual signal would be conveyed to the blind individual through the tactile sense and thus without the use of their eyes. The resolution of the signal was nowhere near that of the human eye, but it allowed blind individuals to "see" rudimentary contrasts and shapes. This "tactile vision device" came as a novel input to the scientific consensus at the time and stood as one of the most iconic pieces of evidence for neuroplasticity. The device has since been advanced to become mobile such that blind individuals now receive the visual information from a thin metal plate on their tongue

(Bach-Y-Rita et al., 1969,p.1f; Doidge, 2007,p.34-38). A person wearing this device would be able to "see" with their tongue, i.e. having a genuinely visual perceptual experience without any "toungeness" to it (ibid.). A burgeoning literature has illustrated how the visual cortex is able process information relevant for its specialized processing regardless of the source (Kupers and Ptito, 2004,p.1-5; Merabet and Pascual-Leone, 2010,p.1-7; Ptito et al., 2005,p.1-3) This is termed "sensory substitution" and is the ability of the brain to use information acquired by a sensory modality to perform a cognitive function which is normally fed by a different sensory modality (Ptito et al., 2005,p.1-3). The visual cortex may be adeptly able to process visual information, yet it is of less importance where the sensors pick up the signal (Doidge, 2007,p.37f; Pinel, 2011,p.68). Although it may be debatable to which extent any given mental function or state is truly microdiscernable from another, it can be argued that at a coarse level of "granuality", the function of "seeing" can be realized by multiple neural or even electronic substrates (Lindeløv, 2010,p.8-10; Overgaard and Mogensen, 2011,p.1-4)

The implication of these lines of evidence which are of prime relevance for neurofeedback is that the brain can adapt to any signals in the environment, whether they originate from biological or non-biological sources. This has led philosopher of mind Andy Clark to argue that humans are "natural born cyborgs", in the sense that the brain can transparently interface readily with electronic devices, just as it transparently interfaces with the peripheral nervous system (Clark, 2001,p.1-10). The findings of Bach-Y-Rita's "tactile vision device" underlines that the brain is not restricted to biological input (Bach-Y-Rita et al., 1969,p.1f; Doidge, 2007,p.1-112; Merabet and Pascual-Leone, 2010,p.1-7). Furthermore, it illustrates that these brain computer interfaces which are gaining momentum have the potential to restore vision for the blind (ibid.). This ability of the brain to attune to computer interfaces is a key component of neurofeedback. In much the same way as a person can learn to perceive visual signals through tactile sensations on the tongue, neurofeedback enables a person to perceive changes in his or her own brain physiology (Clark, 2001,p.50; Kübler and Kotchoubey, 2007,p.1-6)

2.5 Feedback Loops

The human body has an ability for self-regulation in order to appropriately maintain internal balance and order (Kabat-Zinn, 1982,p.144-146). Evolution has endowed our bodies with the autocorrective mechanisms able to adjust deviations for the sake of restoring homeostasis (Breedlove and Watson, 2013,p.393-397). The body accomplishes this self-regulation through finely tuned feedback loops that operate on every level of the organism (Kabat-Zinn, 1982,p.144-146). For instance, when an individual performs a physical exercise, the heart will automatically pump more blood to provide sufficient oxygen, and will return to a normal level when the exercise is over (ibid.).

The use of biomedical devices to monitor and influence physiological processes has traditionally been in use only in critical situations and by the hands of medical professionals. Perhaps the most familiar of all biofeedback devices is that of electrocardiography (ECG) used in modern hospitals (Pinel, 2011,p.110). Imagine a doctor hearing the sound of an ECG machine beeping at regular intervals indicating the heartbeat of the patient. In case the doctor hears a flat lining of the ECG signal, a defibrillator is used in order to provide a brief electrical current to the patient's heart muscles to reestablish normal cardiac rhythm (Kouwenhoven, 1969,p.1). At the moment when the doctor provides the current, he or she enters into a loop, where further perception of the sound of the ECG is now informed by the effects caused by the actions and inactions of the defibrillator. The example is critical in explaining that feedback is only ever present when the output of the system is routed or "fed" back to its own place of origin, such that future effects are informed by previous effects. The discrepancy with this analogy and biofeedback practice is that, in biofeedback, the rains of control are given to the individual and that they enforce the loop themselves. Self-regulation of physiological processes such as heart function is a documented human ability, yet by advancing our technical practices humans have made it possibly to outsource physiological regulation to biomedical devices (Cavazza et al., 2014,p.1-7; Sapolsky, 1994,p.1-33)

2.6 Psychological Biography

From ancient philosophy to the modern cognitive neuroscience, it has been a human goal to "know thyself" (deCharms, 2008,p.1; Wilson, 2009,p.1). Through neurofeedback it is now possible to access both mind and brain through subjective interception and external measurements of one's brain simultaneously. Indeed, neurofeedback could be termed "interoneuroimaging" and presents itself as a promising tool for enhancing self-knowledge (ibid.). There is a sense in which neurofeedback as a psychological technical practice acts both as a literal and a symbolic biography for the subject. The

rather unique characteristic of neurofeedback is the “loopiness” of the process, whereby the attempts at self-regulation is met by immediate feedback based on its success or failure. In daily life, the typical attempts to self-regulate one’s physiology are often unguided and it thus remains uncertain whether these self-regulatory attempts are fruitful or not.

Compared to traditional self-regulation, neurofeedback allows individuals to regulate physiological processes based on measures achieved through high-level computational algorithms that are naturally outside one’s immediate awareness and control (Ramirez et al., 2001,p.1; Strehl, 2014,p.1). It is of cause the very intriguing quality of science and technology to discover measurable phenomena in the world that were previously unknown. As Karl Marx wrote; ”All science would be superfluous if the outward appearance and the essence of things directly coincided” (Marx, 1981,p.570). Indeed, our brains often produce a very coarse version of our world (LeDoux, 1995,p.5), and it is therefore the role of science and technology to extend the scope of the human senses and uncover the hidden layers of complexity in the universe. The telescope had the goal of extending the human eye, the telephone that of the human voice and a camera that of memory of visual scenes. Neurofeedback is equally another method for extending the human view of the world, yet it is unique in that it extends our view inward, towards the capacity for self-regulation of human physiology.

3. Mind Over Chatter

Frank H. Duffy, M.D., Professor and Pediatric Neurologist at Harvard Medical School, stated in an issue of the journal Clinical Electroencephalography that neurofeedback should play a major role in the treatment of mental illnesses (Duffy, 2000 from Hammond, 2011,p.1). "In my opinion, if any medication had demonstrated such a wide spectrum of efficacy it would be universally accepted and widely used", "It is a field to be taken seriously by all" (ibid.). The present chapter will provide an account of electroenchalography (EEG) neurofeedback, on an implementational, algorithmic and computational level of analysis. In doing so, the chapter will feature a brief neurophysiological explanation of EEG as well as the procedures and rationale for practicing EEG neurofeedback. Moreover, the chapter will provide a synthesized systematic review of the wide spectrum of EEG neurofeedback research literature on the treatment of mental disorders. Here, questions regarding the amount of published study-articles and individual research dedicated to a given mental disorder will be addressed. The chapter will present the two competing theoretical models regarding neurofeedback, that of the "conditioning-and-repair" and the "skill-acquisition" model. To fully delineate the two competing models the present chapter will present experimental evidence suggesting district neurophysiological profiles of language learning abilities. Concluding the chapter, two models will be used to generate hypotheses for a future neurofeedback research project.

3.1 The Basis of EEG Neurofeedback

The acronym EEG is short for electroencephalography, which means the graphical reading of the electrical activity arising from the *encephalon* or "within the head". (Pinel, 2011,p.64; Saab, 2008,p.1). It's instructive to begin at the basic level, which is that of individual excitatory (E) and inhibitory (I) neurons organized in a six-layered cortical structure (Collura, 1990,p.1-3; Ros et al., 2014,p.1-10). When E-neurons produce action potentials they activate the I-neurons, which later retroactively silence the E-neurons, and so *ad perpetuum.* Ultimately, this inhibitory recurrent feedback mechanism prevents an overabundance of excitation and ensures that the cortex has a manageable level of activity, which is necessary for adequate information processing. It is the combined activity of these E-I neuronal assemblies that, when scaled-up to the staggering web of billions of neurons in the cortex, contributes to brain oscillations or "brain waves". How quickly the wave cycles shift between rising and falling determines their frequency, typically measured in cycles

per second or Hertz (Hz). The spectrum has traditionally been delineated in the following bands: delta (1-4 Hz), theta (4-7 Hz), alpha (7-12 Hz), beta (15-30) and gamma (> 30 Hz) (ibid.).

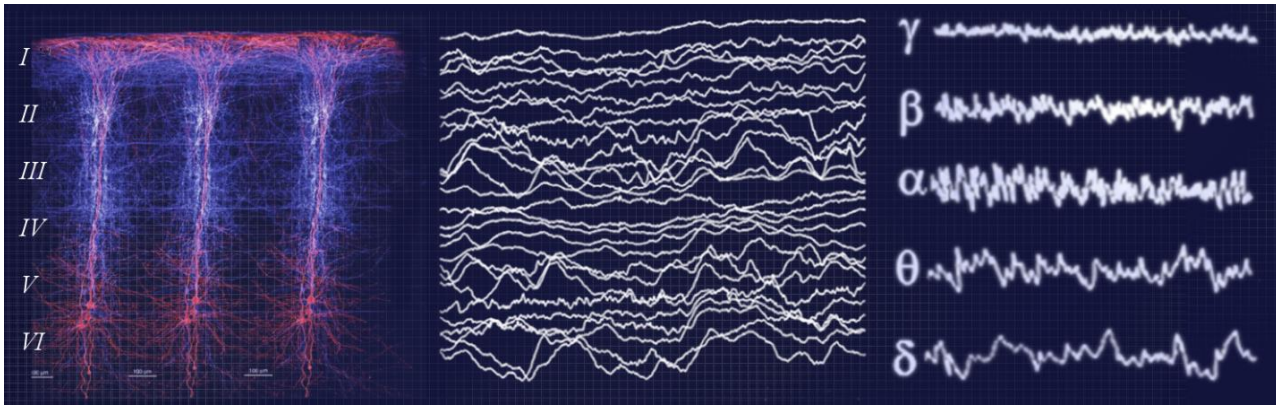

Figure 3. Analysis of neurophysiology through electroencephalography (EEG)
Left: Inhibitory and excitatory neurons organized in a six-layered cortex neurons produce signals measured at the scalp by electrodes **Middle:** 500 milliseconds of raw EEG data as measured by several individual electrodes **Right:** The oscillations can be classified in frequency bands δ: delta (1-4 Hz), θ: theta (4-7 Hz), α: alpha (7-12 Hz), β: beta (15-30) and γ: gamma (> 30 Hz).

These electrophysiological characteristics are interconnected with a panoply of neurotransmitters that work at the synapse of the neuron (Lubar, 1997,p.2-6; Ros et al., 2014,p.2-4). In parallel, the activity of these processes reciprocally determines the cerebral metabolic processes in addition to the neuroplastic changes of local and connective brain tissue (Ghaziri et al., 2013,p.1; Ros et al., 2013,p.1-10, 2010,p.1-8; Başar et al., 2000,p.1-2; Pfurtscheller and Lopes, 1999,p.1-5). These oscillatory electrophysiological processes interconnect with all brain processes, and they have thus implications for neuropsychological processes and the higher psychological level of analysis (ibid.). Historically, EEG patterns were shown to correspond to psychological levels of arousal, from sleep to wakefulness to high alertness (Ros et al., 2014,p.2). Since their discovery, the scientific investigation of electrophysiological brain characteristics have been shown to correspond with several cognitive functions, such as attention, emotion, memory and consciousness (Andreassi, 2013,p.122-143; Polich and Kok, 1995,p.1-34; Ros et al., 2014,4-16; Seth et al., 2008,p.5). These functions are mediated by neuronal synchronization of different frequency bands allowing transient functional integration of neural assemblies (Ros et al., 2014,p.4; Varela et al., 2001,p.1-9). The communicative exchange of information between neurons is similar to the way a radio picks up on a frequency of a particular radio station (ibid.). As such, the transfer of information between neurons (listeners and radio stations) becomes optimal when their frequencies are more prominent and when irrelevant signals (chatter) from other neurons (radio stations) are reduced (Arce-McShane et al., 2016,p.1; Cardin et al., 2009,p.1-4).

It's important to realize that these frequencies occur simultaneously in the brain, however with different amplitudes. Studies have established that the amplitude of these individual frequencies often referred to as the *power* of the frequency, is related to the number of neural assemblies firing at that particular frequency along with the phase-locking (synchronization) of their firing (Ros et al., 2014,p.2). A useful metaphor is to compare these to "standing-waves" generated by a crowd of spectators in a stadium. The amplitude of the frequency is the "agreeableness" of the spectators to contribute to that particular wave cycle in synchrony with others (ibid.). As a general principle, low frequencies integrate information globally in the brain whereas high-frequency oscillations integrate information at local neural assemblies (Bagdasaryan and Le Van Quyen, 2013,p.4-7). At this point, due to the specific progression of this description, the reader may be led to conclude that the causal relationship only goes one way and that activity at local assemblies unidirectionally determines global oscillations. Contrary to this assumption, slower large scale cortical oscillations can, in a top-down manner, entrain faster local oscillations, a process known as cross-frequency coupling. Supporting this view, several lines of evidence highlight the bi-directional nature of global and local oscillatory activity (Canolty and Knight, 2012,p.1-4; Canolty et al., 2009,p.1; Bagdasaryan and Le Van Quyen, 2013,p.4-7). For brevity, in the context of the standing-wave analogy, a bi-directional causal relationships would mean that the crowd of spectators could influence the behaviour of the individual and also reverse.

Supporting the conception of *pathological oscillations* are findings of stable oscillations of one kind in neurologically healthy populations and relatively consistent, different EEG patterns associated with mental disorders (Duff, 2004,p.1-5; Ros et al., 2014,p.5-10). The research on EEG correlations with neurological, neuropsychiatric, and neuropsychological disorders is extensive and the following represents only a subset of this vast literature. For instance, the core symptoms of post-concussion syndrome includes attention and mood disorders, impulsivity, memory difficulties and headaches. Each of which are associated with EEG oscillations, most prominently excessive slow waves (e.g., theta 4-7 Hz) (ibid.). The same neurophysiological pattern is seen in attentional deficit hyperactivity disorder (ADHD), showing excessive theta (see **Figure 4**), in an addition to improvement if ADHD symptomology through upregulating beta or alpha compared to theta (Doppelmayr and Weber, 2011,p.1-14; Martijn Arns et al., 2009,p.1-2; Duff, 2004,p.1-5; Ros et al., 2014,p.5-10).

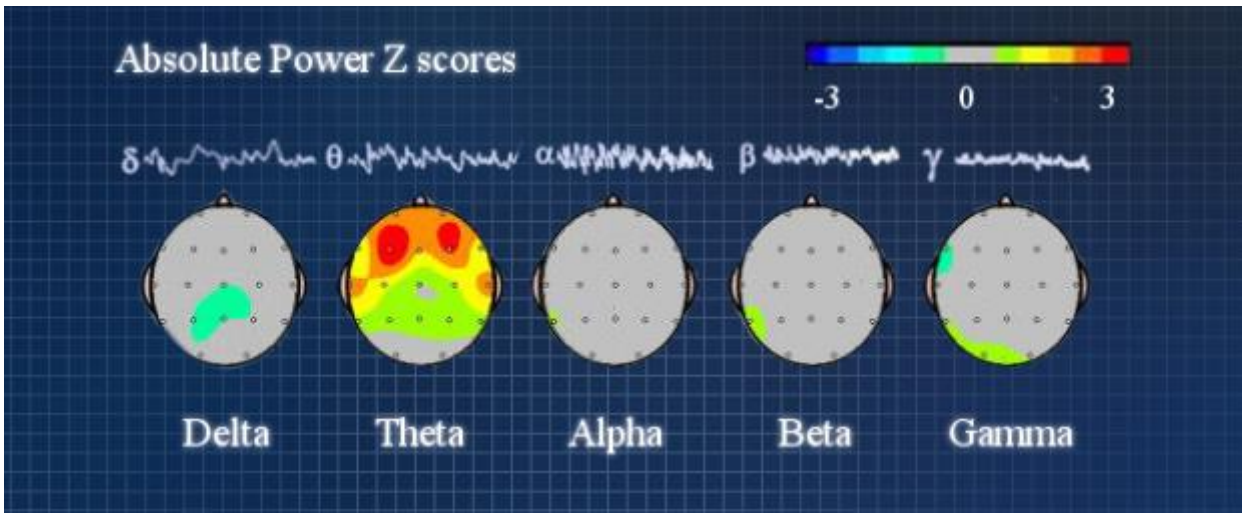

Figure 4. Absolute Power Z score of ADHD Adolescents
The figure shows the power Z score of ADHD with comparison to a standardized database of neurologically healthy adolescents (Collura, 1990,p.1-6), within the five different frequency bands δ: delta (1-4 Hz), θ: theta (4-7 Hz), α: alpha (7-12 Hz), β: beta (15-30) and γ: gamma (> 30 Hz). The regions that are more red correspond to a higher amplitude or power within the corresponding frequency band for adolescents suffering from ADHD as compared with neurologically healthy adolescents. The top right legend shows the colour for the corresponding Z score.

In anxiety disorders such as post-traumatic stress disorder (PTSD), a decrease in the alpha rhythm has likewise been observed, possibly reflecting hyperarousal (Moore, 2000,p.1; Ros et al., 2014,p.5; Wahbeh and Oken, 2013,p.1). In contrasts, disorders such as substance use disorders (SUD) and schizophrenia are characterised by abnormalities in the faster beta and gamma frequencies (Ros et al., 2014,p.5; Sokhadze et al., 2008,p.1-22; Sürmeli et al., 2011,p.1-3). A robust finding in patients with depression is asymmetrical prefrontal activity, highlighting the importance of regional specificity and relative frequency in defining clinical EEG abnormalities (Davidson, 1998,p.1-10, 1992,p.1-4; Hammond, 2005,p.1-3). Moreover, as documented by Bauer (2001) within SUD, baseline EEG beta power was found to be a superior predictor of relapse after a 6 month period, as compared to psychological factors measured through a large battery of neuropsychological tests (Bauer,p.1-9, 2001; Ros et al., 2014,p.5). Specifically, it was shown that beta power improved the predictive accuracy of the model from 56 % to 74 % and significantly outweighing other predictors (ibid.). Importantly, EEG characteristics associated with a particular pathology can be used as a biomarker for prognosis, e.g. in the case of long-term recovery perspectives from ischemic stroke, where delta (1-4 Hz) inversely correlates with perfusion in the lesioned substrate. Similarly, administration of psychostimulants leading to successful outcomes in disorders such as Parkinson's disorder and ADHD also correspond to a normalization of EEG activity (ibid.).

The traditional approach of neurofeedback used by Kamiya and Sterman, was to teach self-regulation by intentionally up- or down-regulating the amplitude of a particular frequency (Cantor and Evans,p.19-49, 2014; Collura, 1990,p.1-6; Egner and Sterman, 2006,p.1-6; Krigbaum and Wigton, 2014,p.1-7; Ros et al., 2014,p.5-10; Vernon et al., 2003,p.1-4). The particular frequency was determined based on prior research literature indicating a plausible association between this frequency and a mental function or dysfunction. A fundamental limitation of this approach is that mental functions and dysfunctions are not necessarily neurobiologically homogenous (Lindeløv, 2015,p.7f; Ros et al., 2014,p.6). In short, psychologically defined constructs based on similar behavioural patterns can arise from dissimilar neural substrates (ibid.). Recently, sophisticated metrics such as frequency power ratios, Z-score neurofeedback, hemispheric synchrony, and phase-lag neurofeedback have been developed in response to these challenges, allowing to address a broader range of neuronal dynamics (Krigbaum and Wigton, 2014,p.1-7; Ros et al., 2014,p.6).

Stating it in the terms of Marr's three levels, the representation of the input and the algorithm for the transformation has shifted with the change of the technological landscape in the last decades. The basic model on the computational level, however, remains the same, namely the association between a measurement of physiological activity and psychopathology and the subsequent attempt to shift this activity. This model means that in relation to any mental disorder, neurofeedback research aims at targeting the associated neurophysiology and at testing whether it results in clinically meaningful improvement. Thus, neurofeedback is a not just a treatment option for some mental disorders, but a multifaceted treatment approach with implications for a wide spectrum of mental disorders (Duffy, 2000,p.1). In the following section, the question of the spectrum neurofeedback research will be addressed, focusing on the amount of research conducted on different mental functions and dysfunctions.

3.2 The Wide Spectrum: a Systematic Review of the literature

3.2.1 Systematic Review Background

Presently, several systematic reviews and meta-analyses of neurofeedback exist. However, such reviews restrict their focus to a single pathological condition or mental disorder such as Epilepsy or ADHD (Arns et al., 2009,p.1; J. Gruzelier, 2014,p.1; Tan et al., 2009,p.1). In a comprehensive bibliography, the International Society for NFB & Research (ISNR) found 629 articles published in scholarly, peer-reviewed journals that discuss or utilize biofeedback (Hammond and Novian,

2013,p.1). Here, the present author undertook a systematic review of study-articles on EEG neurofeedback in order to expand upon the ISNR bibliography in order to address the trend of studies on different mental functions and dysfunctions, taking year and quality into account.

3.2.2 Search Strategy and Screening

A broad search of English-language literature using a range of search terms (for details see appendix 1), restricted to the years between 1999 to 2015 was performed using Google Scholar (GS). The search terms were tailored to have high sensitivity to the previously mentioned bibliography (Hammond and Novian, 2013,p.1). Commercial articles were excluded. The mental disorder or phenomenon that the articles aimed at treating or training was classified. Several subtypes of disorders belonging to a broader class of disorders were collapsed into a single mental disorder or phenomenon (see **Table 2**).

Mental Disorder/Phenomenon	Subtypes
Attention Deficit Hyperactivity Disorder (ADHD)	ADD, Hyperkinetic/Hyperactivity disorder, Impulsivity and Inattention.
Early Onset Behav/Emo Disorders (F91-F98)	Delinquent Behaviour, Criminal behaviour, Criminality, Juvenile Offenders, Conduct Disorder, Tic and Tourette Syndrome, Reactive Attachment Disorder, Attachment Disorder, Neglect, Dissociative Identity Disorder, Somatoform Disorder
Cognitive Enhancement	Working memory, Executive Function, Musical/Creativity/Artistic abilities, Auditory / Visual Discrimination Tasks in Healthy Volunteers. Trainability of absolute, relative, ratio EEG frequencies. Testing different stimuli, contingency awareness, predictors of successful learning etc.
Age Related Cognitive Decline and Neurodegenerative Disease (ARCD and NDD)	Cognitive Enhancement with focus on the Elderly. Dementia, Parkinson's Disease, Alzheimer's, Amyotrophic Lateral Sclerosis.
Pain and Headache	Chronic Pain, Fibromyalgia, Pain Management, Headache and Migraine, Peripheral Neuritis
Substance Abuse	Addiction, Drug Addiction, Psychostimulant Use, Alcohol/Cocaine/Nicotine Dependence
Eating Disorder	Bulimia Nervosa, Disinhibited Eating Pattern, Childhood Obesity
Affective Disorder (F30-F39)	Bipolar/Mood Disorder, Anger Disorder, Mild, Severe and Treatment Resistant Depression
Learning Disability	Dyslexia, Reading Disorder, Dysgraphia, Agraphia, Intellectual disorder, Spelling Disability, Cognitive Impairment & Mild Cognitive Impairment
Sleep / Insomnia	Sleep Disorder and Insomnia, periodic limb movements in Sleep
Subjective Experience	Consciousness, Altered States, Meditation, Wellbeing, Phenomenology, Immersion.
Brain Injury (TBI and CVA)	Traumatic Brain Injury, Cerebrovascular Accidents, Ischemia, Stroke, Hemorrhage, Hematoma, Cerebral Palsy, Myocardiac Infarction.
Balance Disorders	Balance Disorder, Ménère's Disease, Gait.

Stress/Anxiety-Related Disorders (F40-49)	Post-Traumatic Stress Disorder (PTSD), Trauma, Sexual Abuse, Refugee Trauma, Stress Management, Hypertension, Contamination Anxiety, Obsessive-Compulsive Disorder (OCD), Anxiety, Generalized Anxiety, Performance Anxiety,
Autism and Asperger's	Autism, Autistic Spectrum Disorder, Asperger's, Pervasive Developmental Disorder,
Other / Unspecified	Speech Impairment, Swallowing, Restless Leg Syndrome, HIV, Gastrointestinal Disorder, Functional Pregnancy Disturbances, Down Syndrome, Diabetes, Chronic Fatigue, Anosmia, Organic Cognitive Disorder, Premenstrual Syndrome, Unspecified Personality Disorders

Table 2: Mental Disorders and Phenomenon types and subtypes
Left Column: Indicating the Mental Disorder or Phenomena that the study was classified as addressing. **Right Column:** the subtypes of disorders or phenomena belonging to the main disorder. **Disorders without subtypes:** Fetal Alcohol Syndrome and Mental Retardation, Schizophrenia, Epilepsy, Mental and Motor Imagery

An attempt was made to classify sub-disorders into the larger mental, behavioural and neurodevelopmental disorders in ICD10 (WHO, 1992,p.91-228), such as the Affective Disorders (F30-F39) and the Stress-Related Disorders (F40-49). However, ADHD was for emphasis separated from the usual categorization into behavioural and emotional disorders with onset usually occurring in childhood and adolescence (F90-98). Study articles addressing multiple disorders (e.g. Comorbid Insomnia with Affective Disorder) and where participants fulfilled both diagnostic criteria, were counted for each disorder (ibid.). The type of article such as "Research Study", "Book", "Review", "Methods" article sample size (N) in the case of a "Research Study", information on whether the study featured a control group (between-group or crossover design). For inclusion in the subset of studies, the screened articles had to report on a research study using neurofeedback compared against a control or placebo group (including those that compared neurofeedback to a pharmacological alternative) and using more than 9 subjects in total.

3.2.3 Results

From the pool of 1082 screened articles, 771 investigated the effectiveness of neurofeedback for training or treating a specific mental function or dysfunction (See **Figure 5** top pane). To address the annual frequency of controlled studies from the 771 articles were a subset was created conditioned on being a "Research Study" (581) that utilized a controlled design (254), dealing with EEG neurofeedback and having a sample size N >= 9 (227) (**Figure 5** bottom pane). For a detailed overview of the reviewed articles, the database is made freely available[1].

[1]The Database is available at the following webpage: (https://osf.io/vuj7z/).

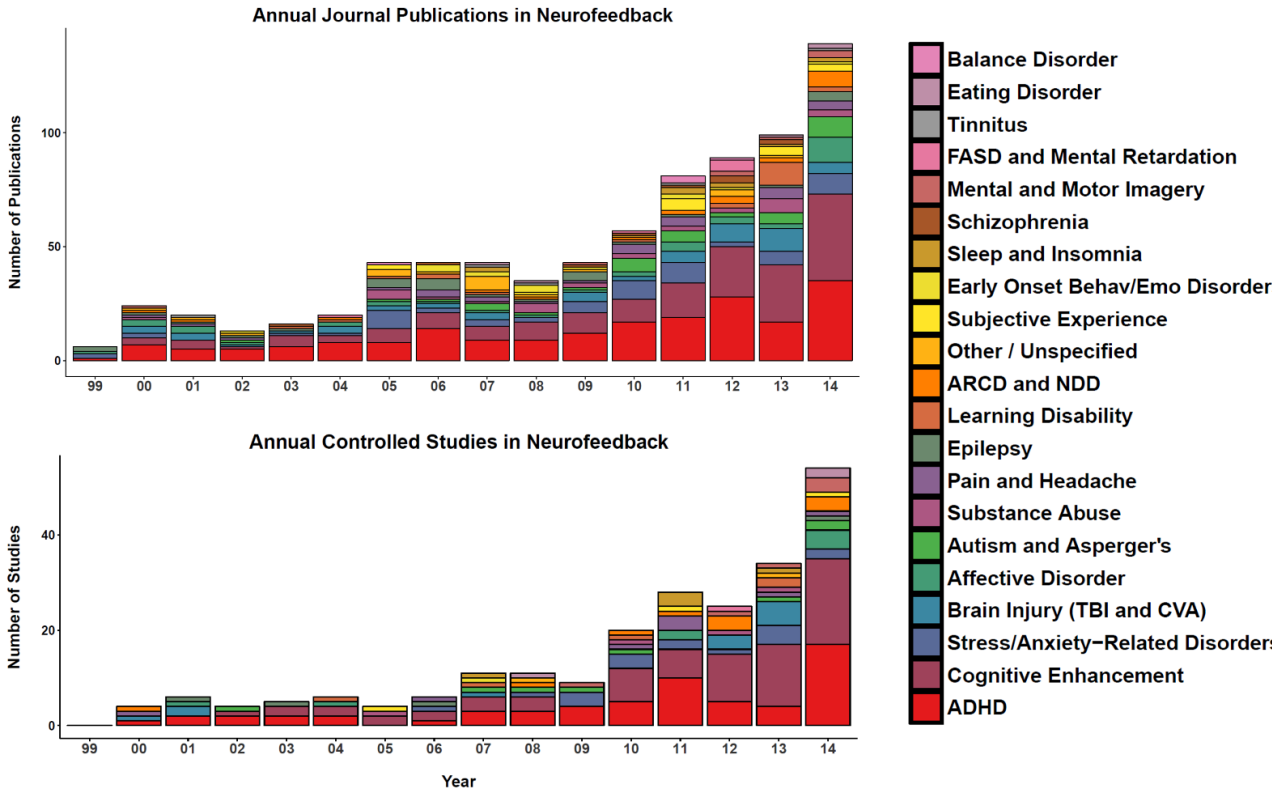

Figure 5. Annual Journal Publications & Controlled Studies in Neurofeedback.
Top Pane: Shows a stacked bar plot of the acquired articles (n) for each year from 1999-2015 along with the specific disorder/mental phenomena in question. **Bottom Pane**: depicts the same time period in the subset of controlled neurofeedback studies (n) with N > 9. Colors for disorders are organized by the inverse of the total publications. FASD: Fetal Alcohol Syndrome, ARCD and NDD: Age-Related Cognitive Decline and Neurodegenerative Diseases, TBI and CVA: Traumatic Brain Injury and Cerebrovascular Accident, ADHD: Attention Deficit Hyperactivity Disorder.

These results show that articles on neurofeedback for ADHD are the most frequently published throughout the years, with Cognitive Enhancement following it. Moreover, neurofeedback research is targeting disorders such as Stress/Anxiety-Related Disorders, Brain Injuries and Substance Abuse to a larger degree than a decade ago. Overall, the pattern shows that there is a nearly three-fold increase in articles over the past 10 years with 43 in 2005 compared to 139 in 2014. The controlled studies also show an increase with an average of 4.3 controlled studies in the initial 99-06 years whereas 2014 alone featured 54 studies.

3.2.4 Systematic Review Findings

Collectively, these data provide evidence that research within neurofeedback is increasing along with the quality of the studies performed in the form of utilizing control groups and higher sample sizes. This could be due to several factors such as popularity, technological innovation, inexpensiveness or scientific increases in scientific publications (Angelakis, 2012,p.1). Presently, there exists a controversy regarding the use of Google Scholar (GS) as an isolated tool for systematic reviews (Bramer et al., 2013,p.1; Giustini and Boulos, 2013,p.1). Moving forward, future systematic reviews

would benefit from using a multitude of databases including Google Scholar, MEDLINE, Cochrane Library, PubMed and Ovid/EMBASE to avoid the limitations of searching with a single database. Future research could also look into the differing types of control such as passive, sham, quasi-active and active control group and the effect-sizes for neurofeedback in those instances. Furthermore, an investigation of the different metrics used in the neurofeedback protocol, such as frequency power ratios, hemispheric synchrony, and phase-lag could be taken into account. This could ultimately lead to a comprehensive review and meta-analysis for neurofeedback within the different mental functions and dysfunctions. The review is both preliminary and superficial in nature, as primarily only reading of abstracts was performed; it is however comprehensive in the number of articles reviewed. Future systematic reviews, bibliometric- and meta-analyses are needed for the investigation into the usefulness of neurofeedback as a therapeutical option.

3.3 Models of the Effects of Neurofeedback

3.3.1 Conceptual confusion

> *The confusion and barrenness of psychology is not to be explained by calling it a 'young science'; its state is not comparable with that of physics, for instance in its beginnings…*
>
> *For in psychology there are experimental methods and conceptual confusion.*
>
> -Wittgenstein, 1953, Philosophical Investigations, Sec. II, p. 232

The famous statement by Wittgenstein written over 50 years ago is acknowledged as forecasting the present psychological discipline (Hutto, 2009,p.1-15). It can be argued that the conceptual confusion is especially applicable to a conceptual understanding of neurofeedback. Without a clear theoretical backdrop, it is often difficult to create a body of knowledge that will constructively foster the deduction of empirical testable hypotheses to either support or refute components of that theory (Hobfoll, 1989,p.1). As stated by Kurt Lewin, "There is nothing as practical as a good theory" (ibid.). Thus, a certain balance between empirical data and conceptual theory is required, as concepts without facts are hollow, so one could equally argue that facts without concepts are meaningless (Novella, 2016). This section presents two prototypical models of explanations as to the working mechanism of neurofeedback (Gevensleben et al., 2014a,p.1-9; Nash, 2005,p.2). These can briefly be described as the "conditioning-and-repair" and the "skill-acquisition" model of neurofeedback effects. As will be discussed below, these competing models have different explanatory power, and posit different

arguments regarding the potential of neurofeedback for informing about mind-brain causal relationships.

Several authors argue that an adequate conceptualization and explanatory model of neurofeedback has generally eluded the investigation of the method (Gevensleben et al., 2014,p.2; Kirlangic and Ivanova, 2003,p.1; Meichenbaum, 1976,p.1-12; Nash, 2005,p.2; Ninaus et al., 2013,p.1-9; Strehl, 2014,p.1-6; Witte et al., 2013,p1-6; Wood et al., 2014a,p.1-3; Brenninkmeijer, 2013,p.1-18). The diverging explanatory models carry with them different assumptions regarding the etiology of the mental disorder and the underlying causality of neuronal and psychological mechanisms of neurofeedback. In addition the models hold different positions on the moderating and mediating factors of the neurofeedback training (e.g., what is the outcome of neurofeedback and how does it transfer to a real life situations?). Furthermore, different opinions may change the interpretation of the clinical efficacy of neurofeedback (ibid.). As an example, Arns and Strehl (2013) and Sonuga-Barke et al (2013) both review the literature on neurofeedback as a treatment option for ADHD using different explanatory models coming to a favourable and dismissive evaluation of neurofeedback respectively (Arns and Strehl, 2013,p.1-2; Sonuga-Barke et al., 2013,p.1-4; Gevensleben et al., 2014,p.1-2). The present section of the thesis will present the "conditioning-and-repair" and the "skill-acquisition" model of neurofeedback. Reflecting on their explanatory power, the extent to which the models show that neurofeedback informs of mind-brain causal relationships will be illustrated. Concluding the chapter, the models will be applied to a hypothesis regarding a future neurofeedback study on language learning abilities.

3.3.2 The conditioning-and-repair model

The "conditioning-and-repair" model represents the traditional approach according to which neurofeedback effects mind-brain causal relationships (Gevensleben et al., 2014b,p.1-9; Nash, 2005,p.2). The fundamental assumption of the model is that the etiology of the mental disorder is due to an underlying neuronal deficit and that the mode of action for neurofeedback is to "repair" the deficit. The model would predict that brain state is highly specific to the mental disorder and that only protocol-specific neurofeedback for the given brain state can and for the brain state to strongly correlate to mental improvement. The model assumes, inter alia, a classical biomedical model and a strict causal relationship from brain to mind. One of the core mechanisms underlying both etiology and alleviation of the symptoms according to the conditioning-and-repair model is that an underlying brain "trait" is causing the maladaptive mental disorder unidirectionally. The model holds that the

brain's electrophysiological and metabolic traits correspond to the individual's mental state and that neurofeedback provides stable change of that trait.

"Monkeys meditate for marshmallows" was the headline in the NewScientist report by Philippens and Vanwersch, who, inspired by Stermans initial findings, had trained monkeys to increase their sensorimotor rhythm and given them marshmallows as rewards (Strehl, 2014,p.1). The argument, being in resonance with the conditioning-and-repair model, is that if animals can learn to do it without explicit instruction, the process of neurofeedback largely involves implicit (unconscious and automatic) processes. According to the law of parsimony it would be unnecessary to postulate higher mental and psychological functions to the processes of neurofeedback (Morgan, 1894,p.53 from Lindeløv, 2015,p.11; Fultz, 2009,p.1-3). In this conditioning-and-repair view of neurofeedback the processes is compared to motor learning and no higher order-cognitive processes are necessarily involved (Gevensleben et al., 2014a,p.4-7). The view reflects what can be termed a neo-behaviourist[2] stance of locating the specific brain abnormality and applying operant conditioning until the brain's "behaviour" is restored to normal, followed by the receding of the mental disorder. According to the "conditioning-and-repair" model, transfer should occur automatically: "[…] when brain behaviour is normalized, the child's behaviour follows"(Steinberg and Othmer, 2004,p.35 from Gevensleben et al., 2014,p.3). The transfer or generalization of the effect to daily life happens by itself without a necessary context dependence between the training and the use of the training. In this regard, the treatment is similar to pharmacology, and explanations of neurofeedback using this model in fact often attributes its causal efficacy in relieving mental disorders to similar mechanisms as psychopharmacology (Gevensleben et al., 2014,p.2-7; Niv, 2013,p.1).

In terms of evidence supporting the model, there have been instances of protocol-specific effects of neurofeedback such as lasting neurophysiological and improved behavioural effects after training of the particular neuronal dysfunction (Monastra et al., 2001,p.1-8) and functional specificity (i.e., double dissociation) of trained spectral bands (Gruzelier, 2014b,p.1-3). There is furthermore evidence that suggests that baseline EEG activity is related to outcome, supporting the notion that "worst cases" improve the most, and that a more pronounced initial neural deficit has a larger potential for improvement on a neurophysiological and psychological level (Gevensleben et al., 2014,p.6, 2009,p.1). In general, the evidence for brain trait in the case of EEG is lacking, as the physiological profile appears to be state-dependent (Gevensleben et al., 2014,p.6; Ros et al., 2014,p.4). For

[2] Neo-behaviourism because a strict behaviourist interpretation would present a conundrum, since neurofeedback relies on neural components underlying behaviour moving the subject matter into the brain rather than on external factors of stimulus and response which behaviourism typically has as its focus (Bechtel, 1994,p.2; Fultz, 2009,p.1-3, 2002,p.1).

example, the oscillatory profiles of ADHD and healthy subjects manifest themselves differently, if at all, depending on the attentional task administered (ibid.). It may be the case that stable EEG changes are only present after abundant training, as it is seen with long-term practitioners of meditation (10.000-50.000h) who show enhanced baseline gamma activity (Gevensleben et al., 2014,p.6;Lutz et al., 2004,p.1). The conditioning and repair model can thus be summarized as targeting a specific underlying neuronal deficit, which is repaired through protocol-specific operant conditioning of the brain assuming a strict unidirectional causal relationship from brain to mind.

3.3.3 The skill-acquisition model

The "skill-acquisition model" also known as the "neuroflexibility" model invokes homeostatic mechanisms and flexibility of nervous system as the explanatory mechanism of neurofeedback (Buckelew et al., 2013,p.1, 2009,p.1; Gevensleben et al., 2014,p.1-9; Nash, 2005,p.2). In contrast to the "conditioning-and-repair model", in this alternative model, neurofeedback doesn't just recondition a specific neuronal deficit, but teaches the individual the skill of avoiding "being stuck" in *any* maladaptive mind-brain state. In fact, for achieving a therapeutic effect with neurofeedback, some authors make the analogy of "rocking" the brain electrophysiology back and forth as one would "rock" a stuck automobile to get out of a snowdrift or mud (Clarke, 2014,p.14). It reflects a certain skill of being able to adjust cortical activation consistent with environmental demands, or "neuroflexibility" (Buckelew et al., 2013,p.1, 2009,p.1; Gevensleben et al., 2014,p.1-9; Nash, 2005,p.2). The "skill-acquisition model" is based on the biopsychosocial model and thus takes into account the psychological factors in increasing the likelihood of transferring the skill to other instances (ibid.). Thus, it aligns with a view on mind-brain causality where cognitive-behavioural and neurophysiological levels represent two sides of the same coin, and the treatment is targeted from both directions (Gevensleben et al., 2014,p.1-9; Kurthen, 2010,p.3-11; Lilienfeld, 2007,p.3). The causal explanatory account is thus one that acknowledges the psychological level of explanation in addition to the neurobiological and sees the effects of the training as moderated and mediated by cognitive factors (Meichenbaum, 1976,p.1-3). In other words, the factors such as the individuals perceptions, attributions, appraisals or his or her internal dialogue about the ability to control the physiological response(ibid.). The "skill-acquisition-model" emphasizes that the mechanism of learning in neurofeedback is controlled, effortful and enhanced through explicit understanding. The model would predict that generalization of the skill to real-life situations would require voluntary effort to achieve (ibid.). Supporting evidence for the skill-acquisition model are instances where neurofeedback targeting specific frequencies results in changes during training, or results in behavioural improvement but not in changes of EEG characteristics (Gevensleben et al., 2014,p.6;

Santarpia, 2008,p.1). One of the strongest pieces of evidence that substantiates the notion of neuroflexibility is provided by Kluetsch et al., (2014), who down-regulated alpha brain waves as opposed to traditional upregulation in a group of individuals diagnosed with PTSD (Kluetsch et al., 2014,p.1-11). The authors found that during training, the alpha became desynchronized but was followed by a significant "rebound" effect of increasing alpha which was positively correlated with subjective ratings of calmness. The neuroflexibility model is often applied in neurofeedback research into insomnia and sleep related problems, where the hypothesis is that sleep disturbances arise due to the an inability to transition between sleep stages (Arns and Kenemans, 2014,p.4-11; Buckelew et al., 2013,p.1, 2009,p.1). A notable challenge to the rivalling conditioning-and-repair model is the generally low consensus as to how to reinforce specific EEG frequencies. Johnson and Bodenhamer-Davis (2009) confronted 13 neurofeedback practitioners (i.e., neurotherapists) with sample clinical cases where the practitioners had to indicate the treatment they would recommend for the given case (Johnson and Bodenhamer-Davis, 2009,p.1). The respondents generally agreed on which brain regions and brain frequencies to train but diverged on their opinions on how to reinforce (down/up-regulate) according to theoretical rationales. This is all to state that neurofeedback might not work by changing towards something specific, but instead through change *per se* and learning to self-regulate this skill in other situations (Gevensleben et al., 2014,p.1-9; Ros et al., 2014,p.1-16). Several authors conceptualize the working mechanism of neurofeedback as "nudging" the brain in the right direction and as such dovetailing with the skill-acquisition model (Baehr, 2009,p.2; Clarke, 2014,p.14; Hammond, 2007,p.2; Larsen et al., 2006,p.3; Ochs, 2006,p.27). The assumption is that neurofeedback facilitates learning of self-regulation in small incremental steps, which the brain then generalizes to use in all self-regulation of its internal dynamics (ibid.). A counter-argument from a conditioning-and-repair model point of view could be the concept of neuronal hydraulics, which states that changing the system without holding sufficient variables equal allows the system to find other outlets of expressing dysregulation (Collura, 1990,p.4). The way of conceptualizing neurofeedback as "nudging" the brain in the right direction seems to coincide with the description of transcranial direct current stimulation (tDCS) (Perry and Lupyan, 2014,p.2; Reinhart and Woodman, 2015,p.2; Sanders, 2014,p.2) Using tDCS allows therapists and researchers to manipulate the membrane potential of neurons which doesn't lead to action potentials directly, but changes the probability of action potentials. As such, neurofeedback and tDCS could be collectively referred to as neurotherapeutic techniques that do not directly cause a particular brain state but rather facilitate or moderate the brain's own ability to achieve the state in question.

Following the prediction of the "skill-acquisition model", several findings support the notion that neurofeedback learning may be mediated and modulated by neuropsychological dispositions prior to training and that these may influence how successfully neurofeedback is learned (Konareva, 2006,p.1, 2005,p.1). Variables like outcome expectation, self-efficacy, achievement, motivation, or locus of control are assumed to be basic modulators of treatment (Borkovec and Sibrava, 2005,p.1; Gevensleben et al., 2012,p.1-7). Keeping in mind that changes of cognitive-behavioural and social variables, are also reflected in changes of the underlying neural networks the "skill-acquisition model" sees these former cognitive factors as equally important to consider when discussing the effect of neurofeedback (ibid.). It has been shown that motivation and attitude towards mastery of the skill correlate positively with increased neurofeedback performance (Nijboer et al., 2010). It has also been shown that attempting to regulate brain activity increases neural activity in networks involved in cognitive control (Ninaus et al., 2013). In addition, neurophysiological measures of executive function have also been shown to significantly predict performance (Doppelmayr and Weber, 2011,p.1-12; Enriquez-Geppert et al., 2014,p.1-4; Ferreira and Dias, 2012,p.1; Knezevic et al., 2010,p.1; Strehl et al., 2005,p.1-6; Siniatchkin et al., 2000,p.1). The stance of the "skill-acquisition model" is that neurofeedback may ameliorate not only the particular neural dysfunction of interest but also encompasses mechanisms on the cognitive-behavioural and social level, which are reflected in underlying neural networks. In other words, neurofeedback promotes reinforcement of compensatory mechanisms on higher interacting levels.

Evidence suggesting that neurofeedback is similar to learning a skill through explicit and controlled cognitive processing lies for example in the original findings by Kamiya (1962,1969) replicated by Frederick (2012), showing that explicit discrimination of alpha brainwaves generalized to voluntary control (Kamiya, 1962,p.6; Kamiya, 1969,p.1-11; Frederick, 2012,p.1-21).This indicates that explicit awareness and discriminatory ability of one's own brain state is somehow fundamentally liked to self-regulation of it (ibid.). The "skill-acquisition-model" does not assume that generalization is ensured automatically (e.g., via an "EEG trait"), but rather generalization is relying on context-dependence with a real-life situation. This suggests a more active role for the participant in transferring self-regulatory strategies in order to induce an "EEG state", learned during neurofeedback, in another context. Recently, the field of neurofeedback research has opened up to incorporating immersive 3D virtual-reality (VR) technology and its potential to make learning more easily transferrable to a situation similar to the one depicted in the virtual environment (Allanson and Mariani,p.1, 1999; Cavazza et al., 2014a,p.1-7, 2014b,p.1; Elgendi et al., 2011,p.1; Hinterberger, 2011,p.1). Similar to exposure therapy, these approaches could change the underlying physiology in

context-specific instances that are characterised by mental disorder (Cavazza et al., 2014b,p.1-6; McNally, 2007,p.5). As an example, Gruzelier et al., (2010) randomized actors to an experimental group presented with an immersive VR environment mimicking a theatre auditorium combined with neurofeedback or to a conventional neurofeedback group (Gruzelier et al., 2010,p.1-5). In a subsequent acting performance, participants in the immersive VR group reported consistently higher scores on the flow state scale and were rated higher by blinded expert raters compared to the traditional neurofeedback group. This line of evidence dovetails with the "skill-acquistion-model" as it points to the context-dependence during the acquisition of the self-regulatory skill of neurofeedback for the ability to transfer it to a new situation.

In summery the "skill-acquisition-model" points to change *per se* and acquisition of the skill in response to change as the driving causal model of the effect of neurofeedback. The model underlines the necessity of incorporating and understanding cognitive-behavioural factors in line with a biopsychosocial conceptualization of mental disorders and treatment. It further predicts neurofeedback to be enhanced by explicit strategies and stresses the acquisition of self-regulation of brain activity to be context-specific in order to generalize to real-life instances.

3.3.4 Evaluating the models

The "conditioning-and-repair" model and the "skill-acquisition" model were presented with the intent to contrast two differing approaches to conceptualize neurofeedback (Gevensleben et al., 2014,p.4). Their assumptions and narrative for an explanation of the rationale and outcome of neurofeedback is also reminiscent of the biomedical and biopsychosocial models from which they descend (Engel, 1977,p.1-7; Gevensleben et al., 2014,p.2-4; Simonsen and Mohl, 2010,p.36-45). It is intrinsic to this discussion that the adequacies and the explanatory power of these models allow inferences regarding mind-brain causal relationships, in particular regarding the possible etiology and the underlying reason of a particular mental disorder. In short, the two models assume different causal explanations how neurofeedback alters the mind-brain relationship, where the "conditioning-and-repair-model" sees specific neuronal deficits as the focal point of neurofeedback, the "skill-acquisition-model" predicts that it is the change *per se* that makes neurofeedback therapeutically effective. The question is whether: 1) neurofeedback tailored to a specific neuronal deficit corresponding to a mental disorder can repair the disorder through implicit automatic means as predicted by the conditioning-and-repair model. As contrasted with 2) neuroflexiblity above anything is related to mental disorder and neurofeedback provides the control to effortlessly acquire the skill to self-regulate in comparable instances. In facilitating an understanding of how hypotheses are generated within neurofeedback research and the predictions heralded by "conditioning-and-repair" and "skill-acquisition" models,

the following section provides a presentation of an on-going project on the electrophysiological profiles of language learning with the intent to provide neurofeedback in a follow-up study.

3.3 Specific Hypothesis: Enhancement of foreign language learning ability

3.3.1 Theoretical Background

As was shown in the systematic review, a large avenue of research within neurofeedback focuses on its potential for ADHD and cognitive enhancement. On the basis of this, one could argue that such treatment options for these mental disorders could be valuable for learning disorders (Cantor and Evans, 2013,p.2). Converging evidence shows that neurofeedback is beneficial in case of disorders such as ADHD, dyslexia and reading disability (Breteler et al., 2010,p.1; Monastra et al., 2005,p.1; Nazari and Mosanezhad, 2012,p.1). There is evidence that suggests that neurofeedback can improve cognitive performance, mood and have other salutogenic effects in healthy individuals (J. Gruzelier, 2014a,p.1-14, 2014b,p.1, 2014c,p.1, 2014d,p.1-3). Furthermore, research indicates that neurofeedback may be able to enhance general mental functions such as working memory and attention (Egner and Gruzelier, 2001,p.1-3; Vernon et al., 2003,p.1-9). No research to date however has examined whether neurofeedback can enhance foreign language learning abilities (Kratschmer et al., 2012,p.1).

3.3.2 Paradigm

To provide the necessary justification to administer neurofeedback training for the enhancement of language learning, the present author sought to, in collaboration with co-authors, empirically investigate the EEG correlates of language learning efficiency (Kratschmer, Leminen, Kvamme and Shtyrov, in prep.). In particular, we wanted to investigate whether learners who are efficient in acquiring foreign vocabulary (fast learners) versus those that are less efficient (slow learners) show different neural activity during basic phonological processing. Prior behavioral experiments have found large variability of Danish individuals in memorizing vocabulary of a foreign language such as Italian (Kratschmer et al., 2006,p.1-16). Furthermore, Danish listeners have noteworthy difficulties discriminating between syllables containing an palatalized lateral consonant which is part of the Italian, but not of the Danish sound system (*gli*,/ʎi/) and syllables containing laterals presents on both sounds systems (*li*,/li/; ibid.). From a series of six hard-to-distinguish Italian phoneme contrasts not present in their native language, Danish listeners achieved at or near ceiling effect discrimination of all contrasts except for /li/ - /ʎi/ (ibid.).

To investigate upon the neural correlates of this discriminatory ability, the mismatch negative (MMN) paradigm was utilized. The basic methodology is a measurement of electrophysiological event-related potential (ERP) responses, that are time-locked to the specific event of frequent or infrequent (i.e., a "deviant") acoustic stimuli (Pulvermüller and Shtyrov, 2006,p.1-19). The MMN paradigm is able to reflect language processing taking place irrespective of attention and thus represents automatic phonological processes, in this case for discriminating the syllables /ʎi/) and /li/. Participants who are unable to discriminate a stimulus will often show a minimal MMN electrophysiological response whereas participants who learn to discriminate the critical sound, have their MMN reliably increased (ibid.). The electrophysiological MMN response is often found to be the strongest in the left perisylvian neuronal assemblies linking together perceptual information stored in the superior-temporal cortex and articulatory action-related information in the inferior frontal cortex (Pulvermüller and Shtyrov, 2006,p.7-19; Pulvermüller, 2001,p.1-6). Thus, we hypothesized a differentiation in neural phonological processing in the left-hemispheric as compared with right-hemispheric areas in learners who were efficient in an online rapid language learning paradigm versus those that were less efficient across the time course of the paradigm.

In the initial phase of the paradigm, healthy volunteers (n=24) performed a memorization round where a Danish word and an Italian word were paired. Subsequently, participants went through a recognition round, where they were presented with a Danish word followed by either an incongruent or congruent Italian word, to which participants had to indicate whether the pairing was correct based on the prior memorization round. As a third task, the participants were exposed to the Danish words as cues for articulating the adequate Italian words into a microphone from memory. These three steps (memorization, recognition and production) were repeated three times. Finally, participants were exposed to two blocks of the MMN paradigm which was based on the syllables /ʎi/and /li/.

3.3.2 Analysis

Based on the participants' performance in the third production round (i.e. their percent correct active memorization), a median split of the group was performed categorizing efficient (fast) learners from less efficient (slow) learners (**Figure 6**)

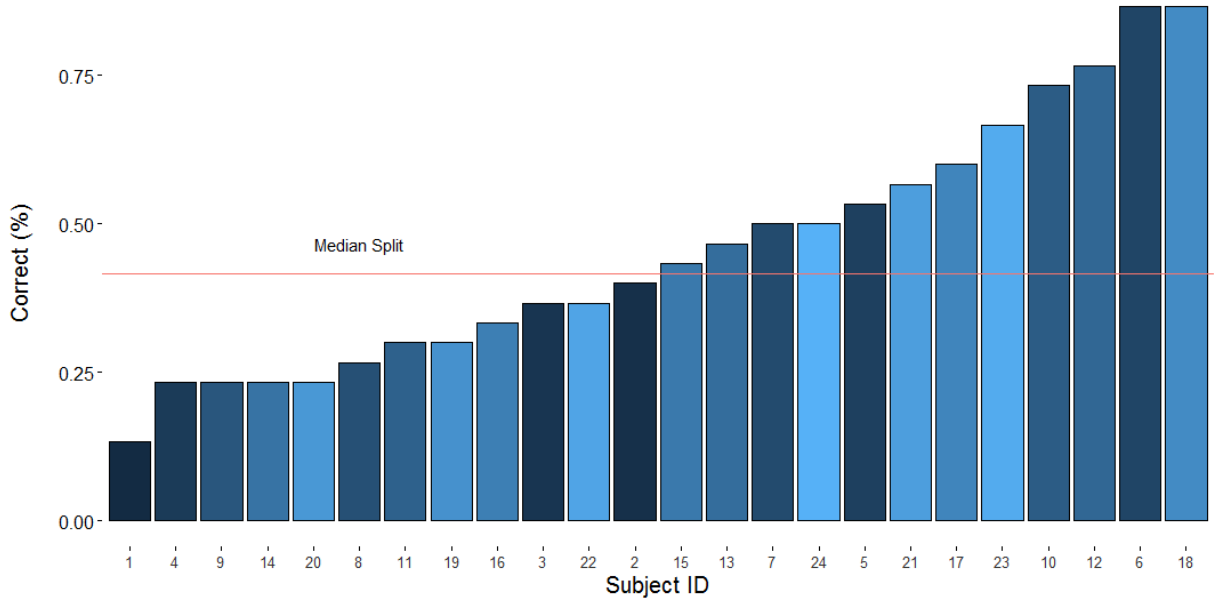

Figure 6: Individual Subjects Correct Percentage in the Production Round
The figure shows the individual subjects correct percentage in the final production round. The red line (-) represents the median split, that formed the 'slow' and 'fast' learners group.

The mean amplitude of the channels left frontal (LF) channels (FC1,FC3,F1,F3) and right frontal (RF) channels (FC2,FC4,F2,F4) were normalized and subtracted from each other to create a lateralization index (LI), where positive values represent asymmetrical left dominance (i.e., LI = (LF amplitude – RF amplitude) / (LF amplitude + RF amplitude)) (Teicher et al., 1997,p.6-8). The lateralization index serves the purpose of increasing the signal to noise ratio of the MMN paradigm in delineating the amplitude dominance of neural assemblies localized in the left-hemispheric regions over the right-hemisphere (Galin and Ellis, 1975,p.1-2; Parker et al., 2005,p.3; Shtyrov et al., 1999,p.1). We compared the lateralization index in a three-way mixed ANOVA with a between-subject factor of learning *Group* (slow, fast) and within-subject factor of *Condition* (/ʎi/, /li/) and *Experience* (1th block and 2nd block of MMN). Statistical analyses and plots were performed using R version (3.3.0) (R Core Team, 2014) with packages ggplot2 (v1.0.1).

3.3.3 Results

Twenty-four individuals (12 = fast, 12 = slow learners) participated in the study, where as expected, the condition factor was significant (F(1,22) = 4.7, p = 0.04, $\eta \frac{2}{G}$ = 0.044). In the critical evaluation of a three- way *Group* × *Condition* × *Experience*, a significant interaction emerged (F(1,22) = 5.8, p = 0.02, $\eta \frac{2}{G}$ = 0.052). Subsequent post-hoc ANOVA split by *Condition* and *Exposure* revealed in the "Gli" only condition a significant *Group* × *Exposure* interaction (F(1,22) = 5.4, p = 0.02, $\eta \frac{2}{G}$ =

0.095) and in the "End" only exposure level a significant *Group* × *Condition* interaction (F(1,22) = 5.5, p = 0.02, $\eta \frac{2}{G}$ = 0.080).

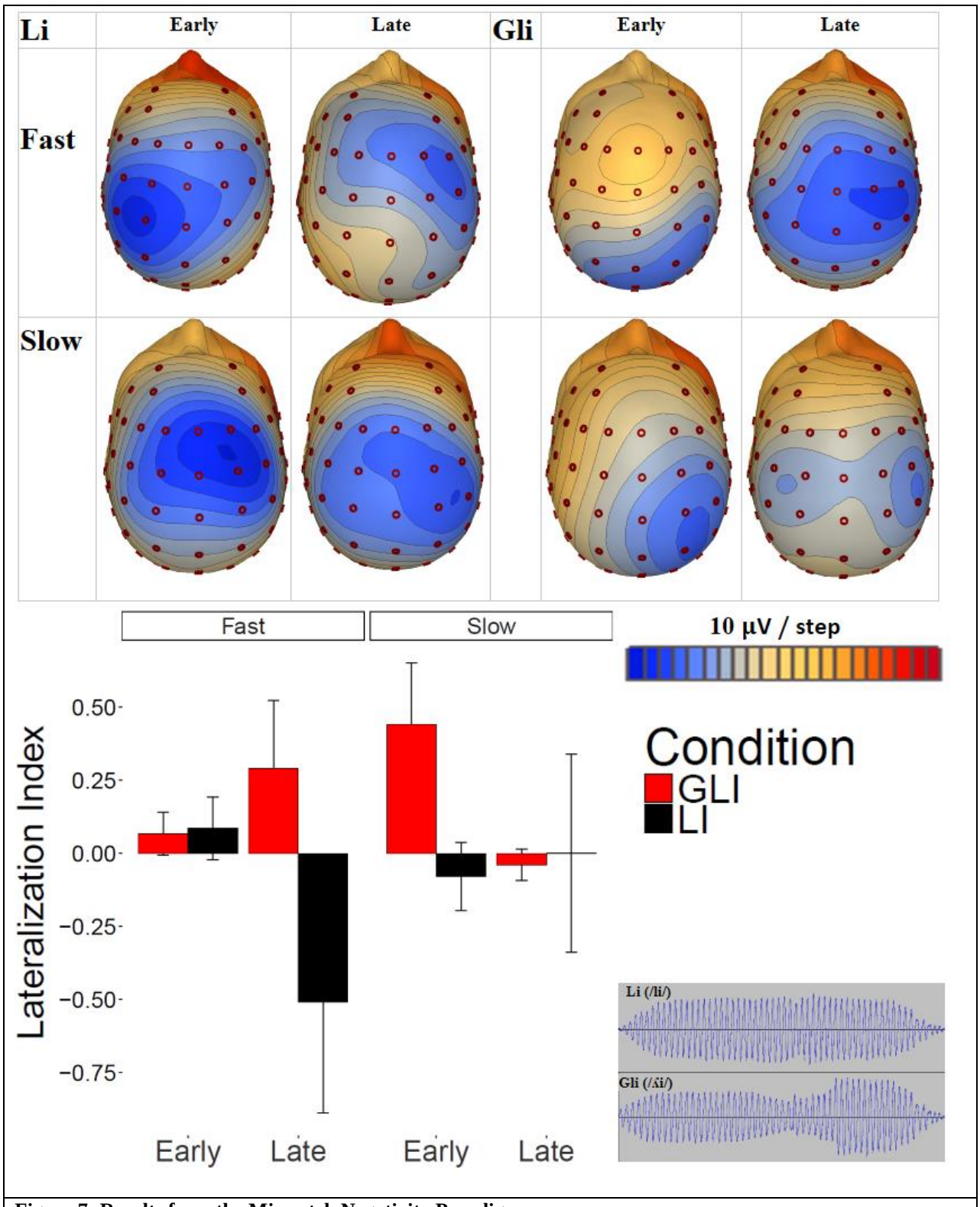

Figure 7: Results from the Mismatch Negativity Paradigm
Top Pane: shows the scalp recordings of the Group × Condition × Experience factors. µV : microvolt. **Bottom Left:** Shows a plot of the mean lateralization index for the different two groups across time. **Bottom Right:** shows the two sound waves of /li/ and /ʎi/.

3.3.4 Main Findings

In this study, using electroencephalography, we show that degrees of efficiency in foreign vocabulary learning correlates with different patterns of neural activity during phonological discriminatory processing. We show an interaction effect in the lateralization index for fast and slow learners in acquiring across experimental blocks the typical neural signatures associated with discriminatory ability. Descriptively, it appears that fast learners initially have no left-hemispheric dominance differences between the two syllables, whereas towards the end of the experiment, they do. Conversely, slow learners start out with an initial difference, which during the course of the experiment is lessened.

We can assume that during the course of the trials, some sort of automatic learning occurs for both groups in distinguishing /ʃi/ and /li/ (Pulvermüller and Shtyrov, 2006,p.1-4). The data at hand provides evidence that changes in left-hemispheric dominance between the two sounds occurs to a greater extent for faster than slower learners. However, at this point it is unclear why the two groups differentiate or even if it plays a role in their language learning ability in general. The present findings are preliminary in nature as the EEG analysis is as yet restricted to the MMN part of the experiment (Kratschmer, Leminen, Kvamme and Shtyrov in prep.). Although it is worth noting that the learning group status was based on the performance during the third production phase of the experiment (as vocabulary memorization the MMN phase resulted in no overt behavioral indication of language learning), yet was shown to correlate with different neurophysiological signatures for sound discrimination.

3.3.5 Future Directions for Neurofeedback

One hypothesis arising from the outcome of the experiment is whether the phonological processes serve a causal role in determining the memorization (and maybe also the recognition) of word pairs, which we used as a beacon for the categorization of our participants into fast and slow learners. The question is whether the degree of neural differentiation during phonological language processing is somehow functionally linked to foreign language learning efficiency. Admittedly, it is a non-trivial assumption, that the neural signatures observed here are linked to perceptual discrimination of phonemes, and with language learning efficiency in general. A demonstrated association between neural activity and cognitive processes cannot rule out that the neural activity is merely epiphenomenal to the cognitive function (Keizer et al., 2010,p.1-4). In order to rule this out, one has to manipulate the neural activity directly and investigate whether that influences the cognitive processes (ibid.). Here, applying the basic computational level model of neurofeedback that is based

on an observed association between a physiological and a mental function or dysfunction, an attempt to shift the activity would have to be performed in order to test such causal claims. Given that neurofeedback has shown efficacy with ADHD, dyslexia and reading disability, one could equally argue that neurofeedback might be beneficial for language learning efficiency (Breteler et al., 2010,p.1; Monastra et al., 2005,p.1; Nazari and Mosanezhad, 2012,p.1). Hence, the argument for performing neurofeedback to induce the neural signature characteristic of efficient language learners during a language learning task would be twofold: to discover if changes in brain state are truly causally related to a change in mental state and to investigate the possibility for providing a novel therapeutic option for learning disabilities.

In terms of evaluating the "conditioning-and-repair" and the "skill-acquisition" models it is possible to derive testable predictions from them in the context of neurofeedback to improve language learning, based on the models' characteristic assumptions regarding the particular mind-brain state (Gevensleben et al., 2014,p.8). For a "conditioning-and-repair" model would assume that it is the particular neuronal deficit in the ability to learn language, in this case the particular similarity of the lateralization index observed by the slow learners towards the end of the MMN experiment that relates to phonological processes and thus language learning. There is evidence to suggest, that brain activity related to cognitive events or ERPs such as is the case with the current discrimination of phonological stimulus are reciprocally influenced by the underlying brain oscillations (Başar et al., 1999,p.1-3). Thus ERPs are compound changes in amplitude superimposed on already-present so called event related oscillations (EROs) which as mentioned interconnect with all of the brain processes, included auditory ones (Başar et al., 2000,p.1-2; Pfurtscheller and Lopes, 1999,p.1-5; Doehnert et al., 2008,p.1-6; Strehl et al., 2006,p.1). Thus, it remains plausible that through the ability of neurofeedback to manipulate brain oscillations, could influence phonological discrimination of phonemes and perhaps, by extension, language processing in general (Doehnert et al., 2008,p.1-6; Strehl et al., 2006,p.1). On the other hand, the "skill-acquisition" model, would assume that slow learners had less neuroflexiblility in their response to the different conditions of /ʎi/ and /li/ and that this inflexibility is causally related to phonological processing and language learning in general. Here, further evaluation of the models could also aim to delineate their claim about the etiology of the mind-brain relationship and its relation to the specific mental dysfunction. Evidence validating either model, would by extension account for the extent of neurofeedback to investigate mind-brain causal relationships.

3.3.5 Study proposal for neurofeedback

An approach would be to apply neurofeedback after the discovery of the impaired learning with the therapeutic goal of ameliorating the impaired learning. The follow-up question, would be to distinguish the explanatory power of the models by applying neurofeedback in different groups with methodological approaches of either model. From an initial pool of volunteers, a pre-test of memorization and recognition would categorize participants into 'fast' and 'slow' learners and the subsequent study addresses whether neurofeedback of the 'slow' learners ameliorates their language learning performance. Here, the slow learners would be divided into different experimental groups the methodology of which align with the assumptions of the models.

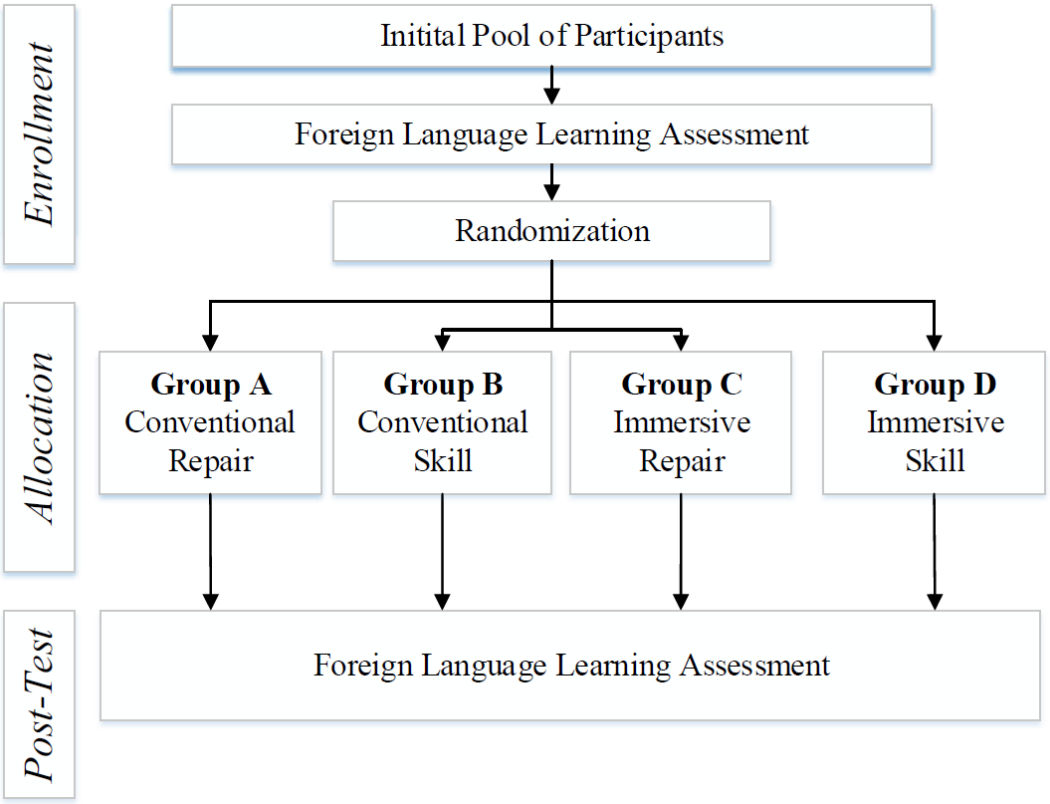

Figure 8: Flowchart depicting the passage of participants through the proposed study
Repair or skill refers to the methodology of the two models of training of up or down-regulating a particular neural measure, whereas conventional or immersive refers to the immersive quality of stimulus presented.

There are at least two ways of providing evidence for the models, by either testing whether it is change towards a specific mind-brain state or change *per se* that influences performance , or testing the different assumptions held by the models regarding transfer. For the first question, a "conditioning-and-repair model" methodology could be protocol-specific neurofeedback up-regulating of the particular EEG-frequency pattern seen by the fast learners, (i.e., heightened amplitude over the left frontal areas). This model would predict that the ability to increase amplitude in left frontal areas would correlate strongly with improve phonological processing and thus language learning abilities..

This would form the basis of Group A (a group receiving conventional neurofeedback for specific neuronal deficit). To validate the "skill-acquisition model" one could apply neurofeedback in the opposite direction (i.e., decrease amplitude in left frontal areas) in expectance of a "rebound effect" or potentially invert the contingencies midsession (Kluetsch et al., 2014,p.1-11; Siniatchkin et al., 2000,p.1-9). This would form the basis of Group B, (a group receiving neurofeedback in differencing directions throughout the training).

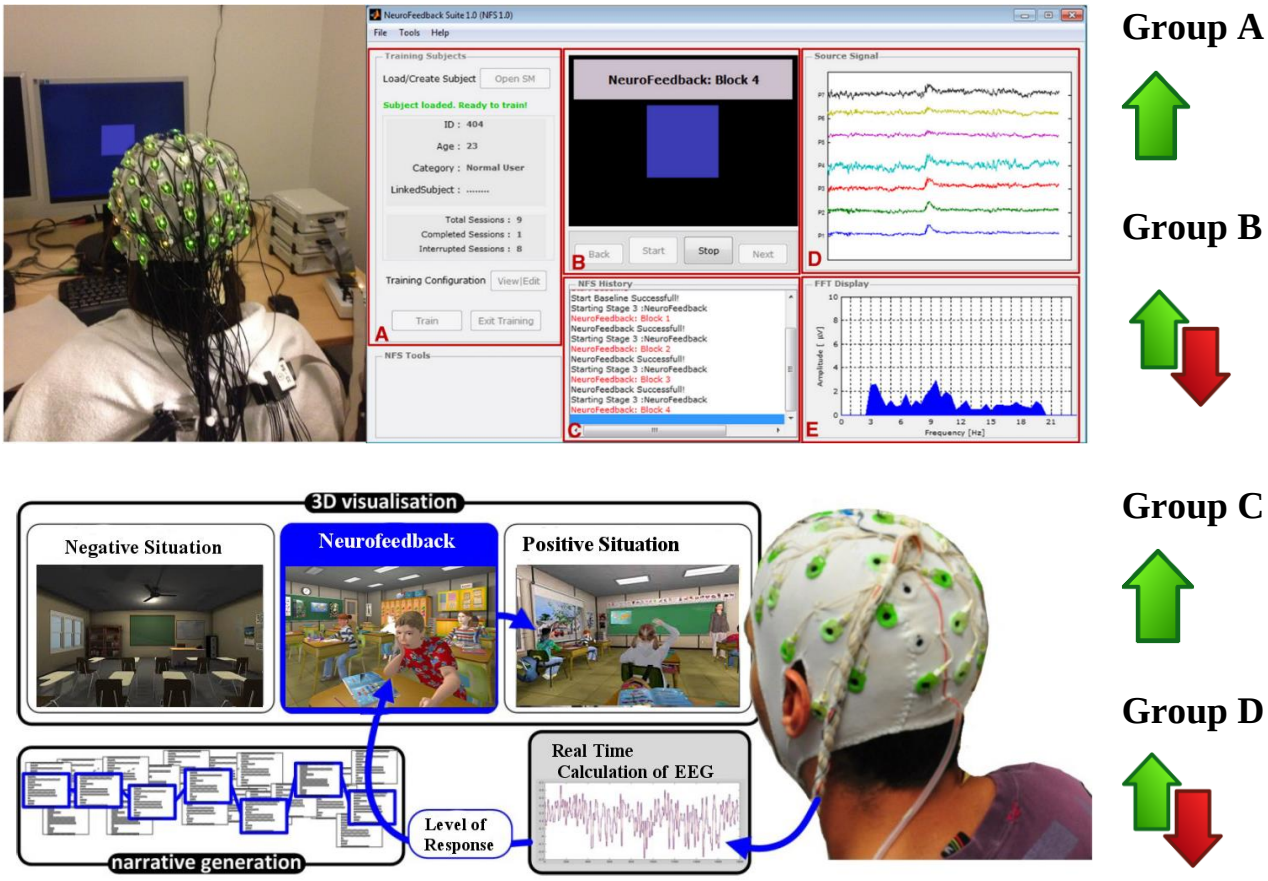

Figure 9. Top Left Pane shows an example of conventional neurofeedback paradigm training, where the colour of object contingent on a specific brain measure. **Bottom Left Pane** shows an example of immersive VR environment depicting a class room that is evolving dynamically contingent on the brain measure**. Right Colum** indicates the Group contingencies of Group A through D and their respective contingencies. A green arrow represents upregulation of the desired neural measure, whereas red represents downregulation.

The second question would aim at the models assumptions regarding transfer, as the "skill-acquisition model" holds that inducing context specific cues with the training would transfer the self-regulatory skill more readily. Here, one option would be to administer neurofeedback in conjunction with immersive VR depicting a classroom, thus creating context specific cues, which would be associated with the place where a follow-up language learning course would be situated. One group, Group C, would receive this immersive VR stimuli, with similar contingencies to brain measure as group A and whereas Group D would receive similar contingencies and group B. Group

A represent a hyperpolarized manifestation of methodology of "conditioning-and-repair" model and the prediction in terms of this model would be that other groups B through D perform similarly to Group A. The "skill-acquisition model" would hold that should other groups should outperform A and in particular group D, as it represents the ultimate manifestation of its methodology.

In this way, it is possible to evaluate whether neurofeedback of the specific brain activity could change the phonological processing or even other aspects of language acquisition in subsequent memorization and recognition rounds. Furthermore, this approach would be able to address the assumptions held by the "conditioning-and-repair" model or the "skill-acquisition" model. In the event that the results of the proposed study favor a "conditioning-and-repair" model a specific mind-brain relationship has been informed of, one that points to changing the brain state "towards" a specific state as leading to a larger degree of efficiency in terms of language learning. In contrast, should evidence favour a "skill-acquisition" model, it is rather the "change" in of brain state itself that is leads to a change in the language learning efficiency. Here, a particular mind-brain relationship is informed of through neurofeedback, one that reflects on the mental capacity to learn a new language. Further scientific causal accounts between brain states and that of efficiency of language learning would have to coherently trace the observed codetermining relationship between a mind state characterized by efficient language learning and brain measures indicated by the outcome of the study. Whether or not it is the account is truly "causal" will be discussed more extensively in subsequent chapters of the thesis. However, should the results of the proposed study show favors any of the two models of neurofeedback's effects a correspondence between the brain and the mind is able to be accounted for.

One may could draw the analogy that language is similar to a particular radio station, and that neurofeedback, by tuning the brain to it pick up on the specific phonotactic rules present in the internal structure of a foreign language, will improve the learning of the language in question (Kratschmer et al., 2012, 2016, p.1-6). In the event of evidence pointing to the "conditioning-and-repair" one could qualify that analogy by stating that it is the specific frequency that more readily leads to the observed mental state. In contrast the, should evidence favour the "skill-acquisition" model, the analogy would be that of changing the knob (i.e., change itself) on the radio as a larger determinant of a change in mental state.

The author of the thesis admits that currently, it is still speculative whether neurofeedback could improve efficiency of language learning, or if the data at hand provide a clear rationale for such future studies. However, if it was shown that neurofeedback holds the potential to improve language

learning abilities, such a novel treatment option would have immense value, both for future scientific inquiry and the therapeutic disciplines.

In short, this chapter has introduced the methodology of EEG along with the rationale for its use in neurofeedback research. In a systematic review of the past 15 years of neurofeedback literature, it was seen that neurofeedback is increasingly used for training and treatment of a wide spectrum of mental functions and dysfunctions. The question regarding neurofeedback's efficacy for treatment of mental disorders will be addressed in later chapters, which the current chapter leaves unaddressed. Lastly, based on an a prior association between a psychological construct and neurophysiological measurement a hypothesis for neurofeedback research was generated which holds a potential for neurofeedback to informing about mind-brain causal relationships.

4. Real-time Functional Magnetic Resonance Imaging

In facilitating the necessary backdrop for a discussion of neurofeedback causal explanatory potential, the following section reviews the basis of real-time functional magnetic resonance imaging (rtfMRI) neurofeedback. The review provides the basis of the measurement of fMRI, as well as noteworthy features of rtfMRI neurofeedback used in later chapters; (i) changing dependent variables to brain measurements, (ii) investigating multiple neural substrates (iii) creation of exogenously controlled loop paradigms.

4.1 The Basis of rtfMRI Neurofeedback

In the early 1990s, it was discovered that one could measure the blood oxygenation level-dependent (BOLD) contrast related to neural activity in the brain, which provides the basis of functional magnetic resonance imaging (fMRI) (Brühl, 2015,p.1-5; Ogawa and Lee, 1990,p.1-2). The BOLD signal is present due to the automatic increase in oxygen consumption in brain areas that increase activity and due to the differential magnetization of oxygenated compared to deoxygenated blood. The signal change is relatively weak, around 0.5-1.5 % compared to baseline and thus, fMRI studies utilize repeated stimulation reliable identify signal changes related to experimental stimuli amongst unsystematic variations in the signal (e.g. fluctuations not related to the stimuli) (ibid.). Moreover, a typical fMRI study will often rely on contrastive analysis, whereby images of this functional brain activity would be acquired when a subject performed a "control" condition (such as receiving non-

painful stimuli) and subtracted with the "active" condition (Amaro and Barker, 2006,p.4). Conventionally, this type of analysis would take researchers days to complete (deCharms, 2007,p.2). Now, with real-time fMRI (rtfMRI), that process has been reduced to seconds (ibid.). A common definition of rtfMRI is thus any process that uses information from a MRI scanner where the analysis and display of the fMRI data keep pace with data acquisition (Sulzer et al., 2013,p.2). Therefore, a hallmark of rtfMRI is its ability to be used for neurofeedback.

Compared to EEG, rtfMRI neurofeedback displays several strengths such as a higher spatial resolution while being able to cover the whole brain including sub-cortical brain structures. Contrary to other intervention techniques such as transcranial magnetic or deep brain stimulation, that apply stimulation to the brain, rtfMRI is a non-invasive method for inducing a particular brain activity (Pinel, 2011,p.106-250; Sulzer et al., 2013,p.6).

4.2 Changing the dependent variable

The usually fMRI experiments study brain activity as the dependent variable (DV) of an independent experimental manipulation, while in rtfMRI the brain activity has become the independent (IV). It can thus serve as important tool to guide and drive the experiment (ibid.). As a consequence it has been argued that rtfMRI neurofeedback has the capacity to go beyond mere correlation and address questions of causality between brain and behavior, thus representing a valuable tool for neuroscientific inquiry (Sulzer et al., 2013,p.6). Taking one of the iconic rtfMRI studies as an example, deCharms et al., (2005) showed that through self-regulation of the BOLD response in the anterior cingulate cortex (ACC) participants could reduce their own pain perception. (deCharms et al., 2005,p.1-6). It's important to recognize that neural activity associated with chronic pain is a vast matrix of several brainstem, thalamic and cortical networks (Petrovic and Ingvar, 2002,p.1; Peyron et al., 2004,p.1, 2000,p.1). However, functional imaging studies seemed to indicate a double dissociation, whereby only the location and discrimination of pain was associated with certain thalamic, somatosensory and insular regions whereas only the emotional and attentional concomitants of pain sensation was associated with increased activity in the ACC. As a consequence, when subjects were suggested to perceive the noxious stimuli as unpleasant ACC activity seemed to increase as compared with when participants were asked to perceive it as less unpleasant (ibid.). The evidence is still only indicative of an association as it is not clear at this point whether the relationship is a causal one (deCharms, 2007,p.5; Keizer et al., 2010,p.2; Van Bockstaele et al., 2014,p.3-28). One causal hypothesis could be that ACC activity causes the change in perceived pain and another view would state that ACC activity is merely a byproduct or "epiphenomena" of the change in pain perception (ibid.).

With the advent of rtfMRI, deCharms and colleagues (2005) were able to provide self-regulation of the ACC region and see its effect on perceived levels of pain (deCharms et al., 2005,p.1-6). Potential confounding variables could be reduced by applying a control group, such as either without feedback, sham feedback, or feedback yoked from another subject or brain region. The researchers were able to feedback the activity of the ACC to patients suffering from chronic pain while they were in the MRI scanner, enabling them to self-regulate their brain activation. The result was a reduction in perception of pain, while in control groups receiving no feedback, sham feedback or yoked feedback the corresponding reduction in pain perception was absent (ibid.). In comparison to the previous where unpleasant pain perception was the IV that was manipulated through hypnosis, with an examination of its effect on brain activity as the DV, in the case deCharms et al., (2005) the variables have been changed, such that brain activity is now the IV and perception the DV (deCharms et al., 2005,p.1-5; Peyron et al., 2000,p.1)

The argument that one can infer causality between activity in the ACC and perception of pain will discussed in subsequent chapters. (**Table 3)** provides a short overview of studies that applied a similar region of interest (ROI) approach, which illuminate how a given cognitive function or disorder can be regulated through rtfMRI-neurofeedback of an anatomical region. The overview is not comprehensive but aims to demonstrate the potential of rtfMRI-neurofeedback for regulation of a multitude of motor, sensory and supra-modal functions along with addiction and mental disorders.

Function / Disorder	**Study**	**Brain Region**	**↑/↓**	**Outcome**
Chronic pain	(deCharms et al., 2005)	Rostral ACC	↑,↓	Patients learned control, associated with decreased pain intensity, compared with no, yoked and sham NF controls.
Motor function / Motor imagery	(Bray et al., 2007)	Motor / somatosensory cortex	↑	Instrumentally induced control over specific regions leading to post-test increases in activity, compared to non-rewarded regions.
Emotional linguistic ability	(Rota et al., 2009)	Right Inferior Frontal Gyrus	↑	Improvement in task on emotional prosodic intonations but not for syntactic processing.
Visual Perception	(Scharnowski et al., 2012)	Early Visual Cortex	↑	Participants who learned to regulate increased their perceptual sensitivity on a visual discrimination task, respective to laterality trained.
Emotional valance appreciation	(Brühl et al., 2014)	Right Amygdala	↓	Down-regulation lead to decreased amygdala activity in subsequent viewing conditions of emotionally laden pictures

Psychopathy (Criminal)	(Sitaram et al., 2014)	Anterior Insula	↑	Increased functional connectivity in emotional network with higher subjective aversive ratings of emotionally aversive pictures (1/4 participants)
Major Depressive Disorder	(Linden et al., 2012)	VLPFC, DLPFC, insular cortex	↑	Successful upregulation of target areas implicated in control of emotion. Clinical improvement on depression scores.
Smoking Cessation	(Li et al., 2013)	ACC mPFC	↓ ↑	Decreased ACC activity lead to decreased cue craving, while increased mPFC activity did not.
OCD - Contamination Anxiety	(Scheinost et al., 2014, 2013)	OFC and anterior PFC	↑,↓	OFC regulation produced lasting changes in connectivity and anxiety. Initial connectivity predicted NF success.
Parkinsons / Motor Function	(Subramanian et al., 2011)	SMA	↑	PD patients who received NF showed improvement in motor symptoms compared to PD matched controls

Table 3. Overview of real-time functional magnetic resonance imaging studies
NF ; neurofeedback, ACC; anterior cingulate cortex, SMA; supplementary motor area, PFC; prefrontal cortex, VLPFC; ventrolateral PFC, DLPFC; dorsolateral PFC, mPFC; middle PFC,OFC; orbitofrontal cortex. ↑/↓ direction of regulation. Table is adapted from (Brühl, 2015,p.5-6)

4.3 Investigating Multiple Mental Strategies and Neural Substrates

A similar strategy that may underline the extent of neurofeedback to investigate causal mind-brain relationships is provided by Hanlon (2013) and Li (2013) and colleagues, who tested whether neurofeedback could reduce cigarette craving tendencies in nicotine-dependent cigarette smokers (Hanlon et al., 2013,p.1-3; Li et al., 2013,p.1-9). The authors instructed participants to manipulate their craving for cigarettes using two different mental strategies. In a "reduce craving" approach, participants were instructed to "reduce craving", while they were "feed" back ACC activity corresponding to a thermometer display that they were told to decrease. In another "increase resistance" approach, participants were instructed to increase resistance while were provided neurofeedback based on their middle prefrontal cortex (mPFC) activity that they were told to increase. The results indicate that the mental strategy of "reducing craving" combined with ACC neurofeedback was successful in reducing cue craving to smoking pictures, whereas "increasing resistance" and mPFC activity was not. Although there may be a multitude of different explanations why the combination of one mental strategy and ROI failed, the study is the one of the first of its kind to hint at a new possible avenue for testing different mental strategies and their neuroanatomical correlates (ibid.). Here, rtfMRI provides the means to test whether different mental strategies (corresponding to the mental state of the participant) holds more prominence in inducing change in the brain activity.

The goal is not just see one's brain in real time or to see if a particular mental strategy can induce a particular brain activity pattern but to develop self-regulatory control over brain activity

corresponding with enhanced in control over the related cognitive processes (deCharms, 2007). Furthermore, different neural substrates such as the ACC or mPFC proposed to be involved in that particular mental function could be ROI targets of the rtfMRI technique, allowing for testing of whether the change in activation in that substrate is significantly more advantageous than another.

4.4 Exogenously controlled closed loop paradigm

The most common form of rtfMRI neurofeedback is endogenous, in which subjects are fed back their self-regulatory efforts via their BOLD response in a continuous loop, similar to the first illustration shown in section 1.1: thesis objective (Sulzer et al., 2013,p.6). This is known as an endogenously controlled loop since each successive signal change is fed back immediately to the participant and made available for themselves to control. In contrast, in exogenous neurofeedback, the feedback signal is not presented to the subject, but rather it is used to trigger an external event or stimuli. Consequently, the key difference between endogenous and exogenous neurofeedback is that in the former the participant is aware and can thus control the feedback signal.

In the first of two experiments by Hinds et al., (2013), the authors show that higher baseline brain activity in a region involved in planning of motor actions called the supplementary motor area (SMA) and lower activity in regions implicated in "lapses in attention" and "mind-wandering" called the default-mode network (DMN) was predictive of reduced reaction time latencies in a vigilance task (Hinds et al., 2013,p.1-9; Mason et al., 2007,p.1-2). In other words, just prior to having to react quickly to an event, the specific constellation of activity brain in regions implicated in planning of motor actions and mind-wandering can inform of how quickly one reacts. The authors then used rtfMRI to measure in real time the ratio of SMA to DMN activity, and used this ratio to trigger the event of having to react quickly. The authors found that the by "waiting" for a particular SMA/DMN ratio they could control the behavioural measurement of reaction time (ibid.). This approach to rtfMRI allows for stimulus presentation to be dynamically dependent on the level of brain activation within a given ROI. It is thus an exogenously triggered stimulus presentation, because it is the experimenter that uses a computer algorithm to "waits" for certain brain activations to occur and uses that to trigger an event. The experimental paradigm takes on an evolving nature where the stimulus presentation is entrained to the brain activity of the individual, serving as a novel approach to investigate neuronal dynamics (Sulzer et al., 2013,p.6f).

5. Neurofeedback for Causal Inference in Neuroscience

The present chapter will wind up the prior mentioned chapters into a discussion of whether neurofeedback has a potential to inform about mind-brain causal relationships. In order to provide an instructive discussion the chapter will first outline how science in general, accounts for causality in empirical relationships. Furthermore, the chapter will examine Hill's (1965) criteria of causation, in addition to pointers on the perspectives of causal inference, such as directionality, necessity and sufficiency. In facing up to question of the potential of neurofeedback for informing about mind-brain causal relationships a discussion of the strengths and limitations in inferring causality through neurofeedback research. The author proposes that there exists several key promising as well as problematic aspects of using neurofeedback for causal inference of mind-brain relationships.

5.1 Causal Inference in Neuroscience

5.1.1 Rank of Scientific Accounts

The process of science seeks to unravel the phenomena of the natural world by discovering and characterising relationships to greater and greater degree of detail. (Machamer et al., 2000,p.1-24). Fundamentally, this is done through asking and answering questions at an ever increasing level of sophistication and difficulty (Leek, 2015,p.1-12). In terms of data analysis, if one were to rank the types of scientific questions by difficulty, one way to do so would be the following way; *Exploratory, Inferential, Predictive, Causal, Mechanistic*. The *exploratory* or descriptive accounts are *prima facie* of a given phenomenon and comes with little or no interpretation of the phenomena and there is no quantification of whether the discovered relationship would hold in the population at large. The exploratory rank is often the first avenue of scientific exploration. An example could be Percival Pott's observation of a heightened degree of cancer in chimney sweepers in the 18th hundred. At the time no biological understanding of the phenomena existed and thus no interpretation towards and underlying cause was made.

The second *inferential* rank of accounts is the most common in formal scientific literature and attempts to quantify whether the observed association is robust enough to be present beyond the sample at hand. As an example the present author used Magnetic Resonance Imaging (MRI) to compare structural brain volume between genders in healthy volunteers (HV) and binge drinkers (BD), characterised by excessive intake of alcohol (Kvamme et al., 2016,p.1-7). Resulting MRI analysis showed several wide-spread brain clusters qualified by group-by-gender interaction,

whereby BD females had increased volume and BD males had decreased volume compared with their HV counterparts. The account is inferential since the association was systematic to such a degree that the opposite (i.e., that the association was not present) is deemed unlikely given the traditional set alpha level of 0.05 (Leek, 2015,p.5f; Nickerson, 2000,p.7). The inferential account can only observe that a particular relationship or association between two measurements can be inferred to exist in the population at large and cannot make causal statements about why it exists (ibid.). Consequently the brain volumetric group-by-gender interaction could be interpreted as either caused by different neurotoxic sensitivities between genders to alcohol or the brain volume differences could be an endophenotypic risk factor for the binge drinking behaviour for either gender (Kvamme et al., 2016,p.1-7). In the first scenario, the intake of alcohol is what causes the brain changes and in the later scenario it is the brain changes that cause the intake of alcohol (ibid.). While the inferential account gives a snap-shot of the association between factors at one specific point in time – that is, it is cross-sectional, the *predictive* account often attempts to use available measures to predict future measurements (Leek, 2015,p.3-6). As an example, Whelan and colleagues measured several psycho-social and biological variables in 14-year old adolescents and applied machine learning techniques to identify predictors of future binge drinkers (Whelan et al., 2014,p.1-17). The authors found that epidemiological, biological and psychosocial variables such as smoking status, genetics, brain measures personality factors and history of prior romantic relationships were able to predict whether adolescents became binge drinkers by age 16. Interestingly the authors show that the accuracy of the statistical model in predicting future binge drinking status was not due any measure in isolation and that bio- and psycho-social factors were equally strong classifiers (ibid.). The predictive account shows that a current measure predicts and predates a subsequent measure without explain why (i.e., it remains unknown if the former is cause of later) (Leek, 2015,p.3-6). In other words, the initiation of binge drinking seen by the 16-year olds in Whelan et al., study (2014) is not necessarily caused by the specific bio-psycho-social pattern observed 2 years prior, and could potentially have occurred regardless (Whelan et al., 2014,p.1-17).

The *causal* rank of scientific accounts requires that one isolated independent variable (IV) is manipulated whilst holding other confounding variables equal with subsequent measurement on a dependent variable (DV) (Coolican, 2014,p.56-65; Leek, 2015,p.3-6; Deacon, 2013,p.8f). This rational underlies the paradigm of the randomized control trials (RTC). In RTCs the participants are randomly assigned to an experimental and control group, that identical to the experimental group in every aspect except for the manipulation in the IV. The RTC paradigm increases the confidence that observed differences in DV is not confounded by placebo, passage of time or Hawthorne effects

(ibid.). In contrast with the inferential and predictive ranks the causal rank of scientific explanations accounts for both the IV average effect on the DV as well as establishes confidence that the direction of the causal relationship goes from the IV to the DV. The leap from a causal to a *mechanistic* explanation of a phenomena is not minor, as in a mechanistic explanation must show that the IV always and exclusively determines the DV. As an example, decades of research have shown a clear causal relationship between smoking and cancer, however it is not a 1:1 relationship as other causes may increase or decrease the risk of cancer. A mechanistic account must show that no other IV(s) need to be accounted for and the change in DV is always and exclusively determined stringently down to mathematical precision by the IV (Leek, 2015,p.3-6; Machamer et al., 2000,p.1-24). If a mechanistic account is represented schematically by **A → B → C** then it would require an account for all of the causal influences determining C as *sine qua non,* with reference to the mechanistic nature of the account. Such accounts happens rarely if ever, outside the realm of math and engineering, however one may argue that the scientific accounts of phenomena such as neurotransmission and DNA base sequences are mechanisms that science is close to give a mechanistic account of (ibid.).

Having thoroughly shown the almost unreachable level or detail required for mechanistic accounts, causal accounts, can be seen as the penultimum of scientific accounts and presents themselves with comparable stringent conditions before they are truly satisfactory. One can argue that within the neuroscientific field, researchers are at a turning point where methods for establishing causal accounts are proliferating in concurrence with increased scientific and technological advancements. Within neuroimaging, causal inference is a central goal and in recent years several technically methods such as granger causality and dynamic causal modelling have been advanced, that focus specifically on inferring causal relationships (Grosse-Wentrup et al., 2016,p.1). Similarly, neurostimulation techniques such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) are also methods that allows for establishing a causal link between brain activity and behaviour (Clarke et al., 2014,p.1; Sliwinska et al., 2014,p.1; Sulzer et al., 2013,p.6). Similar to neurofeedback, TMS can manipulate and investigate brain activity by either temporally suppressing local neural activity or by temporally activating (Pascual-Leone et al., 1998,p.1) As will be discussed further in subsequent chapters, EEG and rtfMRI neurofeedback might also hold a potential to address questions of causality.

5.1.2 Hill's Criteria of Causation

One of the more influential set of criteria for causal inference has been formulated by Sir Austen Bradford Hill (Hill, 1965,p.1-6; Van Bockstaele et al., 2014,p.1-10). He proposed that the confidence in interpreting that one variable causes another can be evaluated on the basis of nine criteria. These are; *the strength of the relation*. It is clear that for A to cause B there should be a relationship between them such the probability of the presence or different levels of B corresponds with the presence or the different levels of A to a degree that is measureable. *Consistency* refers to the generalizability and replicability of findings, i.e., that the association is present in different settings using different methodologies and so on. *Specificity* references to the presence of a 1:1 relationship such that A always an exclusively cause B, which similarly was required in order to satisfy a mechanistic account (Hill, 1965,p.1-6; Leek, 2015,p.3-6; Van Bockstaele et al., 2014,p.1-10). As noted by Hill (1965), many effects have multiple causes, so although specificity indicates causality, the absence of specificity does not negate the possibility of a causal account yet it negates a mechanistic account (ibid.). The criterion of a *biological gradient*, is similar to a dose-response curve meaning that there exists a continuous relationship between every level of A that corresponds to every level of B. For instance knowing that death rate from cancer correlates positively with smoked cigarettes adds more confidence in a causal account compared with knowing only that smokers have a higher death rate than non-smokers. The *plausibility* criterion means that scientific knowledge can give a theoretical explanation as to why it is that it is A that causes B. This comes with an obvious caveat, as mentioned earlier, Pott's observation of a heightened degree of cancer in chimney sweepers was not backed by any plausible explanation, as at the time, the discovered relationship was only exploratory. *Coherence* implies that the suggested causal relation between A and B doesn't' interferer with any knowledge about A, B or another established causal account explaining A and B's co-occurrence. The most crucial criteria for inferring causality according to Hill (1965), are those of temporality and experimental evidence. The *temporality* criteria means that the likelihood that A causes B increases if A precedes B and not the other way around. This parallels the logic that follows from prospective studies that attempt to provide a predictive account. *Experimental studies* showing that manipulating the variable A leads to changes in B is one of the strongest demonstration of causality. One must however precede with caution when drawing the casual conclusion that **A → B** as it may be the case that A could have led to changes in an unidentified process C which resulted in changes in B. This would mean that the causal chain of effect between A and B is indirect (i.e., **A → C → B**) whereby manipulating C would hold more of a strength in manipulation B as compared with A. This case, is still indicative of a causal relationship between A and B, A is however not *causally primary* to B, where C is. The last criterion is that of analogies meaning if scientific knowledge indicates a causal

relationship between the constructs A´ and B´ it makes the causal relationship between A and B more likely.

5.1.3 Inference is not observation

When dealing with the thorny question of causality, there arises the fundamental problem of causal inference which refers to the impossibility of ever observing causality (Holland, 1986,p.1-21). Here, the operative word is *observe* since causal relationships cannot be known through observation but only through *inference,* meaning deriving logical conclusions from factual evidence (ibid.). In inferring causality, it is often the case that any of Hill's criteria may be necessary yet not sufficient to provide a convincing causal account. Here, choosing an example regarding a question of causality that most feel they intuitively know the answer to; does smoking cause cancer? The tobacco industry claimed that the observed correlation between lung cancer and smoking is due to lung cancer causing individuals to start smoking (White, 1990,p.1-10; Novella, 2015,p.159ff). What is the evidence for opposite claim; that smoking causes lung cancer ? The consistency or the strength of the association could be counter-argued by "correlation does not imply causation", and one could even entertain the plausibility criteria that lung cancer victims often feel stressed and since stress may lead to smoking that is the reason for the observed association (Andersen et al., 1994,p.1; Holland, 1986,p.1-21; Novella, 2015,p.159ff; Pomerleau and Pomerleau, 1991,p.1). In other words the strength of the association, consistency and plausibility alone does not provide enough evidence to discern which causal hypothesis is more likely. The reason that it is more likely that smoking causes lung cancer compared with the reverse is because of the temporally criteria. Here, research shows that non-smokers will initiate smoking before the onset of lung cancer and that cancer victims who quit smoking will reduce their risk of dying from cancer compared with those who continue smoking (White, 1990,p.1-10; Novella, 2015,p.159ff). In other words, questions addressed through multiple causal criteria can be used to *inferentially triangulate* the most likely causal hypotheses given the evidence (ibid.).

5.1.4 Directionality, Necessity and Sufficiency.

In explaining causal relationships there exists different perspectives on what qualifies as causality, such as a narrow view of causality which require a unidirectional cause and effect (Lilienfeld, 2007,p.6-7; Van Bockstaele et al., 2014,p.1-9). This view of causality is not dissimilar to the requirements of a mechanistic account. Alternatively, a bi-directional relationship view of causality acknowledges that the relationship between A and B may arise mutually. An even less stringent view of causality is a multi-directional perspective that acknowledges that effects may have multiple causes thus rendering the specificity criterion less relevant. As an example, there is a general consensus for

psychologists nowadays that the causal links to disorders such as anxiety and depression consists of a complex interplay between genes and environment. A useful heuristic that clarifies this multi-directional view of causality, is that of a man falling to the ground resulting in his fatality. If no other factors intervened a unidirectional cause-effect relationship view of causality would point to being pushed out of a plane as the main factor in the etiology of falling to one's death. However, being on the plane in the first place constitutes a vulnerability factor, for a falling death. Such a vulnerability is not necessary since the man could have fallen from a tall building nor sufficient since being on a plane doesn't deterministically result in being pushed out of it. Next, consider the case that falling may not always result in fatality, for instance wearing a parachute counts as an attenuating factor for falling to one's death. Thus, in discussing causal factors, the directionality of A and B is an important consideration. Furthermore, causal relationships may serve as neither necessary nor sufficient for an effect, but rather as attenuating or exacerbating factors that nevertheless cause the effect to be less or more likely (ibid.).

5.2 The Causal Explanatory Potential of Neurofeedback

In the following section, a framework for discussing key aspects of how neurofeedback potential and limitations in informing about mind-brain causal relationships is provided. The present author, proposes that there exists cautions and bold claims regarding neurofeedback's mind-brain causal explanatory potential. An example of a cautions claim could be that "neurofeedback enables researchers to go beyond mere inferential scientific accounts" (Sulzer et al., 2013,p.7). As a contrast a bold claim would that "neurofeedback informs of unidirectional causal relationship from brain to mind" (Crick, 1995,p.3; Franks, 2013,p.107-112). Both claims are proposed for illustrative purposes and represent extreme poles of mind-brain causal inference. As will be discussed below, there exists several key potential advantages and several key limitations in substantiating the cautious and bold claims for inferring causality. The remainder of the chapter will deal with these key potentials and limitations initially and discuss how they reflect on the problem statement of the thesis. Concluding the thesis, the present author based on a synthesis of the discussed material argue that the advantages and disadvantages can be amplified and attenuated respectively when neurofeedback is coupled with other methodological approaches.

In order to approach the question of whether neurofeedback can inform about causal relationships it is useful to distinguish between the easier and harder sub-questions. An example of an easy question would be whether neurofeedback can inform about brain-to-brain causal relation. Here, several

authors advocate for the ability of both EEG and rtfMRI neurofeedback as being able to improve the neuroscientific understanding of causality of brain function (Caria et al., 2007,p.1; Keizer et al., 2010,p.1-8; Lee et al., 2012,p.1-2; Ros et al., 2013,p.5). These questions ask whether neurofeedback (N) that changes one physical brain measure ($\mathbf{P^1}$) causally changes a subsequent physical brain measure (P^2) represented schematically as ($N \rightarrow P^1 \rightarrow P^2$). To name a few; such questions have led to causal accounts of rtfMRI neurofeedback ability to causally increase connectivity between brain networks and EEG neurofeedback ability to causally change subsequent resting EEG activity (ibid.).

The harder question that this chapter aims to tackle regards whether (i); given that neurofeedback changes a physical measure (P) corresponding with a change in the individuals self-reported mental state (M), is it reasonable to conclude (ii) that; we have been informed about a *causal* relationship between M and P ? The question considers both instances where change (Δ) in physical brain measure is corresponding ($\leftarrow\rightarrow$) with change in mental state (Δ-P $\leftarrow\rightarrow$ Δ-M) and where particular brain states (P^1 and P^2) correspond with mental states (M^1 and M^2) represented thusly ($P^1 \leftarrow\rightarrow M^1$ & $P^2 \leftarrow\rightarrow M^2$). To reiterate the main metatheoretical question of the thesis; have we through evidence provided by neurofeedback research been informed of a correspondence between mind and brain so as to satisfy a causal codetermining law between M and P (James, 1890,p.1-10).

Moving forward this section will apply Hill's (1965) causal criteria on the evidence within neurofeedback research (Hill, 1965,p.1-6). In addition, it will be discussed whether neurofeedback research informs of any causal directionality of mind-brain relationship as well as their necessity and sufficiency. The overall goal is to determine, in light of the discussion on causal inference using neurofeedback, whether we now have confidence in transcending our rank of scientific account of that mind-brain relationship from an inferential to a causal one.

In discussing causal inference in neurofeedback research the discussion will assume that Hill's criteria of strength relation and consistency applies to the premise, (i) neurofeedback change of a physical measure (P) resulting in change in the individuals self-reported mental state (M). Such assumptions may in the future be violated should there amount evidence that the relationship repeatedly fails to be replicated. The examples of neurofeedback research are thus not of primary concern to the matter at hand, they are only meaningful, insofar as they inform the discussion regarding the potential of neurofeedback to make causal mind-brain claims. As such the analysis on their causal explanatory potential should function as a template that can be applied to other neurofeedback studies. Another core assumption is that the measures derived from subjective introspection has construct validly in terms of the mental state of the individual, even if such an assumption may be debatable (Nisbett and Wilson, 1977,p.1-27; Overgaard et al., 2010,p.1; Petitmengin and Bitbol, 2009,p.1-11).

5.2.1 Application of Hills criteria to neurofeedback

The criterion of plausibility, requires that there are scientific explanatory links between neurofeedback and induction of a particular brain state in addition to a link between a physical brain measure and an associated mental state. The first link is self-evident in the ability of the method neurofeedback to change a particular brain measure (Cox et al., 1995,p.1-6) Taking deCharms et al., (2005) example of changing ACC activity to change pain perception, the later link is provided by prior neuroimaging studies having generally supported that ACC activity correlate positively with unpleasantness of pain sensations. (Petrovic and Ingvar, 2002,p.1; Peyron et al., 2004,p.1, 2000,p.1; deCharms et al.,2005,p.1-6). On the basis of this, one can conclude it plausible that neurofeedback can causally induce a brain state resulting in a particular mental state.

Following Hill (1965), causal relationship are often characterized by a biological gradient or does-response curve. Such accounts are subject-specific to the mind-brain relationship investigated through neurofeedback. The appearance of a biological gradient for example, with pain perception and ACC activity as investigated by deCharms et al., (2005) would not serve as evidence for a biological gradient for other neurofeedback studies, yet it would serve as a causal criteria of analogy. It can be argued that the most convincing form of biological gradients are those that both take the form of within and between subject measures. As an example it is shown that between individual the higher the cerebral blood flow in the ACC the larger the rating of unpleasantness of pain (Rainville et al., 1997,p.3). Moreover, deCharms et al. (2005) also show that within each individual the more effective neurofeedback decreases ACC activity, the more a decrease in measures of pain perception (deCharms et al., 2005,p.1-6).

As mentioned, one of the stronger types of criteria of causality is that of experiment, that permit the IV claimed as cause to be manipulated differentially in a minimum of two groups and measurement of the effect on the DV that is hypothesized to be an antecedent from the cause. In the case of deCharms et al., (2005) a reduction in perception of pain followed only in the experimental group receiving neurofeedback of the ACC while in placebo groups receiving no feedback, sham feedback or yoked feedback change in pain perception was absent (ibid.). This counts as strong evidence that neurofeedback meditated regulation of ACC activity is causally related to change in pain perception. Since placebo groups received identical instruction and attempted cognitive control over their pain similar to the test group yet with absence of valid ACC rtfMRI information (ibid.). For the experiment not to show a causal link between neurofeedback of ACC and pain perception would require that the neurofeedback process in the test and control groups to somehow determined the random assignment to each group, which obviously isn't the case (deCharms et al., 2005,p.1-6; Grosse-Wentrup et al.,

2016,p.1). The causal relationship can be stated as follows; that neurofeedback of the specific physical brain measure (NP^1), in this case the ACC, causally impacted the physical brain measure (P^1) by decreasing activity with a link between this and the mental state (M^1) in this case less unpleasant pain perception. Represented schematically ($NP^1 \rightarrow P^1$ & M^1) where the arrow represents a causal relationship.

5.2.2 Tertium Quid

From this study involving how ACC modulates pain perception a further strong case can be made about the causal role of ACC modulation and pain perception, taking the form of ($P^1 \rightarrow M^1$). Here, the authors find it conceivable that ACC activity changes may be driven by top–down connections from a higher order region that causally affects both ACC activity and pain perception as independent quantities (deCharms et al., 2005,p.1-6; Sulzer et al., 2013,p.6). Thus, the appearance of a relationship between P^1 and M^1 may arise due to a tertium quid or ("a third thing of indeterminate character") (Field et al., 2012,p.49). In this view, the causal relationship contains an unidentified tertium quid in this case a physical brain region ($P^?$) that intersects the causal relationship such that ($NP^1 \rightarrow P^? \rightarrow P^1 \rightarrow M^1$). This is referred to as the principle of completeness, that any physical brain state will cause other physical brain state (Kurthen, 2010,p.5).

This does not negate the prior mentioned causal relationship that neurofeedback has induced change in P^1 and that there is a corresponding change in M^1 , it is just unclear how it has done so. It is still reasonable to assume that there could be a causal link between change (Δ) in the physical brain measure (P) and mental state (M) represented as so; (Δ-P $\rightarrow$ Δ-M). Stated another way, there isn't any evidence against this causal hypothesis, however there are no data that favour it when compared with causal hypothesis involving a tertium quid. In this case, the argument pointing to a tertium quid is an argument that the ACC region may not have *causal primacy* with respect to the effect on the mental state of unpleasant pain sensation (Desmond, 2004,p.1; Lilienfeld, 2007,p.7). The argument posits that the unidentified brain region is a stronger and more important causal factor of the mental state. Thus far, what has been established is that neurofeedback in isolation cannot truly address whether the particular physical brain measure holds a causal primacy role in determining a given mental state ($P^1 \rightarrow M^1$). It can however address that some causal relationship exists, if not directly between P^1 and M^1, then rather as a tertium quid causally related to them both. It is important to realize, that the argument from tertium quid is actually an empirical objection, that creates new causal hypotheses that can be addressed through research.

The first way of addressing such a causal hypothesis is due to the advent of technically methods in neuroimaging such as granger causality and dynamic causal modelling, as they have as their prime focus the inference of causal primacy (Hamilton et al., 2011,p.1; Palaniyappan et al., 2013,p.1; Roebroeck et al., 2005,p.1). Specifically, they make use of the temporality criteria in addressing causality by looking at whether neuronal activation in another region came prior to activation in the one in question (ibid.). Through such an investigation it may be shown that one brain region connecting with the ACC in a top-down fashion modulate ACC and that this is what holds causal primacy in changing the mental state. A testable prediction that follows from this hypothesis is that increasing the connectivity between this to-be-identified region and ACC through neurofeedback should outperform the traditional modulation of ACC in isolation regarding the one induced in the mental state. Here, through metatheoretical reflection on the neuroscientific arsenal of investigative techniques one can argue that neurofeedback in isolation may not hold a primary role in establishing a causal account (Sonne-Ragans, 2012,p.25-32). However, by applying techniques such as granger causality in unison, they complement each other in order to address the mind-brain relationship in question (ibid.).

Alternatively, one could attempt to provide evidence against the causal hypotheses pointing to a tertium quid by testing whether neurofeedback regulation of other regions results in change in the mental state. Such a strategy is actually already inherent in the use of yoked neurofeedback placebo group, which in case of deCharms et al., (2005) was the posterior cingulate cortex (PCC) a region in relatively close proximity to the ACC but without any plausible relevance to pain perception. What the use of such a placebo group provides evidence for is that the PCC is not the tertium quid in question. Thus, the strategy of testing whether neurofeedback modulation of multiple neural substrates in addition the one in question are causally involved in a given mental state also holds a potential to discover causal mind-brain relationships.

5.2.3 Testing multiple mental strategies and neural substrates

The strategy of testing multiple neural substrates for discovering causal mind-brain relationships is exemplified through through Hanlon (2013) and Li (2013) and colleagues, showing that neurofeedback of specific regions combined with specific mental strategies can reduce cigarette craving (Hanlon et al., 2013,p.1-3; Li et al., 2013,p.1-9). Here, the authors show that the neurofeedback modulation of the ACC region was effective in reducing craving whereas the middle prefrontal cortex (mPFC) did not result in change in subjective craving scores. In other words, neurofeedback of the ACC region (NP^1) was effective in changing physical brain activity of the ACC

and also concurrently (&) the mental state of craving, ($NP^1 \rightarrow P^1$ & M^1), whereas neurofeedback of mPFC (NP^2) changed only the activity in the NP^2 without resulting in change in M^1 ($NP^2 \rightarrow P^2 \neq M^1$). Such later evidence showing a non-relationship is not useless, as it is rather informative that regulation of one physical brain measure is unsuccessful. Arguably such null-results are important to publish within the neurofeedback literature, so as avoid further attempts to induce change in the mental state through the unsuccessful brain measure (Rosenthal, 1979,p.1-2). This kind of information is valuable as showing that one brain region is unlikely to have causal impact on a mental state is a way of gathering evidence for a criteria of specificity for another mind-brain causal relationship. On the other hand it entirely plausible that the mental function could be realized by other neural substrates that the one that is measured, akin to the function of "seeing" mediated by Bach-y-Rita's tactile vision devise (Bach-Y-Rita et al., 1969,p.1f; Overgaard and Mogensen, 2011,p.1-4).

Another problematic aspect of this type of strategy is that it is conceivable that neurofeedback of a given region (say NP^3) does not lead to a change in the physical brain measure (P^3) and does not influence the measured mental state (M^3). This can be represented like this; ($NP^3 \neq P^3$ & M^3). In this case, it would not be safe to assume that because neurofeedback failed to change P^3 and M^3 that the two are not causally related. The physical brain region might causally influence the mental state, yet the physical brain region does not afford neurofeedback training. Meaning that unsuccessful neurofeedback cannot be used to show that the brain measure isn't causally related to mental phenomena through neurofeedback.

An example of this, could be metrics that do not contain the "online" characteristic that fMRI holds such as structural brain volume (Kvamme et al., 2016,p.1-7; Weiskopf et al., 2004,p.1-3). Even if it as possible to measure in real-time the structural MRI ("rtsMRI"), it would still rationally be a dead-end, since changes in structural brain volume would be too slow of a process to learn to regulate through neurofeedback (ibid.). The physical brain measure, in this case is brain volume, might ultimately play a causal role in the mental state, however there is no practical way for neurofeedback to address it. In other words, should the physical brain measure be "untrainable" through neurofeedback the method is not falsifiable, with respect to inferring causality (Sonne-Ragans, 2012,p.48).

Similarly, there could be instances where rtfMRI neurofeedback would be logically impossible for regulating a given mind-brain causal relationship. As an example, in a meta-analysis by Emmert et al., (2015) showed that the anterior insular cortex (AIC) to be involved in neurofeedback regulation per se, independent of the targeted region (Emmert et al., 2015,p.1-5). The authors explain the findings by linking it with prior evidence showing the AIC to be involved in the self-regulation in

domains not involving neurofeedback. Thus, down-regulation of the AIC presents itself as a "catch-22" situation where attempts to regulate it would result in up-regulation rather than down-regulation (A. Brühl, personal communication, April 8, 2015). Here, establishing causal relationships through neurofeedback is deemed unlikely because of the coherence criteria. In other words we can rationally infer that rt-sMRI and down-regulation of AIC is impossible. Yet, one cannot on the basis of this, conclude that the same "untrainable" physical brain measure is not causally involved in the mental state. In fact, in the case of AIC it is very likely that low activity in said region corresponds with a mental state characterized by poor self-regulatory ability, yet neurofeedback cannot directly investigate it.

One can envision future instances of mind-brain causal relationships, where neurofeedback is made impossible through the coherence criteria, rendering the method incapable of investigating such relationships. In terms of neurofeedback as analytical tool, it has a tendency to focus on causal relationships between brain and mind, where the brain can be trained through neurofeedback. As such the use of neurofeedback as a research strategy may make it more likely that one overlooks mind-brain causal relationships where the brain is untrainable. In short, the strategy of testing multiple regions is advantageous and highlights neurofeedback's ability gather specificity for a given mind-brain causal relationship. However in the case where neurofeedback is ineffective, one cannot conclude the non-existence of a causal relationship between mind and brain making its causal inferential potential unpromising.

5.2.4 Unidirectional causal relationships

The bold claim when dealing with neurofeedback and causal inference is that "neurofeedback informs of unidirectional causal relationship from brain to mind". Prima facie the claim may appear correct, as what is seen first is the change of neural activity in the brain and then what is measured is its effect on a subjective mental state. This follows from a perspective taken by a biomedical model holding an eliminative reductionist position where brain states are seen as the inevitable primary causal determinant of the mental state (P → M) (Lilienfeld, 2007,p.2f). Through the lenses of neurofeedback one could be drawn to this argument since the aim of neurofeedback lies in primarily changing a brain state such ACC activity and then seeing the consequence on the mental state such as subjective craving for cigarettes or subjective pain sensation. However, such an argument is flawed since the change in mental state and brain state could happen concurrently.

In the example provided by Hanlon (2013) and Li (2013) and colleagues, regarding how reducing ACC activity was related to a subsequent reduced craving of cigarettes (Hanlon et al., 2013,p.1-3; Li et al., 2013,p.1-9). Here, it appears as if the brain state satisfied the causal criteria of temporality, that just prior to the mental state, the brain was in a particular state so as to causing the mind state in a "bottom-up" fashion. This would be the argumentation from a causal reductionist position, that of brain causing mind. However another interpretation is that neurofeedback change of the brain state and mental state happens concurrently. In fact the method provided by Hanlon (2013) and Li (2013) and colleagues seem to support this insofar as asking participants to perform a particular mental strategy of "reducing craving" and that this holds potential in reducing ACC activity in combination with neurofeedback of the ACC (ibid.). In this way, the authors are recognizing that intrinsic mental change is interconnected with inducing a brain change. One could, equally argue for mental causation whereby the mental strategy of reducing craving has "downward" causation on the physical brain measure (M → P) (Bagdasaryan and Le Van Quyen, 2013,p.1-7; Chalmers, 2003,p.29)

However, on further inspection the temporality criteria is not really present when discussing mind and brain, as the above show no real evidence pointing to mind state "before" or "after" brain state, and one could counter-argue they could just as well codetermine each other continuously. The process of neurofeedback involves the process of viewing brain state and introspective mental state simultaneously, discounting the mental processes manifestation would most likely erroneous. Even in the case of the strongest argument for a mechanistic brain cause mind (P → M) would have to be in case of the exogenously controlled closed loop paradigm. As described, this specific paradigm "waits" until a certain brain activity is in a certain way and then triggers an event. Here, the induction and thus presence of a low ratio of SMA/DMN activity resulted in a larger degree of surprise to a subsequent reaction time test (Hinds et al., 2013,p.1-9). On close inspection however the appearance of a temporality criterion is actually not present, since the decreased ratio of SMA/DMN activity could be happening concurrently with the mental state of being less prepared and this could causally related to the degree of surprise when the stimuli is presented. One can argue that in subject matter of mind and brain the *temporality* criteria of causality is not possible to attain. As contrasted with a typical experimental trial on the toxic effects of a given drug, one can derive a causal account of the drug on a given disease or symptom because the toxin can be introduced before the symptom showing a clear cause and *then* effect relationship. However, in the case of mind and brain, the present author knows no method to achieve brain state that is isolated from a corresponding mind state. Although the exogenously controlled closed loop paradigm "waits" for a specific brain state and measures the

states effect on a subsequent mind state it cannot conclude that the brain state was without an associated mind state.

In other words it seems unlikely that neurofeedback can provide evidence that support a unidirectional causality from brain to mind. This does not negate the ability of neurofeedback to highlight causal relationships, in a way it actually strengthens the notion of causal reciprocity between P and M. In summery the question of whether the brain process unidirectional cause mental process or the reverse cannot be inferred through neurofeedback and one can only presume they are manifestations of the same phenomena evolving together (deCharms, 2007,p.5).

5.2.5 Moderation Factor

As mentioned EEG and rtfMRI neurofeedback satisfy the Hill's (1965) causal criteria of plausibility insofar as they their processes tie in with the rest of the brains processes. For example, since EEG has shown to be causally linked with cerebral metabolism and blood flow, neurotransmitter release etc., it is plausible that these methods could have widespread effects on several mental functions and dysfunctions (Duff, 2004,p.1-5; Ros et al., 2014,p.5-10). Supporting this, it was shown that EEG-neurofeedback has been applied to a wide spectrum of mental disorders. In this respect, the wide-ranging characteristic is advantageous for the plausibility of neurofeedback in informing about mind-brain causal relationships.

However, it may also be presented as a weakness of the method since it is unknown, whether it is the intended physiological target of neurofeedback or the succeeding physiological changes that may be the actual primary reason for the change in mental state. This is also related to the weakness of the "conditioning and repair" model of neurofeedback, since it is often hard to isolate exactly which element of the broad neurofeedback intervention may be contributing to the therapeutic process (Drechsler et al., 2007,p.1f; Egner et al., 2004,p.1f; Othmer et al., n.d.,p.1-4). As an example it was shown that neurofeedback of some frequency bands could propagate throughout a large array of frequencies due to cross-frequency modulation (Canolty and Knight, 2012,p.1-4; Canolty et al., 2009,p.1)

Neurofeedback's broad effects runs the risk of failing to show specificity in terms of a mind-brain causal relationship. It is the very nature of the cognitive neuroscience to isolate the specific biological process that is linked with the mental phenomena (Cromby, 2007,p.11). When taken to the extreme, it would mean that to explain neurofeedback one would have to point to the sbrain in its entirety in order to explain the mental phenomena. Then, the need to specific neurofeedback on an

implementational neurobiological level of analysis carries with it no information. In this case when explanation becomes so broad as it crosses over and could as well be address it in terms of psychology rather than making an appeal to neuroscience.

One crucial consideration when discussing neurofeedback's potential to inform of mind-brain causal relationships regards whether neurofeedback induced change of the brain state acts as primary causal factor in changing the mental state or whether it acted as a moderating factor. This is similar to the therapeutic role of neurofeedback as viewed from the "skill-acquisition" model, mentioned earlier. In this view the way in which neurofeedback exerts it's therapeutic effects are not causally primary, however the method teaches the individual self-regulatory techniques that generalize allowing for other therapeutic processes to exert the primary causal effect. In other words, even if neurofeedback was necessary it may not be sufficient cause, the mind-brain causally induced changed would dependent on another factor.

For instance, the analysis of EEG allows one to create links between mental disorders and specific EEG characteristics. As an example, individuals with a substance use disorder such as alcohol dependence will typically display abnormal patterns in alpha and beta frequencies (Sokhadze et al., 2008,p.1-19). However, non-alcohol-dependent individual who are relatives of alcohol dependent individuals also have similar abnormal patterns in the alpha and beta frequencies as compared with individuals without alcohol-dependent individuals (ibid.). This indicates that the EEG differences may not impact alcohol use directly, but may serve as a vulnerability factor for the development of alcohol-dependence and thus not primary cause. Hence, in the falling man analogy, EEG abnormalities may be akin to the condition of being on the plane, which is not sufficient in making sure the man falls to his death. Similarly, by extension one should be cautious in arguing that EEG-neurofeedback that reduces the abnormally plays a causal role in alleviation of mental dysfunctions associated with alcohol dependence. This does not render EEG neurofeedback useless, in fact it is rather advantageous, to have a therapeutic method serving as moderating preventive factor or as an add-on treatment to other established treatments (Cantor and Evans, 2014,p.265ff).

In a recent review, it was advocated that the EEG-neurofeedback of ADHD may in part be working through a moderating factor rather than as a directly causal factor (Arns and Kenemans, 2014,p.1-10). In short, several lines of evidence indicate that unstable vigilance has repercussions for attentional networks in general and that this may provide a framework for explaining ADHD symptomology. Similarly it has been shown that ADHD symptomology has been associated with worse sleep duration, daytime sleepiness and sleep disorders. Moreover, symptoms traditionally

associated with ADHD can be induced in healthy children with sleep restriction, suggesting an overlap between ADHD symptoms and sleep-disruption. Thus in a consideration of the causal relationship between neurofeedback and alleviation of ADHD symptomology, it could be possible that sleep as a third link in the causal chain intersects the cause and effect. Thus the hypothesis that is brought forth is that neurofeedback may exert it's effects by normalizing brain networks involved in circadian rhythm, and thus through enhanced sleep may relate to improved cognitive factors such as attention and vigilance (ibid.). To summarize, in inferring mind-brain causal relationship, even though neurofeedback ties in with the brain in several ways and thus has plausible explanations for how it may exert an effect, it may do so indirectly. Thus a key limitation of inferring causality through neurofeedback lies in its inability to ascertain whether the neurofeedback intervention is causally primary or rather represents a moderating factor.

5.2.6 Eliminating competing causal hypotheses

Scientific inquiry often seeks to confirm or verify hypotheses by eliminating competing alternatives to the point where only a single well-supported candidate theory remains (Holowchak, 2007,p.102f). As Sherlock Holmes advised Dr Watson, "When you have eliminated the impossible, whatever remains, *however improbable,* must be the truth" (Hill, 1965,p.4). Here, it will be argued that neurofeedback holds a potential not in establishing mind-brain causal relationships but in eliminating competing ones or rather informing of their inability to explain the data at hand.

To date, the exact nature and causal relationship between conscious intention and brain signals preceding movement is debated amongst philosophers and neuroscientists (Haggard, 2005,p.1-2). A common assumption is that of the Cartesian dualist position, that the mind chooses between available actions and then causes the body via the brain to perform the selected action. However as was shown in the seminal papers by Benjamin Libet, preparatory brain signals known as the readiness potential (RP) precedes the conscious intention to move (Haggard, 2005,p.1-2; Libet et al., 1983,p.1-19). One important question that arises from this finding is whether an individual can still exert a conscious "veto" decision and inhibit movement after the onset of the RP (Kühn et al., 2009,p.1-9; Misirlisoy and Haggard, 2014,p.1-4). Alternatively, the onset of the RP triggers a "ballistic" causal chain of events that is sufficient in causing the movement and thus makes any conscious inhibitory overriding of the movement impossible (De Jong et al., 1990,p.1-16). A recent study by Schultze-Kraft et al., (2015) sought to evaluate these mind-brain causal relationships by presenting subjects with a task in which they were rewarded for pressing a button when prompted with a green "go signals" and negatively reinforced should they press the button after a red "stop signal" (Schultze-Kraft et al.,

2015,p.1-5). A key novel aspect of the study was that the subjects RP and muscle activity was being detected by a brain-computer interface (BCI). Prediction of movements were made in real time by the BCI and would present the stop signal in order to interrupt the subjects movement. Thus the paradigm was an EEG based exogenously controlled closed loop, where the neurofeedback was not fed back to the subject but rather, was used to trigger an event, in this case a stop signal. The results showed that subjects could in fact still veto the movement even after the onset of the RP suggesting that the onset of the RP is not sufficient for the final movement. Moreover, cancellation of movement was possible only if the triggered stop signal occurred 200 milliseconds (ms) before movement onset, thereby constituting a point of no return (ibid.). Here, the real-time EEG neurofeedback is used in a manner that allows for an evolving experimental paradigm (Sulzer et al., 2013,p.2-7). Similar, to the way Hinds et al., 2013, who also used an exogenously controlled loop to decide when an external event would occur (Hinds et al., 2013,p.1-9). In this way, the paradigm uses brain measures as the IV and can thus more optimally inform about mind-brain causal relationships by delineating the time points of onset of RP and the point of no return. It was shown that the RP in itself is not sufficient to cause movement but requires the lack of a veto inhibition before it results in any movement (Schultze-Kraft et al., 2015,p.1-5). However, the improved delineation of time points also allowed researchers to provide evidence for a point of no return occurring 200 ms before movement onset. In summary, neurofeedback holds an advantage in comparison with traditional methods and allows researchers to create evolving experimental paradigms able to provide evidence for and against mind-brain causal hypotheses.

5.2.7 Identifying unpredicted cognitive processes

In the following section it will be reviewed how neurofeedback has the potential to uncover mind-brain causal relationships that is unexpected by the theoretical construct (Micoulaud-Franchi et al., 2014,p.1-7). It is informative, first to explain the two traditional ways neuroscience progresses, that of the neuropsychological approach (NP) of analysing the structure and function of the brain as the IV and measuring the corresponding variation in specific cognitive activities as the DV (ibid.). As an example of an NP could be how patients with brain lesions in the ventromedial prefrontal cortex (vmPFC) show a deficit in a certain type of decision-making situation as measured by the Iowa Gambling Task (IGT) when compared with healthy participants (Bechara and Damasio, 2005,p.1-33). Another tradition within neuroscience is that of the psychophysiological approach (PP), which is generally applied to intact brains measured through neuroimaging as the DV obtained while the participant performs a prescribing task containing a cognitive process of interest as the IV which is

captured by an appropriate behavioural measure (Micoulaud-Franchi et al., 2014,p.1-7). For instance, measuring the neural activity related to masked and unmasked stimulus presentation and then inferring based on verbal reports that one was perceptually conscious and another unconscious (Dehaene et al., 2001,p.1;Sandberg et al., 2014,p.1). In both cases (NP and PP) require an externally controlled theoretical construct for the mental phenomena, in this case advantageous decision making in the IGT or perceptual consciousness of masked and unmasked stimuli respectively (Micoulaud-Franchi et al., 2014,p.1-7). The theoretical construct is "externally" controlled since the experimenter externally imposes the cognitive task based on a theoretical construct. The design of the task attempts to eliminate possible confounding factors as well as to ensure the reliability of the task. On the other hand, these approaches fail to take into account those cognitive processes not predicted by the theoretical construct; as they can only take account of those cognitive processes that were expected. In case of the NP approach, it would be circular reasoning to state that cognitive performance measured through behavioural responses directly conveys the function of the localized neural substrate (e.g. "IGT measures vmPFC function"), given that, that task was constructed from behaviour in the first place (e.g. to capture the core deficit of the vmPFC lesioned patients) (Bechara and Damasio, 2005,p.1-33; Bechara et al., 2000,p.3, 1994,p.1-8; Lindeløv, 2015,p.8). Further, the prescribed cognitive task has a tendency to validate its own axiomatic theoretical construct even though such constructs play a large role in prescribing the specific cognitive task. In the case of vmPFC lesions resulting in a deficit in decision-making as measured by the IGT, the results are not surprising since that was the goal of the task, i.e. to show a deficit. One could just as easily envision a cognitive process where vmPFC lesions may be advantageous (Damasio,1994,p.192-194).

In the case of the PP approach, the neural measure is isolated through contrastive analysis of the cognitive process where behavioural responses have been tailored to inform about the theoretical construct. In the paradigm investigating the neural measures of perceptually consciousness, the externally controlled theoretical construct has as a presupposition the all-or-none dichotomy between conscious and unconscious perception (Dehaene et al., 2001,p.1;Sandberg et al., 2014,p.1). The perceptual experience of the participant is being constrained by the theoretical construct into two different manifestations of the mental phenomena without allowing for any measurement of the possible continuum in-between (Ramsøy and Overgaard, 2004,p.1-20). A further common misconception about the PP approach is that the discovered neural processes can be postulated as causing the mental phenomena, even though the neural contrasts were detected by virtue of the mental phenomena measured through a constrained behavioural task (Overgaard and Mogensen, 2014,p.1f). In other words 'How we measure in large part determines what we measure – or, perhaps more

precisely, what we think we are measuring' (Uttal, 2001 cited from Micoulaud-Franchi et al., 2014,p.2).

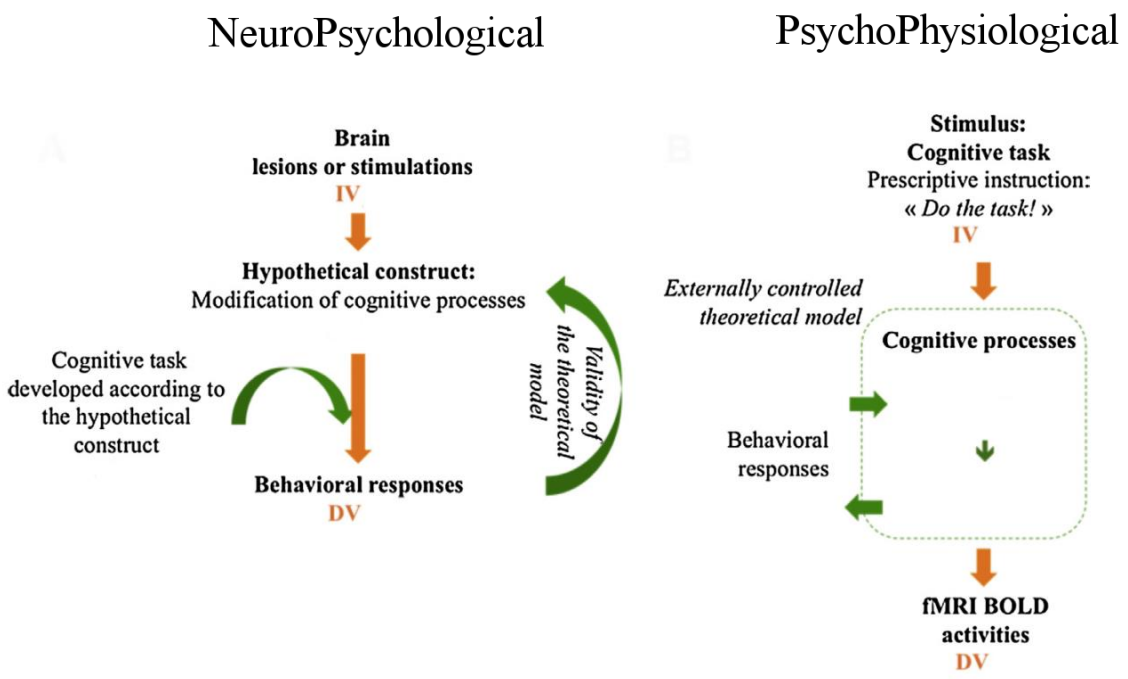

Figure 10. The frameworks compromising the "NeuroPsychological" approach and the "PsychoPhysiological" approach, IV: Independent Variable, DV: Dependent Variable. Adapted from Micoulaud-Franchi et al., 2014,p.4

Neurofeedback has a potential to be fundamentally different from the traditional NP and PP approaches as it can arguable uncover cognitive and mental processes not predicted by the theoretical construct. The theoretical construct in neurofeedback is "internally" controlled rather than externally, since it is the participant inside the neurofeedback loop who controls and thus develops the cognitive task. The cognitive processes is no longer governed by any prescribed task designed for validating a theoretical construct but rather the cognitive process is developed by the participants themselves in an attempt to influence activations in the brain where neurofeedback is derived. (ibid.).

The mental phenomena is the product of "intronеuroimaging" as proposed by deCharms, that of the participants own self-evolving cognitive process that can be perceived phenomenologically while physical processes take place in the brain during such experiences (deCharms, 2008,p.1). In a similar vein, a proposed scientific program in 1996 by Varela, the field of neurophenomenology is an attempt to combine first person subjective reports with third persons neurobiological data (Varela, 1996,p.1-18). From a neurophenomenological point of view, neurofeedback has the potential to facilitate a particular brain activity whereby phenomenological inquiry can enable the subsequent gathering of participants verbatim statements as to their self-evolved cognitive processes in acquiring such brain activity (Bagdasaryan and Le Van Quyen, 2013,p.1-8; Micoulaud-Franchi and Quiles, 2014,p.1-7)

Such a methodology of combined neurophenomenological and neurofeedback approaches was recently used in a rtfMRI neurofeedback protocol to investigate the subjective experience of cognitive processes used in acquiring control over brain activity in the default mode network (DMN) during meditation (Garrison et al., 2013,p.1-8; Micoulaud-Franchi and Quiles, 2014,p.6f). In a study by Garrison and colleagues (2013), the first-person accounts of mental strategies were probed using grounded theory methodology while subjects where meditating and performing rtfMRI neurofeedback of a core region in the DMN called the posterior cingulate cortex (PCC) (Garrison et al., 2013,p.1-8). Activation in the PPC above baseline has previously been found during self-referential thinking, envisioning the future, conceding the perspective of others, mind-wandering and PPC deactivation during meditation or as contemplative traditions call it "being in the moment" (Brewer et al., 2011,p.1; Buckner et al., 2008,p.1-32; Mason et al., 2007,p.1-2). It's important to realize that the previously mentioned mind-brain relationship are acquired using either the NP or PP approaches and thus implicitly use an externally controlled theoretical construct to prescribe the cognitive task in order to investigate the relationship. Here, in the study by Garrison et al., (2013) the authors wanted to investigate whether the up and down regulation of the PCC was associated with any as of yet unexplored subjective experiences (Garrison et al., 2013,p.1-8)

The experiment consisted of experienced meditators going through a protocol aimed at progressively introducing neurofeedback into the meditation practice, thus slowly learning meditators how PCC activity corresponded with their own subjective experience. In breaks throughout the experiment, meditators were asked to describe their subjective experience during the meditation, and were replayed their brain activity during meditation (offline feedback) and asked which strategy they used to change activity. The subjective experiences where then categorized using grounded methodology from open-coded verbatim reports to principal theoretical constructs and it was determined whether those constructs corresponded with decreased or increased PCC activity. The results showed that subjective experiences such as "effortless awareness" , "concentration" and "observing sensory experience" corresponded with PCC deactivation and experiences of "distracted awareness", "interpreting" and "discontentment" with PCC activation. Intriguingly, the authors found several novel qualifiers in terms of the mind-brain relationship in which specific instances of mind-wandering *did not* illicit PPC activation. Below are exempts from the meditators self-reports in unsuccessful attempts to activate PPC which supposedly would occur during mind-wandering (ibid.).

> *"Meditator 134 (run 12): For this meditation, now I just tried not to push it at all, I just wanted to see what would happen with just really resting, not visualizing*

anything, not using anything as a tool, just opening up the space and resting, and I think towards the middle I had some thoughts which I don't see on this graph maybe because I just let them kind of flow by, but I noticed some thoughts. (…)

Meditator 141 (run 14): I was surprised that [the graph] was so blue [PCC deactivation] on that second part. I was observing a lot of what I was thinking, but I was thinking about a lot of things, for example, what I had to do the rest of the day "

(Garrison et al., 2013,p.7)

It is unexpected that such instances of recurrent mind-wandering would result in PCC deactivation given the *a priori* established finding of increased PCC activity in mind-wandering (Mason et al., 2007,p.1-2). On close inspection, the self-report of participants could be interpreted as reflecting instances where mind-waning has a certain quality to it, of not being forced or reactive but rather observing it as a non-judging and non-attached spectator. Mind-wandering leading to PPC activation may be distinguished by such instances where participants thoughts are not attempted to be pushed or shut off, instead they allow their mind to wander and just "let the thoughts be" (Garrison et al., 2013,p.7; Kabat-Zinn, 1990,p 52f & 347f, 1982,p2; Leary et al., 2006,p.20). In contrast, according to Garrison et al., (2013) the subjective experience of mind wandering leading to increased PCC activity may contain a quality of reactivity to mental content or thoughts, such as rumination, desire or aversion toward the mental content akin to the notion of "getting caught up with one's thoughts" (Garrison et al., 2013,p.7; Kabat-Zinn, 1990,p.76).

The results raise a key point, that the combination of neurofeedback and phenomenology allowed the authors to uncover unexpected mental phenomena linked to the particular brain activity, not predicted by the *a priori* theoretical construct (Bagdasaryan and Quyen, 2013,p.1-8; Micoulaud-Franchi and Quiles, 2014,p.1-7). Thus, one of the potentials of neurofeedback for informing about mind-brain causal relationships lies in the synergistic effect of combining it with phenomenological approaches. In contrast, a PP approach that would hold deeply, an axiomatic presupposition of an all-or-none dichotomy between mind-wandering and non-mind-wandering would seek corresponding neural correlates of increased and decreased PCC activity respectively. Then through repeated measurement, a PP approach would gain a contrast of aggregates and mean values that would lead to a conclusion of an overall difference.

The approach would lack any phenomenological constraints and thus be ineffective in uncovering that mind-wandering can be qualified as passively spectated or as a reactive phenomenon, thus failing to detect the subtle nuanced description of the mental phenomena. Here, information from first- and third-person perspectives is braided together in the iterative closed loop, that is internally guided by the participants themselves. In the spirit of Varela's proposal for neurophenomenology the mental phenomena is not purely investigated through the lenses of the cognitive sciences nor phenomenology, but rather what is concluded is mutually constrained by each. This is not to say that the NP and PP approaches should be entirely replaced by neurofeedback, but rather that they suffer from limitations that neurofeedback can ameliorate (ibid.). By no means does neurofeedback in conjunction with neurophenomenology in this instance show a causal relationship between PPC activity and the experience associated with it. Yet, it does provide an approach that can uncover mind-brain relationships not predicted by the theoretical construct which may thus further subsequent investigations into its causal nature.

5.2.8 Methodological pluralism

The above mentioned aspects of neurofeedback's potential and limitations for addressing causality may appear as a neurofeedback"centric" perspective on causal inferred, i.e. focused on making neurofeedback the exclusive tool for addressing causality. In discussing EEG and rtfMRI neurofeedback's potential to inform of mind-brain causality it's crucial to recognize that causal accounts cannot be addressed through neurofeedback alone. Instead, the hypotheses that drive and foster neurofeedback research is made possible through prior psychological and neuroscientific research pointing at the plausibility for neurofeedback to modulate a specific mind-brain causal relationship. For example, the already-established relation between pain sensation and certain brain regions that show that ACC activity corresponds with the extra dimension of the emotional unpleasantness of pain. Here, a burgeoning literature is behind such an observation of the involvement of ACC in this particular mind-brain relationship (Peyron et al., 2000,p.1-21) Thus, neurofeedback as an analytical tool is not the exclusive tool for investigating the mind-brain relationship in question, but acts in unison with the entirety of the neuroscientific investigative arsenal of techniques. In inferring causality, neurofeedback does not hold the final verdict, and must follow the coherence criteria and inform of causal relationships without conflicting with prior knowledge about the mind-brain causal relationships. This was exemplified through the arguments against rt-sMRI neurofeedback and down-regulation of AIC. These unpromising notions show that neurofeedback in certain situations has limitations such as an overfocus on the trainable mind-brain causal

relationships. It becomes paramount, for the future endeavour of neurofeedback researchers to remain wary of such dead-end research questions, that can be avoided on mere scientific coherence in contrast to a trial-and-error empirical agenda.

A beneficial heuristic is to think of causal inference as science slowly triangulating which causal hypothesis is the most likely (Jick, 1979,p.2; Novella, 2015,p.160). One empirical study in isolation cannot be used to infer a causal mind-brain relationship, such inferences are typically the product of gradual piecemeal collection studies pointing towards one hypothesis above another. Methodological triangulation in this context means the "combination of methodologies in the study of the same phenomena" (Denzin, 1978,p.291 from Jick, 1979,p.2). When combining several methodologies in the validation process it ensures that the appearance of the phenomenon in question is reflective of the phenomena and not the methodology (ibid.). In this view, the role of neurofeedback to inform of mind-brain causal relationships achieves a higher degree of explanatory power than when used in isolation. Thus, the framework for establishing causal rather than mere inferential accounts is made possible by embracing methodological pluralism as opposed to purism (du Plessis, 2012,p.1-3; Lilienfeld, 2007,p.1-8).

Throughout this chapter several examples of neurofeedback research bear witness to the advantages of addressing causality using multiple methodologies. In addressing the susceptibility of neurofeedback to tertium quid arguments regarding another brain region having causal primacy in the mind-brain causal relationship. Such causal hypotheses lead to testable empirical predictions, that can be addressed through other technical methods in neuroimaging such as granger causality and dynamic causal modelling. Moving forward neurofeedback could potentially gain an even greater causal explanatory power by merging with other interventional techniques such as TMS and tDCS (Sitaram et al., 2012,p.1; Sulzer et al., 2013,p.6f;Clarke et al., 2014,p.1; Sliwinska et al., 2014,p.1). A testable prediction that would provide increased likelihood of causal primacy between neurofeedback regulation of brain region and a mental phenomenon, would be if TMS disruption limited to said region specifically hindered the acquisition of the neurofeedback learning. Moreover, anodal or cathodal tDCS stimulations should facilitate or attenuate respectively, the learning of neurofeedback for the region expected to be causally primary. Compared with these techniques neurofeedback and in particular rtfMRI allow for a greater whole brain coverage and spatial resolution of anatomical structures that are unreachable to TMS and tDCS. Applying these methods in unison allow for a greater degree of explanatory power as compared with neurofeedback in

isolation. In other words the limitation of neurofeedback is ameliorated by incorporating methodological pluralism.

Methodological pluralism is advantageous within neurofeedback itself, as was seen with Schultze-Kraft et al., (2015) study, aiming to delineate the point of no return in vetoing movements and the causal role of the RP (Schultze-Kraft et al., 2015,p.1-5). Here real-time EEG neurofeedback is the wiser choice, as the temporal resolution of EEG allows for close to millisecond precision whereas rtfMRI has greater temporal delay in its measurements. As a contrast, fMRI measurements allow for investigation of deeper brain structures such as the ACC which was seen in the example by deCharms et al. (2005). Here, methodological pluralism takes the form of researchers eclectically choosing which method is best suited for investigating the particular mind-brain causal relationship (Sonne-Ragans, 2012,p.33-45). Thus, when defining a research question regarding a specific mind-brain causal relationship a key consideration is which neurofeedback modality the relationship affords to be investigated through.

Another core advantage of methodological pluralism in neurofeedback comes with use of mental strategies and the induction of certain mental states used through either hypnosis or meditative techniques. In fact, authors in these disciplines support the notion of methodological and conceptual overlap of meditation and hypnosis and neurofeedback (Batty et al., 2006,p.1-3; Brandmeyer and Delorme, 2013,p.1-3; Gruzelier, 2014a,p.1-9; Warner et al., 2000,p.1-3). In regard to deCharms et al., (2005) the study was influenced by the amounting evidence that hypnosis could influence the specific unpleasant component of the pain sensation (deCharms et al., 2005,p.1-5; Rainville et al., 1997,p.1-3). The result of the study can be viewed both as a replication of the hypnosis findings in addition to an argument for the combination of hypnosis and neurofeedback methodology (ibid.). Moreover, the study by Garrison et al. (2013), the participants were experienced meditators which allowed valuable insights into the subjective experience of effortless awareness associated with PCC activity (Garrison et al., 2013,p.1-8). Furthermore, the study is beneficial for both methodologies, as meditative practices appear to be a prime candidate for improving learning in neurofeedback studies, and neurofeedback may equally provide a medium through which meditative practices become even more compelling in terms of efficacy (Garrison et al., 2013,p.1-8; Hanlon et al., 2013,p.3). If one were to provide an answer as to a question of a short-cut to achieve what contemplatives term “being in the moment” or “one-pointed concentration” based on the results from Garrison et al. (2013), may tentatively be neurofeedback down-regulation of the PCC (Brewer et al., 2011,p.1; Brefczynski-Lewis et al., 2007,p.1f; Garrison et al., 2013,p.1-8). Keeping in mind that, this appeal to neuroanatomy provide only an explanation on the implementational level of analysis, where

neurofeedback and meditation techniques serve as the algorithm to achieve the goal of the subjective experience and therapeutic gains of the mental phenomena, situated at the computational level.

A similar advantage of methodological pluralism is seen with neurofeedback when used in conjunction with a neurophenomenological approach to uncover mind-brain causal relationships not predicted by the theoretical construct. The example provided by Garrison et al. (2013), show the phenomenological approach of taking human first-person experience as a central component that thus allows one to constrain the neuroscientific interpretations of the data for a more nuanced view of the phenomena (Bagdasaryan and Le Van Quyen, 2013,p.1-8; Micoulaud-Franchi and Quiles, 2014,p.1-7; Garrison et al., 2013,p.1-8). Such, a style of inquiry may also be beneficial on behalf of discovering instances where explicit instructions for participants to perform during neurofeedback allow a more efficient self-regulation (Sulzer et al., 2013,p.4).

In summary, neurofeedback research is not exclusively involved in addressing mind-brain causal relationships, in fact the above mentioned material exemplifies the complementary nature of combining neurofeedback with other methodologies. Neurofeedback research often builds on plausible already-established scientific mind-brain relationships and attempts to triangulate which causal relationship is most likely. Here, incorporating a wide variety of quantitative and qualitative methods into neurofeedback research methodology allows a larger degree of explanatory power. Thus, a defining characteristic for the scientific discipline of neurofeedback moving forward in maximizing it's explanatory power is adopting methodological pluralism (Feyerabend, 1993,p.21).

6. Conclusion

Throughout the thesis several key aspects of the degree to which neurofeedback can inform of mind-brain causal relationship arose. In the introductory piece on the principles of biofeedback the root question of induction of certain conscious states were addressed as well as ability of neurofeedback to provide therapeutic benefit. Another important principle was that of how neurofeedback relies on the ability of a plastic nervous system to transparently interface readily with electronic devices and thus extends the human capacity to self-regulate. In the chapter on electroencephalography, the neurophysiological backdrop for the extent of neurofeedback to train and treat a wide spectrum of mental functions and dysfunctions was shown. Here, the "conditioning-and-repair" and the "skill-acquisition" models hold competing assumptions, favour different methodologies and lead to opposing predictions about the ability of neurofeedback to causally effect mind-brain relationships.

In order to facilitate a deeper understanding of neurofeedback and the competing models, exemplary evidence was presented from an on-going investigation into the neural signatures of foreign language learning efficiency. On the basis of this, a series of hypotheses were generated to provide further direct evidence for either model in addition to examining a causal mind-brain relationship. The fourth chapter aimed to review the basis of the second major neurofeedback modality of real-time functional magnetic resonance imaging (rtfMRI). The review's focal point was methodological advantages of rtfMRI to experimentally test multiple brain regions and their activity as the independent variable for given mental phenomena, in addition to designing dynamically evolving paradigms.

In facing up to the question of causality inferred through neurofeedback, the last chapter facilitated an understanding how to attain causal scientific accounts of any phenomenon. Following this, the subsequent discussion deliberated several key limitation in addition to advantages when arguing for the extent of neurofeedback to investigate of mind-brain causal relationships. Here, the present author outlined key challenges of neurofeedback for inferring causality, one of which was susceptibility to tertium quid argumentation. Moreover, at present it seems unlikely that neurofeedback can inform of a brain state to be unidirectional causing a mind state and the method is unpromising in resolving mind-brain states in the face of untrainable brain measures. Through this line of questioning the potential of neurofeedback for informing of mind-brain causality several advantages arose, specifically the extent of the method to provide evidence for the fulfilment of several of Hill's causal criteria such as biological gradients and experimenting with the brain as a dependent measure. Further advantages presented including driving specificity of causal mind-brain relationships by testing multiple neural substrates, that plausibly codetermine the mind-brain relationship. In addition, the methodological advantage of creating dynamic evolving experimental paradigms through exogenously controlled loops able to more clearly delineate mind-brain relationship and pinpoint shortcomings of competing causal hypotheses, was presented. One of the potentials of neurofeedback for inferring causality, came in the form of eliminating causal accounts by its use of an evolving paradigm. This is a strong case against neurofeedback establishing causal relationships, but rather shows it potential to do the opposite, (i.e., to falsify existing causal hypotheses). A noteworthy potential of neurofeedback was the methodological synergy created when the method is paired with the neurophenomenological tradition. Here, an example illustrated how neurofeedback can overcome the shortcomings of the conventional traditions of the neuropsychological approach and the psychophysiological approach and uncover mind-brain relationships not predicted by the theoretical construct. The deliberation of the key pros and cons of neurofeedback for causal inference of mind-brain relationships culminated in the argument that the limitations are ameliorated and the potentials

increased when paired with other methodologies and thus an appeal to methodological pluralism was made. With regard to inferring causal relationships, neurofeedback enters into a reciprocal relationship with other disciplines in order to provide plausibility and coherence for particular mind-brain relationships. While neurofeedback may harbour susceptibility for tertium quid argumentation, such limitations can be ameliorated by pursuing other avenues for inferring causality in neuroscience. A further argument for methodological pluralism was seen in the intriguing mind-brain relationships uncovered when neurofeedback incorporates methodologies such as hypnosis and meditation. In moving forward, the largest potential of neurofeedback for inferring causal mind-brain relationships is more realized through a combined effort of several psychological and neuroscientific methodologies.

Looking back to the present thesis initial conceptualization of the causal rank as a distinct from the inferential rank, one can argue that such a notion is plagued by a false premise. The thorny question of causality and the extent to which neurofeedback can investigate mind-brain causal relationships is one of gradual increases in certainty and not an all or nothing event. Neurofeedback's ability induce change in mental states (M) by manipulating physical brain measure (P) spawns a multitude of causal hypothesis about the nature of the relationship between M and P. It is erroneous to assume that there is a clear demarcation between when something is a causal and when something is *only* inferential. It is a false dichotomy to state that a causal hypothesis can be either wholly justified or utterly discarded, rather hypotheses exist of a continuum of relatively more confidence in a causal hypothesis of a the phenomenon. The denoting of a relationship as "causal" or "inferential" should be proposed only for analytical clarity or didactic purposes as they represent extreme poles of scientific ranks. Thus a new understanding of how mind-brain causal relationships can be informed through neurofeedback, one that highlights the continuum of causal likelihood between an inferential account and a causal one. Inferring causality based on one study alone is highly unlikely, such inferences are usually the product of several studies and methodologies pointing to a common parsimonious causal hypothesis. As proposed by Hill's, his nine criteria for a causal relation represents the *likelihood* of a causal relation, not it's certainty (Hill, 1965,p.1-6). Equally, researchers using EEG and rtfMRI-based paradigms shouldn't state how they *can*, instead how they *might* address questions of causality as opposed to mere correlations (Sulzer et al., 2013,p.6). With the aim of fostering a virtuous scientific research program involving neurofeedback, researchers should be compelled to describe with caution their inferences regarding causality and only make such claims in the event of burgeoning research and meticulous data suggests it. Of cause such notions of the reciprocity of mind and brain are typically assumed implicitly.

The ontological question often arises which is whether the changes in brain activation derive from changes in mind states or whether brain activation causes changes in mind states. With neurofeedback, the presumption is often that the brain activation and mental processes are correlated manifestations of the same phenomena. When discussing whether neurofeedback could provide unidirectional causal relationships it was found that such notions are still unlikely for neurofeedback to addresses. Moving forward researchers within the field of neurofeedback should be compelled to realize that mind and brain change bidirectionally through training (deCharms, 2007,p.5). In fact, as was shown with the ability of neurofeedback to identify unpredicted cognitive processes by braiding first- and third-person perspectives into an iterative closed loop is able to address the mental changes as they occur with changes in the brain.

The present author will argue that what is gained through neurofeedback is more than just an association, since one is consequently more certain of a causal link *within* the mind-brain relationship, as opposed to only knowing that induction of the mental state through experimental means led to a particular brain activity. The later evidence alone cannot rule out that brain activity is epiphenomenal to the mental function or state (Keizer et al., 2010,p.1-4). When inducing the mental state via neurofeedback one has gained the additional information that inducing a particular brain activity have particular mental states associated with it. Even if such a cause-effect relationship is qualified by several reservations such as the exhaustive investigations of multiple regions postulated through tertium quid argumentation and that the relationship is only bidirectional (i.e., no mechanistic or high *specificity* to the causal account).

In culminating on an answer to the problem statement, the present thesis has featured several examples of the potential of neurofeedback to provide evidence for and against mind-brain causal relationships. In light of the discussion and the reviewed evidence, the question posed by thesis of whether "we through the extent of neurofeedback research to investigate mind-brain relationships have consequently satisfied a scientific causal account of a codetermining law between mind and brain" would accordingly be answered; "it depends". It depends on this new understanding of how mind-brain causal relationships can be inferred, one which gradually increases in likelihood. It also depends on the criteria of inferring causality, such as whether unidirectional or a bidirectional causality satisfies as a causal account. It further depends on the whether it is the"conditioning-and-repair" model or the "skill-acquisition" model that most adequately describes the neurofeedback processes, as these models pose different explanatory accounts of the impact neurofeedback had on a mind-brain relationship. Additionally, the causal inference of neurofeedback for mind-brain relationships comes with a susceptibility to tertium quid counterarguments and instances where

neurofeedback may over-focus on trainable brain regions, and thus miss dimensions of the mind-brain relationship. As was shown, the limitations of the neurofeedback method can be ameliorated through the use of methodological pluralism in informing of such mind-brain causal relationships. However most importantly, where neurofeedback does provide an advantage in informing of causality compared with concurrent methods or when it is paired with other methods, it or they cannot do so to any absolute, but rather through a steady incremental increase in the likelihood of a mind-brain causal relationship.

At the present moment, it is thus unknown if neurofeedback will truly allow inference on mind-brain causality in any absolute sense. Although, it can be argued, that in the grand scheme of things the dichotomy between inferential and causal scientific accounts remain entirely justified. Executing this argument, involves a parallel to evolutionary biology. Here, the notion of gradualism states that evolution happens in a steady and gradual transformation of species in a smooth and continuous fashion. This conjecture, dominated evolutionary thinking until Niles Eldredge and Stephen Jay Gould proposed the new theory of punctuated equilibrium, that evolution goes through long periods of stasis followed by rapid bursts of macro change (Eldredge and Gould, 1972,p.1-35). Analogously, I will argue that the progression of the neuroscientific field stand at an inflection point in the progression of scientific ranks of explanations. Here, the key conditions of supporting a potential rapid change is the advent of newer methods, one of which is neurofeedback.

To state in an absolute sense, that an observed relationship has transcended from a mere inferential to a truly causal account is most likely an inappropriate conception as causal hypotheses increase gradually in likelihood. However, in the grand scheme of scientific progression, the neuroscientific discipline stands at decisive moment. A moment where the potential of neurofeedback for causal inference could change the face of it, forever.

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