Mindfulness Training in Dialectical Behavior Therapy

Investigation on Brain Activity by NIRS

Dissertation

der Mathematisch-Naturwissenschaftlichen Fakultät

der Eberhard Karls Universität Tübingen

zur Erlangung des Grades eines

Doktors der Naturwissenschaften

(Dr. rer. nat.)

vorgelegt von

Friederike Gundel

aus Tübingen

Tübingen

2020

Gedruckt mit Genehmigung der Mathematisch-Naturwissenschaftlichen Fakultät der Eberhard Karls Universität Tübingen.

Tag der mündlichen Qualifikation:	17.12.2020
Dekan:	Prof Dr. Thilo Stehle
1. Berichterstatter:	Prof. Dr. Martin Hautzinger
2. Berichterstatter:	Prof. Dr. Birgit Derntl

Content

Summary 6

Personal background/Formulation of Question/ Bias 10

1. Introduction 14

1. Borderline Personality Disorder 14

1.1 Psychopathology and diagnostics of borderline disorder 14

1.2 Etiology 16

1.2.1 Borderline as an emotion regulation disorder 17

1.2.2 The interpersonal disorder model according to Gunderson and Herpertz 18

1.2.3 The theory of identity development/disruption model 19

1.2.4 Diagnosis of borderline disorder according to DSM-5 20

1.3 Psychotherapeutic treatment of Borderline personality disorder 22

1.3.1 Dialectical Behavioral Therapy according to M. Linehan 23

1.3.2 State of research on DBT and mindfulness 26

2. Mindfulness 27

2.1 Definition 27

2.2 Mindfulness and Behavioral Therapy 28

2.3 Modern Definition and Theoretical Models of Mindfulness 28

2.4 Neural Correlates of Meditation Practice 29

2. Meditation and the brain – Neuronal correlates of mindfulness as assessed with near infrared spectroscopy (Study 1) (Friederike Gundel et al., 2018). 38

1. Introduction 38

2. Methods 41

3. Results 46

4. Discussion 54

5. Limitations 63

6. Conclusion 64

3. Effects of Meditation on the Executive Control Network (Study 2) 66

1. Introduction 66

2. Methods 71

3. Results 76

4. Discussion 80

5. Limitations 89
6. Conclusion 91
4. Neural Correlates of Mindfulness in Dialectical Behavior Therapy (DBT): A Pilot Study (Study 3) 92
1. Introduction 93
2. Method 96
3. Results 101
4. Discussion 109
5. Limitations 113
6. Conclusion 114
5. General discussion 116
1. Summary 121
2. Theoretical assumptions: Meditation as a cortical network training 122
3. Theoretical assumptions: Borderline personality disorder as a disorder of neural integration. 126
4. The instability of self-identity as a core pathology of borderline personality disorder 128
5. Conclusions 135
6. Critical reflection of the work 135
6. References 138
Annex 155
1. Course of study 155
2. Text for the instructions for mindfulness measurement 164
3. Instructions Emotional Stroop - Words 165
4. Instruction VFT (word fluid test) 165
5. list of randomizations 168
6. Word lists for emotional Stroop test 169
7. List of abbreviations (alphabetical order) 170
8. Figure list 173
9. Table directory 175
10. Styles and formatting 176
11. Explanation of the own share of the dissertation 176
12. Affidavit 177

Thanksgiving and dedication 177

Summary

In the last years, mindfulness as a therapeutic tool has proven clinical effectiveness on psychiatric patients and in the field of psychotherapy. First research on mindfulness revealed positive effects on chronic pain and stress reduction and mindfulness to be suitable and effective in treating psychiatric patients (Y. Tang & Leve, 2016). So far, it is still unknown if mindfulness skills are more effective than other therapeutic skills. Dialectical behavior therapy (DBT) integrates mindfulness skills (taken from Zen Buddhism) into cognitive behavioral therapy. DBT was developed in the 1980s by Marsha Linehan to treat suicidal patients with emotion regulation problems. Today, this treatment is known to be evidence based for treating borderline patients (Bohus & Schmahl, 2006).

Linehan describes mindfulness as the basic ingredient of DBT. There is still no evidence on the effectiveness of mindfulness skills and the underlying neuronal correlates, and it is still unknown if mindfulness can be successfully learned in an eight-week inpatient setting. This thesis will test this question.

We conducted three studies to get first insights in this topic: In study 1 we tested meditation experts against a group of subjects without meditation experience. We used a paradigm using mindful listening to a sound of a swinging meditation bell. This paradigm used near-infrared spectroscopy (NIRS) as an functional imaging technique and was taken from a pilot study of Erb et al. (2011).

The second study measured executive function and underlying neuronal correlates in both groups of study 1 with a verbal fluency task (VFT) and an emotional Stroop test (EST). Since borderline patients suffer from severe impulse and emotion control issues, we wanted to know if mindfulness would have positive effects on impulsivity and emotion regulation.

The results of study 1 and study 2 should give us first insights for study 3. There, we tested borderline patients with the mindfulness paradigm. We tested psychopathology and underlying neuronal correlates of two groups of borderline patients.

We conducted the following 3 studies for this thesis.

Study 1)

In this study we measured the hemodynamic responses of meditation experts (14 participants) and a control group (16 participants) in a resting and a mindfulness condition. In both conditions, the sound of a meditation bowl was used to find group differences in the auditory system and adjacent cortical areas. Different lateralization patterns of the brain were found in expert meditators while being in a resting state (amplified left hemisphere) or being in mindfulness state (amplified right hemisphere). Compared to the control group, meditation experts had a more widespread pattern of activation in the auditory cortex, while resting. In the mindfulness condition, the control group showed a decrease of activation in higher auditory areas (BA 1, 6 and 40), whereas the meditation experts had a significant increase in those areas. In addition, meditation experts had highly activated brain areas (BA 39, 40, 44 and 45) beyond the meditative task itself, indicating possible long-term changes in the brain and their positive effects on empathy, meta-cognitive skills, and health.

Study 2)

This study investigated if a group of healthy meditation experts had better performances on two executive tasks (emotional word Stroop task and VFT) than healthy controls (same group of participants as in study 1). Besides performance, we measured brain activity (in the prefrontal cortex) of the two groups and tested the influence of a preceding short mindfulness task.

We measured brain function in the prefrontal cortex of two different executive tasks by using near infrared spectroscopy (functional NIRS). Using the affective Stroop task, we tested if meditation experts had better executive function (stronger activation of the prefrontal cortex (PFC)) in terms of emotional control (stability). Using the VFT, we tested differences in word fluency and flexibility among both groups and corresponding differences in brain activation. In addition, we investigated the influence of a 9-minute block of mindfulness practice (9 minutes of mindful listening to the sound of a meditation bowl) conducted before the executive tasks.

Accuracy in Stroop performance was significantly enhanced in the meditation group. In the interference condition of the Stroop Task (emotional words), meditation experts did not perform better.

In addition, we did not find meditation experts to perform better on the VFT.

A preceding short mindfulness task had no effects on performance of the VFT or Stroop task, but enhanced specific brain activation in the PFC as measured by fNIRS.

Study 3)

Neuronal correlates of Borderline Personality Disorder are characterized by an imbalance of frontal-limbic brain areas (hypo- and hyper-activation). Little is known so far about the role of temporo-parietal parts of the brain in the dysfunction of borderline patients. We investigated the effectiveness of mindfulness as a therapeutic tool in the treatment of 29 borderline patients by comparing the therapeutic effects of 8 weeks of DBT therapy with 8 weeks of cognitive behavioral therapy without mindfulness (15 patients).

Both treatments had significant positive effects on specific symptom reduction (borderline symptoms, dissociation, and behavior avoidance motivation), and an increase in mindfulness scores. We also found DBT to be significantly more effective in global symptom reduction and a trend for an increase in reward seeking behavior.

On the neuronal level, the impact of 8 weeks of mindfulness on the temporo-parietal junction (TPJ) and superior temporal gyrus (increase in activity) of both hemispheres was correlated with general symptom reduction (SCL-90-R) and increased mindfulness scores (KIMS-D).

In conclusion, we could show that mindfulness skills can reduce global psychopathology and make an impact on neuronal activity changes in borderline patients.

Personal background/Formulation of Question/ Bias

"Mindfulness is the basis of all skills". By reading these words in Linehan's Skillstraining manual (M. Linehan, 1996) about 10 years ago, I became very curious. As a psychotherapist specialized in Dialectical Behavior Therapy (DBT), this sentence has stuck with me since then. Over the course of the last decade, it has become a core issue in my therapeutic and scientific work and in my personal life.

Why mindfulness as a basis? Isn't DBT much more known for hedgehog balls and stress tolerance skills? Why is mindfulness added to behavior therapy skills in DBT and not e. g. progressive muscle relaxation? In my work with my patients, I repeatedly experienced how important and central the topic of mindfulness became during treatment for my patients even though I saw their difficulties to sit still for three minutes with high tension. I wondered, "Is it possible at all to learn mindfulness on a DBT station within several weeks?" This casual remark (without empirical evidence) by M. Linehan: "Mindfulness is the basis of all skills" has challenged me to do this scientific work. The idea for this research derives directly from my clinical work at a DBT ward (Station 22) at the University Hospital for Psychiatry and Psychotherapy in Tübingen. In the development and course of the research work I was supported by the workgroup “Psychophysiology and Optical Imaging” – specifically by Dr. Ann-Christine Ehlis. I would like to thank her for her excellent and inspiring support! Johanna von Spee, Corinna Klose and Svenja Brosch wrote their diploma and master's theses on this subject and supported the data collection. Similarly, this work would not have been possible without the help of my patients and the mindfulness participants, who all have been my teachers. The paradigm was adopted by Michel Erb. Otherwise, this work is developed directly from my clinical work. The methods suffer because the groups were not randomized for it was difficult to find an age-equal group of meditation experts. For this, a lot of clinical and personal knowledge is incorporated into the work: my professional experience as a DBT therapist with borderline patients (especially the management of the mindfulness group) and my personal meditation experience for many years. A six-month stay (2019) at Tassajara Zen Mountain Center has further deepened my personal knowledge. 7 years of clinical, scientific, and personal work on this topic are now behind me. "Mindfulness is the basis of all skills" is the starting point and finally the central topic of this dissertation. My personal background of the subject must therefore always be taken into account in this scientific work "as a bias", but can also be seen as a "methodological strategy" to integrate phenomenological, clinical and neurobiological knowledge into a research program (Berkovich-Ohana et al., 2020) This is what Varela (1996) called for his neurophenomenological research approach: "an open-ended quest for resonant passages between human experience and cognitive science" (Varela, 1996).

Object, Scientific issue, and Hypotheses of this thesis

The aim of this work is to provide empirical proof that the mindfulness skills in DBT can be acquired within 8 weeks. This learning process should be reflected by specific functional changes in the brain and can be mapped with other measures of change (psychometric tests and performance tests). This means that mindfulness skills should have a therapeutic effect in borderline patients. Therefore, Cognitive Behavioral Therapy (CBT) without mindfulness skills should be less effective. Differences should be seen on a neural level as well as on a behavioral level.

The attempt to provide empirical proof of Linehan's statement also raises the question of the central etiology of borderline disorder and the associated therapeutic tool that Linehan chooses: an inner practice with the longest healing tradition from Zen Buddhism: mindfulness.

In the discussion part of this work, we will focus on etiology and go into the topic of whether borderline disorder is an emotion regulation disorder – as is discussed in science today. Underlying the symptom of emotion regulation, we go into the concept of "personality disorder" or a "disorder of self-development". Then, we will discuss the results found in this study and draw on current research to suggest an underlying neural disorder of borderline personality disorder.

The following hypotheses were made:

1. Subjects with many years of meditation experience show an altered brain function with an acoustic "mindfulness stimulus" compared to mindfulness beginners during a mindfulness exercise.

2. Long-term meditation training improves cognitive performance (word fluency) and emotion control (emotional Stroop test). This is reflected in altered brain function in frontal brain areas (executive network).

3. 8 weeks of DBT with mindfulness skills training significantly improves the psychopathology of borderline patients compared to 8 weeks of cognitive behavioral therapy (CBT) without mindfulness.

In the graphical overview, this dissertation deals with the following topics and interfaces.

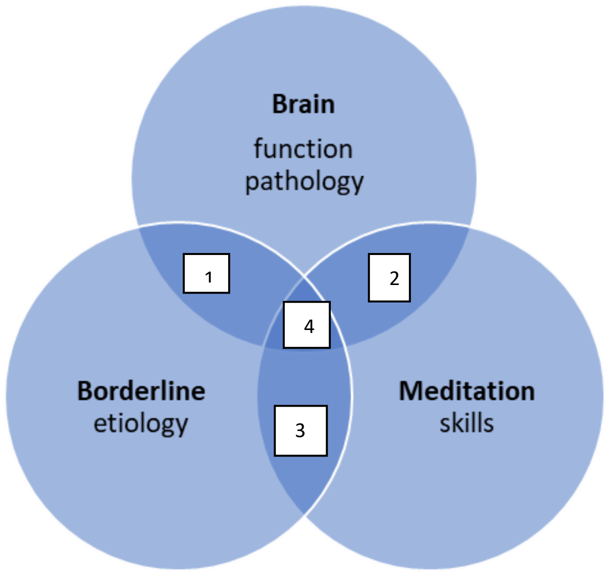


Figure 1: Model based on Simon and Engström(Simon, 2015).

1. Disorder-specific neural pathology of borderline personality disorders

2. Neuronal changes due to meditation practice

3. Therapeutic effectiveness of meditation on symptoms of borderline disorder.

Topics 1, 2 and 3 will be presented in the introduction to this work

4. Meditation as brain training for personality development

Topic 4 will be discussed in the discussion part of this work.

The three studies are assigned to the following interfaces:

Study 1 and Study 2: Interface 2

Study 3: Interface 4

1. Introduction

1. Borderline Personality Disorder

Borderline Personality disorder is a serious mental illness that affects about 3% of the population and causes direct treatment costs of about 4 billion Euros per year (25% of the cost of mental disorders) in Germany. Those affected suffer from strong mood swings, impulsivity, torturous feelings of emptiness and show a dysfunctional interpersonal behavior. This leads to social problems such as poor vocational training, unemployment and early retirement (Bohus & Schmahl, 2006)

1.1 Psychopathology and diagnostics of borderline disorder

At the beginning of this work (2013), the "Diagnostic and Statistical Guide to Mental Disorders" (DSM-IV) of the American Psychiatric Society (APA) was still valid. In May 2013 it was replaced by the DSM-5 as a currently valid manual that is mandatory for psychiatric diagnostics. According to the World Health Organization's (WHO) international criteria (Dilling & Freyberger, 2012) two kinds of emotionally unstable personality disorder are distinguished:

1. An” impulsive type”, mainly characterized by emotional instability and lack of impulse control.

2. A “Borderline type”, additionally characterized by identity problems, fast changing goals, and internal preferences, by a chronic sense of emptiness, by intense but volatile relationships and a propensity for self-mutilation behavior with parasuicidal behavior and suicide attempts.

Patients in this study were diagnosed after DSM IV because there were no diagnostic interviews in German for DSM-5 at that time.

According to DSM-IV, borderline personality disorder is a profound pattern of instability in interpersonal relationships, in self-image and in affect, as well as distinct impulsivity. The beginning is often in early adulthood or puberty and manifests itself in different areas of life.

To be able to make the diagnosis of a borderline personality disorder, 5 out of 9 criteria must be met.

<u>Emotion</u>

(1) Affective instability, which is characterized by a pronounced orientation to the current mood

(2) Chronic feeling of emptiness

(3) Temporary, stress-related paranoid ideation or severe dissociative symptoms

<u>Impulsivity</u>

(4) A stable pattern of Impulsivity in at least two potentially self-harming areas e.g., spending money, substance abuse, reckless driving, eating

(5) Recurring suicide threats, suicide hints or attempts or self-harming behavior

(6) Inappropriate, strong anger or difficulty controlling anger or rage.

<u>Cognition</u>

(7) Identity disorder: a pronounced and persistent instability of self-image or sense of self.

<u>Interpersonal level</u>

(8) Desperate effort to prevent a real or imagined social abandonment: Typical statement: "I do everything you want."

(9) A pattern of unstable and intense interpersonal relationships characterized by a change between extreme idealization and devaluation.

1.2 Etiology

Today, a general biosocial model is usually used in science, which discusses genetic influences as well as psychosocial influences on the development of borderline disorder.

This model has the following empirical basis:

1. A twin study (2000) was able to explain approximately 46% of variance to genetic causes. Approximately 50% of borderline patients also suffer from ADHD (attention deficit and hyperactivity syndrome) in their childhood. There, a genetic disposition is clearly proven.

2. In addition, biographical psychosocial stress factors are usually assumed in the nuclear family: chronically invalidating behavior of the reference persons (binding disorder), severe physical violence (in about 60% of patients) or severe emotional neglect (in about 40% of patients). 65% of patients usually have long-term sexual abuse in their families during their childhood or experienced physical violence (Bohus & Schmahl, 2006).

Phenomenologically, the disturbance is very heterogeneous. Therefore, an attempt was made to reduce the variety of symptoms by factor analysis to three underlying core symptoms (Cheavens, Strunk, & Chriki, 2012).

1) Emotion regulation disorder (Linehan/Bohus)

2) Interpersonal problems (Gunderson/Herpertz)

3) Identity disorder (Kernberg)

In the discussion part of this dissertation, our results will be discussed and classified regarding these three etiological models. Therefore, they are presented in more detail below:

1.2.1 Borderline as an emotion regulation disorder

Today, the most discussed etiological model for borderline personality disorder in Germany outlines an emotion regulation disorder as the main psychopathological component: Patients have a low stimulus threshold and are triggered to high level of arousal, which is hard to reduce. The perception of emotion is low and therefore feelings are usually experienced physically as torturous states of tension, often accompanied by a feeling of depersonalization and derealization (reduced pain perception, dissociation).

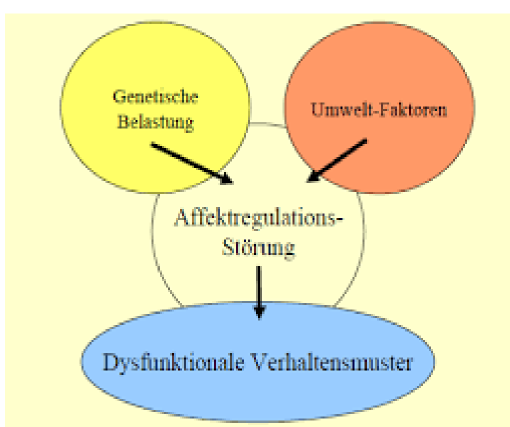


Figure 2: The Bio-Social Model of Borderline Disorder.

from: Linster (Linster, Referat am Institut für Psychologie Freiburg)

This model shows well the relationship between emotion regulation difficulties and behavior (impulsivity). Development and therapy of symptoms can be described easily by operant learning theory: Reduction of stress states through self-harm leads to a negative reinforcement. The advantage of this model is that it can be easily tested.

On the neuronal level, a fronto-limbic dysregulation is proposed. This model consist of a disinhibition syndrome of executive functions with impaired impulse control (Sebastian et al., 2014) and a disturbed emotion regulation with increased affective responsiveness (Sabine C Herpertz et al., 2001). Today, this model has been proven to be empirically sound (siehe Metaanalyse von Visintin et al., 2016).

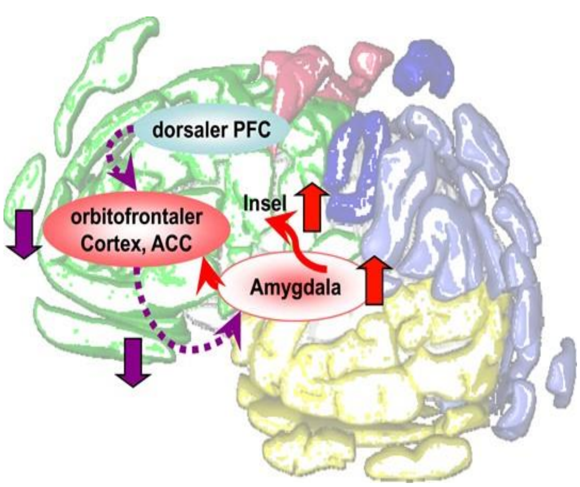


Figure 3: Fronto-limbic dysregulation in borderline patients.

from: Herpertz (2011)

1.2.2 The interpersonal disorder model according to Gunderson and Herpertz

For borderline patients relationships often have the function to define their identity by others (reduction of feelings of emptiness and feelings of self-hatred). The resulting dependence on others is balanced by abrupt counter-regulations (fear of loss of autonomy - breakdown of the relationship, idealization and devaluations, paranoid symptoms) and thus leads to a dysfunctional proximity-distance regulation (Gunderson, Herpertz, Skodol, Torgersen, & Zanarini, 2018). It has been shown that social exclusion triggers extreme feelings of shame and fear of abandonment. This leads to unstable relationships with many neg. consequences for the development of self-esteem and identity. Social integration into society is often strongly endangered (Bohus & Schmahl, 2006).

Following this theory, Herpertz investigates neural foundations of emotion perception and impulse control (by inducing feelings by emotional faces or social games like “cyberball”). Neurobiological correlates can be found, such as stronger activation of the amygdala (Sebastian et al., 2014), the insula region and compensatory, extensive activations in prefrontal brain regions (S. C. Herpertz, 2011; Völlm et al., 2004).

1.2.3 The theory of identity development/disruption model

This etiology of borderline personality disorder has evolved from the psychoanalytic object relationship theory (Kernberg, 1981) and assumes a central personality split as the primary defense mechanism. However, this defensive mechanism must presuppose an existing self-structure. Otherwise, it cannot be an active avoidance. According to Kernberg, the division of the personality is supposed to prevent an integrated concept of self and leads to identity diffusion. The disadvantage of this theory of is that it leaves cause and effect unexplained and is circular closed. The theory is therefore neither scientifically exactly descriptive nor can it be falsified.

Psychoanalytic models emphasized the importance of binding to the primary reference person for first-person development was by (Norden, Klein, Donaldson, Pepper, & M. Klein, 1995). Disorders of mother-child interaction (ambivalent-disorganized) should lead to disturbances in the child's ego development. According to this model, identity disorders then lead to reduced affect regulation, ability to act and mentalization capacity, i.e. to an overly rigid response pattern to social signals (Fonagy, Luyten, & Allison, 2015) Here, authors like Ryle (1999) propose a model that considers multiple self-states to be characteristic of borderline disorder. According to Pollock (2001) fragmentation of the self originates from traumatization. The child's dependence on the primary care providers can lead to serious disturbances in self-development when physical, emotional or sex. assaults, but also emotional and physical neglect take place during childhood. Dissociative processes and the formation of ego states may play a central role here. Binding traumatization can lead to an unclear and confusing attribution of cause (guilt), feelings of exclusion and abandonment, self-hatred, and extreme existential shame.

Due to high complexity, there are hardly any empirical studies on this theory yet (Doering et al., 2012).

1.2.4 Diagnosis of borderline disorder according to DSM-5

But the centrality of the concept of "disturbed self-identity" is now reflected in the new DSM-5 diagnosis system (see Figure 4). There, the focus is placed on the function mode of the personality with the domain self (identity and self-control) and the interpersonal domain (empathy and intimacy) (2012). As a result, the concept of personality has become a focus of research. The DSM-5 defines personality as a constant process of consciousness, perceiving oneself as a unit and adequately maintaining social role boundaries, as well as ascribe a realistic positive self-worth. Added to this is the ability to fully experience, tolerate and regulate own emotions (*Diagnostic and statistical manual of mental disorders (DSM-5)*, 2013).

Borderline-Persönlichkeitsstörung nach DSM-5

Das aktuelle DSM-5 fasst die Borderline-Persönlichkeitsstörung in einem gemischten dimensional-kategorialen Modell. Essenziell sind (A) Störungen der Persönlichkeitsstruktur und -funktion (Selbstbild und interpersonelles Verhalten) sowie störungsspezifische pathologische Persönlichkeitseigenschaften (B).
Diese müssen ausserdem stabil über die Zeit und in unterschiedlichen Situationen auftreten (C), dem soziokulturellen Umfeld unangemessen und dem individuellen Entwicklungsalter nicht entsprechend sein (D), und sie dürfen nicht durch andere medizinische Faktoren (E) verursacht sein (Substanzkonsum, andere hirnorganische Ursache etc.).

Kriterium A: signifikante Beeinträchtigung der Persönlichkeitsstruktur

1. Gestörte Ich-Funktionen
   a) Identitätsstörung
   b) Selbststeuerung

UND

2. Interpersonelle Beeinträchtigungen
   a) Empathiefähigkeit
   b) Fähigkeit zu intimen Beziehungen

Kriterium B: pathologische Persönlichkeitseigenschaften

1. Negative Affektivität (emotionaler Arousal)
   a) emotionale Instabilität
   b) soziale Ängstlichkeit
   c) Trennungsangst und Zurückweisungssensitivität
   d) Depressivität
2. Disinhibitionssyndrom
   a) Impulsivität
   b) erhöhtes Risikoverhalten
3. Antagonismus und Feindseligkeit (erhöhte Kränkbarkeit)

Figure 4: Diagnosis of Borderline Disorder according to DSM-5

from: Swiss Journal of Psychiatry and Neurology (Wrege, 2015)

The new diagnostic system DSM-5 can trigger new basic research on personality disorders and shed light based on the heterogeneity of borderline disorder in the phenotype (Bullis, Boettcher, Sauer-Zavala, Farchione, & Barlow, 2019; Sabine C Herpertz et al., 2017; Koudys, Gulamani, & Ruocco, 2018). First empirical approaches studying identity disorder or personality integration at the neural level has been done (Doering et al., 2012). These Studies focus on the neuronal basis of self-perception (Scherpiet et al., 2015) autobiographical memory (Bozzatello et al., 2019), attribution styles, "Theory of Mind" or empathy (Homan, Reddan, Brosch, Koenigsberg, & Schiller, 2017). Neural key points, such as the cortical midline structures (distinction of stimuli: self/not self) and time-stable cognitive concepts of the self (Damasio, 2010) have increasingly come into research focus. In addition, the brain regions of the "default mode network" for autobiographical memory processes (Whitfield-Gabrieli et al., 2011) have been studied recently. Other brain regions, such as the medial prefrontal cortex, the precuneus, the superior temporal gyrus or the temporo-parietal connection seem to be involved in the formation of the personality/identity and its psychopathology (Takahashi et al., 2010). Disorders in self-development and self-consciousness were found by fMRI studies comparing the activity pattern in The Default Mode Network (DMN) of borderline patients with patterns of healthy volunteers. The results show heightened activity in the central midline structures of the brain in borderline patients (medial prefrontal cortex (mPFC), anterior cingulate cortex (aCC) and precuneus/PCC) and reduced activity in the right lateral temporal cortex (Visintin et al., 2016). Similarly, decreased functional connectivity was found within the DMN and within the Salience Network (SN) (Quattrini et al., 2019). There, the DMN was associated with greater emotional intensity (anger) (Whitfield-Gabrieli & Ford, 2012).

Deriving from these theoretical models and empirical findings, four treatment concepts have been developed, which are available as manuals:

1.3 Psychotherapeutic treatment of Borderline personality disorder

(1) Dialectic-behavioral therapy (DBT) (M. Linehan, 1993): A behavioral therapy approach that integrates mindfulness concepts and a dialectical approach. Evidence of efficacy has been proven (Binks et al., 2006; Soler et al., 2005).

(2) Mentalization Based Treatment (MBT) (Fonagy et al., 2015). Improvement of mentalization was shown according to Bateman & Fonagy.

(3) Schema therapy for BPS (J. E. Young, Klosko, & Weishaar, 2003). According to Young, dysfunctional automated cognitive-emotional patterns ("schemata") can be recognized, questioned, and revised.

(4) Transmission-focused therapy (TFP) (Kernberg, 1981). So far, there have been insufficient empirical effectiveness studies.

Taken together, only 50-60% of patients benefit from the above-mentioned specific treatment approaches. However, non-specific treatments are more likely to be contra-indicated and have high drop-out rates (approximately 50%) (Bohus & Schmahl, 2006).

After this overview of diagnosis, etiology, and treatment of borderline personality disorder, the two central therapeutic concepts of this dissertation will be outlined:

DBT and Mindfulness:

1.3.1 Dialectical Behavioral Therapy according to M. Linehan

The dialectic behavioral therapy was developed in the 1980s by Marsha Linehan for the treatment of suicidal patients (M. Linehan, 1993). It is a disorder-specific cognitive behavior therapy for patients with severe emotion regulation disorders that integrates elements of Zen Buddhism. It teaches both change-oriented and acceptance-oriented skills (dialectic). The therapeutic strategies that at first glance contradict each other, are used to balance extreme thinking patterns and behavior (“black and white thinking”, proximity distance regulation) of the patients. The aim is to integrate these extreme polarities into a reality-adapted integrated "middle path". Linehan calls this "walking the middle way." The integration of body (needs) and mind (mind) is called "wise mind".

The effectiveness of DBT is well documented in Germany: According to the S 2 guidelines of the Association of Scientific Medical Societies (AWMF), DBT is assigned the highest level of evidence for the treatment of borderline personality disorder and an examination as an S3 guideline is requested (Rabenstein, 2020)

Here, we present only the mindfulness module from the skill training of the treatment, which is embedded in an overall therapy concept with individual therapy and telephone consultation.

In the skills training of the DBT, mindfulness is systematically guided and practiced in group setting. The aim of the module is that the patients come to a regular practice and transfer it into everyday life. In the stationary setting, mindfulness is used twice/week 30 min. practiced in a group setting. Short mindfulness exercises are also instructed before each group session, so that patients practice an additional 10 guided short mindfulness exercises per week. Like a physical exercise, this mental skill should be practiced repetitively.

Unlike Mindfulness Based Stress Tolerance (MBSR)(J. Kabat-Zinn, 2003) and Mindfulness Based Cognitive Therapy (MBCT) (Segal & Teasdale, 2018), the mindfulness skills in the DBT are only 3 min. long since the patients are often under very high tension and reduced concentration ability. Exercises with a focus on the outside (e. g. mindful listening) or in action are usually easier for patients at the beginning, as borderline patients avoid contact with their interior (phobia of emotions, emotional pain).

Mindfulness skills are taught as "what-skill" and "how-skill":

"What" means: the focus of the practice: observe, describe, and participate.

"How" means: the inner attitude of the practitioner: non-assessing, concentrated and effective.

In mindfulness training, patients learn to interrupt automated thought patterns and to be conscious and fully focused in the present. In this way a here and now orientation is practiced, and rumination is interrupted. The focus is on the sensory level (listening, smelling, tasting, feeling, seeing). Unpleasant feelings should be perceived, but also the impulse for action that is associated with it. The digression of perception to the mental level should be corrected again and again. These exercises train the integration of feelings and thoughts into a state that Linehan (2015) describes as "wise mind".

In the advanced stage, patients learn to perceive their own thought processes. Here, the technique of "labeling" or counting is used to remain in a metacognitive perspective.

Unlike cognitive behavioral therapy, mindfulness does not use cognitive restructuring. Instead, it is practiced observing cognitions, let go of them and switch the attention to a physical focus.

The meta-cognitive posture helps patients to gradually reduce fixations, dissociations, to perceive aversive emotions without judgement and to tolerate them ("I am not my thought", "I am not my feeling"). This corresponds to the attitude in exposure procedures of behavioral therapy. With the skill "Emotion surfing" this mindful attitude is practiced even under high tension, strong feelings and/or "craving". Change-oriented techniques (exposure) become more effective through mindful awareness.

Bohus and Huppertz (2006) make the following assumptions why mindfulness is effective:

1. Improvement of metacognitive processes, which facilitates the relativization of activated cognitive-emotional schemas.

2. Improving the acceptance of unpleasant internal and external phenomena.

3. Improving emotional activation levels in exposure-based procedures

4. Improving the self-organization of cognitive-emotional structures in psychopathological non-relevant problems

5. spiritual processes are developed.

1.3.2 State of research on DBT and mindfulness

A research group in Barcelona under Soler (2005) has studied the effectiveness of mindfulness training in DBT over the past 15 years:

After DBT mindfulness training, the following changes occur in borderline patients: Reduced borderline symptoms (Elices et al., 2016; Mitchell, Roberts, Bartsch, & Sullivan, 2019), reduced general psychopathology (Soler et al., 2012), attention improvements (Soler et al., 2012), reduced impulsivity (i Farrés et al., 2019; Soler et al., 2016) and increased mindfulness scores (Elices et al., 2016). There has also been evidence that mindfulness training improves distancing ability (Elices et al., 2016). According to Hölzel (2011) the emotion regulation should improve. However, this has not yet been replicated in borderline patients (Feliu-Soler et al., 2014). However, improvements were made on the two scales "emotional clarity" and "feeling acceptance" on the Spanish version of the "Difficulties in Emotion Regulation Scale" (DERS) (Gratz & Roemer, 2008). Greater deactivations in the Default Mode Network in the posterior cingulated cortex and in the precuneus after mindfulness training (10 weeks) was found by Farrés and colleagues (2019). In general, lower mindfulness scores (except for the observation scale) are found in borderline patients compared to healthy volunteers (Tortella-Feliu et al., 2018).

2. Mindfulness

2.1 Definition

“Mindfulness” (Sanskrit: "Sati") is a central aspect of Zen meditation next to “Concentration” (Sanskrit: "Samadhi"). Zen meditation is a 2,500-year-old technique to reduce suffering and in the religious context of Buddhism.

In the Lankavatara Sutra, a basic text of Mahayana Buddhism (ca. 300 A.D.), meditation is described as a technique to reduce delusions, ideas ("imagined reality") and projections ("projections") in order to make a direct experience with reality as it is ("suchness") (Hamlin, 1983). Any form of motivation for change ("greed" – wanting something and "hate" - avoidance) prevents acceptance of what is. The idea of a separate self-identity and the idea of a world separated from myself (subject-object separation) is considered an illusion. The end of "habit-energy" and perception without projections is described as liberation from suffering (Pine, 2012). Long-term exercise leads to a stable state of equanimity and calmness, which goes along with sensory clarity.

Without meditation training, a constant stream of thoughts, feelings and associative leaps is experienced in awake state of rest, which is described in Buddhism as "monkey mind" (Vago & Zeidan, 2016). The fixation on self-related thoughts is described as the cause of suffering and are – in a more extreme form – a sign of psychopathology (rumination in depression e.g.).

The healing path is called the "eightfold path" in Buddhism:

Suffering ends by letting go of adhesion/greed and hatred/avoidance.

This path includes, among other things, "right mindfulness", "right concentration" and "right exercise" ("effort").

2.2 Mindfulness and Behavioral Therapy

Buddhist ideas are unusual for behavioral therapy at a first glance. However, there are many overlapping aspects found in both Buddhism and behavioral therapy (Mikulas, 1978).

Both emphasize the aspect of the "here and now" and are less interested in the past (Buddhist: "emptiness" of memories). Both concepts emphasize the reduction of dysfunctional concepts and the need to practice new behavior. Like behavioral therapy, Buddhism first emphasizes self-observation (attention) and the direction of attention (concentration). Mindfulness of thoughts and feelings can lead to a distancing from oneself. Then it is possible to observe one's own ego-identity as an object (meta-cognition). Confrontational techniques are similar to Buddhist teachings, reducing avoidance behavior and confront (observe) and accept everything without judgment (Robins, 2002).

In contrast to cognitive behavioral therapy, mindfulness practice there is no change in the content of thoughts (no reformulation of dysfunctional thoughts), but thoughts are considered as "empty". Cognitive de-fusion is therefore sought. Self-aspects are separated from external and inner stimuli. Change orientation is described in Buddhism as an illusion, although regular practice is sought. Change is also the most fundamental goal of behavioral therapy. Both methods are thus related, but complementary: mindfulness (practicing the attitude to the world – "how-to-skill", "validation") and behavioral therapy (acting, changing the world).

2.3 Modern Definition and Theoretical Models of Mindfulness

Today, Mindfulness is understood as mental training, as a "non-assessing observation of one's own thoughts, feelings and other experiences centered in the present" (Bishop et al., 2004; J. Kabat-Zinn, 1990). Bishop formulated a two-component model for mindfulness: regulation of attention and an open and accepting attitude towards everything that is there (Bishop et al., 2004)

Hölzel describes 4 components of mindfulness:

1. Regulation of attention

2. Body awareness

3. Emotion regulation/Exposure

4. Change of perspective.

By practicing regularly this simple mental technique (concentration, mindfulness, distancing, re-orientation) trains important basic functions of the brain and over the years, a metacognitive self-regulation is developed: The recognition of clues for digression and the flexible release of self-related cognitions improves the reorientation to the “here and now”. In the end, this practice leads to improved self-regulation and an increase in well-being (Dorjee, 2010).

2.4 Neural Correlates of Meditation Practice

According to Menon's "Triple Network Model"(Menon, 2011) three functionally distinct networks can be found in the brain:

The Central Executive Network (CEN) includes cognitive control functions such as problem solving, working memory, decision-making, and impulse inhibition. The following brain regions are involved: the bilateral dorsolateral prefrontal cortex (dlPFC), the ventrolateral prefrontal cortex (vlPFC), the dorsomedial prefrontal cortex (dmPFC), the lateral posterior parietal cortex (PPC) and the rostro-lateral prefrontal cortex (rlPFC, BA 10). The CEN is more right-hemispheric and is active when external stimuli are processed. Seeley et al. (2007) showed that intrinsic functional connectivity in CEN is related to improved executive performance.

The Default Mode Network (DMN; Raichle, 2015) is activated in daydreaming, biographical memories, future planning and self-perception, i.e. in thought processes that are independent of external stimuli. The brain regions involved include the orbital and ventro-medial prefrontal cortex (vmPFC), precuneus, the posterior cingular cortex (PCC) and the lobulus parietalis superior. The DMN is rather left-hemispheric organized.

Since the DMN is not actually a resting state of the brain, Seeley suggests the term "intrinsic connectivity" (Seeley et al., 2007). The organization of the DMN is directly connected to the functionality of other brain networks (Ross & Cisler, 2020). Psychopathology and therapeutic progress can be made visible in changes/connectivity of the DMN (Simon, 2015).

The Salience Network (SN) filters personal relevant information out of a huge number of internal and external stimuli and initiates adjustment behavior. The anterior insular cortex (AI) and the dorsal anterior Cingular Cortex (dACC) with its connectivity to subcortical and limbic structures are involved. Similarly, the anterior insular region is linked to the lateral prefrontal cortex (CEN), as well as to the medial prefrontal cortex (DMN), which are anti-correlated. One can therefore define the SN as a “switching network” between the DMN and the CEN (Goldberg, 2018), whereby the right insular region is always activated when switching from DMN to CEN, but not the other way around. Prillwitz and colleagues were able to show that fiber tract integrity in the SN is related to the personality trait "self-directedness" in the "Temperament and Character Inventory" (TCI) (Prillwitz et al., 2018). Other authors were able to show that high anxiety goes along with intrinsic functional connectivity in the SN (Seeley et al., 2007). There seems to be an anticorrelation between inner orientation (DMN) and external orientation (CEN), which becomes increasingly flexible in the course of the development from child to adult (Goldberg, 2018). Similarly, networks can change through pathological processes and develop to mental or structural disorders (e. g. personality disorders) (Medaglia, 2017; Quattrini et al., 2019).

Mindfulness is training for all three networks:

The central executive network: By repeatedly concentrating on a meditation object, the dorsal top-down attention system is trained. In beginners of meditation, this area of the brain is particularly involved, and in experts the activity is reduced. Therefore, Emotional Stroop tasks (Allen et al., 2012) are more easily accomplished. CEN is necessary for orientation to the outside (objects) and for the constant observation of one's own experiences, which is part of the meta-consciousness in meditation (Lutz, Jha, Dunne, & Saron, 2015)

The resting state network (DMN) is involved in both self-perception and compassion processes. Both are practiced by meditation. In certain meditation practices with a broad attention focus (e. g. ZEN), thoughts are not actively suppressed, but their appearance and disappearance are only observed (Lutz et al., 2015). The non-assessing attitude means a solution from the first person perspective (de-fusion, de-centering) and leads after repeated training to the realization that thoughts are not accurate representations of reality, but are “empty” in themselves. (Lebois et al., 2015). Similarly, in meditation experienced practitioners, activity in the resting state network decreases (Brefczynski-Lewis, Lutz, Schaefer, Levinson, & Davidson, 2007). Reduced resting state activity is associated with reduced self-referential thoughts (ego perception) and leads to improvement of external orientation (object perception) (Simon, 2015).

The insular region in the **Salience network** is involved in meditation training to detect self-processes, support body perception (Kieran CR Fox et al., 2016), and to notice when the meditation focus is lost (Britta K Hölzel et al., 2007). Damasio (2010) describes a model of "conscious presence". There, the insula region, the thalamus, and the brain stem merge all subjective feelings into a constant neural representation to a subjective second-order consciousness. This second-order consciousness might be the neural basis of the meta-presence practiced in meditation. Processes in the SN seem to be involved (Lutz et al., 2015).

In the translational model (see Figure 5), Tang and colleagues describe how mindfulness affects these three networks: Mindfulness meditation leads to improved self-regulation and improves behavior changes (Y. Tang & Leve, 2016).

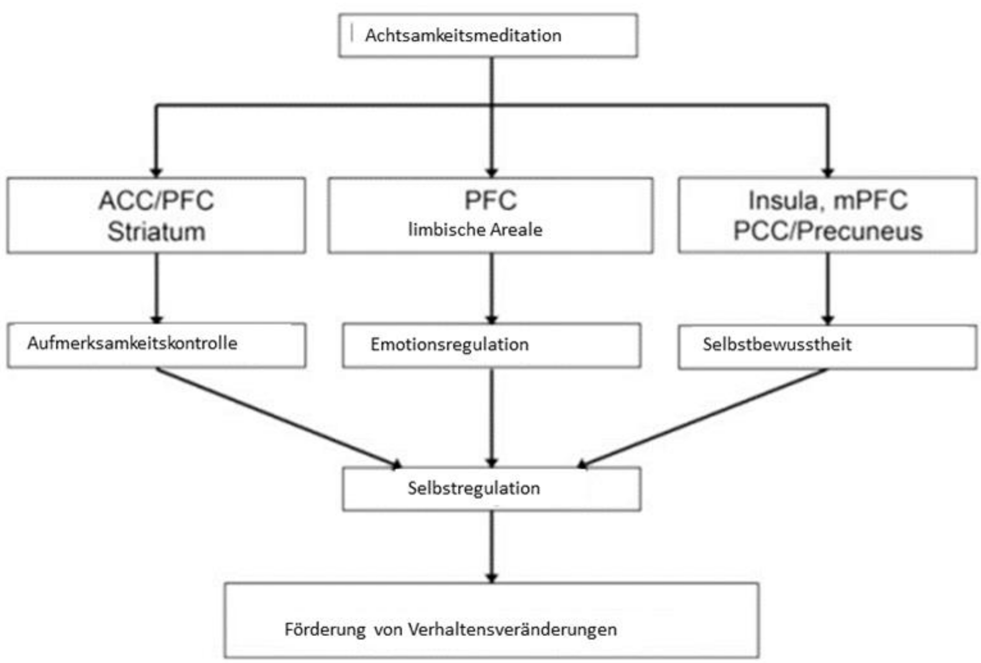


Figure 5: The Translational Model of Mindfulness Meditation (Y. Tang & Leve, 2016)

Empirically, the health-promoting effects of mindfulness are now well documented: mindfulness reduces stress symptoms, pain symptoms, ponders and improves emotion regulation and attention as well as clinical symptoms (Bishop et al., 2004; Gard, Hölzel, & Lazar, 2014; Grossman, Niemann, Schmidt, & Walach, 2004).

Short-term changes through meditation (state)

Many fMRI studies examine the short-term effects of mindfulness exercises on CEN performance and network connectivity. It showed a consistent picture of improved connectivity within and between the three networks DMN, CEN and SN (Brewer et al., 2011; Garrison, Zeffiro, Scheinost, Constable, & Brewer, 2015).

Long-term changes due to meditation (trait)

Long-term changes were found through meditation with reduced DMN activity and positive health changes. On the other hand, meditation experts (regular practice for more than 3 years) showed increased connectivity between DMN and CEN and SN. The focus of mindfulness is usually centered on a meditation object in beginners of meditation, to be distracted by self-related thoughts again and again. Long-term meditators then usually choose an open meditation focus, which makes it possible to observe the flow of thoughts remotely without identifying with it. Practicing meditation over the years, the stable concentration on an object changes to a state of non-duality, to a non-conceptual consciousness and to a dissolution of subject-object relationship. The silence achieved by this open focus is different from the silence created by focused absorption (Vago & Zeidan, 2016). The reduction of DMN activity through meditation is also used to treat mental disorders, which interfere with behavioral processes due to strong rumination and over-attention.

In summary, the long-term effect of meditation can be described as follows: Increasing ability to concentrate without effort with heightened clarity and stability that lead to significantly reduced activation of the DMN. In the course of years of practice, the

DMN may be "converted" into a meditative network (Brewer et al., 2011; Manna et al., 2010). Such structural changes in the brain could be found in several studies (für einen Überblick siehe Fox et al., 2014).

2.5 Classification of the dissertation in the current state of research

Both, the concept of personality disorder and mindfulness as a therapeutic intervention are based on complex meta-mechanisms. Proving the effect of mindfulness on borderline symptoms is not easy. Today, various mediating variables are discussed: reduction of rumination (Selby, Fehling, Panza, & Kranzler, 2016), improved mentalization (Guendelman, Medeiros, & Rampes, 2017) reduction of stress, pain reduction, increased body perception, reduction of dysfunctional assumptions, change in the default mode network or specific personality factors (Lee, 2017). Mindfulness as a meta-cognitive skill seems to be related to changes in overall connectivity in the brain (state), and in the long run to structural changes in the brain (trait; Farrés et al., 2019; Selby et al., 2016)(trait; Farrés et al., 2019; Selby et al., 2016)(trait; Farrés et al., 2019; Selby et al., 2016).

Bohus emphasized in 2009 that the reduction of dissociation is crucial in symptom improvement in borderline personality disorders (Bohus & Schmahl, 2006).

Since dissociation and mindfulness are opposite concepts, mindfulness training could reduce dissociations and thus contribute to the effectiveness of behavioral therapy interventions or directly reduce neural psychopathology. So far, however, studies on the influence of mindfulness on the reduction of dissociations (Bohus, 2009) are lacking.

Instead, the focus of current borderline research has been on the concept of emotion regulation/impulsivity and social hypersensitivity. The model of fronto-limbic imbalance is now considered well established.

Since 2013, the new diagnostic system DSM-5 has brought broader concepts for personality integration into the focus of research. However, in Europe there are hardly any borderline research dealing with the topic of "disorder of personality" and "identity" so far. Disorders of self-integrity and the relationship self/other have been intensively researched in the field of schizophrenia research. Here, temporal/parietal areas of the brain play a central role. These areas of the brain have been less studied in borderline patients so far and could play a role in personality integration, but also in dissociative processes.

M. Linehan's statement that mindfulness is the basis of all skills points to these neglected aspects of this disorder: the disruption of personality development in borderline patients through dissociation and the treatment of these disorders by mindfulness: This work tries to gain initial knowledge of this question and to stimulate further research through theoretical considerations.

Both topics are presented in Table 1 in terms of their psychopathology or their impact on the three networks.

Table 1: Overview of possible interactions at the neural level between borderline psychopathology and mindfulness

	Executive Network	Salience Network	Default Mode Network
Borderline	Emotion regulation Attention deficit Impulsivity.	Hypersensitivity for social stimuli	Disruption of personality/identity “Black and white” thinking, dissociation, paranoia, psychotic symptoms depersonalization, derealization body image
Meditation	Attention control Concentration/Stability.	Detecting loss of focus, Reorientation/flexibility	De-fusion, meta-cognition 3rd person perspective empathy and compassion TOM Features acceptance, non-assessing

The following key assumptions will be examined in this work:

8 weeks of DBT leads to similar changes in brain function in borderline patients as found in long-term meditation experts. After 8 weeks, psychopathology should decrease more significantly and show brain function differently in a mindfulness exercise (like the meditation experts) than in a comparison group of borderline patients after an 8-week cognitive behavioral therapy intervention (CBT) without mindfulness (study 3).

Study 1 replicates the mindfulness paradigm of Erb et al. (2011) with a group of longtime experts in meditation and compares the results with a group of healthy volunteers with no meditation experience.

The same mindfulness paradigm will be used again in Study 3 in borderline patients and two therapeutic approaches (DBT and CBT) will be compared against each other: After 8 weeks, the DBT group should show a stronger symptom improvement than the CBT group, and training in mindfulness should lead to changes in brain function (similar changes as the group of meditation experienced in Study 1).

The mindfulness paradigm consists of 3 X 3 minutes of mindfulness (careful listening to the sound of a singing bowl that is struck every 12 seconds). Before and between the mindfulness periods there are 2-minute time-blocks without mindfulness focus (mind-wandering), with the auditory stimulation continuing. The subjects perform all time-blocks with open eyes.

Study 2 looks at the effect of a mindfulness exercise (mindfulness paradigm) on the function of the frontal brain and on behavioral data. The same groups as in Study 1 are compared here. Both, a word fluid test (VFT) and an emotional Stroop test are performed with and without prior mindfulness exercise.

For all studies, the functional brain imaging method of near-infrared spectroscopy was used. This method was chosen because it is non-invasive, allows an upright posture and is therefore very suitable for measurement in a patient group. Since this imaging method detects neural activity up to 3 cm below the skull calotte, both the auditory cortex and the prefrontal cortex could be investigated easily.

2. Meditation and the brain – Neuronal correlates of mindfulness as assessed with near infrared spectroscopy (Study 1) (Friederike Gundel et al., 2018).

Abstract

Mindfulness meditation as a therapeutic intervention has been shown to have positive effects on psychological problems such as depression, pain, or anxiety disorders.

In this study, we used functional near-infrared spectroscopy (fNIRS) to detect differences in hemodynamic responses of meditation experts (14 participants) and a control group (16 participants) in a resting and a mindfulness condition. In both conditions, the sound of a meditation bowl was used to find group differences in the auditory system and adjacent cortical areas. Different lateralization patterns of the brain were found in expert meditators while being in a resting state (amplified left hemisphere) or being in mindfulness state (amplified right hemisphere). Compared to the control group, meditation experts had a more widespread pattern of activation in the auditory cortex, while resting. In the mindfulness condition, the control group showed a decrease of activation in higher auditory areas (BA 1, 6 and 40), whereas the meditation experts had a significant increase in those areas. In addition, meditation expert had highly activated brain areas (BA 39, 40, 44 and 45) beyond the meditative task itself, indicating possible long-term changes in the brain and their positive effects on empathy, meta cognitive skills and health.

1. Introduction

Today, the practice of meditation is seen as a mental or cognitive training which is accompanied with emotional well-being and amelioration of concentration and attention (state). Practicing over years makes it possible to keep this awareness continuously beyond daily meditation practice (trait) (Erb et al., 2011). All this makes meditation interesting to the field of psychopathology (as a therapeutic intervention) and to the study of underlying functional, physiological, and anatomical correlates of meditation on the brain.

In the 1990s, secular standardized methods of mindfulness-training were developed for therapeutic and clinical use, e. g. Mindfulness-Based Stress-Reduction (MBSR). The effects of these meditation programs in reducing stress-related diseases are still inconclusive: While Gotink et al. (2015) and Spikerman et al. (2016) point at positive effects of these programs in reducing pain, phobias, depression and other emotional disorders, Goyal et al. (Goyal et al., 2014) found only small improvements on stress-related symptoms and even lower evidence when these meditation programs were compared with nonspecific active controls. Recent functional and structural neuroimaging studies have fostered a growing pool of knowledge by examining the effects of meditation training or comparing novices and experts in meditation practice.

A review of this literature has uncovered brain regions associated with mechanisms of mindfulness: medial prefrontal cortex (mPFC) and associated default mode network (DMN) as well as the insula and amygdalae (Boccia, Piccardi, & Guariglia, 2015). Structural imaging studies found changes in gray and white matter of the cortical midline structures (CMS) and the DMN, insula, hippocampus and amygdale (Hölzel et al., 2011) and a meta-analysis of 78 functional neuroimaging investigations (Kieran CR Fox et al., 2016) found dissociable patterns of brain activation for four different types of meditation (focused attention, mantra recitation, open monitoring and loving-kindness).

Little is known so far, as to why changes in brain activity or brain structure might have positive effects on mood: Kemmer at al. (2015) found a less active DMN in meditators during a mindfulness task and Brewer et al. (2011) found trait-based neural differences in long-term meditators suggesting that there are profound changes in the DMN in this group. The reduction of mind-wandering in meditation might play a key role in stabilizing mood and reducing stress (Simon, 2015). The authors also indicate that there might be a connection between sustained metabolic activity in the DMN and mental disorders such as schizophrenia, epilepsy, anxiety, depression, autism, and attention deficit hyperactivity disorder as well as Alzheimer's disease. Today, mindfulness is even seen as a cognitive training for mental enhancement and potential age-defying effects on gray matter atrophy (Luders, Cherbuin, & Kurth, 2015).

Other brain areas active while meditating might have positive effects on emotional aspects. Lamm et al. (2011) found specific changes in the right somatosensory cortices after a training of compassion meditation training.

Due to the diversity of meditation practices, methodological difficulties and the complex nature of meta cognitive function, research on this topic is challenging. Further research on patients with mental disorders is needed to understand relevant therapeutic effects of meditation. This research will further foster our knowledge of under-lying psychopathological brain processes and might help to develop specific therapeutic tools.

Our present study is embedded in a larger research project studying the therapeutic effects of dialectic behavioral therapy (DBT) for border-line personality disorder. This therapy approach uses Zen meditation techniques (mindfulness skills) to train emotion regulation. Since borderline patients are often phobic to intrinsic states (emotions, body sensations), we used an outside focus (auditory stimulus) and just 3 min of meditation time. So far, it is still unclear whether this reduced mindfulness training for borderline patients is effective. To find out differences in brain activity while meditating in a somehow realistic upright position, we used near-infrared spectroscopy (NIRS). This method allows for a non-invasive monitoring of concentration changes in oxygenated (O2Hb) and deoxygenated hemoglobin (HHb) as indicators of brain activation without severe restrictions on body movements and posture. The mindfulness paradigm was taken from a small experimental study by (Erb et al., 2011). The study presented here aimed at examining the effects of regular meditation practice on cortical activation patterns in the auditory cortex and adjacent cortical areas during a mindfulness paradigm guided by an auditory stimulus (meditation bell). We expected to find specific patterns of hemodynamic responses in a meditation expert group while meditating and resting as found in previous studies(Britta K. Hölzel et al., 2008; Lazar et al., 2005; Luders, Toga, Lepore, & Gaser, 2009). A control group of healthy meditation novices was also measured. In a second step – and not presented here – the mindfulness paradigm will be studied on borderline patients before and after a DBT mindfulness training.

2. Methods

2.1. Subjects and Questionnaires

The study comprised two groups of healthy subjects: one with (meditation group) and one without (control group) meditation experience. The meditation group included a total of 14 participants (6 male, 8 females; 1 left-handed) with a mean age of 49.2 ± 9.1 (range: 29–62) years and a mean regular meditation experience of 16.6 ± 10.2 (range: 3–31) years. Mean weekly mediation duration was reported to be 4.8 ± 3.4 h. All the participants of this group followed the Buddhist tradition of Zen (sitting meditation – “Za Zen”) and walking meditation (“Kin Hin”) and were organized in meditation groups practicing together and for themselves. None of the group was trained beforehand to meditate on an auditory task, but all of them were acquainted with the sound of a meditation bowl, which is used in Zen traditionally to signal the beginning and end of a meditation session. Since there were participants with long meditation experience, different meditation techniques might have been learned making this group very heterogeneous. The control group comprised 16 participants (6 males, 10 females; mean age: 22.5 ± 7.7 years (range: 18–50); 1 left-handed) without any meditation experience. The two groups differed significantly in age (t_{28}=8.74, p < 0.001), but not gender distribution (χ^2=0.09, p=0.77). Regarding education, all participants had the German "Abitur". Moreover, they were all German native speakers with no evidence of a current mental disorder (as indicated by self-report). Personality-wise, no significant group differences occurred for any of the Big-Five-Inventory-10 scales (BFI-1)(Rammstedt, Kemper, Klein, Beierlein, & Kovaleva, 2012). Only for the Openness Scale, the meditation group tended to show higher scores (Mann-Whitney U=68.5, p=0.061). The Global Severity Index (GSI) of the Symptom Checklist (SCL-90-R) (Franke, 2002) – as an indicator of psychopathology – also did not differ significantly between groups (t_{28}=1.38, n. s.; mean overall value: 44.85 ± 9.87); however, based on the MWT-B (German: Mehrfach-Wortschatz-Intelligenztest) (S. Lehrl, Merz, J., Burkhard, G., & Fischer, B. , 2005) meditators had a significantly higher intelligence quotient (IQ) (124.21 ± 10.92) as compared to the control group (102.06 ± 13.82; t_{28}=4.82, p < 0.001). Moreover, regarding everyday mindfulness, meditators exhibited significantly higher scores on the Kentucky Inventory of Mindfulness Skills (KIMS-D)(G. Ströhle, Nachtigall, C., Michalak, J., & Heidenreich, T. , 2010) (155.00 ± 13.55 vs. 135.19 ± 15.42; t_{28}=3.71, p < 0.001). The KIMS-D is a questionnaire measuring the tendency to be mindful in everyday life. It is applicable to subjects with and without meditation experience (G. Ströhle, 2006). The KIMS is based on a theory by Kabat-Zinn (J. Kabat-Zinn, 2003) stating that mindfulness is a universal ability at least rudimentarily developed in every person.

Written informed consent was obtained from all participants. The study was approved by the local Ethics Committee (University of Tuebingen) and all procedures were in accordance with the Declaration of Helsinki in its latest version.

2.2. Procedures

The sequence of mindfulness task and the applied questionnaires (see 2.1) was randomized across subjects. Half the participants started with the 17 min mindfulness task and subsequently answered the questionnaires, and the other half completed the questionnaires first and performed the mindfulness task afterwards. Completion of the questionnaires took 15–20 min.

2.2.1. Mindfulness paradigm

The mindfulness paradigm comprised four baseline blocks (2 min each) and three mindfulness periods (3 min each) which were conducted in an alternating fashion. Throughout the whole experiment, the tone of a meditation bowl was presented with one new strike every 12 s. Participants always had their eyes open. During baseline periods, participants were instructed just to rest without a specific focus on the tone. In contrast, during meditation periods, they were asked to focus their attention on the tone in a “mindful” manner.

2.2.2. NIRS

NIRS measurements were conducted using the ETG-4000 Optical Topography System (Hitachi Medical Co., Japan) continuously recording relative changes in the concentration of O_2Hb and HHb from a 10-s starting baseline (preceding the first rest segment of the mindfulness paradigm). For the mindfulness paradigm, two lateral probe-sets (3×5 optodes each; inter-optode distance: 30 mm) were employed comprising a total of 44 (2×22) measurement channels covering an area of 12×6 cm over left and right fronto-temporal areas. For positioning, the middle optode of the lowest row was placed on T3 (left) and T4 (right), respectively; at the same time, the middle optode of the top row was placed as closely as possible to positions C3 (left) and C4 (right) respectively, according to the international 10–20 system for EEG electrode placement (Jasper & Rasmussen, 1958) (see Fig. 1). For the measurement, near-infrared light of two wavelengths (modulated at a distinct frequency for each wavelength and channel; ranges: 695 ± 20 nm and 830 ± 20 nm) was continuously emitted onto the scalp and the amount of reflected light was detected by appropriate photodetectors. Based on a modified Beer-Lambert Law (see Sassaroli & Fantini, 2004), the signals were analyzed and transformed according to their respective wavelength and location, resulting in the time course of concentration changes in O_2Hb and HHb for each of the 44 measurement channels (whereby channels were located midway between each emitter-detector pair; sampling rate: 10 Hz).

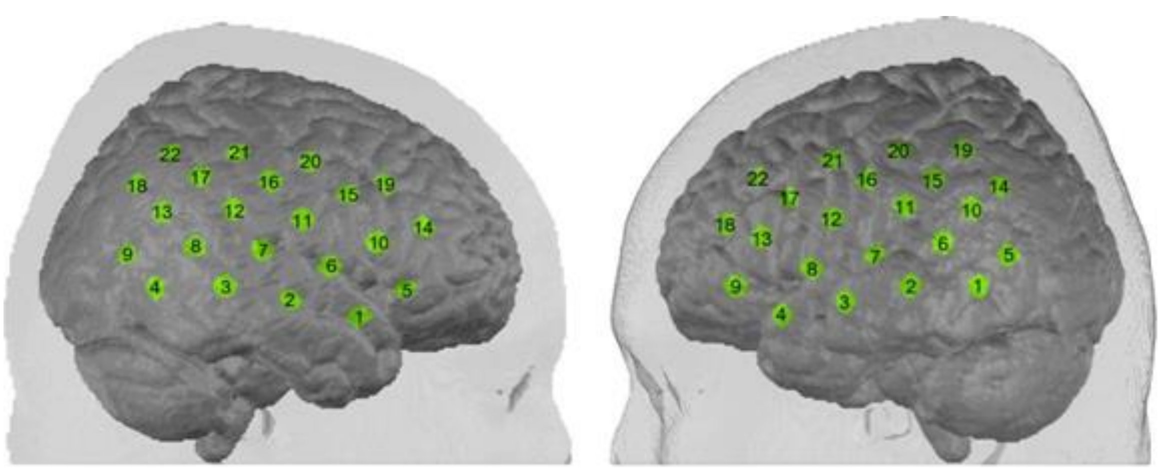


Fig. 1. 3×5 probe set arrangement with numbers indicating NIRS channels on the right and left hemisphere. The correspondence of NIRS channels to underlying cortical areas was estimated based on a placement of the probe sets based on 10–20 system reference positions and the virtual registration method suggested by Singh (2005).

2.2.3. Data analysis and statistics

With the NIRS system, changes in the concentration of O_2Hb and HHb were recorded from starting baseline. For the analysis (using customized Matlab scripts; The MathWorks, Inc., USA), data were individually averaged according to the task condition (rest periods vs. mindfulness) whereby the first 60 s of all mindfulness periods were discarded to give practitioners enough time to reach a meditative state, resulting in a 120 s average for each participant and condition. The very first baseline period was analyzed separately and not included in the average of the rest periods: first, in order to include an equal number of segments/repetitions in the two experimental conditions; second, because the first segment in NIRS data often shows very particular activation patterns that might – in part – be related to an increased arousal at the beginning of an experiment in the lab; and third, due to the consideration that rest periods following periods of mindfulness might differ from rest periods before a state of mindfulness has been reached. In order to correct the NIRS data for slow physiological signals unrelated to the task itself (e.g., spontaneous oscillations in cerebral blood flow; cf. (R. Zhang, Zuckerman, J.H. & Levine, B.D. , 2000), a linear fitting function was used for baseline correction. Moreover, a bandpass filter was applied between 0.008 and 0.05 Hz, followed by an interpolation of noisy channels based on the mean value of all adjacent channels. For statistical analysis, mean values across the task segments were calculated for each condition, NIRS channel and participant (see A. C. Ehlis, Herrmann, Plichta, & Fallgatter, 2007). For reasons of conciseness, out of the different available NIRS parameters (O_2Hb, HHB, total hemoglobin), only HHb data will be reported (which has a superior spatial specificity (Plichta, Heinzel, Ehlis, Pauli, & Fallgatter, 2007) and seems to be less prone to artifacts caused by, e.g., extracerebral perfusion changes (Haeussinger et al., 2014; Heinzel et al., 2013; Kirilina et al., 2012). Importantly, cortical activation should be reflected by a decrease in HHb concentration. To illustrate patterns of activation for both mindfulness and rest periods, t-maps were calculated based on channel-wise comparisons between task conditions or against zero (one-sample t-test). Here, a Bonferroni-based correction was applied to account for the multiple test situation based on the formula provided by (Sankoh, Huque, & Dubey, 1997) (Dubey/Armitage-Parmar algorithm; see also (Sassaroli, Tong, Benes, & Fantini, 2008) and Plichta et al. (2007). The correspondence of NIRS channels to underlying cortical areas was estimated based on a virtual registration method (Rorden, 2000; Singh, 2005; Tsuzuki, 2007).

Statistically, following the illustration of general activation patterns using the above-described t-maps, analyses of variances (ANOVAs) were calculated comprising the within-subject factor “condition” (mindfulness vs. rest) and the between-subject factor “group” (control group vs. meditation-experienced subjects). In case of significant interactions, post-hoc tests were conducted using t-tests for matched and independent samples. Pearson's correlation coefficient was used to examine a potential impact of age and IQ on NIRS data due to group differences regarding these two factors. Two-sided testing procedures were used throughout.

3. Results

3.1. T-maps (topographical brain activation data: HHb concentration changes during rest or mindfulness conditions contrasted against zero (one-sample t-test) for each NIRS channel) (see Table 1).

For the control group, significant activation (decreases in HHb concentration) was observed in rest periods in channels #4 (t_{15} =−2.902, p=0.011), #8 (t_{15} =−2.908, p=0.011) and #9 (t_{15} =−2.619, p=0.019) of the left hemisphere (see blue areas in Fig. 2), which are located within the temporal lobe, adjacent to the primary auditory cortex.

Table 1 Significant Activation in Resting State (as indicated by one-sample t-tests).

Control Group					
Region	Side	Channel	Three	*t*(15)	*p*
Temporopolar	left	#4	BA38	- 2.902	.011
Retrosubicular	left	#8	BA48	- 2.908	.011
Broca´s area	left	#9	BA45	- 2.619	.019
Premotor cortex	right	#20	BA6	- 2.513	.024
Meditation Group					
Region	Side	Channel	Three	*t*(13)	*p*
Middle temporal gyrus	left	#3	BA21	- 2.608	.022
Temporopolar	left	#4	BA38	- 2.881	.013
Retrosubicular	left	#8	BA48	- 2.392	.033
Broca´s area	left	#9	BA45	- 2.324	.037
Subcentral	left	#12	BA43	- 2.441	.030
Supramarginal gyrus	left	#19	BA40	- 2.400	.032
Broca´s area	left	#22	BA44	- 2.805	.015
Subcentral	right	#11	BA43	- 2.511	.026

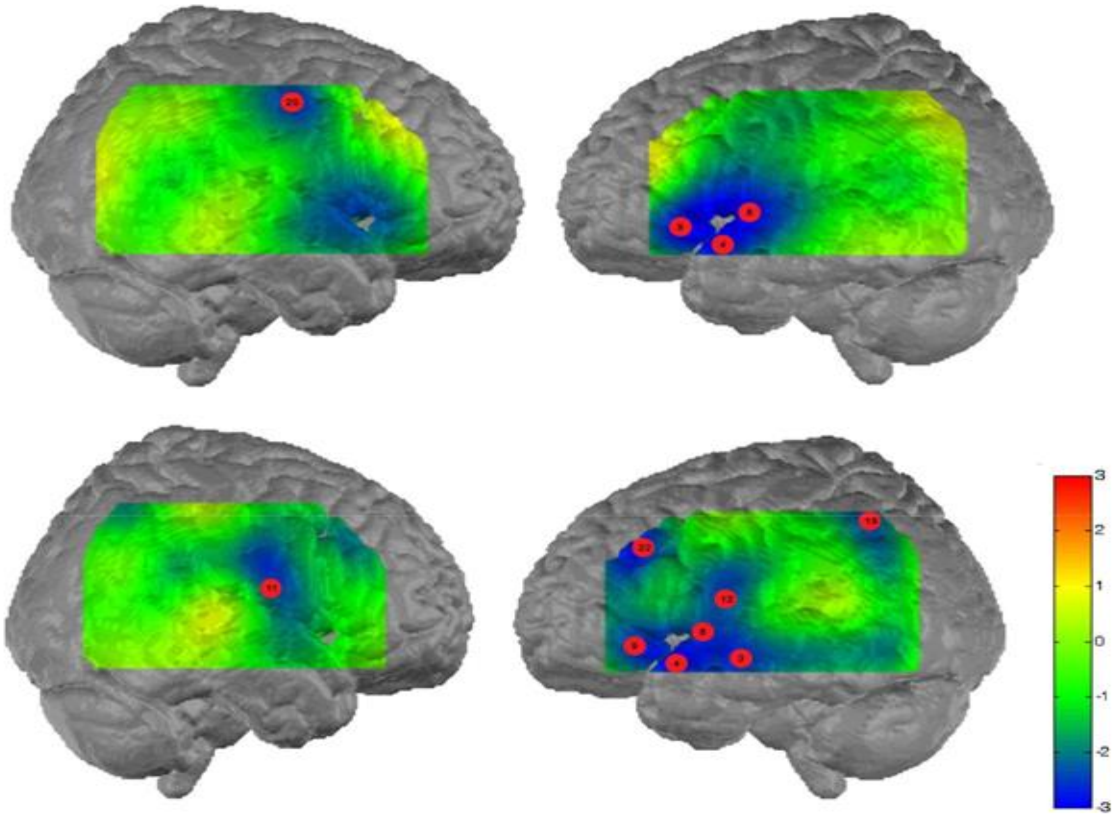


Fig. 2. Resting condition (Baseline): Significant cortical activation for control group (upper panel) and expert meditators (lower panel) (T-values show increases and decreases in HHb concentration contrasted against zero (one-sample t-test). Blue areas indicate decreases in HHb, i.e., cortical activation). Upper panel: Control group showed significant activations mainly in the primary auditory system (for details see also Table 1). Lower panel: Expert meditators had a more widespread activation mainly in the left hemisphere of the auditory system (for details see also Table 1). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

On the right, decreases in HHb were observed in similar channels, however, only channel #20 ($t_{15} = -2.513$, $p=0.024$) reached statistical significance (see Fig. 2), which – according to our localization algorithm – is located within Brodman Area 6 (premotor / supplementary motor cortex). Subjects with meditation experience showed activation in similar areas for the rest condition, with a more widespread activation focus particularly for the left hemisphere. Here, a cluster of adjacent channels #3 (t_{13} =−2.608, p=0.022), #4 (t_{13} =−2.881, p=0.013), #8 (t_{13} =−2.392, p=0.033), #9 (t_{13} =−2.324, p=0.037), #12 (t_{13} =−2.441, p=0.030) as well as channels #19 (t_{13}=−2.400, p=0.032) and #22 (t_{13}=−2.805, p=0.015) showed significant decreases in HHb concentration (i.e. cortical activation), most of which were located within the temporal lobe (middle temporal gyrus, temporopolar area, subcentral area), so again close to the primary auditory cortex. For the right hemisphere, only channel #11(t_{13} =−2.511, p=0.026) showed a significant increase in activation (subcentral area; see Fig. 2) in meditation-experienced subjects (Table 1).

In the mindfulness condition, interestingly, the control group showed no significant activation in any of the NIRS channels as compared to baseline (see also Fig. 3 and Table 2). In contrast, participants with meditation experience showed significant activation in channels #16 (t_{15}=−2.553, p=0.024) and #20 (t_{15} =−3.717, p=0.003) of the left hemisphere (located at the border between the primary somatosensory cortex (BA 1) and supramarginal gyrus (BA 40) and channels #8 (t_{15} =−2.712, p=0.018) (primary auditory cortex / superior temporal gyrus, BA 22), #19 (t_{15} =−2.256, p=0.042) (part of Broca's area, BA44) as well as #12 (t_{15} =−3.138, p=0.008) and #22 (t_{15} =−2.687, p=0.019) (supramarginal gyrus, BA 40) of the right hemisphere.

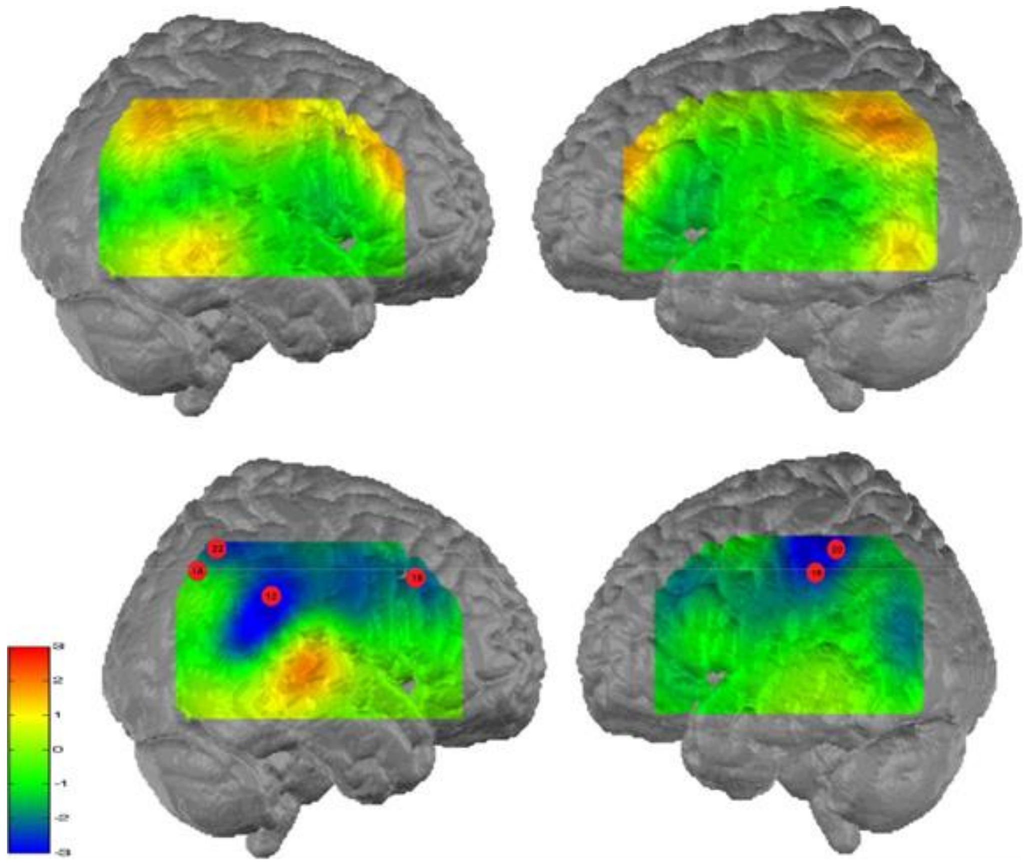


Fig. 3. Mindfulness condition: Significant cortical activation for the control group (upper panel) and expert meditators (lower panel) (T-values show increases and decreases in HHb concentration contrasted against zero (one-sample t-test) Blue areas indicate decreases in HHb, i.e., cortical activation.). Upper panel: Control group: No significant activation was found.

Lower panel: Expert meditators: Significant activation was found mainly in the right hemisphere (see also Table 2). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 2

Significant Activation in Mindfulness-Condition (as indicated by one-sample t-tests).

Mindfulness Group

Region	Side	Channel	Three	*t*(15)	*p*
Primary somatosensory cortex	left	#16	BA1	- 2.553	.024
Supramarginal gyrus	left	#20	BA40	- 3.717	.003
Superior temporal gyrus	right	#8	BA22	- 2.712	.018
Broca´s area	right	#19	BA44	- 2.256	.042
Supramarginal gyrus	right	#12	BA40	- 3.138	.008
Supramarginal gyrus	right	#22	BA40	- 2.687	.019

3.2. ANOVA data ("group" × "condition" for concentration changes in HHb in single NIRS-channels)

The ANOVA analysis (see Tables 3 and 4) revealed a significant main effect of the factor "group" (or trends thereof) for channels #14 ($F_{1,\ 28}$ =3.98, p=0.056, η2=0.124) and 19 ($F_{1,\ 28}$ =6.75, p=0.015, η2=0.194) of Wernicke's area as well as channels #18 ($F_{1,\ 28}$ =5.75, p=0.023, η2=0.170) and 22 ($F_{1,\ 28}$ =4.88, p=0.036, η2=0.148) of Broca's area within the left channel array. On the right, group effects were found for corresponding channels #14 ($F_{1,\ 28}$ =3.19, p=0.085, η2=0.102), #19 ($F_{1,\ 28}$ =11.65, p=0.002, η2=0.294) and #22 ($F_{1,\ 28}$ =6.20, p=0.019, η2=0.181). In all cases, meditation-experienced subjects showed significantly stronger activation (i.e., more negative HHb values) as compared to the control group.

Table 3

ANOVA main effect: Group (meditation versus control group).

Hemisphere									
right					left				
Channel	Three	*F*(1, 28)	*p*	η²	Channel	Three	*F*(1,28)	*p*	η²
#14	BA45	3.19	.085	.102	#18	BA45	5.75	.023	.170
#22	BA40	6.20	.019	.181	#19	BA40	6.75	.015	.194
#19	BA44	11.65	.002	.294	#22	BA44	4.88	.036	.148
					#14	BA39	3.98	.056	.124

Table 4

ANOVA main effect: Group×Condition.

Hemisphere									
right					left				
Channel	Three	*F*(1, 28)	*p*	η²	Channel	Three	*F*(1,28)	*p*	η²
#16	BA1	8.27	.008	.228	#16	BA1	3.40	.055	.125
#20	BA6	7.59	.010	.213	#20	BA40	3.97	.056	.124
#21	BA40	7.71	.001	.216					

Beyond these main effects, significant interactions "group × condition" (see also Table 4) were found for channels #16 ($F_{1,}$ 28=8.27, p=0.008, η^2 =0.228), #20 ($F_{1,}$ 28=7.59, p=0.01, η^2 =0.213) and #21 ($F_{1,}$ 28=7.71, p=0.01, η^2 =0.216) of the right hemisphere. Post-hoc t-tests further confirmed that – for all three channels – significant group differences were only found for the mindfulness (channel #16: t28=2.07, p=0.048; channel #20: t_{25} =2.29, p=0.031; channel #21: t_{24} =2.13, p=0.044) and not for the rest condition (all t < 1, p > 0.3) with more negative values (i.e., stronger activation) in the meditation group (see Fig. 4). Directly comparing the two conditions furthermore showed significantly decreased activation (or trends thereof) in the mindfulness compared to the rest condition in the control group (channel #16: t_{15} =2.77, p=0.014; channel #20: t_{15} =2.97, p=0.009; channel #21: t_{15} =1.92, p=0.074). For channel #21, meditation-experienced subjects showed a significant condition effect in the opposite direction, i.e., stronger activation for mindfulness vs. rest (t_{13} =2.47, p=0.028). Within the left channel array, interaction effects occurred only as statistical tendencies for channels #16 ($F_{1,}$ 28=3.40, p=0.055, η^2 =0.125) and 20 ($F_{1,}$ 28=3.97, p=0.056, η^2 =0.124) with a trend for a between-group difference only for the mindfulness condition in channel #20 (t_{19} =1.93, p=0.069).

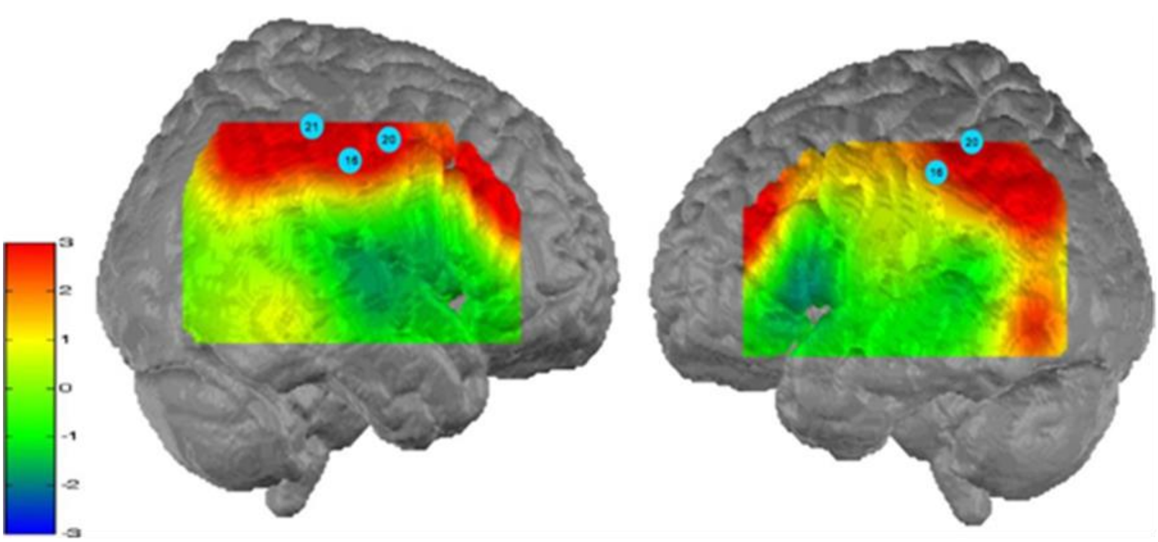


Fig. 4. Significant group differences in mindfulness condition: (T-maps for HHb concentration changes in meditation-experienced vs. control subjects for the mindfulness condition. Red areas indicate relatively stronger activation in the meditation compared to the control group.). **Right:** #16 (BA 1), #20 (BA 6): significantly reduced activity in the control group. #21 (BA 40): significantly higher activation in meditation group. **Left:** only statistical tendencies for #16 (BA 1), #20 (BA 40).

3.3. Correlation analyses of confounding variables "age" and "IQ"

Due to group differences in age and verbal IQ, we exploratively correlated our NIRS data with both confounding variables. Interestingly, age was significantly correlated with the NIRS data in only two channels out of a total of 88 calculated tests (22 channels ×2 probe sets ×2 conditions) within the meditation-experienced group (right probe-set: channel #9, baseline: $r=0.56$, $p < 0.05$; channel #2, mindfulness condition: $r=-0.64$, $p < 0.05$) and in no channel or condition in the control group. For the IQ values derived from the MWT-B, again only two out of 88 tests reached statistical significance in the control group (channel #19, left side, mindfulness condition: $r=-0.50$, $p < 0.05$; channel #17, right side, mindfulness condition: $r=-0.52$, $p < 0.05$); within the meditation group, five out of 88 tests showed significant correlations between IQ and NIRS data (left probe-set: channel #16 and #21 [baseline], channel #20 [mindfulness]; right probe-set: channel #19 and #22 [baseline]; $0.55 \le r \le .65$, all $p < 0.05$).

4. Discussion

In this study, we compared cortical activation patterns between meditation experts and a control group without meditation experience during mindfulness and a baseline condition using a background auditory stimulus and NIRS as a non-obtrusive, ecologically valid neuroimaging method. As expected, in our baseline condition, the auditory cortex was activated in both groups with a somewhat more widespread pattern of activation in meditation experts (see Fig. 2).

In the mindfulness condition (see Fig. 3), we found no significant increase in hemodynamic responses in the control group, but significant activation in areas of the primary somatosensory cortex (BA1), gyrus temporalis superior (BA 22), supramarginal gyrus (BA 40) and Boca's area (BA 44) for meditation experts. Beside this, the ANOVA analysis revealed specific group differences that concerned only the mindfulness condition (interaction effect: Table 4). Over several (neighboring) channels of the right hemisphere, significant group differences were only found for the mindfulness condition with more negative HHb values (i.e., stronger activation) in the meditation compared to the control group (Table 4). While the control group showed a decrease in hemodynamic responses for the mindfulness condition compared to baseline in secondary and tertiary auditory areas (BA 1, 6 and 40), meditation experts showed an opposite pattern of activation changes with a significant increase in activation for the mindfulness condition especially in BA 40 (supramarginal gyrus; Wernecke's area) (see also Fig. 4). The results show brain areas which are specifically active in meditation trained people while being mindful on an auditory stimulus. Our study is the first one to replicate findings of a pilot study by (Erb et al., 2011) indicating that NIRS is an appropriate and handy method to detect changes in the brain in mindfulness paradigms. The use of auditory cues seems to be a suitable method to test the primary sensory system as well as brain areas which are connected to higher mentalization skills, such as language or moral decision making (Kraus & White-Schwoch, 2015). In addition, the auditory system is strongly connected with emotions (Ethofer et al., 2006).

4.1. Right lateralization of the lateral parietal cortex in the state of meditation

We found indications for state-dependent changes in brain lateralization from left to right (see Figs. 2 and 3) when meditation experts changed to the mindfulness task (see also Table 5).

Table 5

Lateralization from left to right in meditation experts when shifting from resting state into a mindfulness condition.

Meditation Group (Resting State Condition)

Region	Side	Channel	Three	*t*(13)	*p*
Middle temporal gyrus	left	#3	BA21	- 2.608	.022
Temporopolar	left	#4	BA38	- 2.881	.013
Retrosubicular	left	#8	BA48	- 2.392	.033
Broca´s area	left	#9	BA45	- 2.324	.037
Subcentral	left	#12	BA43	- 2.441	.030
Supramarginal gyrus	left	#19	BA40	- 2.400	.032
Broca´s area	left	#22	BA44	- 2.805	.015
Subcentral	right	#11	BA43	- 2.511	.026

Meditation Group (Mindfulness Condition)

Region	Side	Channel	Three	*t*(15)	*p*
Primary somatosensory cortex	left	#16	BA1	- 2.553	.024
Supramarginal gyrus	left	#20	BA40	- 3.717	.003
Superior temporal gyrus	right	#8	BA22	- 2.712	.018
Broca´s area	right	#19	BA44	- 2.256	.042
Supramarginal gyrus	right	#12	BA40	- 3.138	.008
Supramarginal gyrus	right	#22	BA40	- 2.687	.019

We presume that neural processing of auditory cues in the baseline condition might be more analytical, whereas in the meditative state, holistic top-down neural processing is more prominent (as in music perception). This is in line with a study identifying cortical topography of tonal structures in music that showed a strong right lateralization mainly in temporal (e.g. BA 21), frontal (e.g. BA 45 and BA 6) and parietal regions (BA 1 and BA 40) (Janata et al., 2002). In an fMRI study, (Erb et al., 2011) found enhanced activation in the right auditory cortex (BA 47, rolandic operculum) by expert meditators in a meditative state. Fan et al. (Fan, Duncan, de Greck, & Northoff, 2011) identified in a whole brain based quantitative meta-analysis of recent fMRI studies two different empathy networks, which were also organized in a lateralized way: The affective component of empathy was located on the right side, whereas cognitive-evaluative empathy was located on the left side. Following this thought, we speculate that there may be two aspects of auditory processing as well: Primary analytical processes located mainly on the left side, whereas affective integration of these primary processes (higher order processing as in mindfulness state) is prominent in the right hemisphere. In our study, meditation experts had higher activation in BA 6 on the right hemisphere. Following Fan, this region is part of the affective-perceptual empathic system. The activation of the empathic system might reflect the training in mindfulness of a non-judging attitude towards everything. In addition to that, (Kieran CR Fox et al., 2016) identified in their meta-analysis of 78 functional neuroimaging investigations the right BA 6 to be involved in meditative states. The authors suggest that this region may play a role in mental manipulation of psychological content and memory and may interact with other brain areas assisting in the intentional regulation to attention. All this is very speculative yet but might foster new research.

4.2. Mindfulness state: The role of the right temporo-parietal junction (rTPJ)

The right temporo-parietal junction (rTPJ) in meditation experts seems to play a crucial role while being in a mindfulness state. On the left hemisphere results are similar, but not statistically significant indicating a possible down-shifting of analytical processes (see previous section). Besides its role in the emotional aspects of speech and music as well as holistic language processes (Poeck & Hartje, 2006), the right TPJ seems to be specifically involved in long-term meditation training and was found to be highly active disengaging from disrupting
inner thought and focusing outwards to auditory stimuli (Lutz, Slagter, Dunne, & Davidson, 2008). Therefore, stronger activity in BA 40 found in our study may reflect the improved ability of meditation experts to dis-identify from one's own perspective and to sustain an attention focus to the here and now (auditory task). Beyond that, BA 40 seems to be related to the ability to separate one's own emotions from emotions of others (theory of mind; (Saxe & Kanwisher, 2003). Therefore, the increased activation of BA 40 in meditation experts reported here might be one of the neurobiological factors underlying the observation that meditation fosters emphatic perspective of others followed by better social integration with its positive effects on health (by, e.g. oxytocin; see (Esch, 2014; Lamm et al., 2011; Uchino et al., 2012). Lamm et al (2011) found in their meta-analysis of fMRI studies of empathy two separate neural networks, whereby the right TPJ was involved in cue-based empathy that requires reflecting and mentalization about the current state of another person. The authors stress that this activity in the rTPJ is necessary to prepare empathic responses. This is in line with Young et al. (2010) who found that disruption of the right temporoparietal junction reduces the role of moral judgments. The authors refer to the fact that moral development in children from 6 to 11 years goes along with the maturation of this brain region.

Krall et al. (2015) analyzed connectivity patterns in this region and could distinguish two different neural networks in the rTPJ: A task positive network in the anterior rTPJ as a core region for a right-lateralized frontoparietal attention network, which reacts to sudden changes in visual, tactile and auditory stimulation, and the posterior rTPJ, which is connected with typical ToM regions enabling social interaction capacities.

The high activation on the rTPJ in a mindfulness state might reflect the underlying process in meditation: Being aware when the focus of attention is shifting away from the meditation focus (auditory cue) and shifting the attention back to focus repeatedly. The strong connectivity of the rTPJ to attention/saliency network regions might be trained by meditating over many years, so that it is possible to interrupt automated, predicted routines: Reorientation of attention and correcting false belief.
On the other hand, Krall et al. (2015) identified the posterior part of the rTPJ to be related with the default mode network reflecting stimulus-independent mental processes which are co-activated with a social network more globally involved in ToM-like abilities. High activation on BA 40 might also be amelioration in auditory performance for meditation experts. This is in line with studies finding better somatosensory performance in meditation trained persons: Ker et al. (2011) found enhanced alpha power modulation in a localized representation in the primary somatosensory neocortex in response to a cue in healthy subjects after 8 weeks of mindfulness meditation training. Haegens et al. (2011) could show that the alpha activity is under top-down control and seems to play an important role for setting the state of sensory regions to optimize processing in a somatosensory spatial attention task. It can be speculated that the detection of auditory cues in our study might be regulated by the same mechanism so that higher activity of BA 40 might also reflect better detection auf auditory cues.

4.3. Long-term effect of meditation practice (trait)

As a more general effect, the ANOVA analysis also revealed main effects of the factor group (Table 3) indicating that meditation-experienced subjects showed significantly stronger activation (i.e., more negative HHb values) in secondary and tertiary auditory brain areas (BA 39, 40, 44 and 45) as compared to the control group independent of the specific task condition. These results point at a more general effect of meditation training beyond the mindfulness-condition. Areas highly active in a meditative state (tertiary auditory system) seem to stay active beyond the meditative task itself (i.e., in resting conditions). Our findings strengthen the hypothesis that meditation training can foster specific long-term effects in the brain, which are not dependent on the task presented, but might represent lasting underlying resting-state changes (trait features).

4.4. Lasting DMN-changes in meditation experts

In our study, BA 40 (TPJ) seen as part of the DMN was more active in meditation experts. This finding does not correspond with results of meta-analyses by Tomasio et al. (2014; Tomasino, Fregona, Skrap, & Fabbro, 2013) and Garrison et al. (2015) showing that a regular practice of meditation reduces DMN activity. Reduced DMN activity is seen as an indicator for a therapeutic effect of meditation in mental disorders such as depression, altering patterns of self-judgment and extended rumination (Farb et al., 2010; Farb et al., 2007) or improvements of attention control (Hasenkamp, Wilson-Mendenhall, Duncan, & Barsalou, 2012). On the other hand, previous findings show that increased resting state activity enhances auditory stimulus detection (Sadaghiani, Hesselmann, & Kleinschmidt, 2009). Doll et al. (2015) found also stronger inter-network intrinsic functional connectivity (inter-iFC) between the DMN and the Salience network (SN) in mindfulness trained persons. The authors found a reduced activity in the anterior

DMN and a stronger connection to the temporo-parietal DMN with the salience network in people with high scores on a mindfulness scale. The authors stress that in this temporo-parietal area, ongoing activity of the DMN and goal directed behavior may overlap. This is in line with results of studies of e.g. Hasenkamp and Barsalou (2012) and Berkovich-Ohana et al. (2014) finding stronger connections in these networks in association with mindfulness. Brewer at al. (2011) speculated that meditation coactivates monitoring/control regions with nodes of the DMN to form a new "default mode" being active during meditation as well as in the resting state. This is in line with experience in long-term practitioners reporting that in the end there is no formal meditation time anymore, but everyday life becomes meditative and that there is a qualitative shift from the quality of the "I" to the "Non-Self" (Dor-Ziderman, Berkovich-Ohana, Glicksohn, & Goldstein, 2013). Tusche et al. (2016) suggested in the context of studies on altruistic giving that there might be a bottom-up shift of attention (from a predominant first-person to a third-person perspective) in the TPJ. Berkovich-Ohana et al. (2012) found in their studies gamma power increases (both state and trait) in posterior brain areas in mindfulness practitioners compared to controls. They suggest a "trait transition from self-reference processing towards an experimental self-reference mode." Future studies will have to further clarify this shift in quality which is not quite understood so far.

A dissociation of temporo-parietal DMN with anterior structures of the DMN and reduced activity there, as shown in Doll et al. (2015), might explain our results with stronger activity in BA 40 as a result of a new "default mode network". Long-term changes in the connectivity of the DMN might explain the salutary effects of meditation in psychopathology as mentioned above.

In our study, bilateral BA 44, and BA 45 (Broca's area) also showed higher activation in meditation experts across different conditions. Forstmann et al. (2008) found in a model-based fMRI analysis BA 44 in the right hemisphere to be involved in selective inhibition processes in go/no-go tasks. This inhibitory function might reflect one of the underlying processes of meditation since suppression of response tendencies is trained in mindfulness tasks to be able to continuously disengage in reflective thinking and to re-attend to the meditative task.

Benuzzi et al. (2008) found in this region a putative mirror neuron system, which might have influence on emphatic feelings, whereas Fan et al. (2011) did not find this structure in their meta-analyses. Lamm et al. (2011) found BA 44 to be involved in an experimental paradigm to invest empathy for pain by viewing pictures of body parts in painful situations (picture-based paradigm). As the authors state, BA 44 is activated when the outcome of shown affective situations is being predicted or understood. BA 44 is supposed to be the core region of this cortical network. Meditation experts – as shown by our study – might have stable interoceptive awareness and a better meta-representation of global emotional moments. The stable amelioration of this brain area might then explain positive effects of mindfulness training on emotional regulation and mood disorders.

Findings in left BA 39, located on the temporo-parietal junction, demonstrated stronger HHb concentration changes in meditation experts. This region plays an important part in the conscious experience of the self and malfunctioning of this area leads to feelings of disembodiment or out-of-body experiences (Blanke & Arzy, 2005). This area is also known to play a crucial role in self-other distinctions, moral decision making (FeldmanHall, Mobbs, & Dalgleish, 2014) retrieval of autobiographical events, and making judgments that are self-relevant (Nelson et al., 2010) and has been linked to feelings of compassion, which develop in the course of long-term meditation (Lutz et al., 2008).

In a fMRI longitudinal study by Hölzel et al. (2008), participants of an eight week mindfulness based stress reduction (MBSR) program (J. Kabat-Zinn, 1990) showed increases in gray matter density in the TPJ (BA 39) and Taylor et al. (J. Kabat-Zinn, 1990)(J. Kabat-Zinn, 1990)(J. Kabat-Zinn, 1990)(J. Kabat-Zinn, 1990)(J. Kabat-Zinn, 1990)(J. Kabat-Zinn, 1990)(J. Kabat-Zinn, 1990)(2013) found a stronger connectivity of the left and right inferior parietal lobes for people experienced in meditation. It can be hypothesized that stronger functional activity over different conditions as seen in this study, based on regular long-term meditation training, might even foster structural changes in gray matter density as found in Hölzel et al. (2011) and Taylor et al. (2013).

5. Limitations

The main limitation of our study concerns the fact that the two groups differed in age and verbal IQ. Significant findings in our study in the ANOVA group effect in channels # 22 and #19 on the right probe set and in the ANOVA interaction effect on channel #20 (right probe set) and in channels #16 and #20 on the left probe set might be influenced by higher IQ in the meditation group. Since random group assignment was not possible in this study (quasi-experimental design), high IQ and a skillful meditation practice might be correlated. Better performance especially on BA 40 in the meditation group could then be a result of higher order performance of the brain in general (higher IQ) as a pretreatment difference and not a training effect. Following Miller and Chapman (2001) there is no statistical way of sorting out or controlling for these confounded variables. Therefore, an ANCOVA would not be indicated here. As the authors stated, the only way to find out about the specific relationship between meditation training and IQ, is to look at large numbers of studies (meta-analysis) to get a quasi-random assignment. Moreover, the small sample size of this study limits general statements on this topic; replication in larger samples is needed, precisely matched with respect to age and IQ. Findings in our study might therefore partly reflect differences in IQ as well as aspects of aging and the results might not be due to meditation training alone. For example Liu and Yan (2007) as well as Freiherr et al. (2013) found data indicating an enhancement of multisensory integration in older adults. However, the reported correlation analyses indicate that our NIRS data were mostly not systematically (linearly) related to these two confounding factors. Even for the IQ data (for which 5 out of 88 tests showed a statistical correlation), the correlations did not show a homogenous pattern in both groups. Based on this evidence, we believe that the main findings of our study were not primarily influenced by group differences in age or verbal IQ.

Another limitation of our study concerns the heterogeneity of the meditation technique. The expert group probably followed different kinds of meditation training over the years which may each have a specific impact on the brain (Travis & Shear, 2010). Here, different meditation techniques should be examined (e. g. focused attention, open attention, and loving kindness) with longitudinal designs. Another critical point concerns the paradigm of our study: Stronger activity in BA 40 could be explained by two opposing neural networks (task positive and DMN)

and our study might not have distinguished these two networks. It is not clear, if listening to an auditory task is demanding enough to trigger the execute network in the brain. Maybe this task is so easy that the DMN becomes active. Here, a study design with two different conditions (eyes open/eyes closed) may give further insight into the interaction of resting state and auditory detection.

Another critical point concerns the short periods of meditation time (3 min) being followed by a 2 min period of resting time. It might have been difficult for expert meditators to quickly switch back from a meditative state into an ordinary resting state. Therefore, longer periods of meditation time should be tested, and resting time should be studied independently. All in all, meditation is a skill that is used on a mental level and it remains unclear whether such a practice was performed by the participants.

6. Conclusion

Despite these limitations, there is growing evidence that regular meditation seems to have a profound impact on changing the connectivity of the brain (DMN, salience network, executive network). Here we could replicate the findings of Brewer et al. (2011). Our study could also show that long meditation training affects the TPJ, which is an important pivot point in the brain for attentional, somatosensory and affective integration. Here, our study is in line with previous findings of Hölzel et al. (2011). In the clinical context, training the brain by mindfulness skills might increasingly play a beneficial role in the treatment of mental disorders. Mindfulness training can therefore be seen as a mental skill to train general health fostering attitudes such as e. g. empathy and compassion, improve attention (Lutz et al., 2009), increase cognitive flexibility (Moore & Malinowski, 2009) and may even delay the onset of Alzheimer's disease (Innes & Selfe, 2014). For an overview of salutary e(Lutz et al., 2009)(Lutz et al., 2009)ffects of meditation see Brown et al. (2007). Even though underlying neural pathways of meditation have not been fully understood yet, meditation adds already a highly effective tool to existing cognitive-behavioral psychotherapeutic approaches (e.g. Hayes & Feldman, 2004; M. Linehan, 1996) and boosts new research of the neural mechanisms of attention, DMN, empathy, ToM, moral decision making, body integration and distinction of self and others.

Conflict of interest

None.

Acknowledgments

Ann-Christine Ehlis was partly supported by IZKF Tübingen (Junior Research Group 2115-0-0).

We would like to thank Ramona Täglich and Betti Schopp for the excellent technical support of this project.

3. Effects of Meditation on the Executive Control Network (Study 2)

Keywords: meditation; executive control network; Stroop task; verbal fluency task; fNIRS

1. Introduction

Today, there are many different approaches to teach mindfulness ranging from a short intervention lasting only five days (Integrative Mind-Body Training, IMBT; (Yi-Yuan Tang, Yang, Leve, & Harold, 2012; Zeidan, Johnson, Diamond, David, & Goolkasian, 2010) to eight weeks of formal training in e.g. mindfulness-based stress reduction, MBSR (Jon Kabat-Zinn, 1982) or cultivating mindfulness on an individual basis over as long as decades following traditional Eastern Buddhist tradition (e.g. Zen).

First, mindfulness was studied with respect to clinical aspects (e. g. stress reduction, pain, depression) in developing new psychological tools. Recently, the study of mindfulness has become the aim of cognitive psychology and neuroscience, since mindfulness meditation can be seen as a metacognitive training enhancing a set of cognitive functions in the prefrontal cortex (PFC) (Ott & Hölzel, 2011). The impact of meditation on executive function becomes obvious when looking at the basic meditation instruction for focused attention meditation (Hasenkamp & Barsalou, 2012):

1. Detection of distraction from meditation object, without judgment and further mind-wandering (Alvarez & Emory, 2006)
2. Refocusing attention and conscious access on the meditation object and
3. Sustaining focus on this object.

There is a cyclic reiteration of these three processing steps during meditation.

Following this simple instruction for 20 minutes over a couple of days or weeks can positively influence cognitive functions: attention processes (attention control, orienting and alertness (Malinowski, 2013) controlling cognitive processes for working memory (Zeidan et al., 2010), planning, decision making, self-regulation, executive inhibition (Gallant, 2016) and enhancing cognitive flexibility (Kim, Johnson, Cilles, & Gold, 2011). Underlying brain structures are positively modified (e.g. Grant, Courtemanche, Duerden, Duncan, & Rainville, 2010); (Lazar et al., 2005; Yi-Yuan Tang et al., 2012) and there is an enhanced performance of executive function in emotion regulation and verbal fluency (Alvarez & Emory, 2006).

Meditating over several years can lead to profound alterations in brain morphology, e.g. long term changes in the default mode network (Simon, 2015) and increases in gray matter in the anterior cingulated cortex. Short-term meditation training (with only four days of 20-minute sessions) already fosters performance on the Stroop task (Stroop, 1935) and verbal fluency (Zeidan et al., 2010).

Executive functions run conscious behavior and are always needed when autopilot behavior and thought must be interrupted by invoking cognitive control. These higher mental processes are needed for self-regulation to reach certain pre-defined goals in the presence of distracting or interfering information. Thereby, flexibility and stability are central features of volitional behavior (Karnath & Thier, 2012).

1. Flexibility is always needed to adapt behavior and cognitive processes to changing problems and goals. Here, patients with prefrontal lesions have problems in flexibly adapting their behavior. Verbal fluency tests are often used to track prefrontal pathology (e.g. Ravnkilde, Videbech, Rosenberg, Gjedde, & Gade, 2002).
2. Stability is the second central feature of executive function. To reach specific goals, irrelevant information from outside or inside (automatic responses) must be dissociated and inhibited. Here, prefrontal pathologies like in attention deficit hyperactivity disorder (ADHD) reduce the ability to pay attention and to keep the focus on long term goals. A typical test to probe inhibition problems is the Stroop task (Shao, Janse, Visser, & Meyer, 2014).

The mental processes described above are both found in mindfulness meditation: Stability – keeping the focus on the object of attention (e. g. the breath) and detecting when the controlled focus is lost, and automatic mind-wandering processes take over. Flexibility – there must be a flexible shifting back from automatic autopilot behavior (activity of the default mode network, DMN) to volitional attention to the meditation focus in the present (executive network) (Bishop et al., 2004).

The potential for mindfulness meditation practice to enhance executive function has been examined with the Stroop task in a range of studies before (for an overview, see Gallant (2016). The Stroop task is seen as an efficient tool to measure inhibition of automatic responses (incongruent information is presented in the same target, e.g. The word “red” is written in green color, whereby the instruction is to ignore the word meaning and simply name the ink color). To test the ability to inhibit emotional responses, emotional Stroop tests have been developed as in Moore and Malinowski (2009) most of the empirical studies have found that the ability to suppress an automatic response was stronger in meditation experts relative to non-meditators (Allen et al., 2012; Teper, Segal, & Inzlicht, 2013). Only in a study of Anderson et al. (2007), no differences in performance in an “elaborative” affective Stroop task (emotional words) could be found between a mindfulness based cognitive training group (MBCT) and a control waiting group. Here, the use of a semantic symbol (written words) might have failed to induce automatic inhibition as in its traditional format.

The impact of mindfulness meditation training on executive function has also been tested by verbal fluency tests. The verbal fluency test (VFT) has a phonetic variant (telling as many words with a given first letter, e. g. “S”, as fast as possible) which is more demanding than the semantic variant (to tell as many words of a given category as fast as possible). The phonetic verbal fluency (PVF) seems to depend on the left inferior and middle frontal cortices, putamen, and thalamus networks (Deppermann et al., 2014; Nishimura et al., 2009). The semantic verbal fluency (SVF) imposes a smaller demand on executive processing with more activity in the temporal lobes (Abreu et al., 2013). Many studies investigated verbal fluency (VF) in healthy subjects to find a robust increase in brain activity in both frontal and temporal areas (Deppermann et al., 2014; Dieler, Tupak, & Fallgatter, 2012; A.-C. Ehlis, Haeussinger, Gastel, Fallgatter, & Plewnia, 2016; Herrmann, Ehlis, & Fallgatter, 2003). Hypo frontality is often found in neuropsychiatric disorders such as schizophrenia, mood disorders, dementia, and anxiety disorders. It also seems connected to eating disorders, ADHD and alcohol dependence (Dieler et al., 2012). Schnitzspahn et al. (2013) found a significant decline of frontal performance in VF in a healthy group of elder people (mean age: 69.3 years) relative to a younger group (mean age: 24.8 years).

As Dieler (2012) point out in their review, functional near-infrared spectroscopy (fNIRS) has many advantages for studying speech related tasks. While in functional magnetic resonance imaging (fMRI) or electroencephalography (EEG) studies subjects are required to sit still or lie in a very narrow and noisy environment, fNIRS is relatively insensitive to movement-related artefacts, while machines are portable and affordable, which makes this method especially useful in the fields of psychiatric (Yokoyama et al., 2015) and language research (e.g. when testing verbal fluency). In fact, in a review on the use of fNIRS in psychiatry, Ehlis et al. (2014) point out that the verbal fluency test (VFT) is the task most frequently applied in fNIRS research and a wealth of previous studies were able to show robust fronto-temporal activation during the VFT using fNIRS (see e.g. Dieler et al., 2012). Methodically, fNIRS is a BOLD-based imaging method providing indirect assessments of cortical function through changes in the concentration of oxygenated (O_2Hb) and deoxygenated hemoglobin (HHb) based on the amount of absorbed and reflected near-infrared light in the brain. Cross-validation with fMRI largely confirms the physiological basis of the fNIRS signal for several cognitive tasks (Cui, Bray, Bryant, Glover, & Reiss, 2011). However, so far, fNIRS studies on the effects of meditation on VFT performance are lacking.

Deepeshwar (2015) tested the effect of 20 minutes mindfulness meditation against a 20-minutes session of random thinking in experienced meditators on the performance of a Stroop Color Word Test. They found significant improvement in cognitive performance after meditation compared to random thinking. In an analysis of fNIRS-data, they found a significant increase in O_2Hb in the left and right PFC during the Stroop task after the meditation session in comparison with random thinking.

In our study, we used a similar design to test if this effect of a meditation session on executive function is only found in meditation experts. We compared performance and brain activity of executive function of two groups: Meditation experts and a group of meditation novices.

We measured activity in the prefrontal cortex during two different executive tasks: An affective Stroop task and a verbal fluency test (VFT). Using the affective Stroop task, we tested if meditation experts had better executive function (stronger activation of the PFC) in terms of emotional control (stability). Using the VFT, we tested differences in word fluency and flexibility among both groups and corresponding differences in brain activation. In addition, we investigated the influence of a 9-minute block of mindfulness practice (9 minutes of mindful listening to the sound of a meditation bowl) conducted before the executive tasks.

Building on previous evidence in mindfulness research, we intended to test the following hypotheses:

1. Meditation experts perform better in reaction time and accuracy in the interference condition (emotional words) of an affective Stroop task than a control group of non-experts.
2. Meditation experts perform better (i.e., they produce a higher number of words) in a VFT in comparison to a control group of non-experts.
3. A preceding short mindfulness task enhances executive functioning as measured by a word fluency task and a Stroop task and these enhancements are connected to activations in specific brain regions, particularly the PFC.

2. Methods

2.1 Subjects

The study compared two groups of healthy subjects with (meditation group) and without (control group) meditation experience (same subjects as in F. Gundel et al., 2018). The meditation group comprised 14 participants (8 female and 6 males; 1 of them left-handed) with a mean age of 49.2±9.1 (range: 29–62) years. The participants had a mean regular meditation experience of 16.6±10.2 (range: 3–31) years. Mean weekly meditation duration was reported to be 4.8±3.4 hours. The control group included 16 participants (10 female and 6 males; mean age: 22.5±7.7 years (range: 18–50); 1 of them left-handed) with no meditation experience. The two groups differed significantly in age with the meditation group to be older (t_{28}=8.74, p<0.001), but not in gender distribution (χ^2=0.09, p=0.77). All participants had the German high school exam "Abitur". All participants were German native speakers. On the Big-Five-Inventory-10 scales (BFI-10) (Rammstedt et al., 2012), no significant group differences were found. But on the "Openness Scale", there was a tendency for higher scores for the meditation group (Mann-Whitney U=68.5, p=.061). The Global Severity Index (GSI) of the Symptom Checklist (SCL-90-R) (Franke, 2002) – as an indicator of psychopathology –did not differ significantly between groups (t_{28}=1.38, n. s.; mean overall value: 44.85±9.87); in terms of intelligence quotient, based on the MWT-B (German: Mehrfach-Wortschatz-Intelligenztest) (S. Lehrl, Merz, J., Burkhard, G., & Fischer, B. , 2005), participants of the meditation group showed a significantly higher intelligence quotient (IQ) (124.21±10.92) as compared to the participants of the control group (102.06±13.82; t_{28}=4.82, p<0.001). In addition to that meditators exhibited significantly higher scores on the Kentucky Inventory of Mindfulness Skills, measuring the tendency to be mindful in everyday life (KIMS-D) (G. Ströhle, Nachtigall, C., Michalak, J., & Heidenreich, T. , 2010) (155.00±13.55 vs. 135.19±15.42; t_{28}=3.71, p<0.001). This inventory is applicable to subjects with and without meditation experience and based on a theory of Kabat-Zinn (1982) stating mindfulness to be a universal predisposition of mankind.

The study was approved by the local Ethics Committee (University of Tuebingen), all procedures were in accordance with the Declaration of Helsinki in its latest version and written informed consent was obtained from all participants.

2.2 Procedures

The sequence of mindfulness task and the executive tasks was counter-balanced across subjects. The questionnaires were always completed in between, which took 15 to 20 minutes. Half the participants started with the 17 minutes mindfulness task and after completion of the questionnaires they performed the executive tasks, and the other half completed the executive tasks first and did the mindfulness task afterwards. The executive tasks were performed en bloc and took 30 minutes in total, with 20 minutes for the affective Stroop task and 10 minutes for the verbal fluency task. The sequence of the affective Stroop task and VFT was also counter-balanced across subjects.

2.3 Mindfulness paradigm

The Mindfulness paradigm consisted of four baseline blocks (2 minutes each) and three mindfulness periods (3 minutes each) which were conducted in an alternating fashion. During the entire paradigm, the tone of a singing bowl was presented with one new strike every 12 seconds. Participants were instructed to rest with eyes open during the baseline blocks, without a specific focus on the tone. In the meditation blocks, the instruction was to focus the attention mindfully to the tone. As for the executive functioning tasks (see below), brain activation data was also recorded for the mindfulness paradigm, the results of which have been reported elsewhere (F. Gundel et al., 2018).

2.4 Affective Stroop task

The affective Stroop task measures executive functioning under emotional influence. Participants are asked to react as fast and correct as possible with keystroke to the font color of a word ignoring its meaning. The words differ regarding their emotional content. This study included 10 neutral, 10 negative emotional and 10 borderline-specific negative emotional words. We used four versions of the affective Stroop task with different allocations of colors and keys, which were balanced across subjects.

2.5 Verbal fluency task

The verbal fluency task consisted of a phonological, a semantic and a control condition. Participants were asked to name as many words as possible with a certain initial in the phonological condition and from a certain category in the semantic condition. The control condition was listing the weekdays. Each condition lasted 30 seconds with a 30 second break in between conditions. This sequence was repeated three times with differing initials and categories. The letters and categories originated from the „Regensburger Wortflüssigkeitstest“ (Aschenbrenner, Tucha, & Lange, 2000). We used two versions of the VFT with different letters and categories, which were randomized across subjects.

2.6 NIRS

NIRS measurements were conducted using the ETG-4000 Optical Topography System (Hitachi Medical Co., Japan) continuously recording relative changes in the concentration of O_2Hb and HHb. A single probe set (3x11 optodes; inter-optode distance: 30 mm) was employed with a total of 52 measurement channels placed over the prefrontal cortex. (see Figure 1). For positioning, the middle optode of the lowest row was placed on FPz and the rear optodes of the lowest row were placed as closely as possible to T3 and T4, according to the international 10-20 system for EEG electrode placement (Jasper & Rasmussen, 1958). Near-infrared light of two wavelengths (modulated at a distinct frequency for each wavelength and channel; ranges: 695±20 nm and 830±20 nm) was emitted continuously onto the scalp and the amount of reflected light was detected by appropriate photodetectors. Based on a modified Beer-Lambert Law (Sassaroli & Fantini, 2004), the signals were analyzed and transformed according to their respective wavelength and location, resulting in the time course of concentration changes in O_2Hb and HHb for each of the measurement channels (whereby channels were located midway between each emitter-detector pair; sampling rate: 10 Hz).

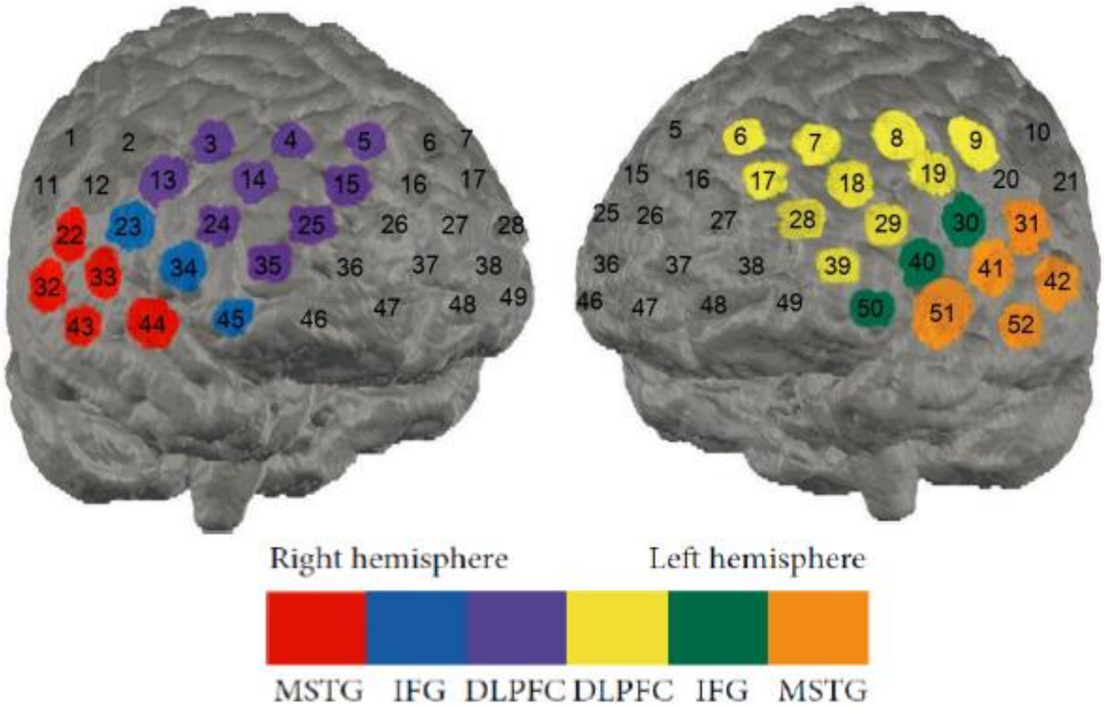


Fig. 1. position of probe set (3x11 optodes).

2.7 Data analysis and statistics

With the NIRS system, changes in the concentration of O_2Hb and HHb were recorded from starting baseline. For analysis of the affective Stroop task, recorded data was directly exported to Matlab for all analyses (using customized Matlab scripts; The MathWorks, Inc., USA). Since the task design was event-related, data was analyzed according to single events, i.e., on a trial basis (in contrast to block design analysis which was conducted for the VFT; see below). A bandpass filter was applied between 0.03 and 0.5 Hz Movement artefacts were corrected using a correlation-based signal improvement procedure (CBSI) proposed by Cui et al. (2010) which utilizes the expected negative correlation between O_2Hb (increase with brain activation) and HHb (typically decrease with brain activation) signals (resulting in a single outcome parameter that was subsequently analyzed). Afterwards, noisy channels were automatically interpolated with a variance criterion of 3.5. For further analysis, a peak detection procedure was used in individually averaged data (per participant, NIRS channel and task condition). Because a maximum of the hemodynamic response was expected after 8 seconds, we chose a peak detection window from 6 to 12 seconds after stimulus presentation and exported the resulting peaks for statistical analysis.

For analysis of the VFT (block-design data), a linear fitting function was used for baseline correction in order to correct the NIRS data for slow physiological signals unrelated to the task (e.g., spontaneous oscillations in cerebral blood flow) (cf R. Zhang, Zuckerman, J.H. & Levine, B.D. , 2000). Moreover, a bandpass filter was applied between 0.008 and 0.05 Hz, followed by an interpolation of noisy channels based on the mean value of all adjacent channels (see above). For the VFT data, the CBSI correction method was not applied as – due to the capillary dominance in this part of the brain – O_2Hb and HHb signals are not necessarily anti-correlated in Broca's area (see Yamamoto, 2002) which is the region most dominantly involved in language production (such as during the VFT). Therefore, O_2Hb and HHb data will be separately reported for this task. For further analysis, VFT data were individually averaged according to the task condition (phonological vs. semantic vs. control task blocks). For statistical analysis of the VFT data, mean values across the last 20 s of all task segments were calculated for each condition, NIRS channel and participant (see A. C. Ehlis, Herrmann, M. J., Plichta, M. M., & Fallgatter, A. J. , 2007).

The correspondence of NIRS channels to underlying cortical areas was estimated based on a virtual registration method (Rorden, 2000; Singh, 2005; Tsuzuki, 2007). Brain activation during the VFT was predominantly expected in the dorsolateral prefrontal cortex (dlPFC), the inferior frontal gyrus (IFG) and the middle and superior temporal gyrus (MSTG; see e.g. Deppermann et al., 2014). Accordingly, we defined a priori ROIs for the VFT paradigm for the left dlPFC (channels 6, 7, 8, 9, 17, 18, 19, 28, 29, 39), right dlPFC (channels 3, 4, 5, 13, 14, 15, 24, 25, 35), left IFG (channels 30, 40, 50), right IFG (channels 23, 34, 45), left MSTG (channels 31, 41, 42, 51, 52) and right MSTG (channels

22, 32, 33, 43, 44). Based on the dominant involvement of the PFC in the resolution of Stroop-conflicts, the described prefrontal ROIs were also considered for the Stroop analysis.

Statistically, following the illustration of general activation patterns by testing peak/amplitude data in t-tests against zero, analyses of variances (ANOVAs) were calculated comprising the within-subject factor “condition” (VFT: phonological vs. semantic vs. control; Stroop task: emotional vs. neutral), the within-subject factor “task sequence” and the between-subject factor “group” (control group vs. meditation-experienced subjects). In case of significant interactions, post-hoc tests were conducted using t-tests for matched or independent samples, as appropriate. Pearson’s correlation coefficient was used to examine a potential impact of age and IQ on NIRS data due to group differences regarding these two factors. Two-sided testing was applied throughout.

3. Results

3.1 Affective Stroop Task

Regarding behavioral data, a 2 × 2 ANOVA with the between-subject factor “group” and the within-subject factors “condition” (neutral vs. negative Stroop words) and “task sequence” revealed a significant main effect “group” for Stroop error rates ($F_{1, 25} = 4.72$, $p <. 05$). Across all Stroop trials, mean error rates were significantly lower in meditation-experienced subjects (3.1 ± 1) as compared to non-meditating controls (8.2 ± 1.9) (See Figure 2). No other main effects or interactions reached statistical significance (all $F < 0.7$, $p > .4$). With respect to reaction times (RTs), no significant main effects or interactions occurred (all $F < 2.5$, $p > .1$). [1]

[1] One participant from the meditation group had to be excluded from the behavioral analysis of the Stroop task as response buttons were incorrectly assigned during the experiment.

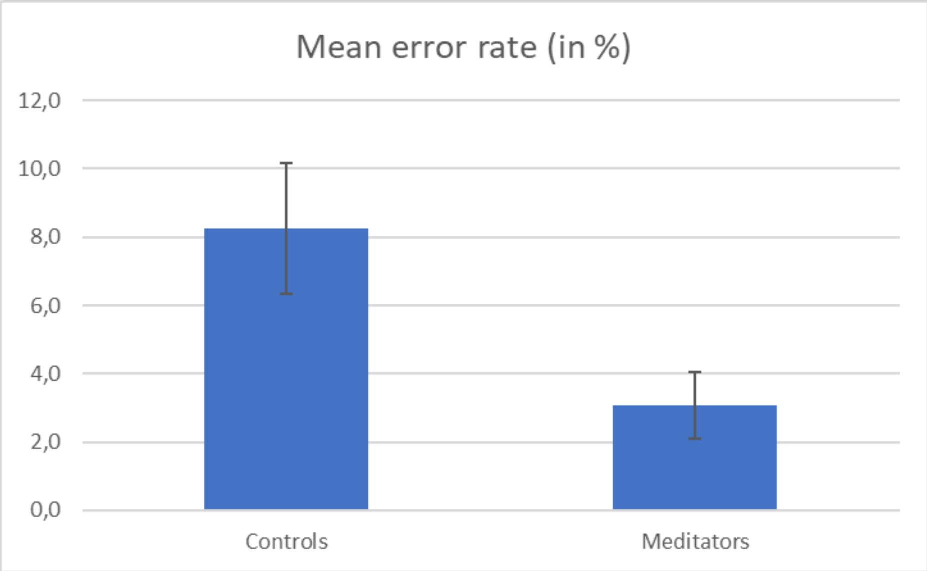


Fig. 2. ANOVA main effect: meditation-experienced subjects had significantly lower mean error rates.

With respect to the fNIRS data, t-tests against zero – illustrating general activation patterns for the different Stroop conditions – indicated significant CBSI-corrected hemodynamic responses (i.e., cortical activation) for both groups. In detail, the control sample exhibited significant increases in cortical activation (Bonferroni-corrected for eight statistical comparisons: 4 ROIs × 2 conditions) for negative Stroop words in the left DLPFC ($t_{15} = 3.26$, $p < .00625$) and right IFG ($t_{15} = 3.37$, $p < .00625$). Meditation-experienced subjects also showed significantly increased cortical activation following negative Stroop words in the left DLPFC ($t_{13} = 4.32$, $p < .00625$); moreover, for the neutral stimulus condition, they additionally showed significant hemodynamic responses in both the left and right IFG ($t_{13} = 3.47$ and 3.10, respectively; $p < .00625$).

After correction for multiple statistical testing, no significant main effects or interactions were observed in the conducted ANOVA directly testing effects of group (meditation vs. control), Stroop condition (negative vs. neutral words) and task sequence (meditation first vs. executive functioning tasks first). However, an exploratory analysis of the peak activation channel (#30) within the left IFG showed (at a regular significance level of $p < .05$) a significant main effect of group ($F_{1, 26} = 5.09$, $p < .05$): Here, participants with meditation experience showed significantly stronger activation (M = 0.0045, SD = 0.0032) than control participants (M = 0.0023, SD = 0.0019) across Stroop conditions.

3.2 Verbal Fluency Task

The ANOVA calculated for the number of words produced during the VFT showed a significant main effect of “task condition” ($F_{1, 26}$ = 106.48, p < .001) with the highest number of words produced for the semantic version of the VFT (“categories”) followed by the control condition (“weekdays”) and finally the phonological condition (“initial letters”). T-comparisons were significant for all resulting contrasts (phonological vs. control: t_{29} = -9.65, p < .001; phonological vs. semantic: t_{29} = -10.85, p < .001; semantic vs. control: t_{29} = 5.48, p < .001) (see Figure 3).

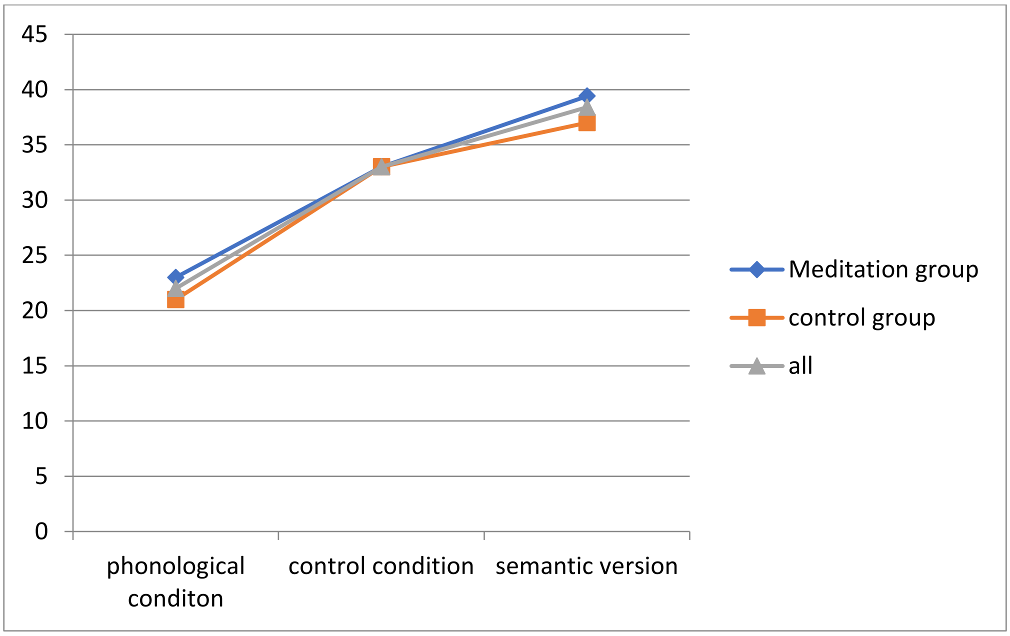


Fig. 3. ANOVA main effect of “task condition”

No other significant main effects or interactions were found.

Regarding the corresponding fNIRS data (general activation pattern), the complete sample (averaged across both groups because no group effects reached statistical significance) showed significant activation (t-tests against zero) for the left and right

DLPFC, left and right IFG as well as left and right MSTG during phonological fluency (O_2Hb; $3.97 \leq t_{29} \leq 7.06$, $p < .001$; see Figure 4). For HHb, only hemodynamic responses in the left DLPFC reached statistical significance ($t_{29} = -3.88$, $p = .001$; $M = -0.0262$, $SD = 0.0369$). No significant activation was observed for the weekday control condition in any of the ROIs. For the semantic version of the VFT (categories), O_2Hb data showed significant activation in the left and right IFG and left and right MSTG ($2.98 \leq t_{29} \leq 5.23$; $p \leq .006$). HHb concentration decreased significantly only in the right MSTG ($t_{29} = -3.11$, $p = .004$; $M = -0.0241$, $SD = 0.0425$).

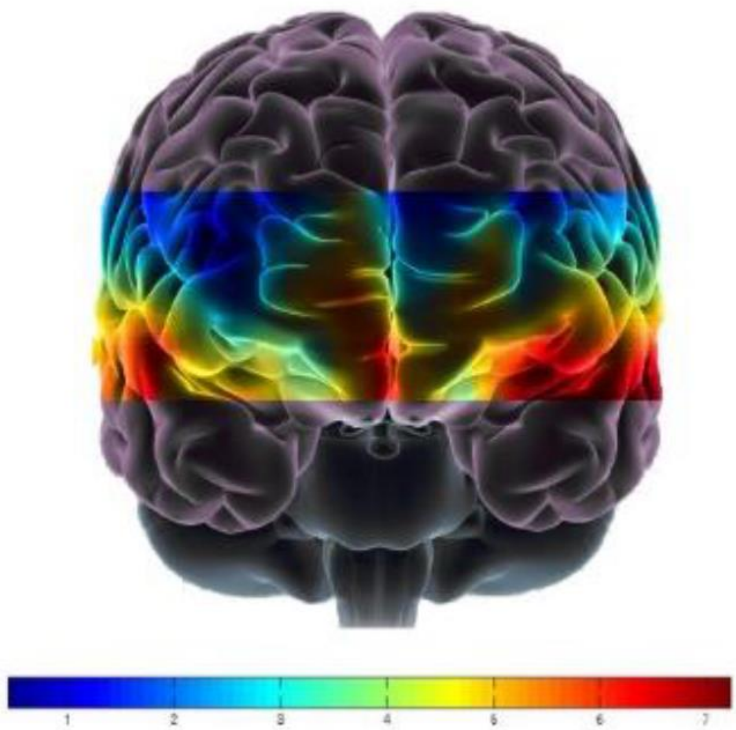


Fig. 4. Changes in O_2Hb concentration during the phonological VFT condition. The map depicts t-values (contrasted against zero) for all NIRS channels of the fronto-temporal probe set (view from the front).

Additionally, a 2 × 2 × 3 ANOVA (group × task sequence × condition) showed a significant main effect of task sequence for O_2Hb in the left DLPFC ($F_{1, 26} = 7.98$, $p = .009$): When the mindfulness condition was conducted first, activation in the left DLPFC during the VFT was significantly stronger (M = 0.0320, SD = 0.0252) than when VFT and Stroop were conducted first (M = -0.0027, SD = 0.0395). Moreover, a main effect condition occurred for O_2Hb concentration in the left DLPFC ($F_{2, 47} = 11.85$), right DLPFC ($F_{2, 52} = 7.97$), left IFG ($F_{2, 52} = 28.37$), right IFG ($F_{2, 50} = 15.10$), left MSTG ($F_{2, 45} = 28.19$) and right MSTG ($F_{2, 47} = 18.91$; all $p < .001$). Thereby, concentration changes during the phonological condition were significantly higher than in the weekday control task in all ROIs ($3.49 \leq t_{29} \leq 6.39$, $p \leq .002$); compared to the semantical fluency condition, they were only significantly higher in the left and right DLPFC, left IFG and left MSTG ($2.77 \leq t_{29} \leq 4.51$; $p \leq .01$). Finally, the semantic VFT version showed significantly higher O_2Hb concentration than the control task in left and right IFG as well as left and right MSTG ($4.31 \leq t_{29} \leq 6.11$; $p < .001$). For HHb, a main effect condition was found for the left DLPFC ($F_{2, 52} = 5.46$, $p = .007$) and left IFG ($F_{2, 49} = 10.04$, $p < .001$) with significantly stronger activation in the phonological VFT as compared to the control condition in both areas ($t_{29} = 3.42$ and 3.76, respectively; $p < .01$). Additionally, in the left IFG also the semantical VFT version showed significantly stronger activation (M = -0.0156, SD = 0.0511) than the control task (M = 0.0127, SD = 0.0512; $t_{29} = 3.43$, $p = .002$).

4. Discussion

This study investigated if a group of healthy meditation experts had better performance on two executive tasks (emotional word Stroop task and VFT) than healthy controls.

In summary, we did not find meditators to perform better in the interference condition of the Stroop task (emotional words). But accuracy in Stroop performance was significantly enhanced in the meditation group (thus, hypothesis 1 was partially confirmed).

In addition, we did not find meditation experts to perform better on the VFT (hypothesis 2 had to be rejected).

Hypothesis 3 was also only partially confirmed: A preceding short mindfulness task had no effects on performance of the VFT or Stroop task, but changed specific brain activation in the PFC as measured by fNIRS.

4.1 Verbal fluency (group effects)

The ANOVA revealed a significant condition effect: Both groups had more verbal responses in the semantic than the phonetic variant of the VFT, which is in line with many previous studies (e.g. Deppermann et al., 2014; Schecklmann, Ehlis, Plichta, & Fallgatter, 2008; Schlösser et al., 1998). On the neurophysiological level, we found stronger brain activation in the left and right dlPFC, left IFG and left MSTG on the phonetic variant in both groups, probably due to the higher executive demand of this condition. Previous studies could show that meditation had a positive effect on verbal fluency performance (Heeren, Van Broeck, & Philippot, 2009; Marciniak et al., 2014; Zeidan et al., 2010). In contrast to that, Kozasa (Kozasa et al., 2017) failed to show that meditation experts had better performance in a lexical decision task.

In the study at hand, we could not find better performance on the VFT in meditation experts, as we expected in our hypothesis. As our meditation expert group was significantly older than the control group (meditation group: mean age: 49.2 years; control group: mean age: 22.5 years), it could be argued that meditation might have augmented verbal fluency, but age-effects might have disguised this improvement.

Executive function decline was found previously in elderly, but there are first results that show that meditation might have age-defying effects in executive function: Newberg et al. (2010) could find better cerebral perfusion in the PFC in meditation experts. Pagnoni and Cekic (2007) found that a group of expert meditators performed as well as a younger control group in a sustained attention task. The authors stress the protective factor of increased grey matter density in meditation practitioners for age-declining in executive function and Lazar (2005) found better attention functioning in this group. Van Leeuwen (2009) could show that older meditators had better performance on the attentional blink task than age-matched non-meditators. The performance of this group was comparable to that of a young control group.

Several theories have been proposed for this age-defying effect of meditation: While Xiong and Doraiswamy (2009) assume enhanced cognitive circuits to be responsible for the increased cognitive capacity, Malinowski and Shalamanova (2017) refer to Steffener and Stern's theory (2012) that training might heighten neural reserve and therefore lead to higher network efficiency, capacity or flexibility. Moreover, meditation might reduce brain ageing and decline of brain structure by reducing stress (Y.-Y. Tang et al., 2009) and positively influencing HPA axis and protective immune functions (Frewen, 2013; Larouche, Lorrain, Côté, & Belisle, 2015). In line with this assumption, Luders (2015) observed that meditators had less gray matter loss than controls.

Besides opposite effects of ageing and meditation – which might have cancelled each other out and led to non-significant group differences – the null effect for the VFT may also have been related to the particular task chosen: Verbal fluency tasks are usually used in psychiatric patient groups (e.g. Noda et al., 2012; Takizawa et al., 2008). Here, we used two healthy groups and thus training might fail to significantly differentiate both groups (ceiling effect).

Taken together, it is not easy to disentangle these different variables and further studies should take aging aspects more stringently into account. In our study, an age-matched group is missing and therefore, interpretation of our results remains partly speculative.

4.2 Verbal fluency (acute effects of a preceding mindfulness task)

Both groups showed higher activation in the left DLPFC when a mindfulness task was done shortly before the VFT. Tomasino and Fabbro (2016) found meditation states to be involved in specific activation and deactivation patterns on the PFC in comparison to a resting state. The increase in cortical activation is usually seen as trigger for a certain performance at the behavioral level. In our study, higher activation in the left DLPFC induced by a preceding mindfulness intervention had no influence on the performance of verbal fluency. This might be due to the above-mentioned ceiling effect or the greater sensitivity of neurophysiological measures (as compared to behavioral data) for subtle neuromodulator effects (see also A.-C. Ehlis et al., 2016; Lahat, Todd, Mahy, Lau, & Zelazo, 2010) .

But why is the left DLPFC activated by the mindfulness task?

The left DLPFC is specialized in the selection of verbal responses in the presence of multiple response options. Colzato (Colzato, Szapora, & Hommel, 2012) found a significant enhancement of mood for both meditation experts and novices after a meditation session. In general, positive mood enhances divergent thinking while negative mood leads to more convergent thinking. In our study, the mindfulness intervention might have had this positive mood effect, thus leading to more activation in the left DLPFC. Divergent thinking processes (brainstorming) might be more effective in finding verbs on a phonetic or semantic level. So far, it is not clear if a meditation session enhances divergent thinking processes first and thus mood is ameliorated or vice versa. But there is a change in how prefrontal problem solving is done (quality shift). A third explanation can be drawn by changes in the DMN which might be triggered by the meditation task in such a way that rumination was diminished. This is in line with Rosenbaum (Rosenbaum et al., 2016) showing reduced left hemispheric (task-related) activity of the PFC among depressed people with higher prefrontal activation in a resting state. The authors stress the negative influence of rumination on prefrontal performance (hypoactivity). Manuello et al. (2016) also state that meditation leads to reduced rumination and that this skill is needed in exploiting attentional resources in a more effective way.

But why did our study fail to show that these neural changes had influence on performance, as other studies did?

Quach et al. (2016) could find better working memory capacity in a meditation group by the Automated Operation Span Task, which contains two simultaneous tasks. The divergent validity of the VFT to differentiate our healthy and well-educated groups might have been not strong enough. Other executive tasks – with more workload – might better show changes in working memory capacity on a performance level, as mentioned above.

4.3 Stroop task (brain activation patterns, group effect)

The Stroop task involves neural circuits subserving attention, working memory, response selection and inhibition (Harrison et al., 2005; Peterson et al., 1999). Meditation can train all the above-mentioned neural circuits together with body awareness, emotion regulation, and change in the perspective of the self (B. K. Hölzel et al., 2011; Slagter et al., 2007). Chan et al. (2007) found reduced Stroop interference testing a meditation trained group against a control group. As in Allen et al. (2012), we failed to find Stroop interference comparing meditation trained subjects with a control group.

The ANOVA analysis revealed a tendency (significance of 5%) that meditation experts had stronger activation in the left IFG. Higher brain activation in these areas might explain better performance (accuracy) in executive function of this group in our study (see below).

4.4 The role of left inferior frontal gyrus

In previous studies using a Stroop task, activity in prefrontal cortex, especially the left IFG, has been found (Laird et al., 2005). The left IFG can be divided into three parts: pars opercularis (BA 44), pars triangularis (BA 45) and pars orbitalis (BA 47). BA 44 and BA 45 are situated in Broca's area, which was initially described by Paul Broca (1861) as a region for language processing. Speech processes are strongly left-lateralized in the brain. Therefore, by using written affective adjectives in our Stroop task, language-processing might cause high activity in left frontal brain regions. The left IFG is also known to be involved in processing selection and processing bias in the incongruent Stroop condition (S. F. Taylor, Kornblum, Lauber, Minoshima, & Koeppe, 1997). In other studies, the left IFG has been associated with impulse control and inhibition of prepotent responses (Swick, Ashley, & Turken, 2008).

But why do meditation experienced subjects have higher activation level in this brain area?

Meditation might directly train the left inferior prefrontal lobe: Scheibner et al. (2017) describe the left inferior prefrontal gyrus as being strongly activated in meditators in refocusing attention after mind-wandering. Swick (2008) found in their meta-analysis that the left IFG is under top-down control, either to use internal representations of goals and the means to achieve them, but also to suppress any other response. The top-down processes of this area reflect the processes which are involved in meditation training by monitoring internal attention processes to stay on task.

Hommel and Colzato (2017) see possible long-term effects of meditation in inducing particular meta-control states that moderate the way individuals exert cognitive control on lower-level processes. The left PFC is said to be involved in top-down generation of emotions together with temporal regions and the cingulate (Ochsner et al., 2009) and might be trained by meditation. Kozasa (2017) found differences in connectivity patterns between PCC and parietal regions in regular meditators and a meditation naive group on a Stroop task.

Fox (2016) found the left inferior frontal gyrus significantly activated (BA 44/45) together with a more left hemisphere activation in BA 6 (premotor cortex) in reviewing and meta-analyzing 25 functional neuroimaging investigations on different styles of meditation. This pattern was found by open monitoring meditation. In our study, most of the meditation group practiced Zen meditation, which is an open monitoring technique. Therefore, left-hemispheric activation in our findings might be due to long-term training of the left IFG and left hemispheric activation as found in this group.

4.5 Stroop Task (behavioral data)

Regarding the (emotional) Stroop effect itself, we did not find any interference effects of affective Stroop words on performance measures in either group. This might be due to the limited impact of incongruence of our negative words used in a healthy group of subjects. These kinds of Stroop tasks might not have enough power to discriminate on the Stroop effect as was also found in a study by Anderson (2007) who used an Elaborative Stroop Task to differentiate between meditation trained subjects and a waiting list.

Babcock and Vallesi (2017) reported that there are a few studies that reported either null or inconclusive results. Köpke and Nespoulous (2006) used the color-word Stroop task using English, French, and bilingual versions in a highly specialized group of professional interpreters and a student group. They also failed to show differences in performance.

Even though we didn´t find a stoop effect, the meditation group had significantly higher accuracy in all categories of the Stroop tasks. Our results support previous studies finding meditation experienced subjects to show better Stroop performance than controls (review of studies: (Gallant, 2016). Our findings result from long lasting meditation training and is seen as a trait effect of meditation.

Hasenkamp and Barsalou (2012) describe functional connectivity differences between high and low practice groups. Increased functional connectivity between attentional systems in the brains of experienced meditators allows for enhanced attentional processing and would explain better performance on executive tasks.

Following the attention model of Posner (2012) besides the executive control network that controls mental states, there are other networks trained by repeated meditation practice: the *alerting network (*establishing and sustaining alertness), the *salience* network (monitoring of mental states) and the *orienting network (*disengaging from distraction and redirecting the attention focus back to the object of meditation). Malinowski and Shalamanova (2017) assume that repeated activation of all these networks during meditation practice will strengthen their functioning and in consequence improve attentional abilities.

The authors point out that improvements in cognitive performance by meditation training appear quite remarkable when compared to typical cognitive training effects, because the enhancement of cognitive skills typically transfers only to tasks, stimuli or contents that are quite similar to the ones trained (Klingberg, 2010). In contrast to such near transfer effects, cognitive enhancement resulting from mindfulness meditation practice appears to demonstrate far transfer.

Far transfer effects might be mediated by the Default Mode Network, which has been found to undergo neuroplastic changes by meditation training (K. C. Fox et al., 2016; Hasenkamp & Barsalou, 2012). Harmelech and Malach (2013) found that resting state activity patterns can be diagnostic of unique personalities or life-styles. Far transfer effects might also be mediated by changes in the Saliency Network of the brain. Kemmer (2015) compared functional connectivity in Zen practitioners and controls in a basic attention-to-breathing protocol. Meditation practitioners exhibited stronger connectivity between frontoparietal parts of the brain with the Saliency Network. The authors interpret these findings as linked to the vigilant attitude that meditators aim to keep detecting and become aware of the fluctuations in one´s own mental state. In context of our affective Stoop task, word meaning is irrelevant and must be ignored to perceive the right color. The meditation experts could do this task more exact than meditation novices.

Hasenkamp and Barsalou (2012) describe the salience network to be implicated in switching between default and executive networks; therefore, meditation training could allow for more efficient switching from the DMN to executive network via the salience network.

Hilger et al. (2017) used functional imaging data from 54 healthy adult participants during wakeful rest and evaluated their individual functional brain networks. Nodal and global measures of efficient network organization (i.e., nodal efficiency and global efficiency) were correlated with intelligence scores (IQ from the Wechsler Abbreviate Scale of Intelligence, WASI).

If regular and repeated training in meditation might positively influence function and network connectivity of the saliency network as described above, there might be a link between meditation, ameliorated processing of salient information, executive performance, and intelligence. Further research in this complex field is needed with longitudinal designs.

4.6 Beginners and Advanced modes of Executive functioning – content orientation versus Meta Cognitive Awareness

Finally, we want to discuss if the group of meditation experts might not only depict changes in one function (e. g. executive function) or in the use of brain networks. Instead, we look at the possibility that meditation might change how we use the brain in general: Josipovic et al. (2012) found experienced Tibetan Buddhist meditators to use the gross functional organization of the cortex in profoundly different ways and exhibit stronger anti-correlation between extrinsic and intrinsic systems during focused attention meditation than fixation with no meditation.

Malinowski and Shalamanova (2017) point at Buddhist meditation instructions (Wallace, 1999) which emphasizes that with increasing experience the initial effort required to balance between all forms of mental agitation and laxity are eventually overcome by expert practitioners.

It can be speculated that meditation experts might establish a higher order cognitive awareness (meta-cognitive shift) which monitors cognitive processing without being engaged into the content of mind-wandering (open monitoring meditation). A stable meta-cognitive perspective with reduced fear for mental and emotional processing might enhance flexibility and reduce working memory capacity. Since working memory capacity is strongly related to performance in other complex cognitive tasks, such as reading or problem solving, higher order representation of things (meta cognition) might reduce the workload associated with self-reflection and emotional evaluating.

Brefczynski-Lewis (2007) used functional magnetic resonance imaging (fMRI) to interrogate the neural correlates of Focused Attention (FA) meditation in experts and novices. Expert meditators with an average of 19,000 hours of practice showed stronger activation in these areas than the novices. Expert meditators with an average of 44,000 practice hours showed less activation. This inverted u-shaped function resembles the learning curve associated with skill acquisition in other domains of expertise, such as language acquisition, and provides support for the notion that after extensive FA meditation training, minimal effort is necessary to sustain attentional focus.

Taken together, all these findings suggest a profound change in brain activity among experienced meditators: a task independent trait-like meta-cognitive monitoring which is characterized both by profound calmness and high vigilance, described possibly as "heightened consciousness" or "enlightenment" in ancient telling.

5. Limitations

There are several limitations to our study that need to be considered. Stroop effect: The affective load of the words presented (neutral, emotional, and borderline-relevant) did not affect reaction times in both groups. The complex nature of detecting word meaning might have failed to arouse enough emotional reaction in the subjects, since this is a top-down process. In the future, emotionally valued pictures might be used to have a stronger impact on limbic regions. Secondly, the affective words were chosen to test a group of Borderline patients. Therefore, this Stroop task might not have had enough differential validity for our two healthy groups.

VFT: This measure, which is extremely sensitive to psychiatric disorders, failed to distinguish our two groups of healthy subjects. Tests with more cognitively demanding tasks should be used for healthy subjects in the future.

NIRS: Because near-infrared light has limited power and penetration depth in brain tissue we were not able to examine deeper brain structures, including the ACC, insular cortex, limbic system, and brain stem in which activation during meditation has been previously reported.

Group Differences: Our practitioners and control subjects differed in many respects: Age and intelligence might have influenced the results in this study and not (solely) meditation training. The meditation expert group was also a preselected group and there might be a selection bias of personality, lifestyle, reduced stress, general health habits or intelligence previously to meditation practice or developed alongside with meditation, so that our results might be explained by these demographic factors.

Heterogeneous meditation techniques: The meditation expert group did not use a homogenous meditation method. Most of them practiced Zen Meditation (open minded meditation), but there were also other kinds of meditation techniques used such as Vipassana and focused attention meditation. While practicing over many years, the meditation experts might have been trained in different styles of meditation and this influence cannot be ruled out.

Impact of the experimental design: To change probe sets, there was a little break (5-10 min) before executive functions could be measured, so that improved Stroop performance or changed brain activation in the VFT might be due to relaxation or moving the body.

6. Conclusion

Long term meditation training might significantly enhance performance on executive tasks. Even a short intervention of mindfulness might significantly change executive function of the brain.

Meta cognitive skills can be trained and have positive impact on how we can deal with stress-related diseases and the challenges of increased information performance in our modern world.

Ethical Standards

The study was approved by the local Ethics Committee (University of Tuebingen), all procedures were in accordance with the Declaration of Helsinki in its latest version and written informed consent was obtained from all participants.

Conflict of Interest

The authors declare that they have no conflict of interest.

4. Neural Correlates of Mindfulness in Dialectical Behavior Therapy (DBT): A Pilot Study (Study 3)

Abstract:

Neuronal correlates of Borderline Personality Disorder are characterized by an imbalance of frontal-limbic brain areas (hypo- and hyper-activation). Little is known so far about the role of temporo-parietal parts of the brain in the dysfunction of borderline patients. We investigated the effectiveness of mindfulness as a therapeutic tool in the treatment of 29 borderline patients by comparing the therapeutic effects of 8 weeks of Dialectical Behavior Therapy (DBT) with 8 weeks of cognitive behavioral therapy (CBT) without mindfulness (15 patients).

Both treatments had significant positive effects on specific symptom reduction (borderline symptoms, dissociation, and behavior avoidance motivation). and an increase in mindfulness scores. We found also DBT to be significantly more effective in global symptom reduction and a trend of increase in reward seeking behavior.

On the neural level, the impact of 8 weeks of mindfulness (DBT) on the temporo-parietal junction (TPJ) and superior temporal gyrus (increase in activity) of both hemispheres was correlated with general symptom reduction (SCL-90-R) and increased mindfulness scores (KIMS-D).

In conclusion, we could show that mindfulness skills can reduce global psychopathology and make an impact on neuronal activity changes in borderline patients.

Keywords:

Borderline personality disorder, Dialectical behavior therapy, Mindfulness, Functional near-infrared spectroscopy, Temporo-parietal junction (TPJ), Superior temporal gyrus

1. Introduction

Borderline Personality Disorder (BPD) is a severe and complex mental disorder and characterized by a persistent pattern of symptoms such as emotion dysregulation, behavior problems (impulsivity), identity instability and interpersonal problems ((*Diagnostic and statistical manual of mental disorders (DSM-5)*, 2013; Lieb, Zanarini, Schmahl, Linehan, & Bohus, 2004)

According to Linehan (1993) emotion dysregulation is the core dysfunction underlying BPD and is caused by biological factors (genetic variables for high emotional vulnerability) and by environmental influences in childhood such as e. g. sexual violence or parental invalidation. These two processes interact and lead to difficulties in tolerating, regulating and moderating emotions. Other symptoms of Borderline patients like impulsive and high-risk behavior, dissociation, feelings of emptiness, suicidal attempts, and self-mutilation are seen as dysfunctional attempts to avoid or suppress high levels of emotions (M. Linehan, 1993).

Dialectical behavior therapy (DBT) was developed by Linehan in the 1980s within a Cognitive Behavior Therapy (CBT) framework and adds mindfulness from Zen Buddhism (Guendelman et al., 2017). DBT is found to be one of the most effective treatments for borderline personality disorders (Higgins et al., 2019). In DBT, individual therapy is combined with group training. The skills training is one of the most effective parts of it (M. M. Linehan et al., 2015). It is divided in skills modules for distress tolerance, emotion regulation, interpersonal effectiveness, and mindfulness. DBT is based on a dialectical viewpoint which balances and integrates opposing ideas such as change skills (taken from cognitive behavioral therapy) and acceptance skills (mindfulness part taken from Zen Buddhism). Mindfulness is part of the acceptance skills and are considered the „core skills“ in DBT providing the basis for change skills, such as emotion regulation (M. Linehan, 1993). Since emotion regulation problems are seen mainly as the core problem underlying borderline symptoms, mindfulness skills seem to be a critical feature of the emotion regulation process and a starting point for treatment (Gross, 2007).

In contrast to Mindfulness Based Stress Reduction (MBSR) or Mindfulness Based Cognitive Therapy (MBCT), DBT mindfulness training has a larger selection of mindfulness skills, which are less formal and shorter (ca. 3-5 min.). Linehan considered this shorter practice as a necessary adaptation for borderline patients. To test Linehan´s model on the neurobiological level, there have been a couple of functional and structural neuroimaging studies on emotion regulation in recent years. In this context, previous findings indicate reduced prefrontal activity (e. g. dorsolateral prefrontal cortex) and a hyperactivity in limbic regions (amygdala and hippocampus) in borderline patients (Minzenberg, Fan, New, Tang, & Siever, 2007). These findings lead to a fronto-limbic dysregulation model. Borderline patients seem to have a hyper-response (in limbic emotion processing areas) triggered by social-emotional cues and a deficient deactivation of these emotional responses by a hypo-response of prefrontal brain areas. A meta-analysis of nineteen functional and structural neuroimaging studies confirmed this model (Schulze, Schmahl, & Niedtfeld, 2016). Borderline patients had increased functional activation in the left amygdala and posterior cingulate cortex while processing negative emotional stimuli compared to healthy controls. On the structural level, borderline patients showed decreased gray matter volume in the left amygdala (Schulze et al., 2016). Other regions have been found to show higher activation by negative emotional stimuli. In a meta-analysis of 18 studies, Ruocco et al. (Minzenberg et al., 2007)(Minzenberg et al., 2007)(2013) found higher activation in the insula, which is sensitive to negative social judgement. In addition, the authors found higher activation in the posterior cingulate cortex, which is involved in processing evaluative aspects of emotions.

On the other side, it can be assumed that mindfulness interventions are influencing these brain areas. Originally, mindfulness is derived from Buddhist Zen meditation and is described in neuroscience as a training of attention and awareness: Cultivating attention towards one´s experiences in the present moment in a non-judgmental attitude (Zinn, 1994). The neurocognitive mechanisms in mindfulness are regulation of emotion, control of attention and self-awareness. The positive impact of mindfulness on mental disorders can be described by an integrated translational framework. There, mindfulness meditation training has an impact on the anterior cingulate cortex (ACC) and prefrontal cortex (PFC) for attention control and emotion regulation. The insula, the medial prefrontal cortex (mPFC), the posterior cingulate cortex (PCC), and precuneus are trained by self-awareness techniques (open monitoring). This neurocognitive training is seen to lead to an ameliorated self-regulation preventing different psychiatric health issues such as e.g. depression or substance abuse (Y. Tang & Leve, 2016).

The impact of mindfulness as a therapeutic tool has been proven in many studies so far (e. g. Bohlmeijer, Prenger, Taal, & Cuijpers, 2010). Mindfulness as an emotion regulation skill was found to be an active cognitive regulation strategy like attention control (top-down) in meditation beginners, while expert meditators might use enhanced bottom-up processing by an automated acceptance attitude. Prefrontal activation was enhanced in meditation beginners whereas this area had a diminished activation in expert meditators (V. A. Taylor et al., 2011). Reward processing might also change in expert meditators leading to enhanced emotion regulation. In this group, heightened activity during rest was found in underlying reward-related brain regions (putamen and caudate) (Kirk, Brown, & Downar, 2015).

Taken together, mindfulness seems to enhance emotion regulation by heightened attention to emotions, altered patterns of appraisal (non-judgmental attitude) and change in response behavior (acceptance instead of suppression).

There is growing interest in studying the link between mindfulness and borderline personality disorder (BPD). Wupperman et al. (2013) describe borderline patients to be phobic for unpleasant internal and external experiences (avoidance behavior, suppression). Eventually, avoidance behavior will lead to a prolongation and amelioration of negative emotions leading to high levels of stress and impulsive behavior There is some evidence that borderline patients tend to have low levels of mindfulness (acceptance skills) which would explain why these patients make extreme efforts to down-regulate negative emotions by dysfunctional behavior (impulsivity) (Baer, Smith, & Allen, 2004). In addition, the neural correlates of borderline personality disorder might reflect the therapeutic effect of mindfulness, since mindfulness training in beginners effectively enhances activity in the prefrontal cortex and diminishes the activity in the amygdala (Y. Y. Tang, Holzel, & Posner, 2015). (Baer et al., 2004)(Baer et al., 2004)(Baer et al., 2004)(Baer et al., 2004)(Baer et al., 2004)(Baer et al., 2004)(Baer et al., 2004)

Research on mindfulness and BPD has just started and there are still many unanswered questions and difficulties. Against this background, the purpose of this study was to test the therapeutic effects of 8 weeks of DBT mindfulness training for borderline personality disorder. We compared two groups of patients with BPD. One group was treated with standardized DBT in an inpatient setting. The outpatient control group, in contrast, was treated with a standard behavioral treatment without mindfulness intervention. We hypothesized that DBT patients had better treatment outcome with respect to reduced borderline symptoms, decreased dissociation heightened mindfulness scores and a reduction of avoidance behavior compared to a group of Borderline patients in a standard behavioral treatment without mindfulness intervention. To gain first insights into neurobiological changes underlying treatment effects, we also correlated changes in symptomatology with activation changes in a mindfulness paradigm as assessed by near-infrared spectroscopy (NIRS). In a previous study (Friederike Gundel et al., 2018) using the same mindfulness paradigm, we found meditation experts to have higher brain activations in the TPJ and temporal gyrus. We therefore hypothesized that mindfulness training had stronger symptom improvements and would be accompanied by stronger activation increases in areas associated with the temporo-parietal junction (TPJ) and temporal gyrus.

2. Method

2.1 Participants

Participants included in this study had to be diagnosed with a borderline personality disorder and report no former training in mindfulness. Only subject between 18 and 55 years and with an IQ > 70 were included. Participants with chronic or acute severe diseases affecting proper brain functioning (e. g. diabetes, severe kidney problems or high blood pressure), acute substance intoxication or acute suicidal thought or behavior were excluded from the study.

The study comprised two groups of borderline patients: The DBT group (n=29) was recruited from an inpatient setting of standardized DBT treatment at the University Clinic of Psychiatry and Psychotherapy in Tübingen, Germany. The patients in the cognitive behavioral therapy group (n=15) were enrolled in ambulant behavior treatment by different ambulant behavior therapist in Tübingen, Germany.

In the DBT group, patients were treated with a standardized German DBT inpatient treatment (Bohus & Bathruff, 2000). Patients were trained in mindfulness skills in two sessions of 30 min./week in a group setting and additionally were instructed on 3 min. mindfulness intervention twice a day and were treated with 25 min. sessions of individualized cognitive-behavior therapy per week.

The control group (outpatient behavioral therapy) was treated with a 50 min. cognitive behavioral therapy session once a week and no training in mindfulness.

2.2 Procedures and Questionnaires

Before and after 8 weeks of DBT and CBT treatment, the NIRS measurement was taken, and self-report Questionnaires were done.

The sequence of the applied questionnaires and the mindfulness task was randomized across participants. Half of the subjects started with the 17 min. mindfulness task followed by answering the questionnaires. The other half answered the questionnaires first and then performed the mindfulness task. Answering the questionnaires took around 15-20 min.

The Big Five Inventory-10 (BFI-10): The BFI-10 is a 10-item version of the Big Five Inventory, BFI-44 (John, Donahue, & Kentle, 1991) and was developed in both English and German. It measures the big five personality core traits „Extraversion“, “Aggreeableness”, „Conscientiousness“, „Neuroticism“ and „Openness“ rated on a five-step scale from 1= „disagree strongly“ to 5 = „agree strongly“ (John et al., 1991)(John et al., 1991)(Rammstedt & John, 2007).

MWT-B: The MWT-B is a multiple-choice vocabulary test (MWT = Mehrfachwahl-Wortschatz-Test, German version). This test can be easily administered in about five minutes and is used as of premorbid tests of intelligence (S. Lehrl, Triebig, & Fischer, 1995).

CTQ: The German version of the Childhood Trauma Questionnaire (CTQ) is a reliable and valid screen for the retrospective assessment of child maltreatment. The CTQ assesses sexual, physical and emotional abuse as well as physical and emotional neglect (Wingenfeld et al., 2010)

The Symptom Checklist (SCL-90-R) (Derogatis, 1977) is a multidimensional psychological test instruments for the assessment of psychological symptoms and psychological distress. It is used for both clinical outcomes measurement and as a psychiatric screening test. All scales are summed up to a Global Severity Index (GSI) indicating global psychopathology.

The short Borderline Symptom List (BSL-23) (Bohus et al., 2009) is a self-rating instrument for specific assessment of borderline-typical symptoms. The BSL-23 can discriminate between patient groups and is sensitive for symptom change.

ARES-K (Action Regulating Emotion Systems Scale) is a widely used personality measure to measure two behavioral systems that are tightly coupled to subjective emotional experience: a behavioral inhibition system (BIS) and a behavioral activation system (BAS). The BIS scale measures anxiety and frustration. The BAS scale assesses goal-directed behavior and reward attainment. We used the short version of the ARES-scales which contains 20 items (Hartig & Moosbrugger, 2003).

FDS-20: The short version of the German Dissociative Experience Scale is called FDS-20. It measures the general degree of dissociative psychopathology and is used as a screening device (Spitzer, Mestel, Klingelhöfer, Gänsicke, & Freyberger, 2004).

The Kentucky Inventory of Mindfulness – German version (KIMS-D) is an multidimensional mindfulness inventory which is based on Linehan´s concept of mindfulness (M. Linehan, 1993) and applied in DBT. The English version was developed by Bear, Smith & Allen (2004) and translated and validated into a German version by Ströhle et al (2010).

Written informed consent was obtained from all participants. The study was approved by the local Ethics Committee (University of Tuebingen) and all procedures were in accordance with the Declaration of Helsinki in its latest version.

2.3 Mindfulness paradigm (NIRS measurement)

The mindfulness paradigm comprised 4 blocks of baseline with normal day-to-day discursive thinking (2 min. each). The baseline blocks were alternated with 3 blocks of mindfulness (3 min. each). There was a continuous auditory stimulation (sound of a singing meditation bells every 12 sec.) both in baseline and meditation blocks.

Participants were asked to sit with open eyes during both conditions. During baseline, subjects were told only to rest, while during meditation periods, they were supposed to focus their attention in a „mindful manner" on the auditory stimulus (see also Friederike Gundel et al., 2018).

2.4 NIRS

NIRS measurements were conducted with the ETG-4000 Optical Topography System (Hitachi Medical Co., Japan). As indicators of brain activity, relative concentration changes of oxygenated (O_2Hb) and deoxygenated hemoglobin (HHb) were continuously recorded from a starting baseline of 10 seconds. The measurement probe sets (two plastic holders with 3×5 optodes each; inter-optode distance: 30 mm) were applied to the left and right side of the head resulting in a total of 44 (2×22) measurement channels covering an area of 12×6 cm over left and right fronto-temporal areas (for more details on the exact positioning of the NIRS probes, see Gundel et al. (2018)). Using this configuration, near-infrared light was continuously emitted onto the scalp and the amount of reflected light was registered by photodetectors. Based on a modified Beer-Lambert Law, the signals were then transformed into concentration changes of O_2Hb and HHb for each measurement channel (which were located midway between each emitter-detector pair) with a sampling rate of 10 Hz.

2.5 Data analysis (demographic variables and questionnaires)

All analyses were conducted using IBM SPSS Statistics. Analyses were conducted only on subjects who had a complete NIRS data set. Statistical significance was set at two-sided $p < .05$.

To describe and compare the two samples, Student's t-test and chi-square statistics were used as appropriate. To evaluate the therapeutic effect of both treatments (DBT, CBT) on changes in psychopathology, mindfulness, and motivational facets, we conducted 2 (group) × 2 (time) repeated-measures analyses of variances (ANOVAs). Group condition (DBT, CBT) was defined as a between-subject factor and time (T1, T2) was defined as a within-subject factor. All clinical and mindfulness scales (BSL-23, SCL-90-R, ARES-K, FDS-20, KIMS-D) were defined as dependent variables. When significant interactions were found, a post hoc analysis was carried out using t-tests for paired or independent samples. Effect sizes were reported by partial eta squared, with values 0.01 considered small, 0.06 moderate and 0.14 large (Cohen, 1988).

2.6 NIRS Data analysis and statistics

O_2Hb and HHb data were computed by means of a modified Bear-Lambert Law. Data preprocessing included: Correction of high amplitude artifacts by the TDDR procedure of Fishburn et al. (2019) a correlation based signal improvement by the procedure of Cui et al. (2010), bandpass filtering (.002 to .1 Hz), interpolation of single noisy channels, correction for global signal changes by the procedure of Zhang et al. (2016) with a PCA based kernel filter with a standard deviation of σ=40, a linear trend correction (to eliminate slow signal changes unrelated to the experimental manipulations) and a z-standardization of the signal by its standard deviation. Data interval from 0-60 s was deleted to allow for an adjustment to the mindfulness condition. Data was averaged over a 60 to 120 s interval following the beginning of the mindfulness or baseline trial with a 5 s baseline correction. Due to the correlation-based signal improvement correction, O_2Hb and HHb data were combined to a single outcome measure ("true O_2Hb") that should increase with increases in brain activation (Cui et al., 2010). For this paper, changes in this activation measure from baseline (t1) to post-testing (t2) were correlated with changes in symptomatology (SCL and BSL: t1 – t2) as well as mindfulness scores (KIMS-D: t2 – t1; note that change scores were calculated to reflect a positive treatment effect [i.e., fewer symptoms or higher mindfulness scores] with positive and a negative treatment effect with negative change score values). Thereby, we focused on data-driven regions of interest by selecting only NIRS channels that showed a "mindfulness effect" (i.e. higher values for the mindfulness condition compared to baseline) in at least one of the two treatment groups. (Cui et al., 2010) (Cui et al., 2010)

3. Results

3.1 Baseline demographical and clinical characteristics

Baseline demographical and clinical characteristics are shown in Table 1. Comparisons between the two groups at pre-intervention indicated a different gender distribution ($p<.1$) with a tendency for more women in the CBT group (100%) compared to the DBT group (82%). The severity of borderline symptoms (BSL-23) and global symptom severity (GSI, SCL-90-R) were significantly lower in the outpatient CBT group than in the inpatient DBT group) (see table 1).

Table 1: Baseline sociodemographic and clinical characteristics

Variable	DBT (n= 29)	CBT (n= 15)	x2	T	p
Gender, n (% of females)	24 (82%)	15 (100%)	2.92		.09
Age, mean (SD)	30.93	31.7[2]		-.232	.82
MWT-B (IQ), mean (SD)	103.75 (13.08)	113.27 (17.23)		-1.87	.074
BFI-10 Personality, mean (SD)					
Extraversion	2.446 (1.10)	2.267 (1.09)		0.51	.61
Aggreeableness	3.23 (1.16)	2.400 (1.08)		2.34	.027
Conscientiousness	3.16 (.83)	2.83 (1.03)		1.06	.301
Neuroticism	4.37 (.73)	3.70 (1.48)		2.02	.05
Openness	3.63 (1.14)	3.03 (1.14)		1.62	.116
Psychopathology, mean (SD)					
BSL-23 (severity of BPD)	2.46 (.75)	1.71 (.88)		2.94	.005
SCL-90-R: GSI (global severity of symptoms index)	79.21 (2.04)	69.87 (11.89)		4.15	.000
CTQ: childhood trauma, mean (SD)	2.41 (1.42)	1.75 (.98)		1.598	.118

[2] n= 5 data points were missing

Sex. Abuse Phys. Abuse Against. Abuse Phys. Neglect Against. Neglect	2.36 (1.289) 3.19 (1.00) 2.37 (1.28) 2.81 (1.27)	1.56 (.59) 3.22 (1.16) 1.92 (.68) 3.29 (.91)		2.27 -.089 1.268 -1.282	.029 .930 .212 .207
FDS-20: Dissociation, mean (SD)	33.23 (22.01)	24.06 (21.75)		1.32	.197
KIMS-D: (Mindfulness), mean (SD)	90.89 (20.22)	106.47 (25.07)		-2.07	.49
Motivation: ARES-K, mean (SD) ARES BIS (inhibition) ARES BAS (reward orientation)	 3.35 (.63) 2.54 (.50)	 3.41 (0.78) 2.98 (0.68)		 -.35 -2.16	 .755 .42

MWT-B = Mehrfachwahl-Wortschatz-Test, German version , **BFI-10** = The Big Five Inventory-10, **BSL-23** = The short Borderline Symptom List, **SCL-90-R** = Symptom Checklist, **CTQ** = Childhood Trauma Questionnaire, **FDS-20** = Fragebogen zu Dissoziativen Symptomen (German Dissociative Experience Scale), **KIMS-D** = Kentucky Inventory of Mindfulness Scale, **ARES-K** = Action Regulating Emotion Systems

3.1 Psychometric results

An ANOVA analysis was conducted and revealed a significant main effect of time for the reduction of borderline symptoms (BSL-23; T1: 2.08 ± .86; T2: 1.7 ± .86; $F_{1, 39} = 5.41$, $p < .05$) with a decrease in symptoms from T1 to T2 across treatment groups (see Fig. 1). Analysis of the global symptom index (SCL-90-R) furthermore revealed statistical trends for a main effect of time (T1: 75.65 ± 8.67; T2: 71.81 ± 10.59; $F_{1, 38} = 3.68$, p = .06; again, indicating an overall decrease in symptoms) as well as an interaction “time × group” ($F_{1, 38} = 3.48$, p = .07; see Fig. 2). The interaction resulted from a significant decrease in symptoms from pre- to post-testing in the DBT group (T1: 79.1 ± 2.1; T2: 74.1 ± 8.1; $t_{25} = 3.26$, p < .01) but not in patients receiving outpatient treatment (CBT; T1: 69.6 ± 12.3; T2: 69.6 ± 12.6; $t_{13} = 0.03$, n. s.); this pattern of change also led to significant between-group differences at the time of baseline testing ($t_{14.4} = 3.02$, p < .01) that were no longer present after the treatment period ($t_{19} = 1.21$, p > .2). For dissociation symptoms (FDS-20) as well as avoidance behavior (ARES-BIS), the corresponding ANOVA showed significant main effects of time (FDS-20: T1: 29.4 ± 21.68; T2: 25.25 ± 21.96; $F_{1, 38} = 4.26$, p < .05; ARES-BIS: T1: 3.41 ± 0.53; T2: 3.19 ± 0.67; $F_{1, 38} = 4.48$, p < .05) with symptom reductions for both groups after 8 weeks of treatment. For the ARES-BAS, however, a trend for an interaction “group × time” ($F_{1, 38} = 3.08$, p = .09) was found. This interaction resulted from a numerical increase in BAS from pre- to post-testing in the DBT group (T1: 2.54 ± .504; T2: 2.73 ± .54; $t_{25} = -1.52$, p < 0.2), and an opposite pattern of change (again only numerical) in patients receiving outpatient treatment CBT (T1: 3.02 ± .68; T2: 2.87 ± .57; $t_{13} = 1.03$, n. s.); this pattern of change also led to significant between-group differences at the time of baseline testing ($t_{41} = -2.36$, p < .05) that were no longer present after the treatment period ($t_{38} = .77$, n. s.; see Fig. 3).

A significant main effect of time for the KIMS-D (T1: 96.49 ± 21.91; T2: 115.24 ± 21.96; $F_{1, 37} = 43.98$, p < .001) indicated that both groups had significantly higher rates in mindfulness (KIMS-D) after treatment (see Fig. 4).[3]

We could also show that improvements in mindfulness (KIMS-D) correlated significantly with improvements in general psychopathology (SCL-90-R; overall: r = .48, p <.01; DBT group: r = .44, p < .05; CBT group: r = .59, p < .05).

[3] Missing data points: KIMS-D: No.6, BSL-23: n=4, SCL-90-R: n=5, FDS-20: n=5, ARES-BIS: n=5

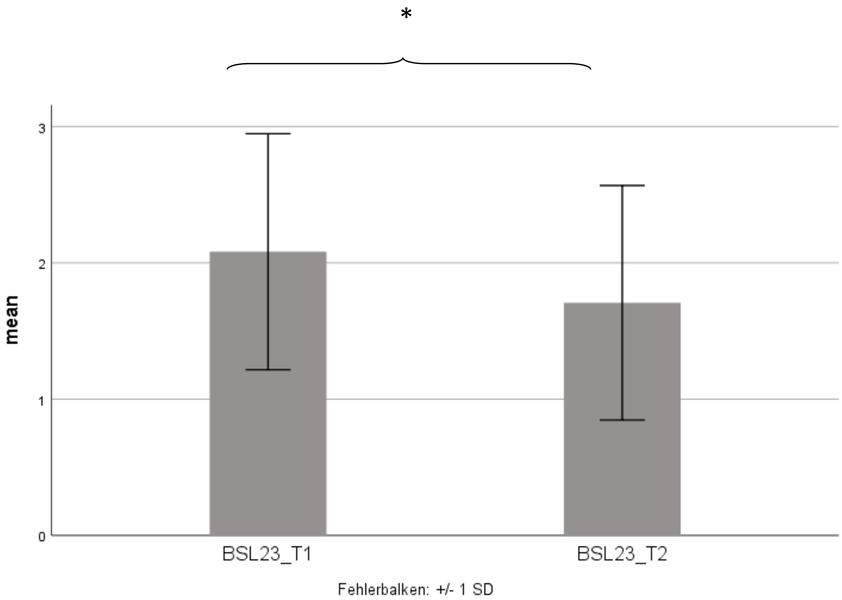


Fig. 1. Reduction of psychopathology: BSL-23 = borderline symptoms

Error bars indicate the standard deviation.

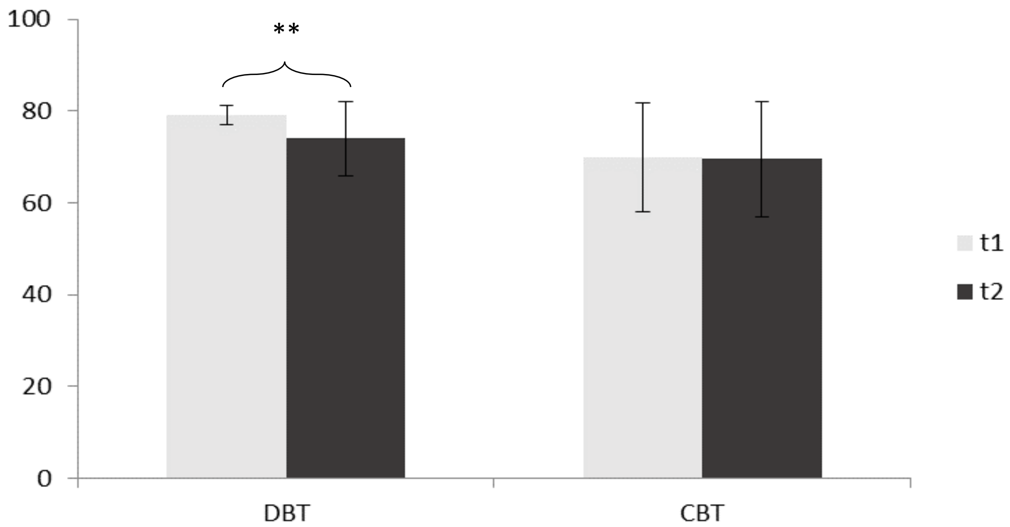


Fig. 2. Reduction of global psychopathology: SCL-90-R

Error bars indicate the standard deviation.

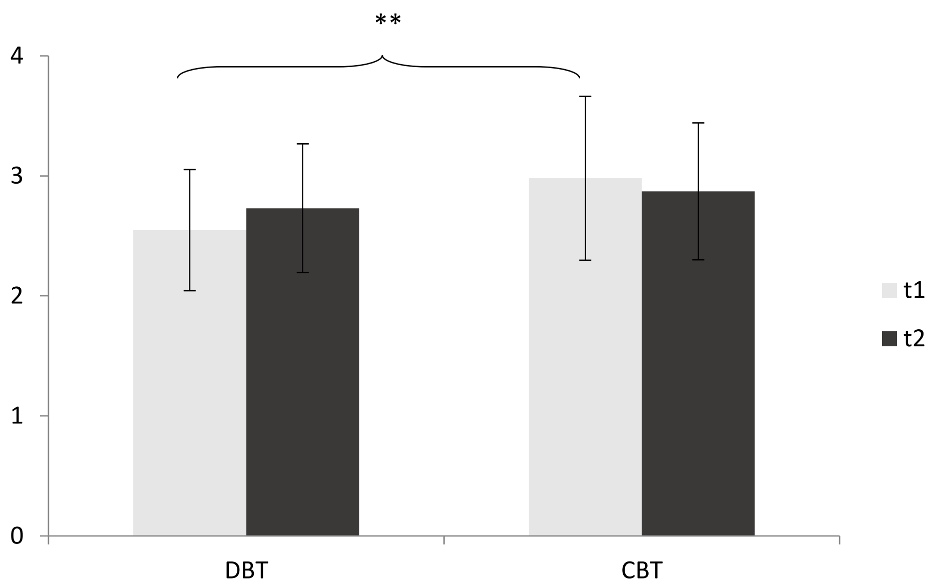


Fig. 3. Changes in motivation (BAS= reward seeking)

(Error bars indicate the standard deviation).

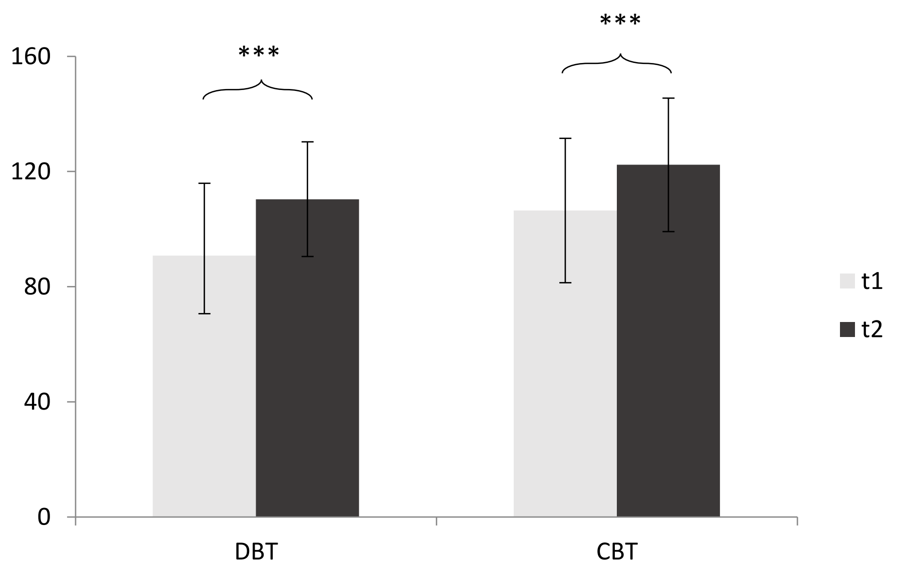


Fig. 4. KIMS-D = Mindfulness (Error bars indicate the standard deviation).

3.3 Neurobiological results

To gain first insights into neurobiological correlates underlying these treatment effects, changes in brain activity from t1 to t2 were correlated with changes in symptomatology focusing on a region of interest located within the superior temporal gyrus and supramarginal gyrus of the left (3 channels) and right hemisphere (4 channels). In the DBT group, activation changes in these two areas correlated significantly with changes in symptomatology as assessed by the SCL (left ROI: $r = .484$, $p < .05$; right ROI: $r = .392$, $p < .05$) as well as changes in mindfulness as assessed by the KIMS-D (left ROI: $r = .427$, $p < .05$; see Fig. 5) indicating – in both cases – positive clinical effects over time (i.e., decrease in symptoms and increase in mindfulness) with increases in brain activation during the NIRS mindfulness condition. In contrast, patients who received out-patient treatment without the mindfulness component (CBT) showed no significant correlation of activation changes in these two ROIs with changes in clinical symptoms or mindfulness over time.

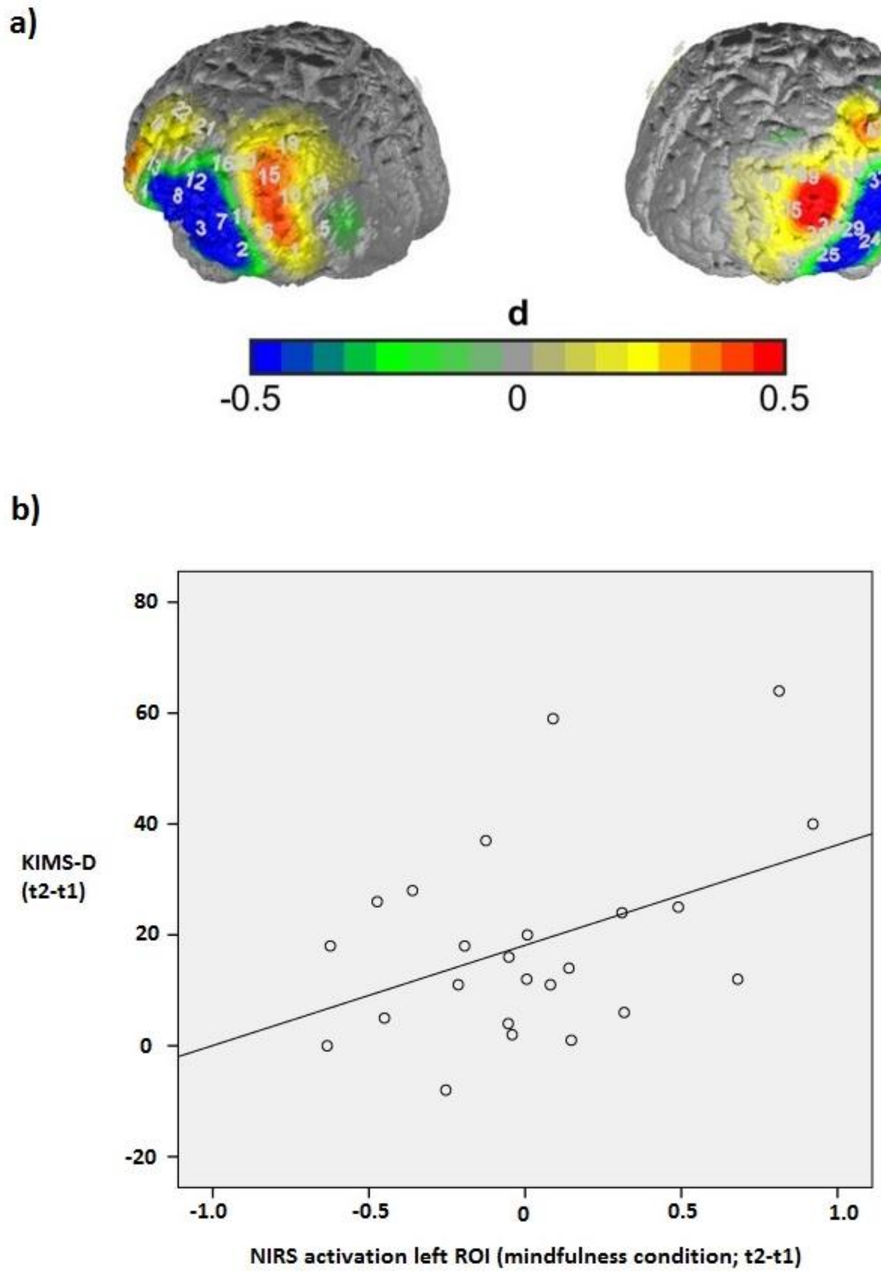


Fig. 5. Correlation between changes in NIRS activation (t2-t1) and mindfulness scores (t2-t1) in the DBT group

a) NIRS activation map (mindfulness vs. baseline condition; colors represent Cohen's d) illustrating the data-driven region of interest (ROI; here: DBT group, t2)

b) Scatter plot illustrating the significant correlation between change scores of NIRS data and mindfulness scores (KIMS-D) in the DBT group.

4. Discussion

To the best of our knowledge, this is the first neuroimaging study using NIRS to compare the effects of 8 weeks of DBT mindfulness skills-training in borderline patients with an active CBT control group. Both groups had significantly reduced psychopathology measures (BSL-23, FDS-20) and a trend for general symptom reduction (SCL-90-R) after 8 weeks of therapy. Furthermore, both groups had significantly improved mindfulness scores (KIMS-D) and reduced avoidance behavior motivation (ARES BIS). We could also show that improvements in mindfulness (KIMS-D) correlated significantly with improvements in general psychopathology (SCL-90-R) and these results correlated with an increase in neural activation in the TPJ and superior temporal gyrus after 8 weeks of DBT.

4.1 Mindfulness

In an ANOVA we found a main effect of time showing that both groups had better self-reported mindfulness scores after 8 weeks of therapy.

A pilot study with healthy participants and healthy meditation experts revealed significantly higher rates of mindfulness in healthy groups with and without meditation experience (Friederike Gundel et al., 2018). Other studies could prove higher levels of negative affectivity to be significantly associated with lower levels of KIMS scores (Baum et al., 2010). These effects are also consistent with the findings of Baer et al. (Baum et al., 2010)(Baum et al., 2010)(Baum et al., 2010)(Baum et al., 2010)(Baum et al., 2010)(Baum et al., 2010)(2004) who found neuroticism, a personality factor that is conceptually like negative affectivity. This is line with our study. Patients in the outpatient CBT group had significantly lower rates on the BFI-10 on the personality traits „ Aggreeableness" and „Neuroticism "(see Table 1). Our results support results of previous studies which found a connection between BPD and basic traits, particularly of high Neuroticism and low Agreeableness and Conscientiousness.

4.2 Psychometric results

In terms of clinical outcomes, both groups had significant reductions of borderline symptom severity (BSL-23), reduced symptoms of dissociation (FDS-20) and reduced levels of avoidance motivation after treatment (ARES BIS). An ANOVA revealed a tendency for a main effect of „group “, and an interaction of „time” and „group“ which suggests the DBT group to be more effective in increasing goal attainment and reward seeking behavior. One possible explanation for this tendency might be that DBT mindfulness training specifically trained the ability to describe feelings and to act with acceptance and awareness fostering positive results in life satisfaction which was previously found (Baer et al., 2004). In addition, we found higher mindfulness rates (KIMS-D) to be positively correlated with a reduction in general symptom reduction (SCL-90-R) and a tendency for the mindfulness training group (DBT) to have better results in reducing general psychopathology symptoms. These results suggest mindfulness training to be effective in borderline patients. DBT might add specific treatment features (acceptance and awareness) to change skills found in cognitive behavior therapy making this approach especially effective for patients with emotion regulation problems and high neuroticism. The specific acceptance skills might help patients to heightened attention, awareness and acceptance of emotions and body and thus, leading to emotional processing, tolerance of distress, habituation processes and more adaptive coping strategies (Baer et al., 2004)(Baer et al., 2004)(Baer et al., 2004)(Baer et al., 2004)(Baer et al., 2004)(Baer et al., 2004)(Baer et al., 2004)(Baer et al., 2004; Hölzel et al., 2011). There might be other ways that mindfulness skills affect borderline symptoms e.g. by reducing stress (Carmody & Baer, 2008) or fostering the ability for compassion (Gilbert & Plata, 2013). Compassion and self-compassion abilities might reduce underlying vulnerability by interpersonal childhood trauma (emotional abuse and neglect found in borderline patients) and thus lead to reduced feelings of loneliness, exclusion, and feelings of paranoia. Acceptance and body awareness might help to reduce feelings of shame and self-hate (Gilbert & Procter, 2006), over-identification and isolation (Neff, 2003).

4.3 Neuroimaging Outcomes

To gain first insights into cortical activation changes underlying improvements in symptomatology, changes in mindfulness related NIRS data from baseline to follow-up were correlated with corresponding symptom changes in both groups. Here, we found an activation increase in a temporo-parietal ROI (superior temporal gyrus, BA22; supramarginal gyrus, BA40) from t1 to t2 during a mindfulness condition to correlate significantly with symptom reductions (SCL-90-R) and increases in mindfulness (KIMS-D), but only in the DBT group. These results suggest mindfulness training to be effective in reducing psychopathology in borderline patients, whereby the neurobiological substrate of this therapeutic effect might be related to an increased involvement of temporo-parietal areas in states of mindfulness. Brain activation of the superior temporal gyrus and supramarginal gyrus was also found in Gundel et al (2018) in meditation experts but not meditation novices measured with the same experimental design as in this study. These results suggested the superior temporal gyrus being affected by mindfulness training. In the present study, the ameliorated activity in the superior temporal gyrus might show a training effect in DBT patients after 8 weeks of mindfulness training. But there are also contrasting results in previous studies: Schnell et al. found reduced activation in the left superior temporal gyrus in borderline patients after DBT treatment (Schnell & Herpertz, 2007) and Goldstein et al. (Schnell & Herpertz, 2007)(Schnell & Herpertz, 2007)(Schnell & Herpertz, 2007)(2009) could not find overall BDP symptom severity to be correlated with BA 22 volume changes. Farrés et al. (2019) also failed to detect DMN changes by fMRI after DBT mindfulness training and interaction training but found other brain areas to be sensitive for clinical changes (left anterior insula and in the calcarine, the cuneus and superior occipital gyri).

These partly conflicting results might reflect differences in study design and might also reflect the complex nature of this brain area, which is part of an integration area for multiple somatosensory input:

The superior temporal gyrus (STG) is associated with processing of eye movements and visual analysis of social information and, therefore, this task is complex. Abnormalities of the STG make it a distinct biomarker in e. g. schizophrenia research. Dysfunction of the STG and associated language areas point at difficulties in converting auditory cues into language (symbolizing, judging). Connecting outside information (social cues) to biographical information might reflect a complex symbolizing task. In the last two decades this area has been extensively examined in the context of auditory hallucinations (schizophrenia) pointing at a dysfunction e. g. of silent inner speech (David, 1999). In terms of borderline personality disorder, Frick and his colleagues examined neurophysiological (fMRI) responses of BPD patients during a 'Reading the Mind in the Eyes' test (RMET). They found BPD patients to discriminate affective eye gazes to mental states significantly better and faster than healthy controls. The authors found healthy subjects to have increased activation in the insula and the superior temporal gyri (Frick et al., 2012). Since BPD patients are vigilant to social stimuli, a higher activation of this area (like in the study at hand) might point at reduced psychopathology after DBT training and a possible training effect of mindfulness skills. (David, 1999)

Other authors (Scherpiet et al., 2015) failed to find correlations between mindfulness questionnaires and brain activation (fMRI data) during mindful self-focused attention in a sample of borderline patients. We could find correlations between an increase of mindfulness (KIMS-D) and brain activation. As discussed in a previous (Friederike Gundel et al., 2018), the supramarginal gyrus (BA 40) plays an important part in theory of mind skills separating one´s own emotions from emotions of others and dis-identify from one's own perspective. This brain area might have been trained by DBT mindfulness skills. Activity of the supramarginal gyrus is involved in empathy and TOM function. Training might ameliorate social integration and reduction of loneliness which is a specific pathology-feature of borderline patients. Meditation expert had heightened activation in this brain area (Friederike Gundel et al., 2018), and this might explain symptom reduction in our DBT group. Schmitgen and colleagues (2019) also found DBT to be more effective for training higher cognitive functions of emotion regulation. High activation in this brain region might also reflect better detection of auditory cues. Kerr et al (2011) found enhanced somatosensory performance in subjects after 8 weeks of meditation training. Krall et al (2015) found the right BA 40 region to be connected to a right-lateralized frontoparietal attention network, which can detect sudden changes in e.g. auditory stimulation (task positive network). Detecting changes in attention focus is explicitly trained in meditation. On the other hand, the posterior part of this region is connected to the default mode network reflecting stimulus-independent mental processes. Both networks seem to be trained by meditation: Getting aware when the focus of attention is shifting away from the meditation focus (here: auditory cue) and shifting the attention back to focus repeatedly. This overlap of DMN activity and goal directed behavior might help Borderline patients trained in mindfulness to stay both connected to an inside and an outside focus of self. Hasenkamp and Barsalou (2012) found stronger connections in both networks in association with mindfulness as well. This trained double feature which Linehan might call "middle way" might reduce typical pathological extremes in borderline patients (integration) and lead to a more stable identity.

Our study contributes to the growing body of mindfulness studies and addresses the question, if DBT mindfulness skills can be acquired by borderline patients and will reduce their specific psychopathology. In the future, a training of meta-cognitive skills might also serve as a prevention method to handle the fast pace of our modern life and to reduce psychopathology features. Further studies are needed to unravel the complex nature of emotion regulation and mindfulness interventions in the future.

5. Limitations

Our study had some major limitations that need to be addressed.

The sample size of the study was relatively small and therefore the statistical power is limited. The results might therefore not be generalizable. The patients were not randomly assigned to both groups and data acquisition was not blinded. The treatments varied not only in setting (inpatient- outpatient), but also in the amount of therapy time.

The outpatient group was affected less by psychopathology, so that groups were not matched properly.

Further, the design of the paradigm used rather long stimulus blocks, resulting in rather wide band-pass filter settings. In future studies, shorter blocks, or analysis of low frequency fluctuations might be used. Studying treatment outcome from a clinical setting generally leads to many uncontrolled variables, which might have influenced our results.

6. Conclusion

The present study provides empirical evidence of the effectiveness of 8 weeks of DBT. We were also able to gain insights in the impact of mindfulness skills on borderline psychopathology reduction. Clinical ratings significantly improved during both therapeutic interventions. We found symptom reductions (SCL-90-R) and increases in mindfulness (KIMS-D) in the DBT group to correlate with an activation increase in a temporo-parietal ROI (superior temporal gyrus, BA22; supramarginal gyrus, BA40) from t1 to t2 during a mindfulness condition. In future studies, the therapeutic potential of mindfulness for borderline patients needs further investigation. In addition, mindfulness as a preventive tool to reduce identity problems should be addressed by studies with longitudinal design.

Acknowledgements

We acknowledge the support by Svenja Brosch and thank Ramona Täglich and Betti Schopp for their excellent technical assistance.

Authors' Contributions

FG: designed the study, wrote the study protocol, recruited participants, conducted NIRS measurements and supported the data and statistical analysis and wrote the first draft of the manuscript.

AE: assisted in designing the study, performed the statistical analysis, supervised the study, and wrote parts of the manuscript.

DR: conducted the NIRS data analysis and statistics and wrote parts of the manuscript.

MH and AF: supervised the study and critically revised the manuscript.

All authors have contributed to and approved of the final manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial or non-profit organizations. Ann-Christine Ehlis was partly supported by IZKF Tübingen (Junior Research Group, grant 2115-0-0).

Compliance with Ethical Standards

The study was approved by the local Ethics Committee (University of Tuebingen), all procedures were in accordance with the Declaration of Helsinki in its latest version and written informed consent was obtained from all participants.

5. General discussion

M. Linehan`s quote that mindfulness is the basis of all skills, was the focus of this dissertation. Are borderline patients able to acquire mindfulness at all in 8 weeks and is it effective for them? Which underlying neural structures are activated by meditation and which structural changes occur over time? These questions have not been sufficiently examined empirically until today and are now topic of this work:

In this dissertation, three studies were developed and carried out on the above questions and several hypotheses were tested. Those are summarized here again. After that, the results are discussed and reclassified in an extended model of borderline psychopathology.

First, **in study 1,** we examined the neural response patterns of two groups of subjects (meditation experts and a group of subjects without meditation experience) in a mindfulness paradigm (mindful hearing and resting state). We wanted to find out, if the groups differ in their neural response pattern to this paradigm. Does long-term meditation cause functional changes in the brain? Study 1 was used to generate hypotheses for study 3.

- The hypothesis of study 1 was:

Hypothesis: Meditation experts show a specific neural response pattern during an auditory mindfulness exercise and in a resting state compared with a group with no meditation experience.

Results:

Hypothesis 1 was confirmed: Meditation experts had higher neural activation in the mindfulness paradigm in BA 39 (left), BA 40 (right) and BA 44, 45 and 47 (bilateral) than in the control group. The results were stable across both states (meditation and rest) suggesting structural change in the brain (trait).

During meditation (state), meditation experts showed higher activations in the right TPJ in the meditative state. We were able to replicate the results of the pilot study of Erb et al. (2011) which also found specific activation patterns in the same paradigm in the meditative state in 8 meditation-experienced subjects. There, increased hemodynamic response patterns were shown by meditation experts in the precuneus (BA 7), which, however, passes into BA 40. There was also an increased activity in the Rolandic Operculum on the right (BA 47). In addition, hemodynamic activity in the inferior frontal gyrus was increased. Frontal areas of the brain were not measurable with our mindfulness paradigm in Study 1 but were studied in our second study.

Study 2 examined whether long-term meditation experience improves performance in executive tests. We also wanted to find out which neural changes are involved (long-term changes – trait). Since borderline patients suffer from deficits in the prefrontal cortex, we were interested in this question in preparation for Study 3. A word fluid test should test cognitive flexibility and the emotional Stroop test should test emotion control. Study 2 was used as preparation for Study 3: Can mindfulness training possibly improve frontal brain performance and thus have a positive effect on typical borderline symptoms such as impulse control and emotion regulation problems?

We also wanted to find out whether a short mindfulness exercise before the executive tests can improve performance in both groups. The short-term effects of mindfulness training on the prefrontal cortex were tested (state).

- For study 2, we made the following 3 hypotheses:

Hypothesis 1: Meditation experts have a better reaction time and make fewer errors in the interference condition of an emotional stroop test than a group of subjects with no meditation experience. These improvements will go along with a typical neural activity pattern in the prefrontal cortex.

Results:

Hypothesis 1 could only be confirmed for the Stroop test: Meditators had a lower error rate compared to a control group. We also found a significant group effect with higher activation in the meditators in the left inferior frontal gyrus.

In contrast to Erb et al. (2011), which found neural activations in the right inferior frontal gyrus during meditation, our study in the left inferior frontal gyrus showed stronger activations during executive tasks. Other studies (Ding et al., 2015; Taren et al., 2017) also found the right inferior frontal gyrus more strongly activated and this part more connected to the dorsolateral prefrontal cortex. The ventral regions, which are mostly right lateralized in their activation, seem to be more responsible for monitoring and re-orientation of salient information. However, these activation ranges were measured at rest and are therefore not very comparable with our results. Another study found structural changes in the left inferior frontal gyrus (BA 47) in meditation experts (Kang et al., 2013). The interplay of activation in the left inferior frontal gyrus and a deactivation of the right anterior superior temporal gyrus (BA 22) found Taylor and colleagues in a modified Stroop Task (S. F. Taylor et al., 1997)

Hypothesis 2: Meditation experts have better performance (name more words) in a word fluid test compared to a control group. The performance increasement correlates with a typical neural activity pattern in the prefrontal cortex.

Results:

Hypothesis 2 had to be discarded because the two groups did not differ in the word fluid test VFT. Both groups showed corresponding neural activations in the prefrontal cortex in all three conditions of VFT (weekdays, semantic and phonetic). Although even a 10-minute mindfulness training per day positively affects verbal memory, Lueke and Lueke (2019) could not show improvements in the general word fluency after meditation. By contrast, other studies found improved verbal fluency after short meditation sessions compared to a reading intervention or a sham meditation (Prätzlich, Kossowsky, Gaab, & Krummenacher, 2016; Zeidan et al., 2010). However, this group was hardly trained in mindfulness. In contrast, our study group consisted of experienced meditation experts. To our knowledge, this is the first study on the word fluency of meditation experts so far.

Hypothesis 3: A previous short mindfulness exercise improves performance in word fluency and in the emo-stroop test in both groups. This performance improvement correlates with a specific neural activity pattern in the prefrontal cortex.

Results:

Hypothesis 3 could also only be partially confirmed. We found no performance improvements in the executive function tests due to the previous mindfulness exercise. Nevertheless, we found specific changes in neural activation patterns after mindfulness: We found stronger neural activations especially in the left dorsolateral prefrontal cortex and in the left inferior frontal gyrus.

Based on the results of studies 1 and 2, **Study 3** should finally verify that mindfulness is effective in borderline patients. For this purpose, it was investigated whether patients benefit more clearly from an 8-week DBT program (reduction of psychopathology) than from an 8-week treatment with cognitive behavioral therapy without mindfulness. Symptoms enhancements after DBT training should also be accompanied with a modified neural response pattern during a mindfulness exercise (as in study 1) and should be like the neural response pattern of the group of meditation experienced participants from study 1.

For study 3, the following 2 hypotheses were made:

Hypothesis 1:

Eight weeks of DBT therapy is more effective than 8 weeks of CBT without mindfulness training. This is reflected in reduced psychopathological symptoms (reduced borderline symptoms, reduced avoidance motivation, reduced dissociation, and increased mindfulness).

Results:

Hypothesis 1 had to be rejected, as both interventions resulted in improvements in psychopathology. However, there was a trend in the improvement of general psychopathology (SCL-90-R), which was only evident in the DBT group.

Generally, an increase in mindfulness scores correlated with symptom improvement in SCL-90-R in both groups.

Hypothesis 2:

The improvement in symptoms due to mindfulness training (DBT) goes along with stronger neural activation in the temporal-parietal junction (TPJ) and temporal gyrus.

Results:

Hypothesis 2 could still be confirmed: only in the DBT group improvements in general psychopathological symptoms (SCL-90-R) correlated significantly with neural activity increases bilaterally in temporal gyrus (BA 40) and supramarginal gyrus (BA 22). Increases in mindfulness levels on KIMS-D were connected to positive clinical effects (reduction of symptoms) and neural activity increases in the left hemisphere in BA 40 and BA 22 during mindfulness exercise in both groups. Our results are in line with the results of a study by Mancke et al. (2018) that found structural changes in the brains of borderline patients after a DBT training. There, the gray matter volume in the superior temporal gyrus and in the supramarginal gyrus was increased. The authors speculated that these neural changes improved mentalization ability (e. g. Theory of Mind) and lead to better emotion regulation in patients. According to these findings, patients in study 3 showed a reduced psychopathology as measured by the SCL-90-R after a DBT training.

1. Summary

Our three studies used a mindfulness paradigm (auditory stimulus) to investigate whether borderline patients after 8 weeks of DBT have specific neural hemodynamic response patterns like meditation experts. We were able to show that meditation experts had more activations in the temporo-parietal compound (BA 40) and in the supra-marginal gyrus (BA 22) than beginners. This neural activity pattern is also apparent in borderline patients after 8 weeks of DBT and goes along increased mindfulness levels and reduced general psychopathology (study 1 and study 3).

To better understand how meditation changes borderline symptoms, we examined the frontal brain in Study 2. We measured the executive performance of meditation experts and a control group. In an Emotion Stroop Task, meditation experts had a reduced number of errors. Other authors found similar results in a group of borderline patients. There, stronger dissociation in an Emotional Stroop Test led to more errors (Winter et al., 2015). Strengthening prefrontal activation through mindfulness exercises could reduce their neural psychopathology (diminished frontal activation) in borderline patients, leading to improved emotion regulation and reduced impulsivity. We found such increased activation in the prefrontal cortex through a previous mindfulness training: Both groups showed stronger hemodynamic response patterns in the left dorsolateral prefrontal cortex and in the left inferior frontal gyrus after mindfulness. Winter et al. found dissociative processes in these two areas of the brain in borderline patients when they had to solve executive tasks (Winter et al., 2015) This result would confirm that mindfulness and dissociations are two opposing concepts. In the word fluency test VFT, however, we could not see any improvements in performance in the meditation group. In borderline patients, the word fluency generally appears to be less impaired (Dinn et al., 2004) so that these results are less relevant anyway for clarifying our initial question.

More interesting, however, are our results on hemodynamic response patterns in the temporo-parietal junction (TPJ) and in the supramarginal gyrus in long-term meditation experts compared to a control group. These areas of the brain are part of the resting state network and are responsible for self- and external perception. Borderline patients show significant changes here. Xu et al (2016) found by functional connectivity analysis that borderline patients showed reduced connectivity compared to healthy volunteers in the core areas of the DMN. Regular meditation training therefore seems to be effective not only through the training in the frontal cortex, but also enhance activity in temporo-parietal areas and thus lead to an improved self- and external perception. The brain region of the TPJ is an integrative area that links different brain areas and different sensory modalities into a higher self-unity. Integrational processes in self-perception might then reduce typical borderline symptoms such as identity diffusion, loneliness, dissociation, and relationship difficulties.

In the final part of this dissertation, the results of our three studies on meditation will merge into an expanded etiological model. For this purpose, the etiological model of borderline disorder as a developmental trauma disorder will be introduced (nach Meares, 2012; Nijenhuis, Lorenz, & Wilmers, 2018). Specific symptoms of borderline personality disorder in relation to the underlying neural network disorders will be explained. In addition, the impact of meditation will be discussed based on the latest empirical research and considering the concepts of ancient Buddhist writings.

2. Theoretical assumptions: Meditation as a cortical network training

Starting point: We were able to show that regular meditation is related to a strong hemodynamic response in the TPJ (study 1 and 3) - a core area of the DMN - with activations in DLPFC for executive tasks (Central Executive Network) and activations in the left inferior frontal gyrus (BA 44 and 45 and 47 (bilateral). This area is active in detecting social cues and is also responsible for symbolism/language (study 2).

We therefore assume that meditation as mental training repetitively trains all three networks in the brain and thereby changes them:

- Frontal cortex: attention to the outside, focused attention to the meditation focus (concentration, Sanskrit: "Samadhi")
- DMN: Attention inward, perception when self-related thoughts come (non-valuing attitude – equanimity, Sanskrit: "Samatha")
- Salience Network: Recognize when the focus of attention turns inward (self-related thoughts). Flexibility in letting go of fixation on self-related thoughts (de-fusion) and returning to focus to the outside -> Shifting (Re-orientation) to Executive Network (Attention, Pali: "Sati")

The basic components in meditation:

1. Concentration ("Samadhi", top-down control) and

2. Mindfulness ("Sati", bottom-up control)

are practiced repetitively and lead over time to a stable meta-cognitive attitude:

3. Equanimity ("Samatha", trait).

We therefore assume that this practice changes the interrelatedness of the three neural networks within and to each other, and that over time the three neural networks are reconnected in a stable way.

This stable reorganization and meta-cognitive attitude are illustrated in the Tibetan description of Namgyal:

"This is like the example of a competent herdsman tending to his cattle. They can roam freely. He does not have to keep bringing them together. It is enough to simply not lose sight of them. Similarly, no matter which thought, or perception occurs, you do not need to block it or keep it under control. Rather, promote a naturally aware presence of mind and thus continue the practice with unbound ease without pinpointing whatever is experienced (Namgyal, 2001)." (Namgyal, 2001)(Namgyal, 2001)

The shepherd monitors the herd without controlling it but keeps an eye on the entire herd.

We translate this into the neuro-cognitive language: external orientation and inner orientation should be active at the same time and there must be a meta-cognitive instance (shepherd) who does not lose his overview (by fixating on only a partial aspect).

Based on these theoretical considerations, regular meditation could train the brain's abilities to simultaneously uphold an outward-facing (executive network) and an inward-facing focus (DMN).

Without meditation experience, DMN and CEN are anti-correlated:

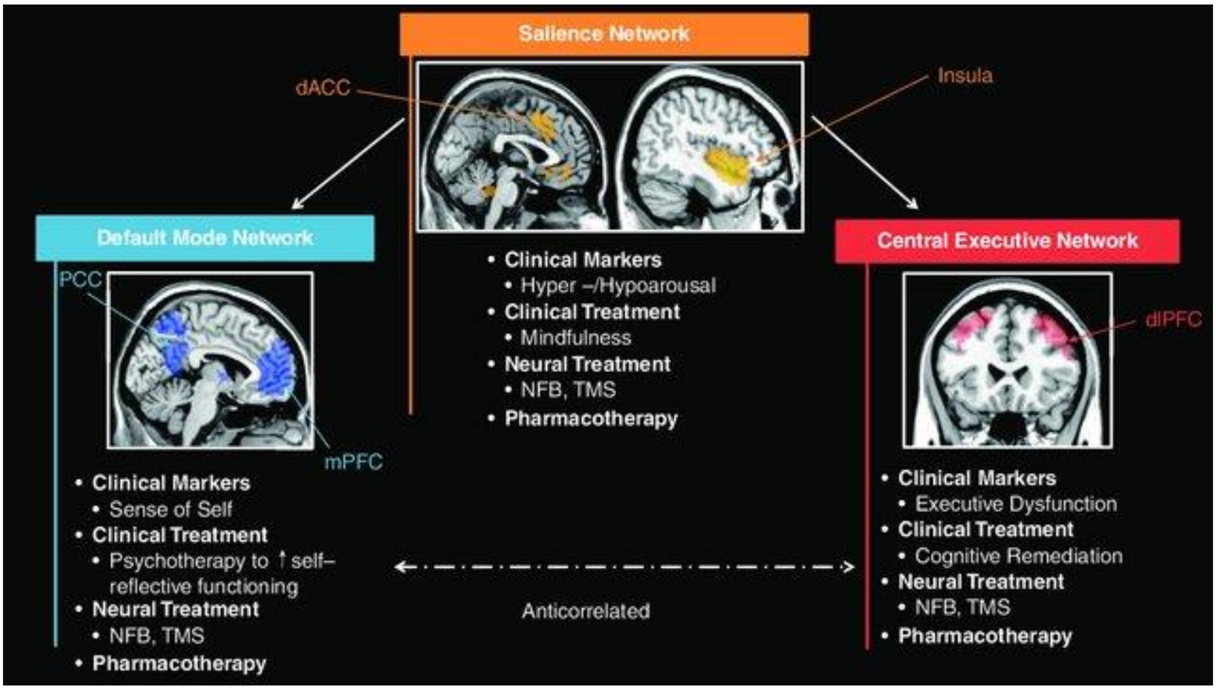


Figure 6: Overarching neural networks of the brain (Lanius, Frewen, Tursich, Jetly, & McKinnon, 2015)

The repetitive mental practice of mindfulness could change the classic pattern of anti-correlation between the Executive Network and DMN. Both orientations (inside/outside) could stay active simultaneously through establishing a higher mental synthesis, a meta-cognition (higher consciousness). One could speculate that this reorganization arises from interruption of the reflexive mental "fusion" both inside and outside (fusion/fixation/control) and by de-fusion of mental content (keep in mind, not merge, non-judgmental, open). The Salience network is probably involved here. Keeping the sitting posture stable (motor stability) the basal embodied self-experience (probably in the insula region) is strengthened and anchored in the present. (anchoring/yoga). Hölzel et al. found e. g. significant structural changes in the insula region after a meditation training (Britta K Hölzel et al., 2007). The basic physical self-strengthening in combination with an extended mental orientation (inside and outside) could then lead to the "self" being embodied temporally and spatially in the present. The mental extension into a "subject ≈ object/self ≈ other" orientation is probably created by the excessive training of all three networks. The hub of these three networks is probably the temporo-parietal connection (TPJ), where this meta-cognitive skill (switching focus of attention inside-outside) is presumably taking place (see also Figures 7 and 8 for an overview of the functionality of the TPJ). The self-consciousness expansion inward and outward is sorted by the underlying orientation on the body into space (here) and time (present). This leads to calmness, mental stability, well-being, mental clarity, personality development, increased performance, and resilience. In borderline disorders, on the other hand, embodiment is often reduced, so that time and space, subject-object/self-other remains disordered and confused. Then, goal orientation and action taking are severely restricted.

Our theoretical concept is confirmed in imaging studies, which initially find an increased activity in the Executive Network (to stabilize concentration) in beginners of meditation. Later, long-time meditation experts will achieve reduced connectivity and activity in the PFC, while reducing connectivity and activity in the DMN and connecting these two networks in paralleled action (Chiesa, Calati, & Serretti, 2011). The two networks, which are classically opposite, are then neuronally reorganized: more in a common network (integrated) than anti-correlated. The increased neural activity in the TPJ in the meditation group from our study 1 supports this model.

3. Theoretical assumptions: Borderline personality disorder as a disorder of neural integration.

In the next step, we briefly describe the etiological model for borderline disorder according to Meares (2012) and explain the effectiveness of meditation on borderline symptoms. First, however, the healthy brain development and the necessary environmental factors are to be discussed, to describe the core pathology of borderline personality disorder.

Based on the attachment theory (Bowlby, 1979; Britta K Hölzel et al., 2007) by the mutual repetitive early mother and child interaction - initially nonverbal, i.e. rather right-hand-hemispheric (Schore, 2002) - a fundamental secure bonding, a basal ability to regulate stress and feelings and a basic "feeling" of the self and the world. If this basic attachment is sufficiently stable and established in the child, healthy brain development can occur. In addition, in the first years of life, the child learns to symbolize these interactions (rather presumably left-hemispheric) by interacting with close reference persons. The later symbolic and linguistic development is necessary to learn concepts such as "Theory of Mind" and more complex interactional behavior and to acquire an increasing social competence (integration of non-verbal, emotional, and linguistic-symbolic aspects). Over the years interacting with the world, basic sensory-motor representations about the world and about the self (analogue) become increasingly differentiated inner representations of the relationship between self and others (social roles, scripts, theory of mind). A basal self-experience in the first-person perspective (phenomenologically) becomes a reflective subject-object relationship over the years and finally a 3rd person-perspective of the self and of the world. This goes along with the development of cortical midline structures, which are involved in the differentiation of self and others and make up a large part of the DMN. Doering et al. (2012) see the anterior parts (ACC) linked to the current self-experience (1st person perspective, mental self), whereas the parietal parts (PCC) of the midline structures of the brain are linked to a feeling of identity (personality, identity, 3rd person perspective, higher moral concepts). This higher mental perspective sets a sense of personality into time and space and integrates information from inside and outside. The temporo-parietal junction (TPJ) is particularly involved in establishing a stable self-experience.

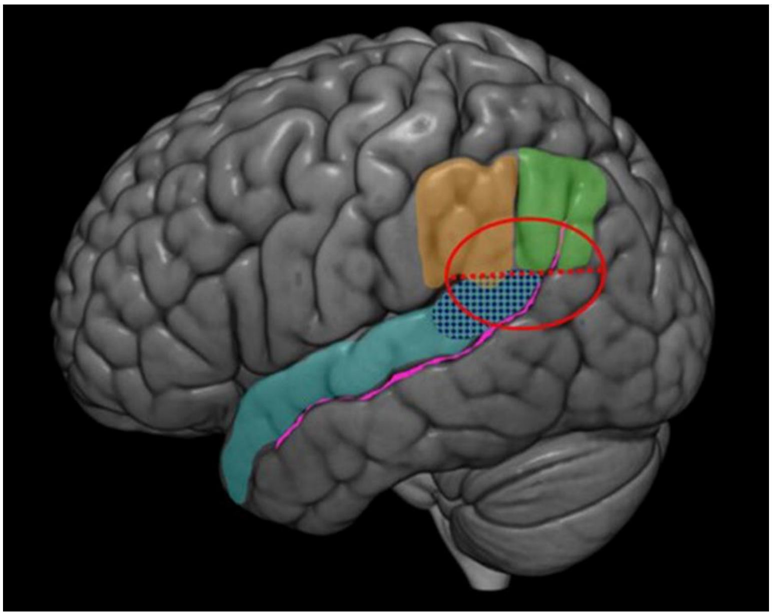


Figure 7: The temporo-parietal connection (Quesque & Brass, 2019).

The temporo-parietal connection (TPJ) is attributed to various functions: social-cognitive functions, self/non-self-differentiation (Bukowski, Lamm, Zeigler-Hill, & Shackelford, 2017) as well as a function that is responsible for switching attention (Serences et al., 2005), language processing (Pulvermüller, 2005), Episodic Memory (Cabeza, Ciaramelli, & Moscovitch, 2012), Moral Judgment (L. Young et al., 2010), Theory of mind (Saxe & Kanwisher, 2003), Empathy (Lamm et al., 2011), and Body Perception (Blanke & Metzinger, 2009).

Mars and colleagues were able to find three functionally distinguishable parts of the TPJ in a structural and functional connectivity analysis that were linked to the following networks:

- The Inferior parietal lobe with the executive network.
- The anterior part of the ventral TPJ with the Salience network.
- The posterior part of the ventral TPJ with the Default Mode Network.

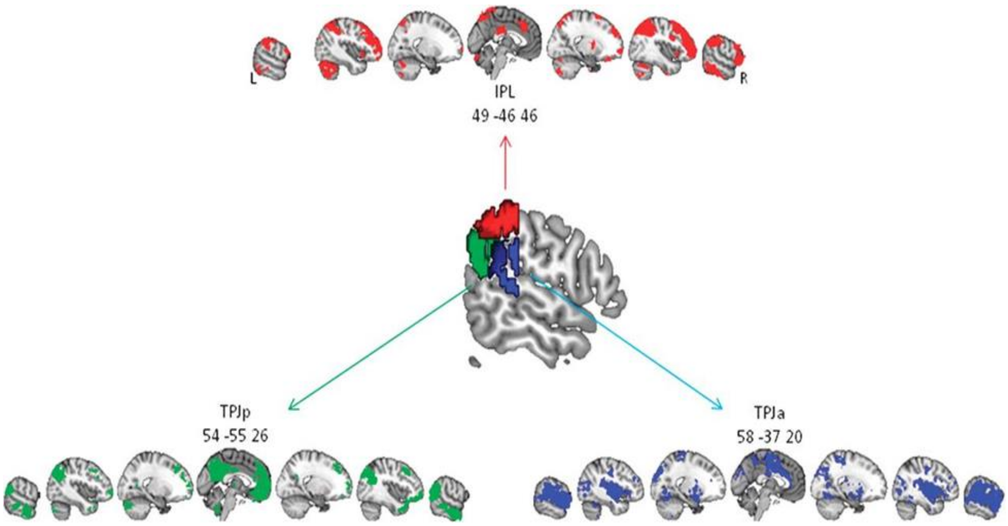


Figure 8: Functional areas of the TPJ (Mars et al., 2012)

The training of this central “pivot point” will probably change the interaction of the three networks. Not only meditation experts show this change, but also borderline patients after 8 weeks of mindfulness training show these changes (study 3).

4. The instability of self-identity as a core pathology of borderline personality disorder

Finally, we want to present the etiological model of borderline disorder according to Meares in order to clarify this theoretical model even further (Meares, 2012). Meares (2012) refers to Pierre Janet (1889) (vgl. Van der Hart & Horst, 1989) and describes an underlying instability of self-identity as the core psychopathology of borderline personality: caused by repeated or ongoing interruption of mother-child interaction (development traumatization) the analog and symbolic level of self-experience in the child cannot be integrated. Therefore, an integration into a coherent sense of self becomes impossible and the feeling of identity remains instable. Meares describes this further on the cortical level as an anti-correlation of the executive and default mode network, which form a common neural basis for self-consciousness. Both are only one half of the self-system ("only with a subject there is an object"). Meares sees the neural basis of incoherent self-esteem in the midline structures of the DMN and especially in the TPJ. Nijenhuis et al. (2018) describe the dissociation of identity in different parts as a creative solution in dealing with too much stress. If this is ongoing and chronic, it will make psychopathological symptoms ("enacted"). The divided self is seen in reduced body perception (depersonalization), reduced self-identity (feelings of emptiness) and identity diffusion, which are typical of borderline patients. Stress increases the de-coupling, resulting in a sudden reduction in mentalization capacity, memory disturbances and a change to a lower state of consciousness and a narrowed field of perception, as well as a narrowing of the visual field.

Nijenhuis et al. (2018) define mental illness by a lack of synthesis of action modes (personification, presentation: orientation in time, symbolization and realization). Like Meares and Nijenhuis, Muller describes borderline psychopathology by the concept of split or dissociation as well (Muller, 1992). The fragmentation of extreme action patterns and lower levels of consciousness (idealization and devaluation, proximity, and distance) cannot be integrated and remain chronically dissociated. Extreme polarized action impulses can only be acted out in an alternated way to stay dissociated separately from each other. Therefore, the basic psychopathology is an integration failure, a disturbance in the maturation of personality. (Muller, 1992)(Muller, 1992)(Muller, 1992)(Muller, 1992)(Muller, 1992)Pierre Janet describes these memory traces as fixated, which were developed by traumatic dissociation, as they lost their capacity to assimilate new experiences (Van der Hart & Horst, 1989). In contrast to dissociative identity disorders, however, the experience of a central self-identity is preserved in borderline patients. However, this integration is unstable and dis-integrates under stress into dissociated self-identities (modes), which show up along natural break points of basic action patterns (escape, attack, everyday management, etc.). Only under extreme stress will the self-identity temporarily disintegrate into psychotic experience. Borderline symptoms such as identity disorder, feelings of emptiness, loneliness, fear of abandonment are all expressions of this underlying disorganized bonding experience (instability). The hypersensitivity of borderline patients to recognize social exclusion situations (hypervigilance), and the rapid switching between hyperarousal (attack, tantrums, etc.) and hypo-arousal or dissociation (feeling nothing, de-realization, depersonalization, psychotic experience, inner voices) also indicate this central des-integrated core symptomatology.

Following this theoretical concept, what kind of treatment for borderline patients will be suitable? In addition to behavioral therapy (interventions to improve executive functions), it seems also necessary to treat the underlying unstable self-experience (DMN, Island, Precuneus, TPJ, network interaction).

The aim of the therapy must be to change the basal reflexive survival patterns (attack flight, etc.) into higher integrated, more differentiated (impulse-controlled) patterns of action. For this purpose, the division (dissociation) of the patterns of action must be overcome and ambiguity and unpleasant feelings must be tolerated. After that, mentalization becomes possible (integration into a higher level of consciousness).

While Linehan called the DBT's goal "walking the middle path" and recognized mindfulness as the basis of all skills, she never explicitly described dissociation as the underlying core pathology of borderline disorder. This step was then made up in 2009 in the extended psychopathology model of DBT. There, the concept of dissociation was included as a central psychopathological factor (Bohus, 2009).

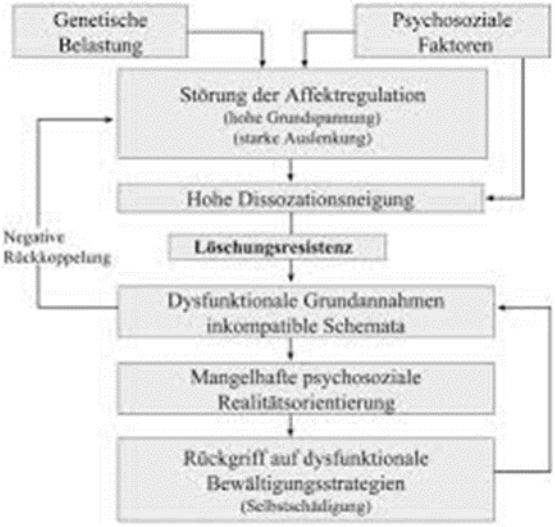


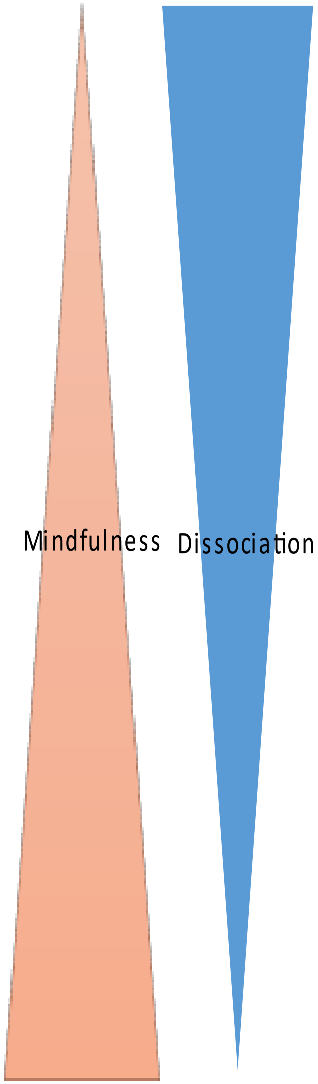
Figure 9: Model of affect regulation (Bohus, 2009)

If we consider the borderline personality disorder as an is insufficient personality maturation (disintegrated self-modes), then mindfulness with its integrative power is the appropriate therapeutic intervention: by practicing a describing and non-judgmental open attitude in mindfulness (meta-cognition), there arises a bonding (confrontation) to inner self-states, which has already in itself healing effects. The reduction of dissociation through mindfulness ultimately leads to a stronger coherence of polar modes of action or self-modes. After being able to look at fixed partial aspects of the self without acting out, there arises a decoupling of evaluation and identification processes (de-fusion or de-reification) and a reorientation to a sensory focus is established (embodiment, sensory level, mindfulness focus). This is done by a repeated switching between a physical-sensory focus and mental concepts. Like the re-processing in EMDR (eye movement desensitization and reprocessing) with the gaze outside, the switching of inner focus in meditation (sensory versus mental) has both an expanding and an integrative effect. Contrasting mental patterns of action and thought (black-and-white thinking) can thus gradually be tolerated and integrated into a higher mental state of consciousness with expanded possibilities for action (a higher concept (Nijenhuis et al., 2018). Instead of "either-or-patterns”) a higher level of integration emerges. This healing process is initiated by empathy (attention) and by an open, non-judgmental attitude, which is practiced repetitively in meditation.

In Figure 10 we integrate the theoretical model of Meares/Nijenhuis with the therapeutic model of DBT. Using this model, the effect of DBT skills in relation to the underlying treatment of self-disorder and the influence of mindfulness as an antidote of dissociation on underlying neural brain activity are made visible.

The results of insufficient self-integration in borderline patients lead to chronic feelings of loneliness. But instead of using mindfulness (turning inside), borderline patients turn to other people to reduce these feelings of loneliness. Since this is a mechanism from early childhood and thus for adults dysfunctional, overly dependent relationship patterns (idealization) and a constant fear of bonding loss arises (hypervigilance for social exclusion, rejection). This is a re-enactment of the traumatic situation (attachment loss). Due to the constant threat of losing bondage, a hypervigilance for social stimuli (triggers) with highly sensitized stress responses (high stress) is created.

Under **high stress (tension > 70%),** the fragile mental self-integration breaks down into the basic sensory-motor experience modes of “attack” and “defense”. This action mode is reflexive and impulsive. The sense of time is lost, and the main goal is to secure survival. Therefore, perception is narrowed and the perception of harmful clues in the outside is increased (hypersensitivity, paranoia). There is a high impulse to act (high muscle tone) and a reduction of body perception against possible injury (reduction of pain perception). In this re-enactment of massive threat, flight-and-fight patterns, freezing or even dying or murder is a possible way out of this perceived bottleneck situation (suicide/murderer).



Stresslevel (DBT)	DBT Skills (therapeutic interventions)	Theory (Meares/Nijehuis)	Neuronal Level
70-100% (high)	Stresstolerance skills Anti-dissociation skills Sensumotoric level power und faint Sensumotoric behavior ameliorating body perception	Sensu-motoric Level Low level of consciousness no perspective, no time, fixed ideas Reflex action 1. person perspective model learning	Boosting prefrontal activity (enhanced inhibition) Basal ganglions
50-70% (medium)	Emotion regulation skills Symbolic/language/interpersonal skills Emotionsregulation by the integration of mental and behavioral level Orientierung over time (being able to wait/put-off). needs (goals) can be regulated by language in social context Regulation of self/ other perspective Acceptance of self/others	Semantic level Subject Object Two-dimensional perspective Time and Space Perception 2. Person Perspektive Reflective action	Ameliorated emotion regulation by strengthening the limbic cortical axis medial prefrontal Cortex /ACC ↑ Amygdala ↓ prefrontal cortex (Inhibition) ↑ Symbolization Higher integrative brain regions: TPJ, IFG, Broca Areal
0-50% (low)	Mindfulness Skills Mental Level Integration von dissociated neuronal networks Meta-Cognitive Skills State of Being Integration of self/other Act on Values	Integrative behavior Three-dimentional Communikative egalitarian Consciousness Highest Integration 3. Person Perspektive	Training of all three neuronalen Networks: DMN PFC SN Integration area: Precuneus, TPJ

Figure 10: Integration Model of DBT Interventions/Theory/Neuronal Level

In medium areas of tension (50-70%), a higher level of consciousness (symbolic, linguistic) is possible. An expanded perception of "me and the world" is possible. Both the internal relationship to oneself (mental <-> physical) and to others (subject <-> object) can be regulated more easily.

In the low-tension range (0-50%), a complete orientation (no action) of the "being-aspects" of the body is possible (embodiment in the here and now). The strong connection to the body allows the mental problem-solving skill to become as flexible and symbolized as possible (mental action). The integration capacity is highest and repeated mindfulness training ultimately reduces psychopathology (splits) at the mental (neuronal) level. This leads to a stable self-integration and complete healing of the self-fragmentation.

Mindfulness processes play a therapeutic role in all three areas of tension and help to expand the ability of the self to act:

> 70%: Get orientation about current state and can stop reflexive behavior to reduce feelings of helplessness.

50-70%: Mental representation and modelling. Learn to acknowledge emotions and strong senses of the body (tolerance = not act/impulse control). To recognize and tolerate others (subject-object relationship). Clarifying own needs and goals. Create a contact with others (reflective goal-oriented action). Dealing with shame and guilt.

0-50%: The self-fragmentation is eliminated by mental practice. The result is an integration of action modes at a high mental level (highest level of consciousness). Through the subject-subject relationship between self and world, there is a stable external and internal orientation and a value-oriented action. Empathic experience (feelings of attachment) lead to a reduction of anxiety and loneliness and mental fixations can be overcome.

5. Conclusions

Mindfulness is the basis of all skills: this dissertation dealt empirically and theoretically with this topic and generated new hypotheses. Based on three empirical studies, we were able to find initial evidence that an 8-week mindfulness training is effective in borderline patients: The reduction of general psychopathological symptoms (SCL-90-R) correlated with specific functional changes in activity in TPJ and supramarginal gyrus. Functional changes in the TPJ and supramarginal gyrus were found in meditation experts. The study results were discussed in the last section in relation to the current state of research and then inductively classified into a new overall model of psychopathology. Taken together, our study results in connection with theoretical models of borderline psychopathology support Marsha Linehan's statement: Mindfulness is the basis of all skills.

6. Critical reflection of the work

The validity of our three studies, their results and conclusions are reduced by many factors, which we summarize here: Overall, the quality of the investigations was severely limited by time, financial and personal limitations. The results of our studies are based on a small number of subjects and therefore have low statistical power/reduced validity.

Similarly, the structure of the investigation showed considerable flaws: the most serious mistake was to place the questionnaires between the investigation of mindfulness and the examination of executive functions. The results of the second study (does a mindfulness exercise before the executive task change performance or neural activation?) are not clearly attributable to the mindfulness exercise but may have been caused by the break or the influence of the questionnaires. The subjects were not randomized and differed in age and other variables (e. g. IQ).

The study design was not blinded and therefore placebo or Rosenthal effects cannot be excluded. Due to the author's personal background with experience in meditation, the work was probably subject to a "confirmation bias" as well as other cognitive biases. The main variable (long-term meditation experience) of the control group studied (meditation experienced) showed a significant age difference, which could not be avoided, as there were no young people with many years of meditation experience. The samples were taken from a clinical setting that included a variety of uncontrollable variables (mindfulness in DBT setting) in addition to mindfulness. Similarly, the comparison of two samples from two different settings (inpatient or outpatient) in the study design is incorrect and reduces the significance of the results. Outpatient behavioral therapy in study 3 has not been further defined, so adherence is not guaranteed.

In the discussion section, the individual results of the studies are generalized to changes in the neural networks. This generalization is derived from a variety of theoretical models and research results. This model is therefore purely hypothetical and not empirically tested but can shed new insights and stimulate further research.

Our measuring method (NIRS) could only detect superficial activation changes of the brain (up to 3 cm). The mindfulness paradigm (focus on auditory stimulus in mindful posture) was performed only mentally. It was therefore not possible to check whether our subjects (especially the borderline patients) could implement this instruction at all. Patients were often tense and stressed during the examination situation.

The group of meditation-experienced experts probably included a pre-selected group of people who had a special lifestyle (regularity, possibly health-oriented) or had special personality traits (conscientious, introverted, etc.). The influence of these covariates on our results could not be adequately controlled.

It should therefore be recommended to repeat the studies in an improved and blinded design. Patients should be randomized, and a comparable control condition should be created, such as e. g. a mindfulness intervention over 8 weeks without further therapy compared to a control group with a relaxation intervention.

The empirical study of meditation is difficult overall, as it is a complex mental training that affects different brain networks and ultimately might change the entire functioning of the brain (cf. "embodied mind" (Damasio, 2010)). It is not easy to operationalize these broad concepts and measure them validly. However, research on underlying neural functions can provide important insights into consciousness, self-perception, and personality (narrative self) that can significantly improve therapeutic treatment.

It is equally challenging to capture the neural changes in personality disorders. Modern imaging and analysis techniques (e. g. fMRI, independence analyses or dynamic causal modelling (DCM)) make it possible to research and answer more complex questions in a more differentiated way. This is important: further research results are urgently needed to be able to diagnose psychopathological developments in patients earlier and to make theories about self and personality development empirically verifiable.

For patient treatment, this basic research means a lot to make new therapeutic interventions more effective, such as e. g. mindfulness interventions could be implemented more specifically or could be used as a prevention method (e.g., mindfulness training in schools). Further research is needed here to make meditation even easier for patients to learn, such as e. g. a neural feedback training, or the use of non-invasive brain stimulation methods to possibly increase the effect of mental training. Behavioral therapists should also be trained more specifically in mindfulness techniques to be able to contact their patients in different modes of action (attachment) as a prerequisite for change. Mindfulness training for therapists as a basic skill in therapeutic training would be an effective and feasible first step.

6. References

Abreu, N., Argollo, N., Oliveira, F., Cardoso, A. L., Bueno, J. L. O., & Xavier, G. F. (2013). Semantic and phonologic verbal fluency tests for adolescents with ADHD. *Clinical Neuropsychiatry, 10*(2).

Allen, M., Dietz, M., Blair, K. S., van Beek, M., Rees, G., Vestergaard-Poulsen, P., . . . Roepstorff, A. (2012). Cognitive-affective neural plasticity following active-controlled mindfulness intervention. *Journal of Neuroscience, 32*(44), 15601-15610.

Alvarez, J. A., & Emory, E. (2006). Executive function and the frontal lobes: a meta-analytic review. *Neuropsychology review, 16*(1), 17-42.

Anderson, N. D., Lau, M. A., Segal, Z. V., & Bishop, S. R. (2007). Mindfulness-based stress reduction and attentional control. *Clinical Psychology & Psychotherapy, 14*(6), 449-463.

APA. (2012). DSM-5 Development. Personality Disorders. In.

Aschenbrenner, S., Tucha, O., & Lange, K. W. (2000). *Regensburger Wortflüssigkeits-Test: RWT*: Hogrefe, Verlag für Psychologie.

Babcock, L., & Vallesi, A. (2017). Are simultaneous interpreters expert bilinguals, unique bilinguals, or both? *Bilingualism: Language and Cognition, 20*(2), 403-417.

Baer, R. A., Smith, G. T., & Allen, K. B. (2004). Assessment of mindfulness by self-report: The Kentucky Inventory of Mindfulness Skills. *Assessment, 11*(3), 191-206.

Baum, C., Kuyken, W., Bohus, M., Heidenreich, T., Michalak, J., & Steil, R. (2010). The psychometric properties of the Kentucky Inventory of Mindfulness Skills in clinical populations. *Assessment, 17*(2), 220-229.

Benuzzi, F., Lui, F., Duzzi, D., Nichelli, P. F., & Porro, C. A. (2008). Does it look painful or disgusting? Ask your parietal and cingulate cortex. *Journal of Neuroscience, 28*(4), 923-931.

Berkovich-Ohana, A., Dor-Ziderman, Y., Trautwein, F.-M., Schweitzer, Y., Nave, O., Fulder, S., & Ataria, Y. (2020). The hitchhiker's guide to neurophenomenology–The case of studying self boundaries with meditators. *Frontiers in Psychology, 11*, 1680.

Berkovich-Ohana, A., Glicksohn, J., & Goldstein, A. (2012). Mindfulness-induced changes in gamma band activity – Implications for the default mode network, self-reference and attention. *Clinical Neurophysiology, 123*(4), 700-710. doi:https://doi.org/10.1016/j.clinph.2011.07.048

Berkovich-Ohana, A., Glicksohn, J., & Goldstein, A. (2014). Studying the default mode and its mindfulness-induced changes using EEG functional connectivity. *Social cognitive and affective neuroscience, 9*(10), 1616-1624.

Binks, C., Fenton, M., McCarthy, L., Lee, T., Adams, C. E., & Duggan, C. (2006). Psychological therapies for people with borderline personality disorder. *Cochrane Database of Systematic Reviews*(1).

Bishop, S. R., Lau, M., Shapiro, S., Carlson, L., Anderson, N. D., Carmody, J., . . . Velting, D. (2004). Mindfulness: A proposed operational definition. *Clinical psychology: Science and practice, 11*(3), 230-241.

Blanke, O., & Arzy, S. (2005). The out-of-body experience: disturbed self-processing at the temporo-parietal junction. *The Neuroscientist, 11*(1), 16-24.

Blanke, O., & Metzinger, T. (2009). Full-body illusions and minimal phenomenal selfhood. *Trends in cognitive sciences, 13*(1), 7-13.

Boccia, M., Piccardi, L., & Guariglia, P. (2015). The meditative mind: a comprehensive meta-analysis of MRI studies. *BioMed research international, 2015*.

Bohlmeijer, E., Prenger, R., Taal, E., & Cuijpers, P. (2010). The effects of mindfulness-based stress reduction therapy on mental health of adults with a chronic medical disease: a meta-analysis. *J Psychosom Res, 68*(6), 539-544. doi:10.1016/j.jpsychores.2009.10.005

Bohus, M. (2009). Borderline-Persönlichkeitsstörung. In S. S. Margraf J. (Ed.), *Lehrbuch der Verhaltenstherapie.* . Berlin, Heidelberg: Springer.

Bohus, M., & Bathruff, H. (2000). Dialektisch Behaviorale Therapie der Borderline-Störung im stationären Setting. *PiD-Psychotherapie im Dialog, 1*(04), 55-66.

Bohus, M., & Huppertz, M. (2006). Wirkmechanismen achtsamkeitsbasierter Psychotherapie. *Zeitschrift für Psychiatrie, Psychologie und Psychotherapie, 54*(4), 265-276.

Bohus, M., Kleindienst, N., Limberger, M. F., Stieglitz, R.-D., Domsalla, M., Chapman, A. L., . . . Wolf, M. (2009). The short version of the Borderline Symptom List (BSL-23): development and initial data on psychometric properties. *Psychopathology, 42*(1), 32-39.

Bohus, M., & Schmahl, C. (2006). Psychopathologie und Therapie der Borderline Persönlichkeitsstörung. Dtsch Aerztebl 103 (49) A 3345–52. In.

Bowlby, J. (1979). The Bowlby-Ainsworth attachment theory. *Behavioral and Brain Sciences, 2*(4), 637-638. doi:10.1017/S0140525X00064955

Bozzatello, P., Morese, R., Valentini, M. C., Rocca, P., Bosco, F., & Bellino, S. (2019). Autobiographical memories, identity disturbance and brain functioning in patients with borderline personality disorder: An fMRI study. *Heliyon, 5*(3), e01323.

Brefczynski-Lewis, J. A., Lutz, A., Schaefer, H. S., Levinson, D. B., & Davidson, R. J. (2007). Neural correlates of attentional expertise in long-term meditation practitioners. *Proceedings of the national Academy of Sciences, 104*(27), 11483-11488.

Brewer, J. A., Worhunsky, P. D., Gray, J. R., Tang, Y.-Y., Weber, J., & Kober, H. (2011). Meditation experience is associated with differences in default mode network activity and connectivity. *Proceedings of the National Academy of Sciences, 108*(50), 20254-20259.

Broca, P. (1861). Remarks on the seat of the faculty of articulated language, following an observation of aphemia (loss of speech). *Bulletin de la Société Anatomique, 6, 330-57., 6*, 330-357.

Brown, K. W., Ryan, R. M., & Creswell, J. D. (2007). Mindfulness: Theoretical foundations and evidence for its salutary effects. *Psychological inquiry, 18*(4), 211-237.

Bukowski, H., Lamm, C., Zeigler-Hill, V., & Shackelford, T. (2017). Temporoparietal junction. *Encyclopedia of Personality and Individual Differences*, 1-5.

Bullis, J. R., Boettcher, H., Sauer-Zavala, S., Farchione, T. J., & Barlow, D. H. (2019). What is an emotional disorder? A transdiagnostic mechanistic definition with implications for assessment, treatment, and prevention. *Clinical Psychology: Science and Practice, 26*(2), e12278.

Cabeza, R., Ciaramelli, E., & Moscovitch, M. (2012). Cognitive contributions of the ventral parietal cortex: an integrative theoretical account. *Trends in cognitive sciences, 16*(6), 338-352.

Carmody, J., & Baer, R. A. (2008). Relationships between mindfulness practice and levels of mindfulness, medical and psychological symptoms and well-being in a mindfulness-based stress reduction program. *Journal of behavioral medicine, 31*(1), 23-33.

Chan, D., & Woollacott, M. (2007). Effects of level of meditation experience on attentional focus: is the efficiency of executive or orientation networks improved? *The Journal of Alternative and Complementary Medicine, 13*(6), 651-658.

Cheavens, J. S., Strunk, D. R., & Chriki, L. (2012). A comparison of three theoretically important constructs: what accounts for symptoms of borderline personality disorder? *J Clin Psychol, 68*(4), 477-486. doi:10.1002/jclp.20870

Chiesa, A., Calati, R., & Serretti, A. (2011). Does mindfulness training improve cognitive abilities? A systematic review of neuropsychological findings. *Clinical Psychology Review, 31*(3), 449-464. doi:https://doi.org/10.1016/j.cpr.2010.11.003
Cohen, J. (1988). Statistical power analysis for the social sciences.
Colzato, L. S., Szapora, A., & Hommel, B. (2012). Meditate to create: the impact of focused-attention and open-monitoring training on convergent and divergent thinking. *Frontiers in psychology, 3*, 116.
Cui, X., Bray, S., Bryant, D. M., Glover, G. H., & Reiss, A. L. (2011). A quantitative comparison of NIRS and fMRI across multiple cognitive tasks. *Neuroimage, 54*(4), 2808-2821.
Cui, X., Bray, S., & Reiss, A. L. (2010). Functional near infrared spectroscopy (NIRS) signal improvement based on negative correlation between oxygenated and deoxygenated hemoglobin dynamics. *Neuroimage, 49*(4), 3039-3046.
Damasio, A. (2010). Self Comes to Mind: Constructing the Conscious Brain by Antonio Damasio. In: Goodreads.
David, A. S. (1999). Auditory hallucinations: phenomenology, neuropsychology and neuroimaging update. *Acta Psychiatrica Scandinavica, 99*(s395), 95-104. doi:10.1111/j.1600-0447.1999.tb05988.x
Deepeshwar, S., Vinchurkar, S. A., Visweswaraiah, N. K., & Nagendra, H. R. (2015). Hemodynamic responses on prefrontal cortex related to meditation and attentional task. *Frontiers in systems neuroscience, 8*, 252.
Deppermann, S., Vennewald, N., Diemer, J., Sickinger, S., Haeussinger, F. B., Notzon, S., . . . Zwanzger, P. (2014). Does rTMS alter neurocognitive functioning in patients with panic disorder/agoraphobia? An fNIRS-based investigation of prefrontal activation during a cognitive task and its modulation via sham-controlled rTMS. *BioMed research international, 2014*.
Derogatis, L. (1977). SCL-90-R (questionnaire form). *Administration, scoring and procedures manual, 1*.
Diagnostic and statistical manual of mental disorders (DSM-5). (2013). American Psychiatric Association.
Dieler, A. C., Tupak, S. V., & Fallgatter, A. J. (2012). Functional near-infrared spectroscopy for the assessment of speech related tasks. *Brain and language, 121*(2), 90-109.
Dilling, H., & Freyberger, H. J. (2012). Taschenführer zur ICD-10-Klassifikation psychischer Störungen. *Huber, Bern*.
Ding, X., Tang, Y.-Y., Cao, C., Deng, Y., Wang, Y., Xin, X., & Posner, M. I. (2015). Short-term meditation modulates brain activity of insight evoked with solution cue. *Social cognitive and affective neuroscience, 10*(1), 43-49.
Dinn, W. M., Harris, C. L., Aycicegi, A., Greene, P. B., Kirkley, S. M., & Reilly, C. (2004). Neurocognitive function in borderline personality disorder. *Progress in neuro-psychopharmacology and biological psychiatry, 28*(2), 329-341.
Doering, S., Enzi, B., Faber, C., Hinrichs, J., Bahmer, J., & Northoff, G. (2012). Personality functioning and the cortical midline structures--an exploratory FMRI study. *PloS one, 7*(11), e49956-e49956. doi:10.1371/journal.pone.0049956
Doll, A., Hölzel, B. K., Boucard, C. C., Wohlschläger, A. M., & Sorg, C. (2015). Mindfulness is associated with intrinsic functional connectivity between default mode and salience networks. *Frontiers in human neuroscience, 9*, 461.
Dor-Ziderman, Y., Berkovich-Ohana, A., Glicksohn, J., & Goldstein, A. (2013). Mindfulness-induced selflessness: a MEG neurophenomenological study. *Frontiers in human neuroscience, 7*, 582.
Dorjee, D. (2010). Kinds and dimensions of mindfulness: Why it is important to distinguish them. *Mindfulness, 1*(3), 152-160.

Ehlis, A.-C., Haeussinger, F. B., Gastel, A., Fallgatter, A. J., & Plewnia, C. (2016). Task-dependent and polarity-specific effects of prefrontal transcranial direct current stimulation on cortical activation during word fluency. *Neuroimage, 140*, 134-140.

Ehlis, A.-C., Schneider, S., Dresler, T., & Fallgatter, A. J. (2014). Application of functional near-infrared spectroscopy in psychiatry. *Neuroimage, 85*, 478-488.

Ehlis, A. C., Herrmann, M. J., Plichta, M. M., & Fallgatter, A. J. (2007). Cortical activation during two verbal fluency tasks in schizophrenic patients and healthy controls as assessed by multi-channel near-infrared spectroscopy. *Psychiatry Research: Neuroimaging, 156*(1), 1-13.

Ehlis, A. C., Herrmann, M. J., Plichta, M. M., & Fallgatter, A. J. . (2007). Cortical activation during two verbal fluency tasks in schizophrenic patients and healthy controls as assessed by multi-channel near-infrared spectroscopy. *Psychiatry Research: Neuroimaging,, 156*(1), 1-13.

Elices, M., Pascual, J. C., Portella, M. J., Feliu-Soler, A., Martín-Blanco, A., Carmona, C., & Soler, J. (2016). Impact of mindfulness training on borderline personality disorder: A randomized trial. *Mindfulness, 7*(3), 584-595.

Erb, M., Ehlis, A.-C., Ernst, L., Chieu, V.-H. N. Q., Triet, M. T. T., Fallgatter, A., . . . Perris, M. C. (2011). Altered Visual and Auditory Processing in Sunyata Meditation: a combined NIRS and EEG Experiment.

Esch, T. (2014). The neurobiology of meditation and mindfulness. In *Meditation–neuroscientific approaches and philosophical implications* (pp. 153-173): Springer.

Ethofer, T., Anders, S., Erb, M., Herbert, C., Wiethoff, S., Kissler, J., . . . Wildgruber, D. (2006). Cerebral pathways in processing of affective prosody: a dynamic causal modeling study. *Neuroimage, 30*(2), 580-587.

Fan, Y., Duncan, N. W., de Greck, M., & Northoff, G. (2011). Is there a core neural network in empathy? An fMRI based quantitative meta-analysis. *Neuroscience & Biobehavioral Reviews, 35*(3), 903-911.

Farb, N. A. S., Anderson, A. K., Mayberg, H., Bean, J., McKeon, D., & Segal, Z. V. (2010). Minding one's emotions: mindfulness training alters the neural expression of sadness. *Emotion, 10*(1), 25.

Farb, N. A. S., Segal, Z. V., Mayberg, H., Bean, J., McKeon, D., Fatima, Z., & Anderson, A. K. (2007). Attending to the present: mindfulness meditation reveals distinct neural modes of self-reference. *Social cognitive and affective neuroscience, 2*(4), 313-322.

Farrés, C. i., C., E., M., S., J., Domínguez-Clavé, E., Martín-Blanco, A., Pomarol-Clotet, E., & ... & Pascual, J. C. (2019). Effects of mindfulness training on the default mode network in borderline personality disorder. . *Clinical psychology & psychotherapy, 26*(5), 562-571.

FeldmanHall, O., Mobbs, D., & Dalgleish, T. (2014). Deconstructing the brain's moral network: dissociable functionality between the temporoparietal junction and ventro-medial prefrontal cortex. *Social cognitive and affective neuroscience, 9*(3), 297-306.

Feliu-Soler, A., Pascual, J. C., Borràs, X., Portella, M. J., Martín-Blanco, A., Armario, A., . . . Soler, J. (2014). Effects of dialectical behaviour therapy-mindfulness training on emotional reactivity in borderline personality disorder: Preliminary results. *Clinical psychology & psychotherapy, 21*(4), 363-370.

Fishburn, F. A., Ludlum, R. S., Vaidya, C. J., & Medvedev, A. V. (2019). Temporal derivative distribution repair (TDDR): a motion correction method for fNIRS. *Neuroimage, 184*, 171-179.

Fonagy, P., Luyten, P., & Allison, E. (2015). Epistemic petrification and the restoration of epistemic trust: A new conceptualization of borderline personality disorder and its psychosocial treatment. *Journal of Personality Disorders, 29*(5), 575-609.

Forstmann, B. U., van den Wildenberg, W. P. M., & Ridderinkhof, K. R. (2008). Neural mechanisms, temporal dynamics, and individual differences in interference control. *Journal of Cognitive Neuroscience, 20*(10), 1854-1865.

Fox, K. C., Dixon, M. L., Nijeboer, S., Girn, M., Floman, J. L., Lifshitz, M., . . . Christoff, K. (2016). Functional neuroanatomy of meditation: A review and meta-analysis of 78 functional neuroimaging investigations. *Neurosci Biobehav Rev, 65*, 208-228. doi:10.1016/j.neubiorev.2016.03.021

Fox, K. C., Dixon, M. L., Nijeboer, S., Girn, M., Floman, J. L., Lifshitz, M., . . . Christoff, K. (2016). Functional neuroanatomy of meditation: A review and meta-analysis of 78 functional neuroimaging investigations. *Neuroscience & Biobehavioral Reviews, 65*, 208-228.

Fox, K. C. R., Nijeboer, S., Dixon, M. L., Floman, J. L., Ellamil, M., Rumak, S. P., . . . Christoff, K. (2014). Is meditation associated with altered brain structure? A systematic review and meta-analysis of morphometric neuroimaging in meditation practitioners. *Neuroscience & Biobehavioral Reviews, 43*, 48-73. doi:https://doi.org/10.1016/j.neubiorev.2014.03.016

Franke, G. H. D., L.R. (2002). *SCL-90-R: symptom-Checkliste von LR Derogatis: deutsche version: manual.* : Beltz Test.

Freiherr, J., Lundström, J. N., Habel, U., & Reetz, K. (2013). Multisensory integration mechanisms during aging. *Frontiers in human neuroscience, 7*, 863.

Frewen, J., Finucane, C., Savva, G. M., Boyle, G., Coen, R. F., & Kenny, R. A. . (2013). Cognitive function is associated with impaired heart rate variability in ageing adults: the Irish longitudinal study on ageing wave one results. *Clinical Autonomic Research, 23*(6), 313-323.

Frick, C., Lang, S., Kotchoubey, B., Sieswerda, S., Dinu-Biringer, R., Berger, M., . . . Barnow, S. (2012). Hypersensitivity in borderline personality disorder during mindreading. *PloS one, 7*(8), e41650-e41650. doi:10.1371/journal.pone.0041650

Gallant, S. N. (2016). Mindfulness meditation practice and executive functioning: Breaking down the benefit. *Consciousness and cognition, 40*, 116-130.

Gard, T., Hölzel, B. K., & Lazar, S. W. (2014). The potential effects of meditation on age-related cognitive decline: a systematic review. *Annals of the New York Academy of Sciences, 1307*, 89.

Garrison, K. A., Zeffiro, T. A., Scheinost, D., Constable, R. T., & Brewer, J. A. (2015). Meditation leads to reduced default mode network activity beyond an active task. *Cognitive, Affective, & Behavioral Neuroscience, 15*(3), 712-720.

Gilbert, P., & Plata, G. (2013). *Compassion focused therapy*: Junfermann Verlag GmbH.

Gilbert, P., & Procter, S. (2006). Compassionate mind training for people with high shame and self-criticism: overview and pilot study of a group therapy approach. *Clinical psychology & psychotherapy, 13*(6), 353-379. doi:10.1002/cpp.507

Goldberg, E. (2018). *Creativity: The human brain in the age of innovation*: Oxford University Press.

Goldstein, K. E., Hazlett, E. A., New, A. S., Haznedar, M. M., Newmark, R. E., Zelmanova, Y., . . . Siever, L. J. (2009). Smaller superior temporal gyrus volume specificity in schizotypal personality disorder. *Schizophrenia Research, 112*(1), 14-23. doi:https://doi.org/10.1016/j.schres.2009.04.027

Golynkina, K., & Ryle, A. (1999). The identification and characteristics of the partially dissociated states of patients with borderline personality disorder. *British Journal of Medical Psychology, 72*(4), 429-445. doi:10.1348/000711299160103

Gotink, R. A., Chu, P., Busschbach, J. J., Benson, H., Fricchione, G. L., & Hunink, M. M. (2015). Standardised mindfulness-based interventions in healthcare: an overview of systematic reviews and meta-analyses of RCTs. *PloS one, 10*(4), e0124344.

Goyal, M., Singh, S., Sibinga, E. M. S., Gould, N. F., Rowland-Seymour, A., Sharma, R., . . . Shihab, H. M. (2014). Meditation programs for psychological stress and well-being: a systematic review and meta-analysis. *JAMA internal medicine, 174*(3), 357-368.

Grant, J. A., Courtemanche, J., Duerden, E. G., Duncan, G. H., & Rainville, P. (2010). Cortical thickness and pain sensitivity in zen meditators. *Emotion, 10*(1), 43.

Gratz, K. L., & Roemer, L. (2008). The relationship between emotion dysregulation and deliberate self-harm among female undergraduate students at an urban commuter university. *Cognitive behaviour therapy, 37*(1), 14-25.

Gross, J. (Ed.) (2007). *Handbook of Emotion Regulation*: New York: Guilford Press.

Grossman, P., Niemann, L., Schmidt, S., & Walach, H. (2004). Mindfulness-based stress reduction and health benefits: A meta-analysis. *Journal of psychosomatic research, 57*(1), 35-43.

Guendelman, S., Medeiros, S., & Rampes, H. (2017). Mindfulness and emotion regulation: Insights from neurobiological, psychological, and clinical studies. *Frontiers in Psychology, 8*, 220.

Gundel, F., von Spee, J., Schneider, S., Haeussinger, F. B., Hautzinger, M., Erb, M., . . . Ehlis, A.-C. (2018). Meditation and the brain–Neuronal correlates of mindfulness as assessed with near-infrared spectroscopy. *Psychiatry Research: Neuroimaging, 271*, 24-33.

Gundel, F., von Spee, J., Schneider, S., Haeussinger, F. B., Hautzinger, M., Erb, M., . . . Ehlis, A. C. (2018). Meditation and the brain - Neuronal correlates of mindfulness as assessed with near-infrared spectroscopy. *Psychiatry Res Neuroimaging, 271*, 24-33. doi:10.1016/j.pscychresns.2017.04.002

Gunderson, J. G., Herpertz, S. C., Skodol, A. E., Torgersen, S., & Zanarini, M. C. (2018). Borderline personality disorder. *Nat Rev Dis Primers, 4*, 18029. doi:10.1038/nrdp.2018.29

Haegens, S., Händel, B. F., & Jensen, O. (2011). Top-down controlled alpha band activity in somatosensory areas determines behavioral performance in a discrimination task. *Journal of Neuroscience, 31*(14), 5197-5204.

Haeussinger, F. B., Dresler, T., Heinzel, S., Schecklmann, M., Fallgatter, A. J., & Ehlis, A. C. (2014). Reconstructing functional near-infrared spectroscopy (fNIRS) signals impaired by extra-cranial confounds: an easy-to-use filter method. *Neuroimage, 95*, 69-79.

Hamlin, E. (1983). Discourse in the Lankavatara Sutra. *Journal of Indian Philosophy, 11*, 267.

Harmelech, T., & Malach, R. (2013). Neurocognitive biases and the patterns of spontaneous correlations in the human cortex. *Trends in cognitive sciences, 17*(12), 606-615.

Harrison, B. J., Shaw, M., Yücel, M., Purcell, R., Brewer, W. J., Strother, S. C., . . . Pantelis, C. (2005). Functional connectivity during Stroop task performance. *Neuroimage, 24*(1), 181-191.

Hartig, J., & Moosbrugger, H. (2003). Die “ARES-Skalen” zur Erfassung der individuellen BIS-und BAS-Sensitivität. *Zeitschrift für Differentielle und Diagnostische Psychologie, 24*(4), 293-310.

Hasenkamp, W., & Barsalou, L. W. (2012). Effects of meditation experience on functional connectivity of distributed brain networks. *Frontiers in human neuroscience, 6*, 38.

Hasenkamp, W., Wilson-Mendenhall, C. D., Duncan, E., & Barsalou, L. W. (2012). Mind wandering and attention during focused meditation: a fine-grained temporal analysis of fluctuating cognitive states. *Neuroimage, 59*(1), 750-760.

Hayes, A. M., & Feldman, G. (2004). Clarifying the construct of mindfulness in the context of emotion regulation and the process of change in therapy. *Clinical Psychology: Science and Practice, 11*(3), 255-262.

Heeren, A., Van Broeck, N., & Philippot, P. (2009). The effects of mindfulness on executive processes and autobiographical memory specificity. *Behaviour research and therapy, 47*(5), 403-409.

Heinzel, S., Haeussinger, F. B., Hahn, T., Ehlis, A.-C., Plichta, M. M., & Fallgatter, A. J. (2013). Variability of (functional) hemodynamics as measured with simultaneous fNIRS and fMRI during intertemporal choice. *Neuroimage, 71*, 125-134.

Herpertz, S. C. (2011). Beitrag der Neurobiologie zum Verständnis der Borderline-Persönlichkeitsstörung. *Der Nervenarzt, 82*(1), 9-15. doi:10.1007/s00115-010-3127-0

Herpertz, S. C., Dietrich, T. M., Wenning, B., Krings, T., Erberich, S. G., Willmes, K., . . . Sass, H. (2001). Evidence of abnormal amygdala functioning in borderline personality disorder: a functional MRI study. *Biological psychiatry, 50*(4), 292-298.

Herpertz, S. C., Huprich, S. K., Bohus, M., Chanen, A., Goodman, M., Mehlum, L., . . . Sharp, C. (2017). The challenge of transforming the diagnostic system of personality disorders. *Journal of Personality Disorders, 31*(5), 577-589.

Herrmann, M. J., Ehlis, A. C., & Fallgatter, A. J. (2003). Frontal activation during a verbal-fluency task as measured by near-infrared spectroscopy. *Brain Research Bulletin, 61*(1), 51-56.

Higgins, J. P., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M. J., & Welch, V. A. (2019). *Cochrane handbook for systematic reviews of interventions*: John Wiley & Sons.

Hilger, K., Ekman, M., Fiebach, C. J., & Basten, U. (2017). Efficient hubs in the intelligent brain: Nodal efficiency of hub regions in the salience network is associated with general intelligence. *Intelligence, 60*, 10-25.

Hölzel, Lazar, S. W., Gard, T., Schuman-Olivier, Z., Vago, D. R., & Ott, U. (2011). How does mindfulness meditation work? Proposing mechanisms of action from a conceptual and neural perspective. *Perspectives on psychological science, 6*(6), 537-559.

Hölzel, B. K., Lazar, S. W., Gard, T., Schuman-Olivier, Z., Vago, D. R., & Ott, U. (2011). How does mindfulness meditation work? Proposing mechanisms of action from a conceptual and neural perspective. *Perspectives on psychological science, 6*(6), 537-559.

Hölzel, B. K., Ott, U., Gard, T., Hempel, H., Weygandt, M., Morgen, K., & Vaitl, D. (2008). Investigation of mindfulness meditation practitioners with voxel-based morphometry. *Social cognitive and affective neuroscience, 3*(1), 55-61.

Hölzel, B. K., Ott, U., Hempel, H., Hackl, A., Wolf, K., Stark, R., & Vaitl, D. (2007). Differential engagement of anterior cingulate and adjacent medial frontal cortex in adept meditators and non-meditators. *Neuroscience letters, 421*(1), 16-21.

Homan, P., Reddan, M. C., Brosch, T., Koenigsberg, H. W., & Schiller, D. (2017). Aberrant link between empathy and social attribution style in borderline personality disorder. *Journal of psychiatric research, 94*, 163-171.

Hommel, B., & Colzato, L. S. (2017). Meditation and metacontrol. *Journal of Cognitive Enhancement, 1*(2), 115-121.

i Farrés, C. C., Elices, M., Soler, J., Domínguez-Clavé, E., Pomarol-Clotet, E., Salvador, R., & Pascual, J. C. (2019). Effects of mindfulness training on borderline personality disorder: Impulsivity versus emotional dysregulation. *Mindfulness, 10*(7), 1243-1254.

Innes, K. E., & Selfe, T. K. (2014). Meditation as a therapeutic intervention for adults at risk for Alzheimer's disease–potential benefits and underlying mechanisms. *Frontiers in psychiatry, 5*, 40.

Janata, P., Birk, J. L., Van Horn, J. D., Leman, M., Tillmann, B., & Bharucha, J. J. (2002). The cortical topography of tonal structures underlying Western music. *science, 298*(5601), 2167-2170.

Jasper, H. H., & Rasmussen, T. (1958). Studies of clinical and electrical responses to deep temporal stimulation in man with some considerations of functional anatomy. *Research Publications of the Association for Research in Nervous & Mental Disease*.

John, O., Donahue, E., & Kentle, R. (1991). The big five inventory-Versions 4a and 54. Berkeley, CA: University of California. *Berkeley, Institute of Personality and Social Research*.
Josipovic, Z., Dinstein, I., Weber, J., & Heeger, D. J. (2012). Influence of meditation on anti-correlated networks in the brain. *Frontiers in human neuroscience, 5*, 183.
Kabat-Zinn, J. (1982). An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: Theoretical considerations and preliminary results. *General hospital psychiatry, 4*(1), 33-47.
Kabat-Zinn, J. (1990). *Full Catastrophe Living*: Delta Publishing.
Kabat-Zinn, J. (2003). Mindfulness-Based Interventions in Context: Past, Present and Future. *Clinical Psychology: Science and Practice, 10*(2), 144-156.
Kang, D.-H., Jo, H. J., Jung, W. H., Kim, S. H., Jung, Y.-H., Choi, C.-H., . . . Kwon, J. S. (2013). The effect of meditation on brain structure: cortical thickness mapping and diffusion tensor imaging. *Social cognitive and affective neuroscience, 8*(1), 27-33. doi:10.1093/scan/nss056
Karnath, H.-O., & Thier, P. (2012). *Kognitive Neurowissenschaften*: Springer.
Kemmer, P. B., Guo, Y., Wang, Y., & Pagnoni, G. (2015). Network-based characterization of brain functional connectivity in Zen practitioners. *Front Psychol, 6*, 603. doi:10.3389/fpsyg.2015.00603
Kernberg, O. F. (1981). Structural interviewing. *Psychiatr Clin North Am, 4*(1), 169-195.
Kerr, C. E., Jones, S. R., Wan, Q., Pritchett, D. L., Wasserman, R. H., Wexler, A., . . . Kaptchuk, T. J. (2011). Effects of mindfulness meditation training on anticipatory alpha modulation in primary somatosensory cortex. *Brain research bulletin, 85*(3-4), 96-103.
Kim, C., Johnson, N. F., Cilles, S. E., & Gold, B. T. (2011). Common and distinct mechanisms of cognitive flexibility in prefrontal cortex. *Journal of Neuroscience, 31*(13), 4771-4779.
Kirilina, E., Jelzow, A., Heine, A., Niessing, M., Wabnitz, H., Brühl, R., . . . Tachtsidis, I. (2012). The physiological origin of task-evoked systemic artefacts in functional near infrared spectroscopy. *Neuroimage, 61*(1), 70-81.
Kirk, U., Brown, K. W., & Downar, J. (2015). Adaptive neural reward processing during anticipation and receipt of monetary rewards in mindfulness meditators. *Soc Cogn Affect Neurosci, 10*(5), 752-759. doi:10.1093/scan/nsu112
Klingberg, T. (2010). Training and plasticity of working memory. *Trends in cognitive sciences, 14*(7), 317-324.
Köpke, B., & Nespoulous, J.-L. (2006). Working memory performance in expert and novice interpreters. *Interpreting, 8*(1), 1-23.
Koudys, J. W., Gulamani, T., & Ruocco, A. C. (2018). Borderline personality disorder: refinements in phenotypic and cognitive profiling. *Current Behavioral Neuroscience Reports, 5*(1), 102-112.
Kozasa, E. H., Sato, J. R., Russell, T. A., Barreiros, M. A. M., Lacerda, S. S., Radvany, J., . . . Amaro, E. (2017). Differences in default mode network connectivity in meditators and non-meditators during an attention task. *Journal of Cognitive Enhancement, 1*(2), 228-234.
Krall, S. C., Rottschy, C., Oberwelland, E., Bzdok, D., Fox, P. T., Eickhoff, S. B., . . . Konrad, K. (2015). The role of the right temporoparietal junction in attention and social interaction as revealed by ALE meta-analysis. *Brain Structure and Function, 220*(2), 587-604.
Kraus, N., & White-Schwoch, T. (2015). Unraveling the biology of auditory learning: a cognitive–sensorimotor–reward framework. *Trends in cognitive sciences, 19*(11), 642-654.

Lahat, A., Todd, R., Mahy, C. E. V., Lau, K., & Zelazo, P. D. (2010). Neurophysiological correlates of executive function: a comparison of european-canadian and chinese-canadian 5-year-olds. *Frontiers in human neuroscience, 3*, 72.
Laird, A. R., McMillan, K. M., Lancaster, J. L., Kochunov, P., Turkeltaub, P. E., Pardo, J. V., & Fox, P. T. (2005). A comparison of label-based review and ALE meta-analysis in the Stroop task. *Human brain mapping, 25*(1), 6-21.
Lamm, C., Decety, J., & Singer, T. (2011). Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *Neuroimage, 54*(3), 2492-2502.
Lanius, R. A., Frewen, P. A., Tursich, M., Jetly, R., & McKinnon, M. C. (2015). Restoring large-scale brain networks in PTSD and related disorders: a proposal for neuroscientifically-informed treatment interventions. *European journal of psychotraumatology, 6*(1), 27313.
Larouche, M., Lorrain, D., Côté, G., & Belisle, D. (2015). Evaluation of the effectiveness of mindfulness-based cognitive therapy to treat chronic insomnia. *Revue Européenne de Psychologie Appliquée/European Review of Applied Psychology, 65*(3), 115-123.
Lazar, S. W., Kerr, C. E., Wasserman, R. H., Gray, J. R., Greve, D. N., Treadway, M. T., . . . Benson, H. (2005). Meditation experience is associated with increased cortical thickness. *Neuroreport, 16*(17), 1893.
Lebois, L. A., Papies, E. K., Gopinath, K., Cabanban, R., Quigley, K. S., Krishnamurthy, V., . . . Barsalou, L. W. (2015). A shift in perspective: Decentering through mindful attention to imagined stressful events. *Neuropsychologia, 75*, 505-524.
Lee, H. (2017). The Role of Mindfulness in the Relationship between Borderline Personality Trait and Psychological Distress. *Korean Journal of Stress Research, 25*(4), 227-232.
Lehrl, S., Merz, J., Burkhard, G., & Fischer, B. . (2005). *Mehrfach-wortschatz-intelligenztest MWT-B.* Balingen: Spitta Verlag
Lehrl, S., Triebig, G., & Fischer, B. (1995). Multiple choice vocabulary test MWT as a valid and short test to estimate premorbid intelligence. *Acta Neurologica Scandinavica, 91*(5), 335-345.
Lieb, K., Zanarini, M. C., Schmahl, C., Linehan, M. M., & Bohus, M. (2004). Borderline personality disorder. *Lancet, 364*(9432), 453-461. doi:10.1016/S0140-6736(04)16770-6
Linehan, M. (1993). *Diagnosis and treatment of mental disorders. Skills training manual for treating borderline personality disorder.*: Guilford Press.
Linehan, M. (1993). *Skills training manual for treating borderline personality disorder.* (Vol. 0898620341): Guilford Press.
Linehan, M. (1996). *Dialektisch-Behaviorale Therapie der Borderline-Persönlichkeitsstörung.*: CIP-Medien.
Linehan, M. M., Korslund, K. E., Harned, M. S., Gallop, R. J., Lungu, A., Neacsiu, A. D., . . . Murray-Gregory, A. M. (2015). Dialectical behavior therapy for high suicide risk in individuals with borderline personality disorder: a randomized clinical trial and component analysis. *JAMA psychiatry, 72*(5), 475-482.
Linster. (Referat am Institut für Psychologie Freiburg). Borderline-Persönlichkeitsstörung. from Institut für Psychologie Freiburg
Liu, X. Z., & Yan, D. (2007). Ageing and hearing loss. *The Journal of Pathology: A Journal of the Pathological Society of Great Britain and Ireland, 211*(2), 188-197.
Luders, E., Cherbuin, N., & Kurth, F. (2015). Forever Young (er): potential age-defying effects of long-term meditation on gray matter atrophy. *Frontiers in psychology, 5*, 1551.
Luders, E., Toga, A. W., Lepore, N., & Gaser, C. (2009). The underlying anatomical correlates of long-term meditation: larger hippocampal and frontal volumes of gray matter. *Neuroimage, 45*(3), 672-678.

Lueke, A., & Lueke, N. (2019). Mindfulness improves verbal learning and memory through enhanced encoding. *Memory & Cognition, 47*(8), 1531-1545. doi:10.3758/s13421-019-00947-z

Lutz, A., Jha, A. P., Dunne, J. D., & Saron, C. D. (2015). Investigating the phenomenological matrix of mindfulness-related practices from a neurocognitive perspective. *American Psychologist, 70*(7), 632.

Lutz, A., Slagter, H. A., Dunne, J. D., & Davidson, R. J. (2008). Attention regulation and monitoring in meditation. *Trends in cognitive sciences, 12*(4), 163-169.

Lutz, A., Slagter, H. A., Rawlings, N. B., Francis, A. D., Greischar, L. L., & Davidson, R. J. (2009). Mental training enhances attentional stability: neural and behavioral evidence. *Journal of Neuroscience, 29*(42), 13418-13427.

Malinowski, P. (2013). Neural mechanisms of attentional control in mindfulness meditation. *Frontiers in neuroscience, 7*, 8.

Malinowski, P., & Shalamanova, L. (2017). Meditation and cognitive ageing: the role of mindfulness meditation in building cognitive reserve. *Journal of Cognitive Enhancement, 1*(2), 96-106.

Mancke, F., Schmitt, R., Winter, D., Niedtfeld, I., Herpertz, S. C., & Schmahl, C. (2018). Assessing the marks of change: how psychotherapy alters the brain structure in women with borderline personality disorder. *Journal of psychiatry & neuroscience: JPN, 43*(3), 171.

Manna, A., Raffone, A., Perrucci, M. G., Nardo, D., Ferretti, A., Tartaro, A., . . . Romani, G. L. (2010). Neural correlates of focused attention and cognitive monitoring in meditation. *Brain research bulletin, 82*(1-2), 46-56.

Manuello, J., Vercelli, U., Nani, A., Costa, T., & Cauda, F. (2016). Mindfulness meditation and consciousness: An integrative neuroscientific perspective. *Consciousness and cognition, 40*, 67-78.

Marciniak, R., Sheardova, K., Čermáková, P., Hudeček, D., Šumec, R., & Hort, J. (2014). Effect of meditation on cognitive functions in context of aging and neurodegenerative diseases. *Frontiers in behavioral neuroscience, 8*, 17.

Mars, R. B., Sallet, J., Schüffelgen, U., Jbabdi, S., Toni, I., & Rushworth, M. F. (2012). Connectivity-based subdivisions of the human right “temporoparietal junction area”: evidence for different areas participating in different cortical networks. *Cerebral cortex, 22*(8), 1894-1903.

Meares, R. (2012). *A Dissociation Model of Borderline Personality Disorder (Norton Series on Interpersonal Neurobiology)*: WW Norton & Company.

Medaglia, J. D. (2017). Graph Theoretic Analysis of Resting State Functional MR Imaging. *Neuroimaging Clinics, 27*(4), 593-607. doi:10.1016/j.nic.2017.06.008

Menon, V. (2011). Large-scale brain networks and psychopathology: a unifying triple network model. *Trends in cognitive sciences, 15*(10), 483-506.

Mikulas, W. L. (1978). Four noble truths of Buddhism related to behavior therapy. *The Psychological Record, 28*(1), 59-67.

Miller, G. A., & Chapman, J. P. (2001). Misunderstanding analysis of covariance. *Journal of abnormal psychology, 110*(1), 40.

Minzenberg, M. J., Fan, J., New, A. S., Tang, C. Y., & Siever, L. J. (2007). Fronto-limbic dysfunction in response to facial emotion in borderline personality disorder: an event-related fMRI study. *Psychiatry Research: Neuroimaging, 155*(3), 231-243.

Mitchell, R., Roberts, R., Bartsch, D., & Sullivan, T. (2019). Changes in mindfulness facets in a dialectical behaviour therapy skills training group program for borderline personality disorder. *Journal of clinical psychology, 75*(6), 958-969.

Moore, A., & Malinowski, P. (2009). Meditation, mindfulness and cognitive flexibility. *Consciousness and cognition, 18*(1), 176-186.

Muller, R. (1992). Is there a neural basis for borderline splitting? *Comprehensive psychiatry, 33*(2), 92-104.

Namgyal, D. T. (2001). *Clarifying the natural state: A principal guidance manual for Mahamudra*: Rangjung Yeshe Publications.

Neff, K. D. (2003). The development and validation of a scale to measure self-compassion. *Self and identity, 2*(3), 223-250.

Nelson, S. M., Cohen, A. L., Power, J. D., Wig, G. S., Miezin, F. M., Wheeler, M. E., . . . Schlaggar, B. L. (2010). A parcellation scheme for human left lateral parietal cortex. *Neuron, 67*(1), 156-170.

Newberg, A. B., Wintering, N., Khalsa, D. S., Roggenkamp, H., & Waldman, M. R. (2010). Meditation effects on cognitive function and cerebral blood flow in subjects with memory loss: a preliminary study. *Journal of Alzheimer's Disease, 20*(2), 517-526.

Nijenhuis, E., Lorenz, S., & Wilmers, F. (2018). *Die Trauma-Trinität: Ignoranz-Fragilität-Kontrolle: Enaktive Traumatherapie*: Vandenhoeck & Ruprecht.

Nishimura, Y., Tanii, H., Hara, N., Inoue, K., Kaiya, H., Nishida, A., . . . Okazaki, Y. (2009). Relationship between the prefrontal function during a cognitive task and the severity of the symptoms in patients with panic disorder: a multi-channel NIRS study. *Psychiatry Research: Neuroimaging, 172*(2), 168-172.

Noda, T., Yoshida, S., Matsuda, T., Okamoto, N., Sakamoto, K., Koseki, S., . . . Higuchi, T. (2012). Frontal and right temporal activations correlate negatively with depression severity during verbal fluency task: a multi-channel near-infrared spectroscopy study. *Journal of Psychiatric Research, 46*(7), 905-912.

Norden, K. A., Klein, D. N., Donaldson, S. K., Pepper, C. M., & M. Klein, L. (1995). Reports of the early home environment in DSM-III-R personality disorders. *Journal of Personality Disorders, 9*(3), 213-223.

Ochsner, K. N., Ray, R. R., Hughes, B., McRae, K., Cooper, J. C., Weber, J., . . . Gross, J. J. (2009). Bottom-up and top-down processes in emotion generation: common and distinct neural mechanisms. *Psychological science, 20*(11), 1322-1331.

Ott, U., & Hölzel, B. (2011). Meditationsforschung: Neuroanatomische Befunde. *Deutsche Zeitschrift fuer Akupunktur, 54*(3), 17-19.

Pagnoni, G., & Cekic, M. (2007). Age effects on gray matter volume and attentional performance in Zen meditation. *Neurobiology of aging, 28*(10), 1623-1627.

Peterson, B. S., Skudlarski, P., Gatenby, J. C., Zhang, H., Anderson, A. W., & Gore, J. C. (1999). An fMRI study of Stroop word-color interference: evidence for cingulate subregions subserving multiple distributed attentional systems. *Biological psychiatry, 45*(10), 1237-1258.

Pine, R. (2012). *The Lankavatara Sutra: A Zen Text*: Counterpoint Press.

Plichta, M. M., Heinzel, S., Ehlis, A. C., Pauli, P., & Fallgatter, A. J. (2007). Model-based analysis of rapid event-related functional near-infrared spectroscopy (NIRS) data: a parametric validation study. *Neuroimage, 35*(2), 625-634.

Poeck, K., & Hartje, W. (2006). Lehrbuch: Klinische Neuropsychologie. In: Georg Thieme Verlag KG.

Pollock, P. H. (2001). Cognitive analytic therapy for borderline erotomania: forensic romances and violence in the therapy room. *Clinical Psychology & Psychotherapy: An International Journal of Theory & Practice, 8*(3), 214-229.

Posner, M. I. (2012). Imaging attention networks. . *Neuroimage, 61*(2), 450-456.

Prätzlich, M., Kossowsky, J., Gaab, J., & Krummenacher, P. (2016). Impact of short-term meditation and expectation on executive brain functions. *Behavioural Brain Research SreeTestContent1, 297*, 268-276. doi:https://doi.org/10.1016/j.bbr.2015.10.012

Prillwitz, C. C., Rüber, T., Reuter, M., Montag, C., Weber, B., Elger, C. E., & Markett, S. (2018). The salience network and human personality: Integrity of white matter tracts within anterior and posterior salience network relates to the self-directedness character trait. *Brain Research, 1692*, 66-73. doi:https://doi.org/10.1016/j.brainres.2018.04.035

Pulvermüller, F. (2005). Brain mechanisms linking language and action. *Nature Reviews Neuroscience, 6*(7), 576-582.

Quach, D., Mano, K. E. J., & Alexander, K. (2016). A randomized controlled trial examining the effect of mindfulness meditation on working memory capacity in adolescents. *Journal of Adolescent Health, 58*(5), 489-496.

Quattrini, G., Pini, L., Pievani, M., Magni, L. R., Lanfredi, M., Ferrari, C., . . . Cobelli, M. (2019). Abnormalities in functional connectivity in borderline personality disorder: Correlations with metacognition and emotion dysregulation. *Psychiatry Research: Neuroimaging, 283*, 118-124.

Quesque, F., & Brass, M. (2019). The Role of the Temporoparietal Junction in Self-Other Distinction. *Brain Topography, 32*(6), 943-955. doi:10.1007/s10548-019-00737-5

Rabenstein, R. (2020). Evidenzbasierte und Leitlinien-gestützte Psychotherapie–die aktuelle Evidenz in der Verhaltenstherapie bei Erwachsenen. *Resonanzen–E-Journal für biopsychosoziale Dialoge in Psychosomatischer Medizin, Psychotherapie, Supervision und Beratung, 7*, 26-42.

Raichle, M. E. (2015). The brain's default mode network. *Annual review of neuroscience, 38*, 433-447.

Rammstedt, B., & John, O. P. (2007). Measuring personality in one minute or less: A 10-item short version of the Big Five Inventory in English and German. *Journal of research in Personality, 41*(1), 203-212.

Rammstedt, B., Kemper, C. J., Klein, M. C., Beierlein, C., & Kovaleva, A. (2012). Eine kurze Skala zur Messung der fünf Dimensionen der Persönlichkeit: Big-Five-Inventory-10 (BFI-10).

Ravnkilde, B., Videbech, P., Rosenberg, R., Gjedde, A., & Gade, A. (2002). Putative tests of frontal lobe function: a PET-study of brain activation during Stroop's Test and verbal fluency. *J Clin Exp Neuropsychol, 24*(4), 534-547. doi:10.1076/jcen.24.4.534.1033

Robins, C. J. (2002). Zen principles and mindfulness practice in dialectical behavior therapy. *Cognitive and behavioral practice, 9*(1), 50-57.

Rorden, C., & Brett, M. (2000). Stereotaxic display of brain lesions. *Behavioural neurology,, 12*(4), 191-200.

Rosenbaum, D., Hagen, K., Deppermann, S., Kroczek, A. M., Haeussinger, F. B., Heinzel, S., . . . Ehlis, A.-C. (2016). State-dependent altered connectivity in late-life depression: a functional near-infrared spectroscopy study. *Neurobiology of aging, 39*, 57-68.

Ross, M. C., & Cisler, J. M. (2020). Altered large-scale functional brain organization in posttraumatic stress disorder: A comprehensive review of univariate and network-level neurocircuitry models of PTSD. *NeuroImage. Clinical, 27*, 102319-102319. doi:10.1016/j.nicl.2020.102319

Ruocco, A. C., Amirthavasagam, S., Choi-Kain, L. W., & McMain, S. F. (2013). Neural correlates of negative emotionality in borderline personality disorder: an activation-likelihood-estimation meta-analysis. *Biological psychiatry, 73*(2), 153-160.

Sadaghiani, S., Hesselmann, G., & Kleinschmidt, A. (2009). Distributed and antagonistic contributions of ongoing activity fluctuations to auditory stimulus detection. *Journal of Neuroscience, 29*(42), 13410-13417.

Sankoh, A. J., Huque, M. F., & Dubey, S. D. (1997). Some comments on frequently used multiple endpoint adjustment methods in clinical trials. *Statistics in medicine, 16*(22), 2529-2542.

Sassaroli, A., & Fantini, S. (2004). Comment on the modified Beer–Lambert law for scattering media. *Physics in Medicine & Biology, 49*(14), N255.

Sassaroli, A., Tong, Y., Benes, C., & Fantini, S. (2008, 2008). *Data analysis and statistical tests for near-infrared functional studies of the brain*.

Saxe, R., & Kanwisher, N. (2003). People thinking about thinking people: the role of the temporo-parietal junction in "theory of mind". *Neuroimage, 19*(4), 1835-1842.

Schecklmann, M., Ehlis, A.-C., Plichta, M. M., & Fallgatter, A. J. (2008). Functional near-infrared spectroscopy: a long-term reliable tool for measuring brain activity during verbal fluency. *Neuroimage, 43*(1), 147-155.

Scheibner, H. J., Bogler, C., Gleich, T., Haynes, J.-D., & Bermpohl, F. (2017). Internal and external attention and the default mode network. *Neuroimage, 148*, 381-389.

Scherpiet, S., Herwig, U., Opialla, S., Scheerer, H., Habermeyer, V., Jäncke, L., & Brühl, A. B. (2015). Reduced neural differentiation between self-referential cognitive and emotional processes in women with borderline personality disorder. *Psychiatry Research: Neuroimaging, 233*(3), 314-323.

Schlösser, R., Hutchinson, M., Joseffer, S., Rusinek, H., Saarimaki, A., Stevenson, J., . . . Brodie, J. D. (1998). Functional magnetic resonance imaging of human brain activity in a verbal fluency task. *Journal of Neurology, Neurosurgery & Psychiatry, 64*(4), 492-498.

Schmitgen, M. M., Niedtfeld, I., Schmitt, R., Mancke, F., Winter, D., Schmahl, C., & Herpertz, S. C. (2019). Individualized treatment response prediction of dialectical behavior therapy for borderline personality disorder using multimodal magnetic resonance imaging. *Brain and behavior, 9*(9), e01384-e01384. doi:10.1002/brb3.1384

Schnell, K., & Herpertz, S. C. (2007). Effects of dialectic-behavioral-therapy on the neural correlates of affective hyperarousal in borderline personality disorder. *Journal of psychiatric research, 41*(10), 837-847.

Schore, A. N. (2002). Dysregulation of the right brain: a fundamental mechanism of traumatic attachment and the psychopathogenesis of posttraumatic stress disorder. *Australian & New Zealand Journal of Psychiatry, 36*(1), 9-30.

Schulze, L., Schmahl, C., & Niedtfeld, I. (2016). Neural correlates of disturbed emotion processing in borderline personality disorder: a multimodal meta-analysis. *Biological psychiatry, 79*(2), 97-106.

Sebastian, A., Jung, P., Krause-Utz, A., Lieb, K., Schmahl, C., & Tüscher, O. (2014). Frontal dysfunctions of impulse control–a systematic review in borderline personality disorder and attention-deficit/hyperactivity disorder. *Frontiers in human neuroscience, 8*, 698.

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., Kenna, H., . . . Greicius, M. D. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *Journal of Neuroscience, 27*(9), 2349-2356.

Segal, Z. V., & Teasdale, J. (2018). *Mindfulness-based cognitive therapy for depression*: Guilford Publications.

Selby, E. A., Fehling, K. B., Panza, E. A., & Kranzler, A. (2016). Rumination, mindfulness, and borderline personality disorder symptoms. *Mindfulness, 7*(1), 228-235.

Serences, J. T., Shomstein, S., Leber, A. B., Golay, X., Egeth, H. E., & Yantis, S. (2005). Coordination of voluntary and stimulus-driven attentional control in human cortex. *Psychological science, 16*(2), 114-122.

Shao, Z., Janse, E., Visser, K., & Meyer, A. S. (2014). What do verbal fluency tasks measure? Predictors of verbal fluency performance in older adults. *Frontiers in psychology, 5*, 772.

Simon, R., Engström, M. (2015). The default mode network as a biomarker for monitoring the therapeutic effects of meditation. *Frontiers in Psychology, 6*, 776.
Singh, A. K., Okamoto, M., Dan, H., Jurcak, V., & Dan, I. (2005). Spatial registration of multichannel multi-subject fNIRS data to MNI space without MRI. *Neuroimage, 27*(4), 842-851.
Slagter, H. A., Lutz, A., Greischar, L. L., Francis, A. D., Nieuwenhuis, S., Davis, J. M., & Davidson, R. J. (2007). Mental training affects distribution of limited brain resources. *PLoS biology, 5*(6), e138.
Soler, J., Elices, M., Pascual, J. C., Martín-Blanco, A., Feliu-Soler, A., Carmona, C., & Portella, M. J. (2016). Effects of mindfulness training on different components of impulsivity in borderline personality disorder: results from a pilot randomized study. *Borderline personality disorder and emotion dysregulation, 3*(1), 1.
Soler, J., Pascual, J. C., Campins, J., Barrachina, J., Puigdemont, D., Alvarez, E., & Pérez, V. (2005). Double-blind, placebo-controlled study of dialectical behavior therapy plus olanzapine for borderline personality disorder. *American Journal of Psychiatry, 162*(6), 1221-1224.
Soler, J., Valdepérez, A., Feliu-Soler, A., Pascual, J. C., Portella, M. J., Martín-Blanco, A., . . . Pérez, V. (2012). Effects of the dialectical behavioral therapy-mindfulness module on attention in patients with borderline personality disorder. *Behaviour research and therapy, 50*(2), 150-157.
Spijkerman, M., Pots, W. T. M., & Bohlmeijer, E. T. (2016). Effectiveness of online mindfulness-based interventions in improving mental health: A review and meta-analysis of randomised controlled trials. *Clinical Psychology Review, 45*, 102-114.
Spitzer, C., Mestel, R., Klingelhöfer, J., Gänsicke, M., & Freyberger, H. J. (2004). Screening und Veränderungsmessung dissoziativer Psychopathologie: Psychometrische Charakteristika der Kurzform des Fragebogens zu dissoziativen Symptomen (FDS-20). *PPmP-Psychotherapie· Psychosomatik· Medizinische Psychologie, 54*(03/04), 165-172.
Steffener, J., & Stern, Y. (2012). Exploring the neural basis of cognitive reserve in aging. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease, 1822*(3), 467-473.
Ströhle, G. (2006). Empirische Erfassung der Achtsamkeit: ein Vergleich der deutschsprachigen Achtsamkeitsskalen.
Ströhle, G., Nachtigall, C., Michalak, J., & Heidenreich, T. . (2010). Die Erfassung von Achtsamkeit als mehrdimensionales Konstrukt. *Zeitschrift für Klinische Psychologie und Psychotherapie.*
Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of experimental psychology, 18*(6), 643.
Swick, D., Ashley, V., & Turken, U. (2008). Left inferior frontal gyrus is critical for response inhibition. *BMC neuroscience, 9*(1), 102.
Takahashi, T., Chanen, A. M., Wood, S. J., Yücel, M., Kawasaki, Y., McGorry, P. D., . . . Pantelis, C. (2010). Superior temporal gyrus volume in teenagers with first-presentation borderline personality disorder. *Psychiatry Research: Neuroimaging, 182*(1), 73-76.
Takizawa, R., Kasai, K., Kawakubo, Y., Marumo, K., Kawasaki, S., Yamasue, H., & Fukuda, M. (2008). Reduced frontopolar activation during verbal fluency task in schizophrenia: a multi-channel near-infrared spectroscopy study. *Schizophrenia research, 99*(1), 250-262.
Tang, Y.-Y., Ma, Y., Fan, Y., Feng, H., Wang, J., Feng, S., . . . Li, J. (2009). Central and autonomic nervous system interaction is altered by short-term meditation. *Proceedings of the national Academy of Sciences, 106*(22), 8865-8870.
Tang, Y., & Leve, L. D. (2016). A translational neuroscience perspective on mindfulness meditation as a prevention strategy. *Translational behavioral medicine, 6*(1), 63-72.

Tang, Y. Y., Holzel, B. K., & Posner, M. I. (2015). The neuroscience of mindfulness meditation. *Nat Rev Neurosci, 16*(4), 213-225. doi:10.1038/nrn3916

Tang, Y. Y., Yang, L., Leve, L. D., & Harold, G. T. (2012). Improving executive function and its neurobiological mechanisms through a mindfulness-based intervention: Advances within the field of developmental neuroscience. *Child development perspectives, 6*(4), 361-366.

Taren, A. A., Gianaros, P. J., Greco, C. M., Lindsay, E. K., Fairgrieve, A., Brown, K. W., . . . Marsland, A. L. (2017). Mindfulness meditation training and executive control network resting state functional connectivity: a randomized controlled trial. *Psychosomatic medicine, 79*(6), 674.

Taylor, S. F., Kornblum, S., Lauber, E. J., Minoshima, S., & Koeppe, R. A. (1997). Isolation of specific interference processing in the Stroop task: PET activation studies. *Neuroimage, 6*(2), 81-92.

Taylor, V. A., Daneault, V., Grant, J., Scavone, G., Breton, E., Roffe-Vidal, S., . . . Benali, H. (2013). Impact of meditation training on the default mode network during a restful state. *Social cognitive and affective neuroscience, 8*(1), 4-14.

Taylor, V. A., Grant, J., Daneault, V., Scavone, G., Breton, E., Roffe-Vidal, S., & ... & Beauregard, M. (2011). Impact of mindfulness on the neural responses to emotional pictures in experienced and beginner meditators. . *Neuroimage, 57*(4), 1524-1533.

Teper, R., Segal, Z. V., & Inzlicht, M. (2013). Inside the mindful mind: How mindfulness enhances emotion regulation through improvements in executive control. *Current Directions in Psychological Science, 22*(6), 449-454.

Tomasino, B., Chiesa, A., & Fabbro, F. (2014). Disentangling the neural mechanisms involved in Hinduism-and Buddhism-related meditations. *Brain and Cognition, 90*, 32-40.

Tomasino, B., & Fabbro, F. (2016). Increases in the right dorsolateral prefrontal cortex and decreases the rostral prefrontal cortex activation after-8 weeks of focused attention based mindfulness meditation. *Brain and cognition, 102*, 46-54.

Tomasino, B., Fregona, S., Skrap, M., & Fabbro, F. (2013). Meditation-related activations are modulated by the practices needed to obtain it and by the expertise: an ALE meta-analysis study. *Frontiers in human neuroscience, 6*, 346.

Tortella-Feliu, M., Soler, J., Burns, L., Cebolla, A., Elices, M., Pascual, J. C., & ... & García-Campayo, J. (2018). Relationship between effortful control and facets of mindfulness in meditators, non-meditators and individuals with borderline personality disorder. *Personality and mental health, 12*(3), 265-278.

Travis, F., & Shear, J. (2010). Focused attention, open monitoring and automatic self-transcending: categories to organize meditations from Vedic, Buddhist and Chinese traditions. *Consciousness and Cognition, 19*(4), 1110-1118.

Tsuzuki, D., Jurcak, V., Singh, A. K., Okamoto, M., Watanabe, E., & Dan, I. . (2007). Virtual spatial registration of stand-alone fNIRS data to MNI space. *Neuroimage, 34*(4), 1506-1518.

Tusche, A., Böckler, A., Kanske, P., Trautwein, F.-M., & Singer, T. (2016). Decoding the Charitable Brain: Empathy, Perspective Taking, and Attention Shifts Differentially Predict Altruistic Giving. *The Journal of Neuroscience, 36*(17), 4719. doi:10.1523/JNEUROSCI.3392-15.2016

Uchino, B. N., Cawthon, R. M., Smith, T. W., Light, K. C., McKenzie, J., Carlisle, M., . . . Bowen, K. (2012). Social relationships and health: Is feeling positive, negative, or both (ambivalent) about your social ties related to telomeres? *Health Psychology, 31*(6), 789.

Vago, D. R., & Zeidan, F. (2016). The brain on silent: mind wandering, mindful awareness, and states of mental tranquility. *Annals of the New York Academy of Sciences, 1373*(1), 96-113. doi:10.1111/nyas.13171

Van der Hart, O., & Horst, R. (1989). The dissociation theory of Pierre Janet. *Journal of traumatic stress, 2*(4), 397-412.

van Leeuwen, S., Müller, N. G., & Melloni, L. (2009). Age effects on attentional blink performance in meditation. *Consciousness and cognition, 18*(3), 593-599.

Varela, F. J. (1996). Neurophenomenology: A methodological remedy for the hard problem. *Journal of consciousness studies, 3*(4), 330-349.

Visintin, E., De Panfilis, C., Amore, M., Balestrieri, M., Wolf, R. C., & Sambataro, F. (2016). Mapping the brain correlates of borderline personality disorder: a functional neuroimaging meta-analysis of resting state studies. *Journal of affective disorders, 204*, 262-269.

Völlm, B., Richardson, P., Stirling, J., Elliott, R., Dolan, M., Chaudhry, I., . . . Deakin, B. (2004). Neurobiological substrates of antisocial and borderline personality disorder: preliminary results of a functional fMRI study. *Criminal Behaviour and Mental Health, 14*(1), 39-54.

Wallace, B. A. (1999). The Buddhist tradition of Samatha: Methods for refining and examining consciousness. *Journal of Consciousness Studies, 6*(2-3), 175-187.

Whitfield-Gabrieli, S., & Ford, J. M. (2012). Default mode network activity and connectivity in psychopathology. *Annual review of clinical psychology, 8*, 49-76.

Whitfield-Gabrieli, S., Moran, J. M., Nieto-Castañón, A., Triantafyllou, C., Saxe, R., & Gabrieli, J. D. (2011). Associations and dissociations between default and self-reference networks in the human brain. *Neuroimage, 55*(1), 225-232.

Wingenfeld, K., Spitzer, C., Mensebach, C., Grabe, H. J., Hill, A., Gast, U., . . . Driessen, M. (2010). Die deutsche Version des Childhood Trauma Questionnaire (CTQ): Erste Befunde zu den psychometrischen Kennwerten. [The German Version of the Childhood Trauma Questionnaire (CTQ):Preliminary Psychometric Properties]. *Psychother Psych Med, 60*(11), 442-450. doi:10.1055/s-0030-1247564

Winter, D., Krause-Utz, A., Lis, S., Chiu, C.-D., Lanius, R. A., Schriner, F., . . . Schmahl, C. (2015). Dissociation in borderline personality disorder: Disturbed cognitive and emotional inhibition and its neural correlates. *Psychiatry Research: Neuroimaging, 233*(3), 339-351.

Wrege, J., Walter, M., Lang, U. E, Borgwardt, S. (2015). Neuropsychiatrie der Borderline-Persönlichkeitsstörung. *Schweizer Zeitschrift für Psychiatrie & Neurologie.*

Wupperman, P., Fickling, M., Klemanski, D. H., Berking, M., & Whitman, J. B. (2013). Borderline personality features and harmful dysregulated behavior: the mediational effect of mindfulness. *J Clin Psychol, 69*(9), 903-911. doi:10.1002/jclp.21969

Xiong, G. L., & Doraiswamy, P. M. (2009). Does meditation enhance cognition and brain plasticity? *Annals of the New York Academy of Sciences, 1172*(1), 63-69.

Xu, T., Cullen, K. R., Mueller, B., Schreiner, M. W., Lim, K. O., Schulz, S. C., & Parhi, K. K. (2016). Network analysis of functional brain connectivity in borderline personality disorder using resting-state fMRI. *NeuroImage: Clinical, 11*, 302-315.

Yamamoto, T., & Kato, T. . (2002). Paradoxical correlation between signal in functional magnetic resonance imaging and deoxygenated haemoglobin content in capillaries: a new theoretical explanation. *Physics in Medicine & Biology, 47*(7), 1121.

Yokoyama, C., Kaiya, H., Kumano, H., Kinou, M., Umekage, T., Yasuda, S., . . . Nishimura, Y. (2015). Dysfunction of ventrolateral prefrontal cortex underlying social anxiety disorder: A multi-channel NIRS study. *NeuroImage: Clinical, 8*, 455-461.

Young, J. E., Klosko, J. S., & Weishaar, M. E. (2003). Schema therapy. *New York: Guilford, 254*.

Young, L., Camprodon, J. A., Hauser, M., Pascual-Leone, A., & Saxe, R. (2010). Disruption of the right temporoparietal junction with transcranial magnetic stimulation reduces the role of beliefs in moral judgments. *Proceedings of the national Academy of Sciences, 107*(15), 6753-6758.

Zeidan, F., Johnson, S. K., Diamond, B. J., David, Z., & Goolkasian, P. (2010). Mindfulness meditation improves cognition: Evidence of brief mental training. *Consciousness and Cognition, 19*(2), 597-605. doi:https://doi.org/10.1016/j.concog.2010.03.014

Zhang, R., Zuckerman, J.H. & Levine, B.D. . (2000). Spontanous fluctuations in cerebral blood flow: Insights from extended-duration recordings in humans. *JAm J Physiol Heart Circ Physiol, 278*(6), 1848-1855.

Zhang, X., Noah, J. A., & Hirsch, J. (2016). Separation of the global and local components in functional near-infrared spectroscopy signals using principal component spatial filtering. *Neurophotonics, 3*(1), 015004.

Zinn, J. K. (1994). Wherever you go, there you are: Mindfulness meditation in everyday life. *Hyperion*, 78-80.

Annex

1. Course of study

Theoretical background

Against the background of cognitive neuroscience, a stimulating field for mindfulness research has opened in recent years: Using mindfulness, both decreased shock reactions (Zeidler, 2007) and altered EEG activity (Lutz et al. 2004) and neural structural changes have been detected (Hölzel, 2011). Especially in the prefrontal parts of the frontal lobe (attention processes and executive functions), parietal lobe and the insula (internal perception) and the sensu-motor cortex an increase in the gray matter.

Pilot study of Erb (2010)

A first pilot study with a group of meditation-experienced subjects (Sitaram, R. 2010) was able to detect specific changes in the brain circulation of these individuals using a NIRS and EEG measurement: The state of mindfulness was compared with a state of normal discursive thinking. This study also found evidence that NIRS measurement is particularly well suited as a method to test less people with experience of meditation (seat position, silent).

Near infrared spectroscopy (NIRS)

Due to the light absorption, which differs in the near-infrared range characteristically for oxidized (oxygen-carrying O_2Hb) and deoxidized hemoglobin (low-oxygen hemoglobin HHb), changes in concentration of both parameters can be measured and thus conclusions can be drawn on the regional blood flow in the cortex.

Aims of study.

An alternative functional measurement of the brain (fNIRS) is intended to demonstrate changes in specific brain regions (e.B. parieto-lateral) of borderline patients after 3 months of DBT treatment. A combined test with NIRS and neuropsychological procedures (Stroop test) is intended to demonstrate changes in emotion regulation and attention control through DBT treatment. At the same time, subjective improvements in mindfulness will be recorded using a questionnaire (KIMS-D) and whether these are associated with changes in psychopathology (SCL-90-R). In the future, this could lead to new procedures in the treatment of borderline patients, such as a direct neurofeedback procedure with NIRS.

Course and duration of studies

In an outpatient preliminary interview (Borderline Consultation) (T0), the borderline patients are diagnosed based on a diagnostic interview (IPDE - International Personality Disorder) and the severity of the disease is determined with the help of the BSL-23 (Borderline Symptom List). Socio-demographic and anamnestic data are also collected. Only Patients who meet the diagnostic criteria of an emotionally unstable personality disorder will be included in the study.

After a waiting period (approx. 1-6 months), the pat. for inpatient DBT treatment.

A NIRS measurement is performed within the first two weeks of treatment. In addition, questionnaires on mindfulness (KIMS-D), for determining the severity of psychopathological symptoms (SCL-90-R), for determining the tendency to dissociation and for the presence of post-traumatic stress disorder are carried out. It also determines whether the pat. Experience in meditation or mindfulness (T1).

This first NIRS measurement (T1) is performed on two other comparison groups (not on station 22):

Persons with at least 1 year of regular mediation experience (Zen, Vipassana, etc.)

Persons without regular meditation experience.

Outpatient borderline patients.

In the penultimate week of treatment (10th week) a second NIRS measurement and will be carried out. The severity of borderline disease (BSL-23) and psychopathological stress (SCL-90-R) and KIMS-D are re-collected at the end of treatment (T2).

Overview of the course of studies:

Pre-Treatment I-- 12-week inpatient DBT treatment:------------------------------I

T_0 ⟶ T1▼ ⟶ T_2

Week 1 Week 12

Screening/Diagnostics Anamnesis and socio-demo. Data • BSL-23 • BFI-10 • CTQ • Dissoz. Frageb.	• NIRS • Stroop • VFT • SCL-90-R • KIMS-D • BSL-23 • ARES		• NIRS • Stroop • VFT • SCL-90-R • KIMS-D • BSL-23 • ARES

Study population

Recruitment

Patients are recruited to introduce themselves to the borderline consultation for an inpatient admission. Only Patients who meet the inclusion criteria and are included for inpatient treatment will be included in the study.

The comparison group of the meditator is recruited from meditation groups.

The group of outpatient borderline patients are recruited from ongoing outpatient behavioral therapies (letters from outpatient behavioral therapists). Due to the high time required (three NIRS measurements with 1.5 hours each, plus travel), this control group receives an expense allowance of 50 euros.

The comparison group of healthy volunteers who receive an 8-week mindfulness training is recruited via a flyer via the e-mail mailing list at the University of Tübingen.

5.2 inclusion criteria

The inclusion criteria for participation in this study are patients who meet the diagnostic criteria (minimum 5 out of 9 criteria) of a borderline disorder in a preliminary interview. These criteria (consistent with the DSM IV criteria) are collected based on a structured clinical interview (at least five out of nine criteria from the IPDE: International Personality Examination Disorder, Loranger, 1998).

- Age between 18 and 55 years
- Ability to consent. If there are doubts as to the ability to consent, a second independent doctor should be consulted to check the ability to consent.
- By written consent after detailed clarification, the participant expressed a willingness to participate in the study (see appendix).

Exclusion criteria

- Lack of consent (if there are doubts about a patient's ability to consent, it will be reviewed by a doctor not involved in the study).
- Patients with schizophrenic disease or other acute or chronic diseases (also anamnestic) that can affect brain metabolism:
- vorbekannter Diabetes mellitus (E10-E14 nach ICD-10)
- Renal insufficiency from stage 3 of the Kidney Disease Outcomes Quality Initiative
- Unadjusted hypertonus (I10.x according to ICD-10)
- Moderate or severe cranial brain trauma (GCS 3-12) or 2nd or 3rd degree skull trauma with unconsciousness of > 30 minutes

- Pat. with an IQ <70.
- Acute substance abuse
- Acute danger to oneself or external crisis.
- The subjects of the outpatient comparison group of borderline patients must not have any experience in mindfulness.
- The subjects of the outpatient healthy comparison group must not have any experience in mindfulness.

Study group: Borderline patients (Station 22)

After detailed information/information of the prospective students and their written consent to study participation, the first step is to check all inclusion and exclusion criteria and to make a diagnosis by means of a standardized diagnostic interview (International Personality Disorder Examination (IPDE) (Loranger, 1998), Big-Five-Inventory-10 (BFI-10) (Rammstedt et al., 2012) and the severity of symptoms by the Borderline Symptom List (BSL-23, Bohus, 2001). In case of abnormalities (see inclusion and exclusion criteria), the subject will not be included in the study.

Comparison group: meditation experts

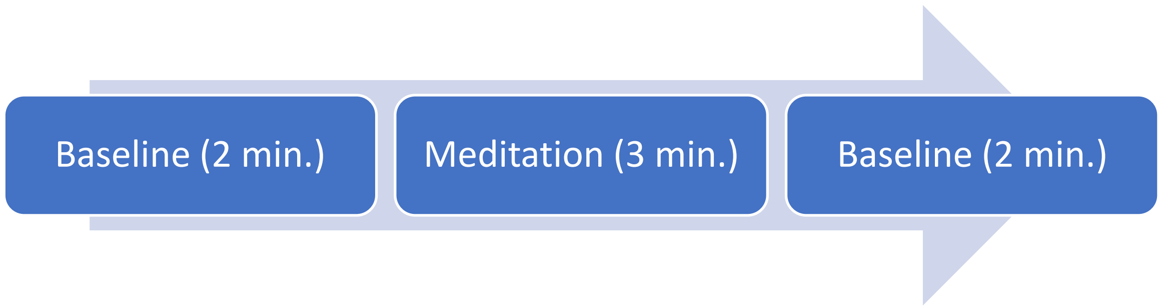
The comparison group of meditator scants are tested in T1 for psychopathological exposure (SCL-90-R and BFI-10) and IQ (MWT). Prob. with at least one year of regular meditation experience (at least 120 min. meditation exercises per week) are included in the comparison group (NIRS testing).

Functional paradigms (NIRS measurement)

Different blocks of meditative and non-meditative states are measured using different acoustic stimuli. It will be the Pat. continuous acoustic stimulation (in total 17 min.).

Continuous acoustic stimulation:

4 blocks baseline (2 min. normal thinking) are interrupted by 3 blocks of meditation (3 min.) alternating. In this first block of 17 minutes, the subjects continuously hear a meditation bowl, which is used every 12 sec. is struck.



Demographic data and tests

The demographic data are collected based on a questionnaire to be completed by the subject. Information on anamnesis, medication, family anamnesis and acute illnesses will be provided in a short interview and, if necessary, in the following interview. recorded with the help of the medical records.

The following data are collected in all subjects (borderline patients):

- standardized diagnostic interview (International Personality Disorder Examination (IPDE) (Loranger, 1998)
- Big-Five-Inventory-10 (BFI-10) (Rammstedt et al., 2012)
- Sociodemographic and anamnestic data
- Kentucky Inventory of Mindfulness, German version (KIMS-D, Ströhle, 2004)
- Borderline Symptom List (BSL-23) (Bohus et al., 2001)
- Questionnaire on dissociative symptoms (FDS) (Freyberger et. al., 1998)
- Scales for the sensitivities of action-regulating emotion systems (ARES) (Hartig and Moosbrugger, 2003).

- Symptom Checklist (SCL-90-R) (Derogatis, 1986)
- Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 2003)

Tests:

- Stroop-Test (Stroop, 1935)
- Verbal learning and memory test (VLMT, Helmstaedter, 2001),
- Multiple Vocabulary Intelligence Test (MWT) (Assessment of Premorbid Intelligence, Lehrl, 2005).

Data management (data collection, evaluation, transfer)

Data collection and data storage

It collects socio-demographic personal data, data on the disease and possibly. Patient therapy, clinical test results, responders' responses in psychometric test instruments and reaction and psychophysiological data (NIRS data) recorded during the various experiments.

Evaluation

The NIRS data is processed and evaluated using the routine software implemented in the ETG-4000 device, as well as MATLAB (The MathWorks Inc.), a commercial software based on numerical calculations using matrices and can be used for off-line analysis of hemoglobin concentration changes. The software packages EXEL (Microsoft inc.) and SPSS are also used for statistical analysis. In the statistical analysis, measurement-repeated variance analyses (ANOVA) as well as correlation and regression analyses are carried out. In the case of statistically significant interactions between two or more independent variables, post hoc analyses are carried out in the form of t-tests for independent or paired samples for a closer examination of the effects. The fulfilment of the requirements of variance analysis methods is verified by means of further significance tests: Levene test for the verification of the degree homogeneity, Kolmogorov-Smirnov test for testing for normal distribution of data points. To counteract a cumulative α error in the case of multiple statistical tests, the Bonferroni correction of the probability of error is implemented.

Privacy issues

When treating the data confidentially, the data protection law of the federal and state governments is complied with. The recording of all collected data takes place in encrypted form (i. e. pseudonymized, without attribution), thus ensuring that no assignment of the findings to the person is possible during the scientific publication of the results. All documents through which a personal assignment of the collected data (patient consent and patient identification list) is possible remain in the study center and are only accessible to the study staff. The medical data collected in the case of psychiatric subjects will be treated confidentially and will only be passed on in encrypted form unless the legal provisions preclude this.

Sociodemographic and clinical variables are first recorded on paper, then entered pseudonymously into a statistical program. The collection and storage of the experimental data takes place exclusively in digital form on a password-protected drive of university medicine at the Clinic for Psychiatry and Psychotherapy, which is only accessible to the applicants and project participants mentioned on the cover. All data collected during the investigation will be retained for 10 years after the evaluation. Only applicants have access to the re-identification list after data storage. All persons involved in the study are subject to medical confidentiality. It is not permitted to share personal information with those not involved in the study.

Ethical concerns

All participants in the study will be informed in detail about the nature, scope and implementation of the investigation and must give their consent in writing for their participation. The information is provided orally by the study doctor and in writing by means of a fact sheet. The text of written consent to study is attached to the annex. Only persons who can understand, judge, and give consent are included for the course of the study.

There is no personal benefit for the subject from participating in the examination. Three measurements with near-infrared spectroscopy are carried out on loads over the course of three months (35 min each), as well as some test psychological examinations (approx. 60 min.). We assume that the burdens on the target group can be classified as moderate. Health risks do not arise from the studies contained in the study design. The medical confidentiality is observed. There are therefore no risks for the subjects (in compliance with the precautions).

Insurance and financing

The subjects do not receive any additional medication. The psychophysiological examination does not carry any known risks. For these reasons, insurance is not available here, as there is no tangible risk to insurance. There is no insurance for the way. The study is financed from hospital funds.

Educating study participants

The investigations were planned in compliance with the 1964 Helsinki Declaration ("Ethical Principles for Medical Research Involving Human Subjects") as amended in 2008 by the 59th General Assembly of the World Medical Association in Seoul, South Korea.

All study participants are over 18 years of age and can be given consent. They shall be informed in writing and orally of the investigations and any associated risks and will be informed of their right to withdraw their consent to carry out the investigation at any time and to terminate the investigation without giving reasons and without any disadvantages thereof. Only after written consent will participants be included in the study.

General provisions

The legal provisions within the framework of data protection and patient safety are complied with. The sheets with the names and personal data of the patients are destroyed after pseudonymized input into the evaluation software. After completion of the study, the results will be published in a well-known journal.

2. Text for the instructions for mindfulness measurement

Dear participant,

this study explores how the brain functions. For this purpose, we measure brain activity with near-infrared light. The examination takes a total of about 1 hour and you will do several small and easy tasks that have to do with attention. There is nothing you can do wrong.

The first task is quite simple and maybe a bit boring. It takes a total of 17 minutes. During this time, you hear every 12 seconds the sound of a meditation bell. Then, you will have two different tasks.

When the word "baseline" appears on the screen, you do not have to do anything special, just wait. The baseline condition lasts 2 minutes.

After that, the word "mindfulness" appears on the screen. Then, your task is to focus your attention on the sound of the singing bowl, only perceive this sound, just like a recording device and your ears are like a recorder. Everything is recorded just as it appears. This should be done in an attitude that is accepting and focused on only this one task. When thoughts and feelings appear (which always happens and is not bad...), you simply perceive these thoughts and then turn your attention back to the mere perception of the sounds. This task takes 3 minutes.

After the end of the mindfulness exercise, the word "baseline" appears again, and it means that you can wait for the next block of mindfulness. You can rest. The waiting time is again 2 minutes.

In total, the mindfulness condition is repeated three times, always with the baseline recovery phases in between.

The first task is then finished, and you have time to complete some questionnaires. During this time, they are put on a different hood.

The second task consists of a concentration task.

3. Instructions Emotional Stroop - Words

Dear proband,

in the following task, emotional and neutral words will appear on the display written in one of the four colors red, yellow, green, or blue. Your task is to decide at the touch of a button, regardless of the word content, which of the colors you have seen.

Before the actual experiment begins, there is a practice run in which you should learn how to map colors and keys. During this exercise, the corresponding color key assignment will still be displayed in the display. However, it is important that you memorize them because they will no longer appear in the actual experiment.

4. Instruction VFT (word fluid test)

This word fluid test is about naming as many words as possible with a specific initial letter or category within 30 seconds. The investigator will tell you exactly when to start or stop enumerating the words at any time. During the whole measurement, it is important that you stay calm and have your eyes closed. Please do not bite your teeth tightly. No speaking is allowed during the resting times, unless you are not well, or you want to cancel the measurement.

Phase 1

First, they are given any letter of the alphabet. You then please say so many main words that come to mind that begin with this letter. No names, cities or countries. Example: If the investigator calls the letter "B", then they say "bee, bush, birch, bible, bath" and so on. If you cannot think of any more terms or very few or no ones, please avoid angry exclamations, but just stay calm until the rest of the time has elapsed.

Rest

This is followed by a rest period of 30 seconds. During this period of rest, please keep sitting and keep your eyes closed. Please do not think about the words during this phase!

Phase 2

After that, please name the days of the week for the next 30 seconds. Start on Monday and count them up one by one every weekday until the investigator says "stop." If you have listed every 7 days of the week before they receive the stop signal, then start again (i.e., on Monday).

Rest

A rest of 30 seconds follows. Please do not speak here and do not think about the previous task! Relax.

Phase 3

Now you will be given any category. After the start command, you will list as many words as possible that belong to this category. Example furniture: chair, table, armchair, stool, bench and so on. Again, if you do not think of any more terms or even very few or no ones, please avoid angry exclamations, but just stay calm until the rest of the time has elapsed.

Rest

Now there is another period of rest.

The described sequence of tasks (phase 1 - phase 3 with subsequent pauses) is repeated a total of 3 times during the experiment. After about 10 minutes, the task is over.

Please also try not to repeat the letters and categories. If this happens, proceed with the task as normal. Please do not deduce words, e.B. bookend, bookend, book author and so on.

If you still have questions or have not understood it correctly, please contact the investigator.

Thank you!

5. list of randomizations

Borderline	groß - klein	1	1	VFT - Stroop		groß - klein	2	2	VFT - Stroop
Borderline	groß - klein	1	1	Stroop - VFT		groß - klein	2	2	Stroop - VFT
Borderline	klein - groß	1	1	VFT - Stroop		klein - groß	2	2	VFT - Stroop
Borderline	klein - groß	1	1	Stroop - VFT		klein - groß	2	2	Stroop - VFT
Borderline	groß - klein	1	2	VFT - Stroop		groß - klein	2	3	VFT - Stroop
Borderline	groß - klein	1	2	Stroop - VFT		groß - klein	2	3	Stroop - VFT
Borderline	klein - groß	1	2	VFT - Stroop		klein - groß	2	3	VFT - Stroop
Borderline	klein - groß	1	2	Stroop - VFT		klein - groß	2	3	Stroop - VFT
Borderline	groß - klein	1	3	VFT - Stroop		groß - klein	2	4	VFT - Stroop
Borderline	groß - klein	1	3	Stroop - VFT		groß - klein	2	4	Stroop - VFT
Borderline	klein - groß	1	3	VFT - Stroop		klein - groß	2	4	VFT - Stroop
Borderline	klein - groß	1	3	Stroop - VFT		klein - groß	2	4	Stroop - VFT
Borderline	groß - klein	1	4	VFT - Stroop		groß - klein	2	1	VFT - Stroop
Borderline	groß - klein	1	4	Stroop - VFT		groß - klein	2	1	Stroop - VFT
Borderline	klein - groß	1	4	VFT - Stroop		klein - groß	2	1	VFT - Stroop
Borderline	klein - groß	1	4	Stroop - VFT		klein - groß	2	1	Stroop - VFT
Borderline	groß - klein	2	1	VFT - Stroop		groß - klein	1	2	VFT - Stroop
Borderline	groß - klein	2	1	Stroop - VFT		groß - klein	1	2	Stroop - VFT
Borderline	klein - groß	2	1	VFT - Stroop		klein - groß	1	2	VFT - Stroop
Borderline	klein - groß	2	1	Stroop - VFT		klein - groß	1	2	Stroop - VFT
Borderline	groß - klein	2	2	VFT - Stroop		groß - klein	1	3	VFT - Stroop
Borderline	groß - klein	2	2	Stroop - VFT		groß - klein	1	3	Stroop - VFT
Borderline	klein - groß	2	2	VFT - Stroop		klein - groß	1	3	VFT - Stroop
Borderline	klein - groß	2	2	Stroop - VFT		klein - groß	1	3	Stroop - VFT
Borderline	groß - klein	2	3	VFT - Stroop		groß - klein	1	4	VFT - Stroop
Borderline	groß - klein	2	3	Stroop - VFT		groß - klein	1	4	Stroop - VFT
Borderline	klein - groß	2	3	VFT - Stroop		klein - groß	1	4	VFT - Stroop
Borderline	klein - groß	2	3	Stroop - VFT		klein - groß	1	4	Stroop - VFT
Borderline	groß - klein	2	4	VFT - Stroop		groß - klein	1	1	VFT - Stroop
Borderline	groß - klein	2	4	Stroop - VFT		groß - klein	1	1	Stroop - VFT
Borderline	klein - groß	2	4	VFT - Stroop		klein - groß	1	1	VFT - Stroop
Borderline	klein - groß	2	4	Stroop - VFT		klein - groß	1	1	Stroop - VFT
Gruppe	Kappenfolge	VFT	Emo-Str.	Reihenfolge	Datum	Kappenfolge	VFT	Emo-Str.	Reihenfolge
Kontrolle_geübt	groß - klein	1	1	VFT - Stroop		groß - klein	2	2	VFT - Stroop
Kontrolle_geübt	klein - groß	1	1	VFT - Stroop		klein - groß	2	2	VFT - Stroop
Kontrolle_geübt	groß - klein	1	2	VFT - Stroop		groß - klein	2	3	VFT - Stroop
Kontrolle_geübt	klein - groß	1	2	VFT - Stroop		klein - groß	2	3	VFT - Stroop
Kontrolle_geübt	groß - klein	1	3	VFT - Stroop		groß - klein	2	4	VFT - Stroop
Kontrolle_geübt	klein - groß	1	3	VFT - Stroop		klein - groß	2	4	VFT - Stroop
Kontrolle_geübt	groß - klein	1	4	VFT - Stroop		groß - klein	2	1	VFT - Stroop
Kontrolle_geübt	klein - groß	1	4	VFT - Stroop		klein - groß	2	1	VFT - Stroop
Kontrolle_geübt	groß - klein	2	1	Stroop - VFT		groß - klein	1	2	Stroop - VFT
Kontrolle_geübt	klein - groß	2	1	Stroop - VFT		klein - groß	1	2	Stroop - VFT
Kontrolle_geübt	groß - klein	2	2	Stroop - VFT		groß - klein	1	3	Stroop - VFT
Kontrolle_geübt	klein - groß	2	2	Stroop - VFT		klein - groß	1	3	Stroop - VFT
Kontrolle_geübt	groß - klein	2	3	Stroop - VFT		groß - klein	1	4	Stroop - VFT
Kontrolle_geübt	klein - groß	2	3	Stroop - VFT		klein - groß	1	4	Stroop - VFT
Kontrolle_geübt	groß - klein	2	4	Stroop - VFT		groß - klein	1	1	Stroop - VFT
Kontrolle_geübt	klein - groß	2	4	Stroop - VFT		klein - groß	1	1	Stroop - VFT
Kontrolle_ungeübt	groß - klein	1	1	VFT - Stroop		groß - klein	2	2	VFT - Stroop
Kontrolle_ungeübt	klein - groß	1	1	VFT - Stroop		klein - groß	2	2	VFT - Stroop
Kontrolle_ungeübt	groß - klein	1	2	VFT - Stroop		groß - klein	2	3	VFT - Stroop
Kontrolle_ungeübt	klein - groß	1	2	VFT - Stroop		klein - groß	2	3	VFT - Stroop
Kontrolle_ungeübt	groß - klein	1	3	VFT - Stroop		groß - klein	2	4	VFT - Stroop
Kontrolle_ungeübt	klein - groß	1	3	VFT - Stroop		klein - groß	2	4	VFT - Stroop
Kontrolle_ungeübt	groß - klein	1	4	VFT - Stroop		groß - klein	2	1	VFT - Stroop
Kontrolle_ungeübt	klein - groß	1	4	VFT - Stroop		klein - groß	2	1	VFT - Stroop
Kontrolle_ungeübt	groß - klein	2	1	Stroop - VFT		groß - klein	1	2	Stroop - VFT
Kontrolle_ungeübt	klein - groß	2	1	Stroop - VFT		klein - groß	1	2	Stroop - VFT
Kontrolle_ungeübt	groß - klein	2	2	Stroop - VFT		groß - klein	1	3	Stroop - VFT
Kontrolle_ungeübt	klein - groß	2	2	Stroop - VFT		klein - groß	1	3	Stroop - VFT
Kontrolle_ungeübt	groß - klein	2	3	Stroop - VFT		groß - klein	1	4	Stroop - VFT
Kontrolle_ungeübt	klein - groß	2	3	Stroop - VFT		klein - groß	1	4	Stroop - VFT
Kontrolle_ungeübt	groß - klein	2	4	Stroop - VFT		groß - klein	1	1	Stroop - VFT
Kontrolle_ungeübt	klein - groß	2	4	Stroop - VFT		klein - groß	1	1	Stroop - VFT

6. Word lists for emotional Stroop test

Table take from psytest.psy.med.uni-muenchen.de/home/Beate Ruppel/Diplomarbeit_Beate_Ruppel_LMU_Muenchen_zweiseitig.pdf

Borderline-specific	Negative	Neutral
Restless	Grim	analog
Unstable	plump	Valid
Sad	haemic	Visually
Helpless	Unwise	Mountainous
Unable	disapproving	digital
Angry	Bidder	Structurally
Furious	antisocial	Clean
Angry	Icy	neutral
dick	brummig	formal
Lonely	Fresh	Logical
Envious	Irritated	Internally
Stupid	Dark	Flat

These words did not specify where the word series came from. Nor was it specified whether the negative and neutral word series were appropriately selected by syllable length or frequency.

In the same article, a negative priming test was performed. There, reference is made to a work by Herpertz and Schnell (2003).

These words are:

Borderline-specific	Neutral	Negative
Depending on	Abstract	arrogant
Repellent	Structurally	Malicious
Aggressive	diagonal	Selfish
Anxious	service	Unsuccessful
Excited	Monochrome	Hostile
Depressed	Empirically	geistlos
emotional	Professionally	humorless
Exhausted	Liquid	Miserable
Frustrated	Graphically	Childish
Hectic	Municipal	Petty
Helpless	Logical	Criminal
Impulsive	Machine	Ridiculous
Fainting	Methodically	Slowly
Restless	neutral	disapproving
Guilty	Visually	Envious
Unsure	Partial	Scandalous
Hated	rational	worrying
Crazy	Factual	antisocial
Worthless	Simply	Dogged
Disgusting	Synchronously	Bitter

Test zum negativen Priming aus: Domes G, Winter B, Schnell K, Vohs K, Fast K, **Herpertz SC** (2006) Inhibitory functioning in borderline personality disorder and the influence of emotions. *Psychological Medicine*, 36:1163-1172

7. List of abbreviations (alphabetical order)

aCC	anterior cingular cortex
ADHD	Attention Deficit and Hyperactivity Syndrome
AI	anterior insular Cortex
ANOVA	analyses of variance
APA	American Psychiatric Society
AWMF	Working Group of the Scientific Medical Societies
BFI-10	Big-Five-Inventory-10 scales
CBSI	correlation-based signal improvement procedure
CBT	Cognitive Behavior Therapy
CEN	Central Executive Network
dACC	dorsal Anterior Cingular Cortex
DERS	Difficulties in Emotion Regulation Scale
DBT	dialectical behavioral therapy
dlPFC	dorsolateral prefrontal cortex
DMN	Resting state network.
DSM-5	Diagnostic and statistical manual of mental disorders (DSM-5)
dmPFC	dorsomedial prefrontal cortex
EEG	electroencephalography
EST	emotional Stroop Test

fMRI	Functional magnetic resonance imaging
GSI	Global Severity Index
HHb	deoxygenated hemoglobin
IFG	inferior frontal gyrus
inter-iFC	inter-network intrinsic functional connectivity
IQ	intelligence quotient
KIMS-D	Kentucky Inventory of Mindfulness Skills, German translation
MBCT	Mindfulness Based Cognitive Therapy
MBSR	Mindfulness Based Stress Reduction
MBT	Mentalization Based Treatment
mPFC	medial prefrontal Cortex
MSTG	middle and superior temporal gyrus
NIRS	Near infrared spectroscopy
O2Hb	oxygenated hemoglobin
PCC	posterior parietal cortex
PFC	prefrontal cortex
rlPFC	rostro-lateral prefrontal cortex
RMET	Reading the Mind in the Eyes' test
SN	Salience Network
RTs	reaction times
SCL-90-R	symptom checklist 90
STG	superior temporal gyrus

SVF	semantic verbal fluency
TCI	Temperament and Character Inventory
TFP	Transmission-Focused Therapy
TOM	Theory of Mind
TPJ	temporo-parietal junction
VFT	Verbal fluency test
vlPFC	ventrolateral prefrontal cortex
vmPFC	ventro-medial prefrontal cortex
WHO	Wold Health Organization

8. Figure list

The illustrations were numbered in the framework part of the dissertation (introduction and overall discussion). In the English-language studies, the numbering of figures has been maintained internally.

Introduction:

Figure 1: Model based on (Simon, 2015) p. 13

Figure 2: The Bio-Social Model of Borderline Disorder. p. 17

Figure 3: Fronto-limbic dysregulation in borderline patients. p. 18

Figure 4: Diagnosis of borderline disorder according to DSM-5 p. 21

Figure 5: The Translational Model of Mindfulness Meditation p. 32

Study 1:

Fig. 1. 3×5 probe set arrangement p. 44

Fig. 2. Resting condition (Baseline): Significant cortical activation p. 48

Fig. 3. Mindfulness condition: Significant cortical activation p. 50

Fig. 4. Significant group differences in mindfulness condition p. 53

Study 2:

Fig. 1. position of probe set (3x11 optodes). p. 74

Fig. 2. ANOVA main effect. p. 77

Fig. 3. ANOVA main effect of "task condition" p. 78

Fig. 4. Changes in O_2Hb concentration p. 79

Study 3:

Fig. 1. Reduction of psychopathology: BSL-23 p. 105

Fig. 2. Reduction of global psychopathology: SCL-90-R p. 105

Fig. 3. Changes in motivation (BAS= reward seeking) p. 106

Fig. 4. KIMS-D = Mindfulness p. 106

Fig. 5. Correlation between changes in NIRS activation p. 108

Discussion:

Figure 6: Overarching neural networks of the brain p. 124

Figure 7: The temporo-parietal connection p. 127

Figure 8: Functional areas of TPJ p. 128

Figure 9: Model of Affect Regulation p. 131

Figure 10: Overview model DBT p. 133

9. Table directory

The tables were numbered in the framework part of the dissertation (introduction and overall discussion). In the English-language studies, the tables numbering has been maintained internally.

Introduction

Table 1: Table of effects p.36

Study 1:

Table 1: Significant Activation in Resting State p.47

Table 2: Significant Activation in Mindfulness-Condition p. 51

Table 3: ANOVA main effect: Group p. 52

Table 4: ANOVA main effect: Group×Condition p. 52

Table 5: Lateralization from left to right in meditation experts p. 56

Study 3:

Table 1: Baseline sociodemographic and clinical characteristics p. 102

10. Styles and formatting

For simplification and better readability, the male form was basically used in this work, e. B. "borderline patients". But both sexes are always meant. In the English-language text, the style of the APA was published in the6th. edition used.

The individual chapters of this dissertation are fully numbered. On the other hand, the figures and tables in the framework of the dissertation (introduction and overall discussion) were numbered in themselves. In the English-language studies, the numbering of figures and tables has been maintained internally.

11. Explanation of the own share of the dissertation

The work was carried out in the University Hospital for Psychiatry and Psychotherapy under the supervision of Prof. Dr. Martin Hautzinger and Prof. Dr. Andreas Fallgatter. The study was conceived in collaboration with Dr. Ann-Christine Ehlis, head of the Psychophysiology and Optical Imaging Group, and Michael Erb. The tests were carried out by me independently and with the support of Johanna von Spee, Corinna Klose and Svenja Brosch. The statistical evaluation was carried out after consulting by the workgroup Psychophysiology and Optical Imaging according to the guidance of Ann-Christine Ehlis, Florian Haeussinger, Sabrina Schneider, and David Rosenbaum. I assure that I have written the manuscript on my own and that I have not used any sources other than those I have indicated.

Tübingen, 22.08.2020

Signature

12. Affidavit

I hereby declare that I have independently written the work submitted for the doctorate entitled : "Mindfulness Training in the DBT: Investigation of Brain Activity by Means of NIRS", used only the specified sources which are marked as such. I declare that the guidelines for ensuring good scientific practice of the University of Tübingen (Senate decision of 25.5.2000) have been observed. I assure by oath that this information is true and that I have not concealed anything. It is well known that the wrong delivery of an insurance to oaths is punishable by up to three years or a fine instead of a custodial sentence.

Tübingen, 22.08.2020

Signature

Thanksgiving and dedication

I thank my parents, family and friends for their patience and support over the last few years. Kira must not be forgotten either.

A special thanks goes to my partner Marty Smith for all his love, especially in the form of his cooking skills.

I dedicate this dissertation to my children Tarjar and Lukas.

Curriculum Vitae

Dipl. Psych. Friederike Gundel
geb. Bunke
*28.09.1967 in Tübingen
Wh.: Amselweg 7, 72076 Tübingen
Familienstand: gesch., zwei erwachsene Kinder

Schulausbildung:

1987	Abitur am Uhlandgymnasium Tübingen

Bildungsweg:

1988-1995	Studium der Klinischen Psychologie an der Phillips-Universität Marburg (24.11.1995 Diplom)
1989-1992	Weiterbildung als Gestalttherapeutin, IGTC Marburg
1992	Praktikum an der psychiatrischen Poliklinik in Trondheim, Norwegen
1999-2000	Weiterbildung in Systemischer Paartherapie, Hans Jellouschek, Entringen
1999-2004	Verhaltenstherapeutische Ausbildung, TAVT in Tübingen
2002	Praxis Dr. Martin Jung, Tübingen, psychotherapeutisches Praktikum als PIA

2002-2003	Institut für Klinische Psychologie, Bürgerhospital Stuttgart, als PIA (Alkoholentzugsstation)
2003	Zusatzausbildung: VT bei Kindern und Jugendlichen, TAVT
13.10.2003	Approbation als psychologische Psychotherapeutin, Richtlinienverfahren: Verhaltenstherapie
18.11.2004	Eintrag in das Arztregister KV Südwürttemberg, Nr. 09187
2005	Zusatzausbildung: VT als Gruppenverfahren, TAVT
2014-2015	EMDR Fortbildung
2011-2012	DBT Fortbildungen
24.10.2016	Fortbildungsabschluss als DBT Therapeutin
2017-2020	Basis-, Fortgeschrittenen- und Masterkurs Strukturelle Dissoziation bei Ellert Nijenhuis

Beruflicher Werdegang:

1996-2001	Kurleitung am DRK Mutter-Kind-Kurheim in Pfalzgrafenweiler, Schwerpunkt: Essstörungen bei Frauen.
1999-2001	freiberufliche Tätigkeit als Paartherapeutin, Tübingen
2003	Drogenentzugsstation DEMOS, Klinikum Stuttgart (50%)
2004-2005	Gemeindepsychiatrisches Zentrum West, Klinikum Stuttgart (50%)
2003-2012	Arbeit als psychologische Psychotherapeutin (Entlastungsassistenz) in der Praxis Dr. M. Jung (50%)
2005-2010	Klinische Psychologin an der Psychiatrische Institutsambulanz, Bürgerhospital Stuttgart (50%), 1.10.2008-31.12.2010: 38,46%

Ab 2011 Akademische Mitarbeiterin (Station 22: Schwerpunkt Borderline und komplexe Traumafolgestörungen), Universitätsklinik für Psychiatrie und Psychotherapie, Tübingen (50%)

Promotionsprojekt: „Achtsamkeit in der DBT“ an der Universitätsklinik für Psychiatrie und Psychotherapie.

27.03.2012 Zulassung als Psychotherapeutische Einzelpraxis, Schwerpunkt Verhaltenstherapie (BSNR 626907900) in Tübingen (50%)

Veröffentlichungen

2018 Gundel, F., von Spee, J., Schneider, S., Haeussinger, F. B., Hautzinger, M., Erb, M., ... & Ehlis, A. C. (2018). Meditation and the brain–Neuronal correlates of mindfulness as assessed with near-infrared spectroscopy. *Psychiatry Research: Neuroimaging*, *271*, 24-33.

2018 Knoblich, N., Gundel, F., Brückmann, C., Becker-Sadzio, J., Frischholz, C., & Nieratschker, V. (2018). DNA methylation of APBA3 and MCF2 in borderline personality disorder: potential biomarkers for response to psychotherapy. *European Neuropsychopharmacology*, *28*(2), 252-263.

2018 Thomas, M., Knoblich, N., Wallisch, A., Glowacz, K., Becker-Sadzio, J., Gundel, F., ... & Nieratschker, V. (2018). Increased BDNF methylation in saliva, but not blood, of patients with borderline personality disorder. *Clinical epigenetics*, *10*(1), 109.

2019 Thomas, M., Banet, N., Wallisch, A., Glowacz, K., Becker-Sadzio, J., Gundel, F., & Nieratschker, V. (2019). Differential COMT DNA methylation in patients with Borderline Personality Disorder: Genotype matters. *European Neuropsychopharmacology*, *29*(11), 1295-1300.

2019 Nieratschker, V., Thomas, M., Knoblich, N., Wallisch, A., Glowacz, K., Gundel, F., ... & Brueckmann, C. (2019, January). INCREASED BDNF METHYLATION IN SALIVA, BUT NOT BLOOD, OF PATIENTS WITH BORDERLINE PERSONALITY DISORDER. In *EUROPEAN*

NEUROPSYCHOPHARMACOLOGY (Vol. 29, pp. 1297-1298). RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS: ELSEVIER.

Reviews

2018 Kozasa, E. H., Balardin, J. B., Sato, J. R., Chaim, K. T., Lacerda, S. S., Radvany, J., ... & Amaro Jr, E. (2018). Effects of a 7-day meditation retreat on the brain function of meditators and non-meditators during an attention task. *Frontiers in human neuroscience*, *12*, 222.

Reviewed by David R. Vago, Vanderbilt University Medical Center, United States.

Friederike Gundel, Department of Psychiatry and Psychotherapy, University Hospital Tübingen, Germany

Kooperationen

Arbeitsgruppe um Jun.-Prof. Dr. Vanessa Nieratschker:

Datensammlung und Beteiligung an den Veröffentlichungen für das Forschungsprojekt „Epigenetik der Borderline-Persönlichkeitsstörung und Effekte der DBT auf die DANN-Methylierungsmuster.

Station 22 (Prof. A. Rapp): Traumatherapie, Klinische Arbeit, Beteiligung an Veröffentlichung (in press) zu Traumaexposition in der Schwangerschaft.

Tübingen, den 23.04.2021 Friederike Gundel