Mindfulness-Based Interventions: Mechanisms of Action

Thorsten Barnhofer
Rationale
Depression

Pathology consists not so much of the mood state per se, but an “increased tendency to enter into”, and an “inability to disengage from this mood state” (Holtzheimer & Mayberg, 2011, p. 1)
Mindfulness-Based Cognitive Therapy: Core Skill

“...ability, at time of potential relapse, to recognize and disengage from mind states characterized by self-perpetuating patterns of ruminative, negative thought.” (Segal, Williams, & Teasdale, 2002)
Mindfulness

“the awareness that emerges through paying attention on purpose, in the present moment, and non-judgmentally to the unfolding of experience moment to moment” (Jon Kabat-Zinn, 2003)

Pali: sati, Sanskrit: smrti: open-hearted knowing, meanings include elements of “remembrance, reminiscence, thinking of or upon, calling to mind, memory”
Current Findings
Treatment-Related Changes in Decentering (Bieling et al., 2012)

Table 5

Interactive Effects of Potential Mediators in the Prediction of Depressive Symptoms From Randomization to 6-Month Follow-Up

<table>
<thead>
<tr>
<th>Order of entry</th>
<th>Predictor 1</th>
<th>Predictor 2</th>
<th>B1</th>
<th>B2</th>
<th>t1</th>
<th>t2</th>
<th>Cumulative $R^2$</th>
<th>F for increment in $R^2$ for set</th>
<th>df</th>
<th>Partial correlation (pr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HRSD T2</td>
<td></td>
<td>0.39</td>
<td>0.24</td>
<td>1.34</td>
<td></td>
<td>0.06</td>
<td>1.19</td>
<td>1, 34</td>
<td>0.23</td>
</tr>
<tr>
<td>2</td>
<td>ΔEQ-W</td>
<td>Group</td>
<td>1.29</td>
<td>-1.25</td>
<td>1.59</td>
<td></td>
<td>0.06</td>
<td>1.43</td>
<td>2, 32</td>
<td>0.27</td>
</tr>
<tr>
<td>3</td>
<td>ΔEQ-W × Group</td>
<td></td>
<td>2.38</td>
<td>0.49</td>
<td>2.11</td>
<td></td>
<td>0.21</td>
<td>4.45**</td>
<td>1, 31</td>
<td>0.35</td>
</tr>
<tr>
<td>1</td>
<td>HRSD T2</td>
<td></td>
<td>0.17</td>
<td>0.12</td>
<td>0.70</td>
<td></td>
<td>0.01</td>
<td>0.37</td>
<td>1, 31</td>
<td>0.13</td>
</tr>
<tr>
<td>2</td>
<td>ΔTMS-C</td>
<td>Group</td>
<td>1.38</td>
<td>-0.37</td>
<td>2.07</td>
<td></td>
<td>0.08</td>
<td>1.26</td>
<td>2, 29</td>
<td>0.19</td>
</tr>
<tr>
<td>3</td>
<td>ΔTMS-C × Group</td>
<td></td>
<td>2.30</td>
<td>0.48</td>
<td>2.70</td>
<td></td>
<td>0.19</td>
<td>7.30**</td>
<td>1, 28</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Note. HRSD T2 = Hamilton Rating Scale for Depression, randomization session (pretreatment); EQ-W = Experiences Questionnaire, Wider Experiences; TMS-C = Toronto Mindfulness Scale. Curiosity; Group = mindfulness-based cognitive therapy (MBCT), medication, placebo. Δ = standardized residualized change in mediator variable from randomization to post treatment (i.e., 8 weeks). All analyses use depression severity (HRSD T3 6 months) as the outcome. df = degrees of freedom.

*p < .05. ** p < .01.
Interoceptive Awareness and Decentering (Barnhofer et al., in prep.)

![Diagram showing the relationship between Treatment, MAIA Attention Regulation, EQ Decentering, and BDI-II Depressive Symptoms]

<table>
<thead>
<tr>
<th>Antecedent</th>
<th>M1 (ΔMAIA AR)</th>
<th>M2 (ΔEQ Decentering)</th>
<th>Y (ΔBDI-II)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coeff.</td>
<td>SE</td>
<td>p</td>
</tr>
<tr>
<td>Treatment</td>
<td>a₁</td>
<td>-5.31</td>
<td>.000</td>
</tr>
<tr>
<td>M₁ (ΔMAIA AR)</td>
<td>a₂</td>
<td>d₂₁</td>
<td>.27</td>
</tr>
<tr>
<td>M₂ (ΔEQ Decentering)</td>
<td>b₁</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>iM₁</td>
<td>12.23</td>
<td>.000</td>
</tr>
</tbody>
</table>

\[ R^2 = .18 \]
\[ F(1, 58) = 13.5, p = .000 \]

\[ R^2 = .40 \]
\[ F(2, 57) = 19.0, p = .000 \]

\[ R^2 = .35 \]
\[ F(3, 56) = 10.4, p = .000 \]
Interoceptive Awareness and Decentering (Barnhofer et al., in prep.)

\[
a_1 d_{21} a_2 = .58, \ SE = .43, CI = [.07, 1.92]
\]

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Treatment</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(X) Treatment</td>
<td></td>
<td>(a_1)</td>
<td>-5.31</td>
<td>1.44</td>
<td>.000</td>
<td>(a_2)</td>
<td>-5.10</td>
<td>1.30</td>
<td>.000</td>
<td>(c')</td>
<td>4.50</td>
<td>2.52</td>
<td>.079</td>
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<tr>
<td>(M_1) (ΔMAIA AR)</td>
<td></td>
<td>(d_{21})</td>
<td>.27</td>
<td>.10</td>
<td>.011</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>(M_2) (ΔEQ Decentering)</td>
<td></td>
<td>(b_1)</td>
<td>-.39</td>
<td>.19</td>
<td>.045</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td></td>
<td>(iM_1)</td>
<td>12.23</td>
<td>2.23</td>
<td>.000</td>
<td>(iM_2)</td>
<td>9.29</td>
<td>2.24</td>
<td>.000</td>
<td>(i_Y)</td>
<td>-16.07</td>
<td>4.38</td>
<td>.000</td>
</tr>
</tbody>
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\(R^2 = .18\)
\(F(1, 58) = 13.5, p = .000\)
\(R^2 = .40\)
\(F(2, 57) = 19.0, p = .000\)
\(R^2 = .35\)
\(F(3, 56) = 10.4, p = .000\)
Interoceptive Awareness and Decentering
(Barnhofer et al., in prep.)

$$a_1b_1 = 2.11, \ SE = 1.02, \ CI = [0.34, 4.50]$$

<table>
<thead>
<tr>
<th>Antecedent</th>
<th>M1 (ΔMAIA AR)</th>
<th>M2 (ΔEQ Decentering)</th>
<th>Y (ΔBDI-II)</th>
</tr>
</thead>
<tbody>
<tr>
<td>X Treatment</td>
<td>$a_1$</td>
<td>$a_2$</td>
<td>$c'$</td>
</tr>
<tr>
<td>$M_1$ (ΔMAIA AR)</td>
<td>$-5.31$</td>
<td>$-5.10$</td>
<td></td>
</tr>
<tr>
<td>$M_2$ (ΔEQ Decentering)</td>
<td>$-0.27$</td>
<td>$-0.39$</td>
<td>$b_1$</td>
</tr>
<tr>
<td>Constant</td>
<td>$12.23$</td>
<td>$9.29$</td>
<td>$i_M$</td>
</tr>
</tbody>
</table>

$$R^2 = .18$$ $F(1, 58) = 13.5, \ p = .000$ $R^2 = .40$ $F(2, 57) = 19.0, \ p = .000$ $R^2 = .35$ $F(3, 56) = 10.4, \ p = .000$
Interoceptive Awareness and Decentering
(Barnhofer et al., in prep.)

\[ a_2 b_2 = 1.99, \ SE = 1.17, \ Cl = [0.27, 5.06] \]

<table>
<thead>
<tr>
<th>Antecedent</th>
<th>( M_1 (\Delta \text{MAIA AR}) )</th>
<th>( M_2 (\Delta \text{EQ Decentering}) )</th>
<th>( Y (\Delta \text{BDI-II}) )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coeff.</td>
<td>( SE )</td>
<td>( p )</td>
</tr>
<tr>
<td>( X ) Treatment</td>
<td>( a_1 )</td>
<td>-5.31</td>
<td>1.44</td>
</tr>
<tr>
<td>( M_1 (\Delta \text{MAIA AR}) )</td>
<td>( d_{21} )</td>
<td>.27</td>
<td>.10</td>
</tr>
<tr>
<td>( M_2 (\Delta \text{EQ Decentering}) )</td>
<td>( b_2 )</td>
<td>-.39</td>
<td>.22</td>
</tr>
<tr>
<td>Constant</td>
<td>( iM_1 )</td>
<td>12.23</td>
<td>2.23</td>
</tr>
</tbody>
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\( R^2 = .18 \)
\( F(1, 58) = 13.5, p = .000 \)

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\( R^2 = .35 \)
\( F(3, 56) = 10.4, p = .000 \)
Cognitive Reactivity (Barnhofer et al., in press)
Cognitive Reactivity (Kuyken et al., 2010)

- MBCT versus m-ADM
- Post-trial cognitive reactivity *higher* in MBCT
- Treatment moderates relation between cognitive reactivity and symptoms at end of follow-up
- Change in self-compassion moderates relation between cognitive reactivity and symptoms in MBCT group
SWAD Dismantling Control Comparison (Williams et al., 2014)

Williams, Crane, Barnhofer, Brennan, Duggan, Fennell, ... & Russell (2014). *Journal of Consulting and Clinical Psychology.*
Future Perspectives

From Buckner et al. (2008)

From Hamilton et al. (2011)
**Pizzagalli (2011): Frontocingular Dysfunction as a Biomarker of Treatment Response**

**TABLE 1. Summary of Neuroimaging Studies Investigating rACC Activity as a Predictor of Treatment Response in MDD Subjects**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Study</th>
<th>Imaging</th>
<th>Task</th>
<th>Numbers of subjects</th>
<th>Increased pre-treatment rACC in responders</th>
<th>Effect size (Cohen’s d)</th>
</tr>
</thead>
</table>
| Pharmacology

- Paroxetine
  - Madsen et al., 2007: PET, Reading, 8 Resp. vs 10 Non-Resp., X<sup>+</sup> 1.43
- Paroxetine
  - Drevets et al., 1999: PET, Reading, 9 Resp. vs 17 Non-Resp., Reversed finding
  - Rizzagalli et al., 2001: PET, Reading, 9 Resp. vs 8 Non-Resp., X<sup>+</sup> 1.43
- Paroxetine
  - Saxena et al., 2005: PET, Reading, 44 MDD subjects, X<sup>+</sup> 0.80
- Venlafaxine
  - Davidson et al., 2003: PET, Picture processing, 12 MDD subjects, X<sup>+</sup> 1.04
- Galantamine or Rivastigmine
  - Mulert et al., 2007a: EEG, Reading, 10 Resp. vs 10 Non-Resp., X<sup>+</sup> 1.33
- Fluoxetine
  - Chen et al., 2007: PET, Face perception, 16 MDD subjects, X<sup>+</sup> 2.34
- Escitalopram
  - Langenecker et al., 2007: PET, Go/NoGo, 16 MDD subjects, X<sup>-</sup> -1.23
  - Kornreich et al., 2009: PET, Reading, 16 Resp. vs 18 Non-Resp., Reversed finding, X<sup>-</sup> -1.49
- Venlafaxine + lorazepam
  - Matts et al., 2003: PET, Reading, 11 Resp. vs 22 Non-Resp., Null finding<sup>+</sup>, Not available
- Venlafaxine or Paroxetine + lorazepam
  - Korb et al., 2009: PET, Reading, 22 Resp. vs 16 Non-Resp., X<sup>-</sup> -0.70
- Ketamine
  - Salvadore et al., 2009: MEG, Face perception, 11 MDD subjects, X<sup>-</sup> -2.27

| Sleep deprivation

- Total SD
  - Ebert et al., 1991: SPECT, Reading, 5 Resp. vs 3 Non-Resp., X<sup>-</sup> -2.46
  - Bartels et al., 1999: PET, Reading, 11 Resp. vs 9 Non-Resp., X<sup>-</sup> -2.46
  - Kold et al., 1997: SPECT, Reading, 9 Resp. vs 6 Non-Resp., X<sup>-</sup> -0.81
  - Wu et al., 1999: PET, Reading, 12 Resp. vs 24 Non-Resp., X<sup>-</sup> -0.67
  - Full SD
    - Ebert et al., 1994: PET, Reading, 11 Resp. vs 9 Non-Resp., X<sup>-</sup> -1.56
    - Sakai et al., 1997: PET, Reading, 6 Resp. vs 6 Non-Resp., X<sup>-</sup> -1.23
  - Total SD
    - Holsboer et al., 1999: SPECT, Reading, 8 Resp. vs 6 Non-Resp., X<sup>-</sup> -3.40
    - Clark et al., 2005: PET, Reading, 6 Resp. vs 12 Non-Resp., X<sup>-</sup> -1.14

| ECT

- McCormick et al., 2007: PET, Reading, 5 Resp. vs 5 Non-Resp., Reversed finding, X<sup>-</sup> -1.77

| tFMS

- Tanaka et al., 1999: SPECT, Reading, 6 Resp. vs 6 Non-Resp., Null finding<sup>+</sup>, Not available
- Montaghi et al., 2009: PET, Reading, 17 MDD subjects, Reversed finding<sup>+</sup>, Not available
- Naccache et al., 2002: PET, Reading, 8 MDD subjects, X<sup>-</sup> -1.48
- Lang et al., 2007: PET, Reading, 24 MDD subjects, X<sup>-</sup> -1.01
- Kato et al., 2003b: PET, Reading, 6 Resp. vs 8 Non-Resp., X<sup>-</sup> -1.36

| CSF

- Siegel et al., 2008: IMRI, Self-referential task, 14 MDD subjects, Null finding<sup>+</sup>, Not available

Abbreviation: Resp, responders; Non-Resp, non-responders.
*#hypothesized pattern was observed.
1. Failure to a correlation between pre-treatment rACC activity and changes in depression severity.
2. Not included in the meta-analysis (no information was provided allowing the computation of effect sizes pertaining to ACC regions).
3. Effect size for an aggregate "limbic system" (ACC, amygdala, and hippocampus).
4. Effect size for an aggregate region (OFC and basal ACC).
5. Included in the meta-analysis.
Reflective Thinking and Depressive Thinking
(Brennan, Barnhofer et al., 2015)
Affect Labeling (Creswell et al., 2007)
Affect Labeling and Trait Mindfulness (Creswell et al., 2007)
Affect Labeling and Trait Mindfulness (Creswell et al., 2007)
Changes in Amygdala Activity following Mindfulness Training or Active Control
Changes in PFC Activity following Mindfulness Training or Active Control
Amygdala-PFC Functional Connectivity (Hoelzel et al., 2013)
Conclusions
Thank you