# The Amsterdam Resting-State Questionnaire

*Measuring and characterizing resting-state cognition and its neural correlates*

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*“The mind is the effect, not the cause.”*
Daniel Dennett

# Contents

# Chapter 1
# General introduction

*Consciousness, then, does not appear to itself chopped up in bits. Such words as 'chain' or 'train' do not describe it fitly as it presents itself in the first instance. It is nothing jointed; it flows. A 'river' or a 'stream' are the metaphors by which it is most naturally described. In talking of it hereafter, let us call it the stream of thought, of consciousness, or of subjective life.*

**William James, 1890**

## The tension between introspection and behavior

As so vividly described by William James (James & Miller, 1890), consciousness appears to us as undivided, flowing and continually being refreshed with both internal and external impressions. These conscious states emerge from the myriad, often spontaneous, dynamics of ongoing neuronal activity within the human brain (Seth, 2010) and enable us to reflect on our past, anticipate future events and to interpret the behavior of others by placing ourselves in their shoes, a concept known as theory of mind (Buckner & Carroll, 2007; Saxe & Kanwisher, 2003). Although the human brain is not unique in its capability to produce conscious states (Edelman & Seth, 2009)—evidence suggests that even non-mammalian species (ravens) may express sophisticated behavior suggestive of theory of mind (Bugnyar & Heinrich, 2005; Massen, Pašukonis, Schmidt, & Bugnyar, 2014)—only humans appear to unequivocally possess meta-consciousness, self-awareness, and the ability to report on their inner experiences. This allows, in principle, for the exploration of potential relationships between inner experiences and the neural activity from which these experiences originate.

The study of inner experiences continues to play a key part in the psychological and cognitive sciences, despite its historical controversy (Boring, 1953; Costall, 2006; Danziger, 1980). The early psychologists of the 19th century were divided on what constitutes the 'proper' scientific method for gaining knowledge about the human mind (in the broadest sense of the word). Famous examples are William James and his concept of the 'stream of consciousness' who, in line with the British tradition influenced by John Stuart Mill, accepted (trained) introspection as a valid source of information. On the other end of the spectrum were experimental psychologists such as Wilhelm Wundt, who attempted to elevate the psychological science to a level of reliability and objectivity on par with the physical sciences—even if it meant severely limiting their methodology to a select number of carefully controlled experiments and trained subjects (Danziger, 1980). In the early 20th century, John B. Watson, the founding father of behaviorism denied inner experiences any scientific value, mainly due to their apparent unreliability and subjectivity, and declared the study of behavior alone as the 'correct' form psychology should take on (Boring, 1953; Costall, 2006). However, neither of these (widely) disparate positions could account for a complete picture of human consciousness and its relation to underlying biology—after all, the early Würzburg school of psychology already attempted to expand on the restricted experimental paradigms of Wundt by including subjective reports (Danziger, 1980).

The prevalent argument against the use of self-reports as method is the presumed unreliability of said reports. While human memory can be certainly prone to (sometimes severe) error under special circumstances (Nisbett & Wilson, 1977), doubting the value of human recollection and inner experience also undermines the plethora of social and economic institutes of society—even Watson, staunch crusader of behaviorism admitted the value of advertising psychology (Danziger, 1980). More importantly, however, is the fact that even the earliest psychologists were aware of the danger of potential unreliability of subjective reports, and consequently put considerable effort and thought into methods to control assessment. Self-reports, in other words, have been with the psychological and cognitive sciences from their early beginnings, and successfully so considering Freud's extensive legacy (Howe, 1991).

Simultaneously, there can be no doubt about the tremendous advances and insights provided by psychophysiological research. Important examples include Donders' reaction time experiments, Weber's famous just-noticeable difference equation, Hans Berger's electroencephalography (EEG)—still forming a basic tool in clinical and cognitive neuroscience (Berger, 1929)—and highly influential models of memory (Baddeley, 1992) and visual processing (Marr & Poggio, 1976). In recent years the crucial dimension of brain activity, usually accessed via neuroimaging techniques such as electroencephalography, magnetoencephalography or functional magnetic resonance imaging, has been added to the standard repertoire of the (cognitive) neuroscientist (Calvert et al., 1997; Griffiths et al., 1998; MacDonald, Cohen, Stenger, & Carter, 2000; Monto, Palva, Voipio, & Palva, 2008; E. E. Smith & Jonides, 1999).

## Return of the wandering mind

Traditionally, neuroimaging experiments have strongly relied on event-related or task-based paradigms (McCarthy & Donchin, 1981), where experimental blocks alternate with passive rest periods thought to serve as a suitable baseline condition. These rest conditions commonly take on the form of relaxed wakefulness with closed eyes and their use has a long tradition in clinical settings, for instance as baseline EEG measurements in epileptic patients (Fenton, 1984). However, the idea of resting-state brain activity reflecting mere unstructured, spontaneous "idling" has been convincingly rejected by studies showing that beside the expected event-related activations, specific functional brain networks reliably decrease in metabolic activity during tasks (M E Raichle et al., 2001). These same "task-negative" networks by contrast appear to be most active during resting periods and the most prominent of these networks, involving the medial temporal lobe, medial prefrontal cortex, posterior cingulate cortex and precuneus, has since been referred to as the default mode network (Buckner & Vincent, 2007; Michael D Greicius, Krasnow, Reiss, & Menon, 2003; M E Raichle, 2006; M E Raichle et al., 2001). The paradigm-shifting discovery of the default mode network (DMN) has sparked an explosive growth in the number of studies dedicated to the exploration of the resting-state and its functional correlates (see Figure I-1). Yet despite our rapidly increasing understanding of the physiological and functional mechanisms of the brain, fueled by technological advances and readily available and affordable computational equipment, our knowledge regarding the meaning of spontaneous brain activity in terms of conscious experience remains strongly limited.

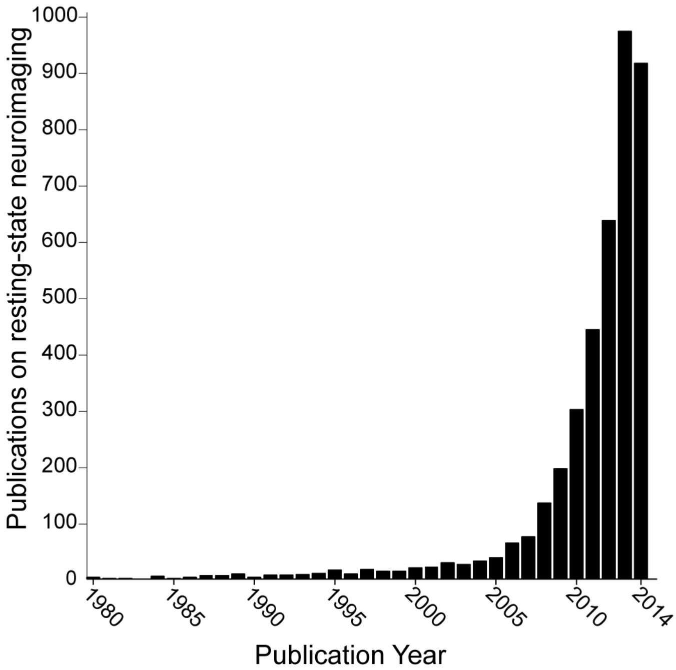


**Figure 1.1** Research into resting-state neuroimaging has witnessed exponential growth over the first decade of the 21st century, highlighting the interest generated by the field. Shown is a histogram based on a PubMed keywords search (September 2014) using the query: "Resting-state & (EEG OR fMRI OR PET OR Neuroimaging OR MEG)".

Many of these conscious inner experiences take on the form of daydreaming or mind wandering, and are generally defined as thoughts unrelated to a specific task or focus (McVay & Kane, 2009). These tasks need not be external in nature, nor does mind wandering imply not paying attention to any task at all, as is illustrated by an anecdote in which famous psychologist William James supposedly countered the accusation of being absent-minded by stating he was merely *present-minded* to his own thoughts. Indeed, it could be argued that the wake-state nervous system always selects an object of attention, even if it is self-generated as in the case of inner thoughts.

However, a precise definition of mind-wandering, even when limited to the behavioral domain, appears difficult as reflected by its multitude of proposed descriptors throughout the past decennia, including "stimulus-independent thoughts" (Antrobus, 1968), "zone-outs" (Schooler, Reichle, & Halpern, 2004) and "task-unrelated thoughts" (McVay & Kane, 2009). Potential differences (Smallwood, 2010) aside, this predominantly behavioral operationalization of mind wandering has provided invaluable insights into psychophysiological correlates of mind wandering, e.g., reaction time increases and the role of task-load (Smallwood & Schooler, 2006), and its place in cognitive theories of executive control and working memory (Dehaene, Changeux, Naccache, Sackur, & Sergent, 2006; McVay & Kane, 2010; Smallwood, 2010). Pioneering work on mind wandering dates back to the nineteen sixties (Antrobus, Singer, Goldstein, & Fortgang, 1970; Antrobus, Singer, & Greenberg, 1966; Antrobus, 1968; J. L. Singer, 1974), but wider attention was only recently achieved (Schooler & Schreiber, 2004; Smallwood & Schooler, 2006), possibly fueled by discoveries made in resting-state neuroimaging experiments. An elegant and common example of detecting mind wandering episodes is by measuring lapses in attention towards external tasks through reaction time increases (Smallwood, McSpadden, & Schooler, 2008), which can be readily merged with existing resting-state neuroimaging protocols (Andrews-Hanna, Reidler, Huang, & Buckner, 2010).

This approach, however, neglects much of the "subjective" dimension of mind-wandering, i.e., the qualities of the underlying stream of conscious evaluation even though it is known that we spend much of our waking time on inner experiences which, as some have suggested (Killingsworth & Gilbert, 2010), may affect psychological well-being negatively. On the other hand, recent studies suggest that (deliberately) engaging in "mind wandering", that is focusing conscious evaluation inwards, could have a positive impact on creativity and problem solving (Baird et al., 2012). In addition, individual differences in mind-wandering experience or the impact of disease status on inner experiences are domains still open to systematic study. Fortunately, as with the classical disparity between behaviorism and introspectionism, there is no need to a priori forfeit subjective accounts of inner experiences, as these can be combined with physiological and behavioral assessments, potentially offering a richer and more complete picture of mind wandering. The necessity to further investigate the semantics of mind wandering becomes evident when one considers the substantial interest in default mode network activity during the resting state and its relation to mind wandering (Brewer et al., 2011; Buckner & Carroll, 2007; Buckner & Vincent, 2007; Christoff, Gordon, Smallwood, Smith, & Schooler, 2009; Guldenmund, Vanhaudenhuyse, Boly, Laureys, & Soddu, 2012; Hasenkamp, Wilson-Mendenhall, Duncan, & Barsalou, 2012; Smallwood, Tipper, et al., 2013).

Before proceeding, an important clarification needs to be made. Although mind wandering has evolved into an umbrella term encompassing both the occurrence of an attentional shift inwards as well as the accompanying conscious representation. Whereas the switch in focus constitutes an observable deviation deserving distinguishing nomenclature, it is less clear whether or not the subjective experience of mind wandering is also different from "on-task" subjective experience. Therefore, the general term conscious evaluation is introduced when referring to this subjective component explicitly.

## A global workspace model of conscious thought

Consciousness presumably involves the coordinated and integrated interplay of a wide array of different neural processes and associated neural substrates, a notion captured by global workspace theory (Dehaene et al., 2006), which postulates the existence of networked specialized neural modules (for instance sensory processing) and a distributed, but interconnected set of entities providing a neural workspace. This workspace facilitates the continuous and global exchange of information between different cognitive processes, e.g., long-term memory (Addis, Wong, & Schacter, 2007) and verbal report, and hence between underlying anatomical regions such a prefrontal structures involved in executive control and decision-making. As such, activation of the global workspace—the availability of integrated information to a global network—may give rise to consciousness, allowing for (the guidance of) intentional behavior (Smallwood, 2010). The global workspace then provides a fine theoretical framework in which to place mental evaluation during mind-wandering episodes, given that mind wandering is necessarily reportable (otherwise its subjective dimension could not be queried) and hence *conscious* (Dehaene et al., 2006; Dehaene & Naccache, 2001; Smallwood, 2010).

The generation of mind-wandering episodes may be governed, at least in part, by automatic processes triggered by (external) cues (McVay & Kane, 2010). These processes in turn strive to minimize discrepancies between desired end-states or goals and the current state. As goals are set, their resolution process may evolve into a current concern (Klinger, Barta, & Maxeiner, 1980), i.e., the generation of recurring thoughts related to a set topic such as the anticipation of future events (Antrobus et al., 1966; Buckner & Carroll, 2007). Depending on the success of this resolution process, the result can be either constructive, as in overcoming a personal tragedy, or unconstructive (e.g., refusing to let go of an unreachable goal) potentially resulting in (excessive) rumination (Martin & Tesser, 1996; McVay & Kane, 2010). Importantly, the various thought-generating concerns and desires are assumed to compete for conscious attention and, thus, their gating into awareness must be regulated accordingly by means of executive control (McVay & Kane, 2010; Smallwood & Schooler, 2006; Smallwood, 2010). Failure of proper executive control of current tasks can lead to mind wandering triggering processes gaining access to global workspace, resulting in task-unrelated thoughts to enter consciousness potentially, diverting processing resources from the task at hand and, thereby, producing lapses in attention or performance (Smallwood, 2010).

Conscious evaluation most frequently occurs under conditions that present few constraints on the subject's attention (Smallwood, 2010), such as during the resting-state, where default mode network (DMN) activity is predominant (M E Raichle et al., 2001; Smallwood, Brown, Baird, & Schooler, 2012). In addition, the proposed neural organization of global workspace theory is quite compatible with the distributed neuronal structures underlying the DMN (Fair et al., 2009; M D Fox, Zhang, Snyder, & Raichle, 2009). These findings corroborate to support the hypothesis that the default mode network and associated brain areas are at least in part involved with generating consciousness and, by extension, creating the prerequisites for the subjective experiences attributed to mind wandering and resting-state cognition (Doucet et al., 2012; He & Raichle, 2009; Larson-Prior et al., 2009; Spreng, Mar, & Kim, 2008; Tononi & Koch, 2008). In summary, the global workspace hypothesis provides a useful framework for integrating cognitive theory and neurophysiological observations associated with conscious evaluation.

## A standardized approach to studying resting-state cognition

The resting state appears to be an ideal condition for gathering data about the many facets of subjective experience, given its unrestricted nature which is deemed conducive to the generation of inner thought (Smallwood, 2010). In addition, a short period of wakeful rest is readily implemented in a wide range of (experimental) contexts and its limited demands form a low threshold for a variety of different populations, especially within clinical settings where neurological screenings using resting-state assessments have a long tradition (Berger, 1929).

Inner experiences have been frequently studied through the use of the experience sampling method, a customizable self-report method that randomly probes participant experiences several times a day, over the course of typically one week (Csikszentmihalyi & Larson, 1987). As such experience sampling is well suited to investigate and track the link between behavior and psychological experience over time and different settings. Owing to its flexibility, it can also be adapted to focus on subsets of inner experiences such as thought patterns (Heavey & Hurlburt, 2008; Hurlburt & Akhter, 2008) or emotion (Zelenski & Larsen, 2000). However, despite the fruitful history of research focusing on inner experience inspired by the experience sampling method (Csikszentmihalyi & Larson, 1987; Heavey & Hurlburt, 2008; Kahneman, Krueger, Schkade, Schwarz, & Stone, 2004; Zelenski & Larsen, 2000), also in relation to neuroscience (Christoff et al., 2009; Lehmann, Grass, & Meier, 1995; Lehmann, Strik, Henggeler, Koenig, & Koukkou, 1998; Spreng et al., 2008; Stawarczyk, Majerus, Maj, Van der Linden, & D'Argembeau, 2011; Wackermann, Pütz, Büchi, Strauch, & Lehmann, 2002), the specific application to cognition during rest, is a relatively recent development (Killingsworth & Gilbert, 2010).

Especially within this context, the term "resting-state cognition" is preferred over the broader denomination of mind wandering as it specifically refers to a condition of no external task demand, but which is nevertheless conducive to the generation of inner experiences (Delamillieure et al., 2010; Smallwood, 2010). In a pioneering study, Delamillieure et al. (2010) developed a questionnaire specifically targeted at exploring facets of resting-state cognition after a period of resting in a fMRI scanner (Delamillieure et al., 2010; Doucet et al., 2012), thereby providing a first step towards a taxonomy of important dimensions of thought associated with the resting state. However, this approach has not been without criticism, as the retrospective assessment of experience may be subject to memory degradation, exacerbated by increasing intervals between the realization of subjective experience and its actual assessment (Fell, 2013; Schwarz & Sudman, 1993). The manner of assessment may also invite bias, for example participants may give less accurate accounts of their experiences when interviewed in person compared to the more private context provided by self-reports (Nederhof, 1985). Furthermore, given the significant operational costs of many modern neuroimaging experiments, time efficiency is paramount. Post resting state interviews, while offering exhaustive accounts of inner experiences, remain time-intensive and not well-suited for large-scale assessment.

To conclude, as interest in resting-state cognition and its potential relation to brain activity increases, so does the need for specialized cognitive tools to effectively measure and characterize resting-state cognition in order to extend the scope of the "neuroscience of mind wandering" (Gruberger, Ben-Simon, Levkovitz, Zangen, & Hendler, 2011).

## Clinical relevance of subjective experience

One may wonder as to whether subjective experience is at all of relevance to the (pre-)clinical practice. After all, physiological and behavioral observables often provide sufficient diagnostic information regarding disease (or disorder) state and progression. Inclusion of the additional dimension of subjective experience could, however, be used to discern typologies within patient groups and co-capture the substantial inter-individual variation among patients, leading to potentially more sensitive diagnostics.

Still, the refinement of classification procedures should not be seen as the sole motivation to study (changes in) subjective experience in clinical populations. Considering the importance of conscious thought to (mental) life, the characterization of subjective thought attaches meaning to a possibly debilitating disease beyond the 'objectivity' of diagnostics, thereby generating a view on the personal, individual narrative of patients (Clark, 2015; B Hurwitz, 2000; Brian Hurwitz & Charon, 2013).

Structured self-report tools aimed at exploring conscious subjective experience, such as the Amsterdam-Resting State Questionnaire, have the benefit of serving both of these motivations. Because many neurological assessments involve at least one resting-state recording (for example EEG or (f)MRI) they offer an efficient opportunity to gather subjective experience samples alongside standard diagnostic protocols and observables, paving the way for analyses focused on improving patient / disease classification, the impact on (resting-state) cognition and their mutual relationship.

## Aim and outline of the thesis

This thesis embodies an effort to expand the toolset of cognitive neuroscience by introducing an instrument and associated protocol that provides for efficient and informative exploration of resting-state inner experiences, allowing broad application and ease of implementation. The Amsterdam Resting-State Questionnaire (ARSQ, pronounced “\ˈask” or “ˈäsk”) represents the fruit of this effort (see Figure 1.2).

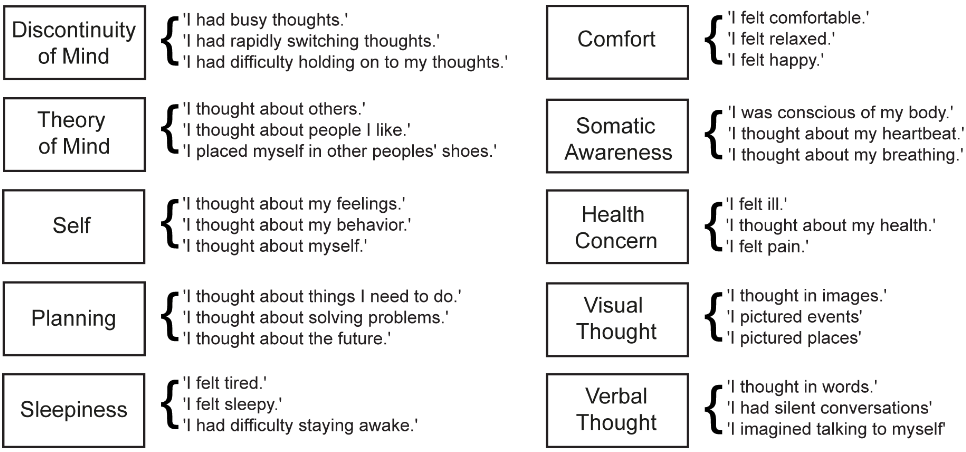


**Figure 1.2** The dimensional structure and associated questionnaire items of the (revised) Amsterdam Resting-State Questionnaire (ARSQ), which represents the foundation of this thesis.

A key focus during the development of the ARSQ rested on its ability for large-scale characterization of mind wandering correlates across a wide variety of (clinical) populations. The ARSQ attempts to both minimize the impact of potential negative effects on memory introduced by assessment lag and maximize the range of potential participants by specifying 1) a standard protocol for obtaining resting-state data of mind wandering and 2) employing a compact, computerized self-report survey with Likert-type items, allowing for near-immediate sampling of resting-state cognition under most conditions. As such the ARSQ aims to combine neurophysiological and psychological data obtained from the resting-state, opening a window on both mind and brain. In line with this aim, **Chapter 2** describes the development of the ARSQ and the derivation of specific dimensions of resting-state cognition from a large sample of participants using confirmatory factor analysis (Ackerman & Heggestad, 1997; Digman, 1997; Hoekstra et al., 2011; Jensen, 2006; Schreiber, Nora, Stage, Barlow, & King, 2006; Tully, Winefield, Baker, Turnbull, & de Jonge, 2011; Van Der Sluis, Vinkhuyzen, Boomsma, & Posthuma, 2010), with each dimension tapping into a facet of mind wandering (see Figure 1.2). Subsequent investigations address the question of whether the obtained interrelation between these dimensions remain stable across different experimental settings, such as fMRI and EEG measurements. Finally, it is shown how these dimensions of resting-state cognition are associated with different measures of mental well-being.

In **Chapter 3,** a revised version of the ARSQ is presented and validated, which expands on the number of resting-state dimensions by introducing measures for visual and verbal thought, previously suggested to be of importance (Delamillieure et al., 2010; Duncan & Cheyne, 1999) as well as a more specific dimension related to participants disposition towards health concern (see Figure 1.2). Simultaneously, assessment and computation of dimensional scores were standardized, thus streamlining assessment of resting-state cognition data further. Utilizing the revised ARSQ, the test-retest correlation of ARSQ (dimensional) scores was further investigated over several time periods. Given the observed test-retest correlations, the question was addressed whether the observed stability in resting-state cognition data were related to personality traits, such as Cloninger's Temperaments and Character Inventory (Cloninger, Svrakic, & Przybeck, 1993; De Fruyt, van de Wiele, & Van Heeringen, 2000).

After rafter having developed and refined a tool to investigate subjective experience, **Chapter 4** investigates the potential relationship between resting-state cognition and functional connectivity in several intrinsic connectivity networks (S. M. Smith et al., 2009; Tomasi & Volkow, 2011, 2012; Zuo et al., 2010) within a large sample of dizygotic twins and their immediate family members. Ratings on "Sleepiness", "Visual Thought" and "Discontinuity of Mind" all exhibit significant associations with connectivity networks in visual, auditory, executive and sensorimotor areas, leading to the interesting hypothesis that what is observed when large-scale functional connectivity increase in actuality represent cognitive *disengagement* rather than active conscious deliberation.

In **Chapter 5**, it is explored whether a combination of self-assessments of subjective experience as well as theta-band EEG biomarkers derived from the resting-state provides information about how quickly participants fall asleep. In addition, potential associations between theta activity and ARSQ-ratings were analyzed as well as changes in cognition as the result of the transition from wakefulness to stage 1 sleep (Yang, Han, Yang, Su, & Lane, 2010). Post resting-state ARSQ-ratings on "Discontinuity of Mind", "Theory of Mind", "Self", "Planning" and "Sleepiness" were each significantly associated with theta-activity. However, subjective experience after sleep or wake trials respectively (matched in length) was generally best predicted not from EEG-biomarkers but from pre-trial resting-state ARSQ-ratings. Except for "Planning" and, as expected, "Sleepiness" no other ARSQ-dimensions were affected by the transition from wakefulness to stage 1 sleep. Finally, it is shown that a theta-based measure of long-range temporal correlations (DFA-exponent) and "Sleepiness", both obtained from resting-state trials, significantly contribute to explaining variation in sleep-onset latency. These results support the interesting notion that a combination of eyes-closed based ARSQ-ratings and EEG-biomarkers could be utilized to help improve sleep quality for individuals suffering from (mild) insomnia, possibly by integration into a health monitoring or biofeedback device.

Considering the vast improvements and rapid developments in the field of brain-computer interfaces and their entry into (clinical) neuroscience in the form of neuro-feedback, **Chapter 6** will focus on a review of EEG-biofeedback literature for the treatment of ADHD and sleep disorders. While clinical neurofeedback has had somewhat of a checkered past, especially in terms of methodological rigor, current developments show exceeding improvements in this regard.

Finally, **Chapter 7** as the general discussion integrates the obtained results of the present research and in addition to deliberating on the results and potential caveats of the here presented data, an outlook on future research is provided.