"Exploring the brain and behavioral mechanisms of MBIs for depression and anxiety"

Day:	Time:	Track:
Thursday 12th July 2018	10:45 – 12:00	Working Mechanisms

The goal of this symposium is to share results of four studies that examined the brain and behavioral mechanisms of change during MBCT for remitted depressed patients and MBSR for adults with social anxiety disorder. One study examines an online version of MBCT in women at high risk of depressive relapse. A second study is a prospective, randomized, clinical, neuroimaging study comparing in-person MBCT to a wellness-based CBT intervention. The third presentation provides further analyses of the aforementioned RCT and describes an evaluation of viscerosomatic suppression as a biomarker of MDD vulnerability. The fourth study compares MBSR to CBT and waitlist control for adults with with social anxiety disorder. All studies use fMRI to examine brain changes that potentially elucidate how MBCT and MBSR produce therapeutic improvement in mood and anxiety disorders.

Symposium overview

Presenter 1	**Clara Lopez-Sola*** - Brain and mind changes after an online Mindfulness Based Cognitive Therapy (MBCT) intervention in women at high risk of depressive relapse
Presenter 2	**Le-Anh Dinh-Williams** - Changes in Reward Processing Following Mindfulness-Based Cognitive Therapy and Lasting Wellness
Presenter 3	**Norman Farb** - Mindfulness Training, Stress-Evoked Viscerosomatic Suppression, and Depression Vulnerability
Presenter 4	**Philippe Goldin** - Investigating brain and behavioral indices of emotion regulation and mindfulness skills during an RCT of CBT versus MBSR for social anxiety disorder
Chair:	*Philippe Goldin*

* On behalf of Marina Lopez-Sola

Brain and mind changes after an online Mindfulness Based Cognitive Therapy (MBCT) intervention in women at high risk of depressive relapse

Marina Lopez-Sola [1,2] et al. **PRESENTED BY <u>Clara Lopez-Sola</u>** [3]

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Background and objectives: Depression is the leading cause of illness and disability worldwide (WHO, 20171), and its recurrent nature is a medical challenge that antidepressants have not been able to resolve (Fournier et al. 20102). MBCT was specifically developed as an intervention to prevent depressive relapse long-term (Segal et al. 20123), but objective, mechanistic evidence for its protective effects is needed. In this study, we aim to understand the neurophysiological and psychological mechanisms of vulnerability to depressive relapse and the protective effects of MBCT, delivered in an online fashion. The study hypotheses are: (i) MBCT will significantly reduce depressive symptoms (PHQ-9), in part by first enhancing self-compassion; (ii) these symptom improvements will be associated with changes in brain processing of negative self-referential autobiographical memories.

Methods: We enrolled 25 recurrent major depressive patients with residual symptoms of depression and 25 matched healthy women. Two subjects per group discontinued the study (N=23 subjects/group). Participants underwent a functional MRI scanning visit and completed a set of questionnaires before and after an 8-10-week online MBCT intervention.

Results: At baseline, patients showed greater depression scores (t=8.76, p<.00005), and lower self-compassion (t=-7.52, p<.00005) compared with healthy women. After only two weeks of MBCT, we found a significant increase in self-compassion (t=2.93, p=.007). Reductions in PHQ-9 depression scores were observed after 8 weeks of treatment (t=-2.11, p=.04), and remained significant two weeks later (t=-3.45, p=.002). Mixed-effects GLM models indicated a significant group-by-time interaction effect for PHQ-9 depression scores (linear decrease significantly greater for patients than controls: t=-2.68, p=0.01) and self-compassion (linear increase significantly greater for patients than controls: t=4.20, p=.0002). Increases in self-compassion from week 7 onwards mediated reductions in depression scores (mediation path a*b: t= 1.70; p = .04). Neuroimaging analyses are still in progress.

Conclusions: Online MBCT significantly reduced depressive symptoms in female recurrent MDD patients at high risk of relapse. The mediation analysis indicates that early increases in self-compassion are one significant mechanism via which MBCT reduces depression. We are working to establish the relationships between these changes in psychological functioning with changes in brain processing of affective self-referential information.

Changes in Reward Processing Following Mindfulness-Based Cognitive Therapy and Lasting Wellness

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Background and objectives: Mindfulness-Based Cognitive Therapy (MBCT) is increasingly gaining recognition as an effective strategy in the promotion of positive emotions in previously depressed patients (PE), a population significantly at risk of re-experiencing depression. This is important because theories on PE and resilience would argue that these gains are likely to help promote lasting wellness and reduce the subsequent risk of re-experiencing depression. The issue is that no study to date has examined the relationship between MBCT, positive emotions, and lasting wellness.

Methods: To address this gap, we conducted a prospective, randomized, clinical, neuroimaging study. A sample of seventy-seven previously depressed participants were randomized to receive either MBCT or a cognitive behavioral intervention adapted for Wellbeing (CBT-WB). Using fMRI, we examined BOLD reward-related responses during a gambling task, as an objective neurobiological measure of PE, before and after treatment and monitored for the return of depressive symptoms during a two-year follow-up. This design allowed us to identify: (a) neurobiological changes in PE following MBCT and CBT-WB; (b) relationship between changes in reward processing and lasting wellness; and (c) markers of enduring MDD vulnerability, that is reward-related neurobiomarkers that were present before treatment, resistant to change, and associated with the return of depression.

Results and Discussion: Interestingly, no changes in reward processing following MBCT or CBT-WB were observed in this study, contradicting the growing consensus that mindfulness training brings about changes in PE. In regards to enduring MDD vulnerability, this study found that responses to the anticipation of a reward, but not the reception of it, were predictive of relapse. More specifically, individuals whom relapsed demonstrated chronic reductions in the ventromedial prefrontal cortex before and after treatment while anticipating a potentially rewarding event. This region plays a major role in the tracking of reward-related probabilities and their incentive value. Together, these finding suggest that the inability to anticipate something pleasant during periods of uncertainty is an important predictor of the recurrence of depression and that this response may be resistant to mindfulness and cognitive training. Potential limitations of reward processing tasks and relapse prevention interventions will be discussed in this presentation.

Mindfulness Training, Stress-Evoked Viscerosomatic Suppression, and Depression Vulnerability

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Background: Relapse and recurrence following recovery from Major Depressive Disorder (MDD) are common and debilitating outcomes with enormous social costs. Encouragingly, mindfulness-based interventions such as Mindfulness-Based Cognitive Therapy (MBCT) have shown efficacy in reducing MDD vulnerability following episode remission. However, the mechanisms underlying MDD prophylaxis are unclear. This makes it difficult to assess the need for prophylactic interventions such as MBCT, and likewise challenging to know whether a patient's relapse vulnerability has changed following intervention. Established vulnerability markers, such as personality, family history, and clinical history reflect fixed factors largely insensitive to an individual's changing vulnerability over time. Stress-evoked avoidance of body sensations is commonly observed in MDD, but is relatively understudied in neuroscience research. Our prior work indicates that negative mood provocation leads to suppression of the viscerosomatic brain regions such as the somatosensory cortex and insula, and that such suppression predicts greater MDD symptoms in a community sample. We therefore performed an fMRI study to evaluate viscerosomatic suppression as a biomarker of MDD vulnerability.

Methods: Participants (N=84) remitted from MDD were randomized to receive either 8 weeks of MBCT or an active control wellness-based Cognitive Behavioral Therapy intervention. Participants were scanned both before and after the 2-month preventative treatment period, prior to a 2-year follow-up period of bimonthly MDD relapse screening.

Results: In both pre- and post-intervention fMRI scans, negative mood induction consistently evoked viscerosomatic suppression, which proved to be a reliable biomarker of future MDD relapse vulnerability, hazard ratio = .14, 95% CI [.05 to .44]. Incorporating treatment-related biomarker change improved prediction $X2(1) = 19.4$, $p < .0001$. While some differences between MBCT and the active control condition were observed, both groups were equally protected from MDD relapse and showed similar rates of biomarker change.

Discussion and conclusion: The identification of a reliable and dynamic biomarker of MDD vulnerability represents an important step in stemming the rising prevalence of depression worldwide. The lack of group differences in addressing viscerosomatic suppression suggests that there may be multiple avenues for strengthening embodied awareness in the face of stress-implications for matching participants to their ideal treatments will be discussed.

Investigating brain and behavioral indices of emotion regulation and mindfulness skills during an RCT of CBT versus MBSR for social anxiety disorder

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Background: Cognitive-Behavioral Group Therapy (CBGT) and Mindfulness-Based Stress Reduction (MBSR) are both effective treatments for anxiety disorders. Theoretical models suggest that CBT and MBSR work by different therapeutic mechanisms, namely, increases in cognitive reappraisal and mindfulness skills. However, few studies have directly examined whether changes in these proposed mechanisms predict treatment outcome. Thus, the goal of this study was to investigate potential therapeutic mechanisms of CBT versus MBSR in adults with social anxiety disorder (SAD) by assessing (1) weekly changes in emotion regulation and mindfulness skills during treatment, and (2) pre-to-post changes in reappraisal and acceptance brain networks using fMRI.

Methods: 108 unmedicated adults with SAD were randomly assigned to 12 weeks of CBGT, MBSR and waitlist control groups. All participant completed weekly assessment of emotion regulation strategies and mindfulness skills, as well as administered an fMRI emotion regulation of negative self-beliefs task that assessed brain and behavioral indices of reappraisal and acceptance brain networks.

Results: CBGT and MBSR produced similar decreases in social anxiety and increases in reappraisal and mindful attitude. CBGT produced greater increases in disputing anxious thoughts/feelings and reappraisal success than MBSR. MBSR produced greater acceptance of anxiety and acceptance success than CBGT. Lead-lag analyses revealed increases in weekly reappraisal and reappraisal success predicted subsequent decreases in weekly social anxiety during CBGT (but not MBSR), and that increases in weekly mindful attitude and disputing anxious thoughts/feelings predicted subsequent decreases in weekly social anxiety during MBSR (but not CBGT). Neurally, both CBGT and MBSR produced similar changes in the brain network activation during reappraisal and acceptance.

Discussion and conclusion: This examination of weekly temporal dynamics and pre/post changes of proposed emotion regulation and mindfulness mechanism identified shared and distinct changes during CBGT and MBSR that both support and challenge current conceptualizations of these clinical interventions. CBT may have an impact on mindfulness skills and MBSR on emotion regulation. One key challenge is how to integrate and sequence CBT and MBSR training to make them optimal in a transdiagnostic manner (i.e., across diagnostic categories) and even on an individual patient level.