Effects of mindfulness meditation on brain structure and function

Trial protocol

Part 1

Summary

Mindfulness describes the ability to consciously engage in a state of non-judgemental, present moment attendance. Mindfulness can be trained through the practice of mindfulness meditation. Research has demonstrated that mindfulness meditation has beneficial effects on health and cognition. However, the underlying neural mechanisms are not yet fully understood. This study aims to extend knowledge on these mechanisms. This can help to improve applications of mindfulness meditation in clinical and non-clinical settings. Healthy adults between 18 and 65 with little or no meditation experience are recruited via public advertisement and are assigned to either 31 days of mindfulness meditation training or an active control condition. In the mindfulness meditation training, an experienced mindfulness meditation instructor provides information on mindfulness meditation and guided meditation sessions. In the active control condition, information on various topics of general health is provided. Training sessions are in video or audio format. Both training programs can be accessed via an online platform and are delivered in training sessions of 15 minutes. Before and after the intervention, participants undergo (functional) magnetic resonance imaging (MRI). Participants also complete questionnaires on subjective levels of mindfulness. Analysis of brain activation and functional connectivity will be performed. Mindfulness meditation is expected to promote brain activation in regions associated with attention and to alter functional connectivity.

General Information

Investigators:

Benno Bremer [1,2], Qiong Wu [1,2,3], María Guadalupe Mora Álvarez [1,2], Britta Karen Hölzel [1,2*], Maximilian Wilhelm [2,4], Elena Hell [5], Ebru Ecem Tavacioglu [2,5], Alyssa Torske [1,2,6], Kathrin Koch [1,2,6*].

Affiliations:

[1] Department of Neuroradiology, School of Medicine, Klinikum Rechts der Isar, Technical University of Munich, Munich, Germany

[2] TUM-Neuroimaging Center (TUM-NIC), Technical University of Munich, Munich, Germany

[3] Institute of Medical Psychology, Ludwig-Maximilians-Universität München, Munich, Germany

[4] Heidelberg University Hospital, Heidelberg, Germany

[5] Department of Psychology, Ludwig-Maximilians-Universität München, Munich, Germany

[6] Graduate School of Systemic Neurosciences, Ludwig-Maximilians-Universität München, Martinsried, Germany

* Principal investigators

Contributions

B.B., M.G.M.Á., B.K.H., M.W. and K.K. designed the study. B.B., M.G.M.Á., M.W., E.H. and E.E.T. acquire the data.

Rationale & background information

Mindfulness practice has experienced a surge of interest over the past twenty years and has been widely applied in clinical, educational, and work-related contexts. It is usually defined as the conscious engagement in present-moment attendance with an attitude of acceptance, curiosity, and openness (Bishop et al., 2004). Mindfulness can be trained through the practice of mindfulness meditation. Various programs have been established to impart theoretical knowledge and to provide guided meditation exercises, the most prominent of these being mindfulness-based stress reduction (MBSR) (Kabat-Zinn, 1990).

Along with the general interest, the number of scientific publications related to mindfulness has increased. Various studies show a multitude of positive effects on cognitive processes (Chiesa, Calati, & Serretti, 2011), physical, and psychological health (Creswell, 2017). This raises questions for the underlying mechanisms. Prior research has postulated that mindfulness practice exerts its effects by promoting attention control, emotion regulation and modulating self-awareness (Y.-Y. Tang, Hölzel, & Posner, 2015). Neuroscientific studies could demonstrate that brain regions associated with attention, executive processing, and emotion regulation are relevant to these changes. The anterior cingulate cortex (ACC), which is known to play an important role for executive attention (van Veen, 2002), was found to be more active in experienced meditators, compared to non-meditators (B. K. Hölzel et al., 2007), and to show increased activation following meditation training (Y. Y. Tang et al., 2009). The amygdala, which is widely known for its relevance to the processing of fear and other emotions, was found to show less activation in response to emotional stimuli in mindfulness meditation practicing individuals suffering from generalized anxiety disorder (Britta K. Hölzel et al., 2013). Self-awareness can be associated with the medial prefrontal cortex and posterior cingulate cortex, regions pertaining to the default mode network (DMN) (Buckner, Andrews-Hanna, & Schacter, 2008). These regions were observed to show less activation in experienced meditators, when compared to non-meditators (Brewer et al., 2011).

While large advances have been made, scientific knowledge on the neurobiological mechanisms behind mindfulness remains fragmentary. Existing studies have been conducted under diverse methodological conditions and only few studies implemented longitudinal study designs. Among these, most interventions were either designed for a few days (Y. Y. Tang et al., 2009) or followed standard eight week procedures such as MBSR (Goldin & Gross, 2010). Both training intensities come with challenges: Training effects coming from a few days of training should differ from those coming from more intensive mindfulness meditation practice. On the other hand, long training procedures of eight weeks and longer, require bigger organizational efforts and carry a larger risk of participant loss. Hence, we decided to pursue a longitudinal study protocol with a mindfulness meditation training of 31 days as we expect this to be a good balance between training intensity and feasibility. The training sessions will be delivered via an online platform. Thereby extensive training programs like ours can be

easily integrated into the daily routine of our participants. Prior studies have found web-based mindfulness interventions to come with good effects on various aspects of psychological health (Fish, Brimson, & Lynch, 2016). In this study, we plan on assessing the effects of a 31-days web-based mindfulness meditation training on brain structure and function.

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Study design

General information:

- Monocentric
- Longitudinal
- Control group design

Inclusion criteria:

- Age 18-65
- General MRI suitability
- Ability to provide consent
- Written informed consent
- Right-handedness

Exclusion criteria:

- Presence of psychiatric or neurologic disorders

- Meditation experience of more than three meditations within the past year or more than ten during the entire life span
- Use of psychotropic drugs
- Pregnancy

Randomisation: Simple

Blinding: One-sided (subject only)

Expected duration of data acquisition: 12-18 months

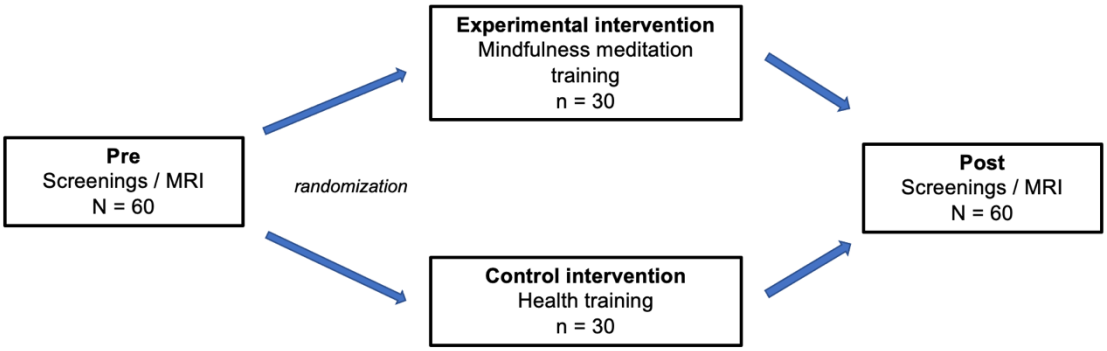
Study population: Recruitment through hospital bulletin boards, online, word-of-mouth

Methodology

Screenings:

- Confirmation of inclusion/exclusion criteria by help of standardized questionnaires
- Written informed consent
- Short version of DSM-IV (M.I.N.I., Sheehan et al. 1998) to exclude psychiatric conditions
- Mindful attention awareness scale (MAAS, Brown et al. 2003)

Screenings are to be conducted immediately before and after the training / control intervention. Two consent forms are to be signed, one is to be handed out to the participant, one is to stay with the investigators.



Interventions:

Training programs are accessible via an online platform ("teachable", https://teachable.com/). Both trainings will consist of 31 sessions each. Each session is laid out for 10-15 minutes and contains either a video clip or an audio recording. The first session contains a video and the following two sessions are presented as audios followed by another video and two audios and so on.

The experimental condition (mindfulness meditation training, MMT) was developed by Britta Hölzel who is a certified MBSR instructor and has been adapted to the delivery format by the other investigators. It is designed to convey both practical meditation exercises as well as general information on mindfulness. It is based on the MBSR program.

The control condition (health training, HT) was designed as a strictly informative control intervention without the practice of meditation. It contains excerpts from popular science broadcasting formats. These cover a broad range of health-related topics. Topics were not allowed to be mindfulness- or meditation-related. Other than this no criteria were applied.

For a full list of contents of either training procedure see below.

		MMT		HT
Session	**Format**	**Theoretical training**	**Practical training**	**Theoretical training**
1	Video	Introduction to mindfulness	Mindful breathing A	Sleep

2	Audio	*(Practice only)*	Mindful breathing A	Chronic pain
3	Audio	*(Practice only)*	Mindful breathing A	Light exposition and health
4	Video	Arriving in presence	Mindful breathing B	Sleep disturbances
5	Audio	*(Practice only)*	Mindful breathing B	Body memory
6	Audio	*(Practice only)*	Mindful breathing B	Migraine
7	Video	Arriving in the body	Bodyscan A	Burnout
8	Audio	*(Practice only)*	Walking meditation	Nutritional supplements
9	Audio	*(Practice only)*	Bodyscan A	Social inequality and health
10	Video	Subjectivity of perception	Bodyscan B	Sore muscles / Vegan diet
11	Audio	*(Practice only)*	Walking meditation	Time perception
12	Audio	*(Practice only)*	Bodyscan B	Gender specific health experience
13	Video	Communicating mindfully	Mindful attention to body sensations	Vitamins
14	Audio	*(Practice only)*	Mindful attention to body sensations	Health impacts of dieting
15	Audio	*(Practice only)*	Mindful attention to body sensations	Aging
16	Video	Non-judgement	Mindful attention to body sensations	Sugar
17	Audio	*(Practice only)*	Mindful listening	Maintaining a diet
18	Audio	*(Practice only)*	Mindful listening	Self-deceit
19	Video	Dealing with stress	Mindfully approaching emotions	Raw foods
20	Audio	*(Practice only)*	Mindfully approaching emotions	Migration and health
21	Audio	*(Practice only)*	Mindfully approaching emotions	Epigenetics
22	Video	Turning towards instead of turning away	Turning towards instead of turning away	Sensible footwear
23	Audio	*(Practice only)*	Approaching unpleasant feelings	Obsessive-compulsive disorder
24	Audio	*(Practice only)*	Awareness of thinking	Self-efficacy
25	Video	Positive qualities	Loving kindness	Busting breakfast myths
26	Audio	*(Practice only)*	Loving kindness	Cardiovascular diseases
27	Audio	*(Practice only)*	Loving kindness	Hypnotherapy
28	Video	Decentring	Open monitoring	Staying active in the office
29	Audio	*(Practice only)*	Open monitoring	Negative empathy
30	Audio	*(Practice only)*	Silent meditation	Pain perception
31	Video	Reflecting the course	Silent meditation	Physical activity

MRI acquisition

Imaging data will be collected on a 3T Philips MRI scanner with a 32-channel head coil at Klinikum Rechts der Isar, München, Germany.

Sequences:

- T2*-weighted resting state functional images (EPI), Multiband factor 2, TR 2.7s, TE 33ms, flip angle 90°. FOV 192 mm x 192 mm x 141 mm. Matrix size 96 x 96 x 64. Slice thickness 2 mm. 200 volumes. Duration ~ 9 minutes. Subjects are instructed to keep eyes closed, awake and to refrain in engaging in any trains of thought.
- T1-weighted anatomical images (MPRAGE), TR 11ms, TE 5.2ms, flip angle 8°. Matrix size 384 x 384 x 230. 0.7mm^3 isotropic voxels.

Safety considerations

It is to be assumed that the MRI measures will be well tolerated by the participants. The duration of the measure is not expected to exceed 45 minutes and therefore should be tolerable. All participants will be informed about the course, duration, and potential risks of the study beforehand. Only participants with written informed consent will be admitted to the study procedure. Participants may withdraw their consent and thereby dropout at any point. In summary, the risks of participation are considered to be low.

Follow up

Aside from the post-interventional measure no follow up examinations are planned.

Data management

The following data are going to be assessed:

- Documentation of inclusion criteria and biographic information that led to the participation
- Questionnaire-based information
- Written informed consent
- MR-images on PACS and copies of the raw data on HDD
- Documentation of any participant-reported adverse effects

Data are stored in the PACS / TUM-NIC file system on hospital servers as well as on external HDD. Data are saved for at least 10 years. Only registered users have access to these data. Data are not to be shared with third parties

Every participant is assigned a pseudonym under which their data are saved. The investigators own a list that links this pseudonym to participant details. This list is kept confidential.

Originals of all central study documents are stored for at least 10 years after creation of the final report. The principal investigator is responsible for storage of these documents.

Participants are informed that in case of withdrawal of consent all data created up to this point will be stored for the analysis. Participants have the right to be informed about their stored data and to require their deletion.

Statistical analysis

Sample size: 30 subjects per group (strong effects (d = 0.8) possible with a power of ~ 0.86 via *t*-tests or Pearson correlation (independent samples, two-sided *t*-tests, β / α ratio = 1); power for rm-ANOVA: γ = 0.94 – 0.96)

Questionnaire-based information are to be manually evaluated and the results are to be collected digitally. Statistical analyses are conducted with SPSS v26.0 or R.

Imaging data are processed with common toolboxes and/or in-house scripts. Toolboxes include SPM12, GIFT, and CONN and may be extended to further toolboxes in case of further analyses. Potential analyses include an independent component analysis, static functional network connectivity and dynamic functional network connectivity as well as seed-based functional connectivity. Time-by-group interactions are to be assessed by repeated measures analyses of variance. Alternatively, group differences are to be assessed by t-tests for paired samples.

Only complete data sets (first and second timepoint) are used for the final analysis. Missing data for one of the timepoints will lead to the exclusion of the associated data set.

Expected outcomes of the study

The results can help to gain a better understanding of the mechanisms underlying the beneficial effects of mindfulness meditation. This can be of significant value to the further development and tailoring of existing applications.

Scientific publications will be created by the investigators altogether. Individual roles are yet to be discussed.

Duration of the project

Data acquisition is expected to take approximately 12 months. Analyses and writing of potential manuscripts are expected to take another 18 months.

Ethics

This study has been approved by the ethics committee of the Klinikum Rechts der Isar, München. There are no ethical concerns to be disclosed. All participants are to be personally informed about the study contents and procedure prior to providing written informed consent. All participants are to be informed that they can withdraw their consent at any point during the study.

Part 2

Budget

B.K.H. acquired private funding through donations which is to be used to provide each participant with a monetary compensation of 100€. This project is supported by a Bundesministerium für Bildung und Forschung (BMBF) grant given to K.K. (grant number: BMBF 01EA1807H). The remaining costs are carried by the department of neuroradiology.