



“Uncovering the neurocognitive mechanisms of meditation using functional Magnetic Resonance Imaging”

Day: Wednesday 11th July 2018 Time: 3.30 – 4.45 pm Track: Working Mechanisms

General background:

The basic neurocognitive underpinnings of the beneficial effects of meditation practices, in particular mindfulness based interventions, are largely unknown. With evidence for clinically relevant effects across a range of psychiatric classifications and general stress-related phenomena, such as rumination and neuroticism, meditation practices carry an important potential for improving health-care in relation to stress-related disorders. Clarifying the neurocognitive mechanisms through which meditation leads to beneficial outcomes might enable us to better identify effective agents of symptom reduction and use these to optimise comprehensive treatment strategies. In this symposium new neuroscientific research will be presented in search for these effective agents of symptom reduction.

Symposium summary:

In the first talk Sevinc will present an RCT on the effects of mindfulness based stress reduction (MBSR) on the neural mechanisms underlying fear extinction. This study addresses the hypothesis that mindfulness-based interventions create a context akin to behavioral exposure therapy by diminishing cognitive avoidance and thereby inducing internal exposure. Assessment of brain activation by means of fMRI during fear extinction before and after MBSR suggests that MBSR improves the retention of extinction memory through enhancing neural activity in regions associated with attentional input to memory. Implications for our understanding of beneficial effects of mindfulness in stress-related symptoms after MBSR will be discussed. In the second talk van der Velden will address hypotheses and preliminary data of an innovative fMRI resting state study. This study focussed on default-mode network connectivity before and after mindfulness based cognitive therapy during rest and during rumination induction. This RCT was set up against the background of an extensive review of the field of neuroscience and mindfulness, which will also be addressed. In the third talk, Barnhofer will present an overview of findings from a study that investigated the effects a brief and intensive mindfulness intervention in patients with a persistent history of depression. Effects of the two-week intervention were compared against an active control and baseline deficits established in comparisons against a healthy control group. In the fourth talk, Sevinc will present a study investigating common and dissociable psychological changes and neural activation patterns associated with two well-known stress reduction courses - the Relaxation Response (RR) or the Mindfulness-Based Stress Reduction (MBSR) program.



Symposium overview

- Presenter 1** **Gunes Sevinc** - Learning Not to Fear: Mindfulness Improves Retention of Fear Extinction - A randomized controlled fMRI investigation
- Presenter 2** **Anne Maj van der Velden** - Neural mechanisms of mindfulness-based cognitive therapy in the treatment of recurrent major depressive disorder: study protocol
- Presenter 3** **Thorsten Barnhofer** - Reversing latent vulnerabilities: effects of a brief intensive mindfulness training in patients with persistent depression
- Presenter 4** **Gunes Sevinc** - Common and Dissociable Mechanisms of Stress Reduction following the Mindfulness-Based Stress Reduction and Relaxation Response Programs
- Chair:** ***Dirk Geurts***



Learning Not to Fear: Mindfulness Improves Retention of Fear Extinction - A randomized controlled fMRI investigation

Gunes Sevinc¹, Jonathan Greenberg¹, Tim Gard^{1,3}, Britta Holzel^{1,2}, Muhammed Milad⁴, Sara Lazar¹

¹*Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, United States;* ²*Department of Neuroradiology, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany;* ³*Institute for Complementary and Integrative Medicine, University Hospital Zurich and University Zurich, Zurich, Switzerland;* ⁴*Psychiatry Department, University of Illinois, Chicago, United States*

Background and objectives: Mindfulness based stress reduction (MBSR) programs have been widely utilized to ameliorate psychiatric and stress-related symptoms, however the neural mechanisms that underlie the reported improvements are still largely unknown. Mindfulness meditation involves refraining from cognitive avoidance and thus provides a basis for internal exposure to aversive stimuli. Thus, we hypothesized that mindfulness-based interventions create a context akin to behavioral exposure therapy and thereby alter participants' neurobiological responses to the aversive stimuli.

Methods: In a randomized controlled longitudinal study with healthy but stressed, meditation-naïve individuals, we tested this hypothesis and investigated neural activation patterns associated with extinction memory using a well-established 2-day fMRI fear-conditioning and extinction protocol. Participants completed either 8-week MBSR (n=42), or stress management education (SME, n=25) programs. Behavioral changes and alterations in neural activation patterns associated with extinction memory from pre to post interventions were assessed.

Results: The results demonstrated that both interventions decreased perceived levels of stress (Cohen's $d=0.56$, for MBSR and $d=0.57$, for SME). However, MBSR resulted in further improvements in levels of anxiety (Cohen's $d=0.43$), rumination (max Cohen's $d=0.82$), mindfulness (Cohen's $d=0.56$), and self-compassion (max Cohen's $d=0.83$). The groups exhibited differential changes in neural activation patterns during extinction recall. MBSR was associated with a greater increase in neural activity in a cluster in left temporoparietal junction (FWE corrected, $p<0.05$), suggesting the involvement of attentional control in retention of fear extinction. Moreover, neural activation in this cluster correlated with improvements in mindfulness levels only for the MBSR group.

Discussion and Conclusions: The current results indicate that MBSR improves the retention of extinction memory through enhancing neural activity in regions associated with attentional input to memory. Overall, these results indicate that MBSR leads to improvements in stress and stress-related symptoms, through improving retention of fear extinction memory. Considering that the ability to recall that a stimulus is no longer associated with threat is critical for healthy emotional functioning, these results suggest the improvement in this ability may be a key mechanism through which mindfulness meditation yields beneficial effects.



Neural mechanisms of mindfulness-based cognitive therapy in the treatment of recurrent major depressive disorder: study protocol

Anne Maj van der Velden¹, Gaëlle Desobres², Mia o'Toole³, Else-Marie Elmholdt⁴, Catherine Harner⁵, Catherine Crane⁵, Jonathan Smallwood⁶, Lone Fjorback¹, Andreas Roepstorff¹, Willem Kuyken⁵

¹*Department of Clinical Medicine, Aarhus University, Aarhus, Denmark*

²*Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Boston, United States*

³*School of Business and Social Sciences, Aarhus University, Aarhus, Denmark*

⁴*NIDO at Aarhus University Hospital, Herring, Denmark*

⁵*Department of Psychiatry, University of Oxford, Oxford, United Kingdom*

⁶*Department of Psychology, University of York, York, United Kingdom*

Background and objectives: Mindfulness-Based Cognitive Therapy (MBCT) is an effective prophylactic treatment for prevention of relapse risk amongst individuals with a history of recurrent MDD. However, only about half experience sustained remission following MBCT. To optimize outcomes of evidence-based treatments we need to identify markers to speak to which individuals will demonstrate long-term benefit from treatment and identify key therapeutic mechanisms of change. Within the field of mental health research it has been argued that the interplay of psychological and biological processes holds great potential to enhance our understanding of mechanisms of change. Despite the promise of such integrative approaches and a rapidly growing literature on the neuroscience of mindfulness meditation, there is currently a paucity of studies looking at the neural mechanisms of MBCT in the treatment of recurrent MDD. The default-mode network (DMN) has received much attention in the context of the clinical neuroscience of depression, and has been suggested as a marker of rumination and vulnerability to depression. In this study, we examine changes in DMN connectivity at rest or during rumination induction following the MBCT programme, and the extent to which change in DMN connectivity may predict proximal and distal clinical outcomes. Furthermore, we employ experience sampling to explore how individual differences in affective and cognitive thought content relate to brain dynamics.

Methods: Participants with a history of recurrent MDD shall be randomized 2:1 to MBCT N=50 in addition to treatment as usual (TAU) or TAU (N=25). We shall examine functional connectivity in the DMN using a fMRI paradigm consisting of resting state fMRI, rumination induction and mindfulness meditation from the MBCT programme. Symptom severity will be measured before and after treatment and at 3, 6, 9 and 12 months follow-up.

Results and Discussion: This study examines changes in DMN connectivity at rest and during rumination induction following the MBCT program, and the extent to which change in DMN connectivity may predict proximal and distal clinical outcomes. Study hypotheses will be presented and discussed in the light of a review of the field.



Reversing latent vulnerabilities: effects of a brief intensive mindfulness training in patients with persistent depression

Thorsten Barnhofer

University of Exeter, Exeter, United Kingdom

Depression is increasingly seen as a neuroprogressive disorder in which repeated exposure to previous episodes and the stress associated with them leads to alterations in neural and physiological functioning that serve as latent vulnerabilities conferring an increased risk for further exposure. Recent research has elucidated how the stress of depressive episodes translates into neural changes underlying this process. Given its stress-buffering effects, mindfulness training may be particularly helpful in addressing, and potentially reversing, such changes.

This talk will present an overview of findings from a study that investigated the effects a brief and intensive mindfulness intervention in patients with a persistent history of depression. Effects of the two-week intervention were compared against an active control and baseline deficits established in comparisons against a healthy control group. I will present findings pertaining to effects of the interventions on a) symptoms and cognitive vulnerabilities such as cognitive reactivity, b) depressive deficits in attentional processes as assessed by event-related potentials in EEG, c) patterns of spontaneous EEG activity during resting state reflecting self-organisation processes in the brain, d) emotion regulation and fMRI amygdala reactivity, and e) resting fMRI connectivity. Based on findings from the project, I will argue that even brief periods of intensive mindfulness training can serve to counter neuroprogression in persistent forms of depression.



Common and Dissociable Mechanisms of Stress Reduction following the Mindfulness-Based Stress Reduction and Relaxation Response Programs

Gunes Sevinc¹, Javeria Hashmi², Jonathan Greenberg¹, Britta Holzel³, Sara Lazar¹

¹*Massachusetts General Hospital & Harvard Medical School, Charlestown, MA, United States*

²*Department of Anesthesia, Pain Management & Perioperative Medicine, Dalhousie University, Dalhousie, Canada*

³*Department of Neuroradiology, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany*

Background and Objective: Most meditation based clinical programs are modeled on one of two well-known stress reduction courses - the Relaxation Response (RR) or the Mindfulness-Based Stress Reduction (MBSR) program. Although both programs are based on meditation, the scientific philosophies and meditative traditions upon which each is founded are distinct. The RR program emphasizes the induction of a relaxed physiological state, whereas the MBSR program is hypothesized to work by cultivating mindfulness. The goal of this study is to investigate common and dissociable psychological changes and neural activation patterns associated with each program.

Methods: Participants were randomized to the RR or the MBSR programs. Improvements in levels of perceived stress, mindfulness, self-compassion and rumination were assessed using self-report measures. Following each program, neural activity during 'relaxing' or 'mindful' bodyscan meditations was investigated using fMRI (n=34).

Results: Both programs were associated with decreased levels of stress (Cohen's d for RR and MBSR, 0.50 and 1.02, respectively) and increased mindfulness (maximal Cohen's d for RR and MBSR, -0.98 and -1.74, respectively). Conjunction analyses revealed functional coupling between ventromedial prefrontal regions and supplementary motor areas. The RR bodyscan was exclusively associated with stronger functional connectivity of the right inferior frontal gyrus – an important hub of intentional inhibition and control- with supplementary motor areas during the bodyscan. The MBSR bodyscan was associated with improvements in self-compassion and rumination and with significant functional connectivity of the right anterior insula – an important hub of sensory awareness and salience- with pregenual anterior cingulate during bodyscan meditation compared to rest.

Discussion: Conjunction analysis results may reflect the present moment awareness and focused attention to the body that is integral to both bodyscan meditations. While differential coupling during the relaxing body scan may reflect increased control of physical/autonomic relaxation, differential coupling during the mindful body scan may reflect increased interoceptive awareness.

Conclusions: These findings indicate that the bodyscan exercises in each program were associated with both overlapping and differential functional coupling patterns. These results may have implications for the differential effects of these programs for the treatment of diverse conditions.