Unexpected results in the treatment of depression

Peter Wilhelm

28.3.2018
Overview of Today’s Lecture

• Validity of controlled clinical trials of psychotherapy

• Component analysis of Cognitive Behavioral Treatment
  – Experiment of Jacobson et al. (1996)

• Replication of component analysis of Cognitive Behavioral Treatment and comparison to Antidepressant medication
  – Experiment of Dimidjian et al. (2006); Dobson et al. (2008)
Validity of controlled clinical trials of psychotherapy: Findings from the NIMH Treatment of Depression Collaborative Research Program

J. S. Ablon & E. E. Jones

Background

- Theoretical Assumption: Particular Treatment causes specific effect:
  - Therapists adhere to manuals
    - use only techniques specified in manual
    - but abstain from others

- Analysis of therapists’ behavior (Ablon & Jones, 1998):
  - Many therapist behaviors are not school specific
    - E.g. correction of wrong cognitions und irrational beliefs in psychodynamic therapy
  - Similar therapist behaviors in different approaches
Research Questions and Hypotheses

- Whether and how theories of IPT and CBT were translated into practice (observed in therapist-patient interaction)?
  
  - H1: techniques and processes in manualized psychotherapies (IPT, CBT) studied in RCTs overlap
  
  - H2: Intervention strategies common to IPT and CBT promote improvement
Reanalysis of data from NIMH Treatment of Depression Collaborative Research Program (see lecture L3)
Identifying prototyps of therapist behaviors for IPT and CBT

- Identifying prototyps of ideal treatments:
  - leading theoreticians and practitioners: CBT (N = 10), IPT (N = 11)
  - Describe ideal treatment for CBT and IPT with Psychotherapy Process Q-Set:
    - 100 Items to assess therapist patient interactions independent of theoretical orientation

- Interrater-Reliability of expert ratings high (Cronbach’s Alphas => .95)
Psychotherapy Process Q-Set

- 100 Items to describe therapist-patient-interaction on a behavioral level
- Unit of observation: 1 session
- Rating from 1 = 'least characteristic' / 'negatively salient' to 9 = 'most characteristic' / 'salient'

- PT-theory independent
- Developed to compare PT-processes of different PTs
### TABLE 1. Rank Ordering, by Factor Score, of the 20 Most Characteristic Psychotherapy Process Items in an Ideal Regimen of Cognitive Behavior Therapy

<table>
<thead>
<tr>
<th>Psychotherapy Process Item</th>
<th>Factor Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>There is discussion of specific activities or tasks for the</td>
<td>1.93</td>
</tr>
<tr>
<td>patient to attempt outside of session</td>
<td></td>
</tr>
<tr>
<td>Discussion centers on cognitive themes, i.e., about ideas or</td>
<td>1.68</td>
</tr>
<tr>
<td>belief systems</td>
<td></td>
</tr>
<tr>
<td>Patient's treatment goals are discussed</td>
<td>1.51</td>
</tr>
<tr>
<td>Therapist encourages patient to try new ways of behaving</td>
<td>1.49</td>
</tr>
<tr>
<td>with others</td>
<td></td>
</tr>
<tr>
<td>Therapist actively exerts control over the interaction (e.g.,</td>
<td>1.45</td>
</tr>
<tr>
<td>structuring, introducing new topics)</td>
<td></td>
</tr>
<tr>
<td>Therapist adopts supportive stance</td>
<td>1.43</td>
</tr>
<tr>
<td>Dialogue has a specific focus</td>
<td>1.38</td>
</tr>
<tr>
<td>Therapist asks for more information or elaboration</td>
<td>1.37</td>
</tr>
<tr>
<td>Patient's current or recent life situation is emphasized in</td>
<td>1.35</td>
</tr>
<tr>
<td>discussion</td>
<td></td>
</tr>
<tr>
<td>Therapist gives explicit advice and guidance</td>
<td>1.32</td>
</tr>
<tr>
<td>Therapist presents an experience or event in a different</td>
<td>1.28</td>
</tr>
<tr>
<td>perspective</td>
<td></td>
</tr>
<tr>
<td>Therapist is confident or self-assured (versus uncertain or</td>
<td>1.21</td>
</tr>
<tr>
<td>defensive)</td>
<td></td>
</tr>
<tr>
<td>Therapist behaves in a teacher-like (didactic) manner</td>
<td>1.17</td>
</tr>
<tr>
<td>Patient is committed to work of therapy</td>
<td>1.14</td>
</tr>
<tr>
<td>Therapist explains rationale behind technique or approach to treatment</td>
<td>1.13</td>
</tr>
<tr>
<td>Patient brings up significant issues and material</td>
<td>1.09</td>
</tr>
<tr>
<td>Patient understands the nature of therapy and what is</td>
<td>1.08</td>
</tr>
<tr>
<td>expected</td>
<td></td>
</tr>
<tr>
<td>Patient feels helped</td>
<td>1.06</td>
</tr>
<tr>
<td>Therapist accurately perceives the therapeutic process</td>
<td>1.05</td>
</tr>
<tr>
<td>Therapist encourages independence of action or opinion in</td>
<td>1.02</td>
</tr>
<tr>
<td>patient</td>
<td></td>
</tr>
</tbody>
</table>

**a** From the Psychotherapy Process Q-Set, 100 statements describing the therapist-patient interaction during the treatment hour designed to provide a standard language for the therapeutic process and allow quantitative comparison and analysis of different forms of psychotherapy. Each statement is rated on a 9-point scale (1=least characteristic or negatively salient, 9=most characteristic or salient).

**b** Derived from ratings of the 100 Psychotherapy Process Q-Set items by 10 expert cognitive behavior therapists.

### TABLE 2. Rank Ordering, by Factor Score, of the 20 Most Characteristic Psychotherapy Process Items in an Ideal Regimen of Interpersonal Psychotherapy

<table>
<thead>
<tr>
<th>Psychotherapy Process Item</th>
<th>Factor Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s interpersonal relationships are a major theme</td>
<td>2.22</td>
</tr>
<tr>
<td>Therapist emphasizes patient’s feelings in order to help them</td>
<td>1.65</td>
</tr>
<tr>
<td>experience them more deeply</td>
<td></td>
</tr>
<tr>
<td>Patient talks of feelings about being close to or needing</td>
<td>1.62</td>
</tr>
<tr>
<td>someone</td>
<td></td>
</tr>
<tr>
<td>Love or romantic relationships are a topic of discussion</td>
<td>1.58</td>
</tr>
<tr>
<td>Therapist explains rationale behind technique or approach to</td>
<td>1.55</td>
</tr>
<tr>
<td>treatment</td>
<td></td>
</tr>
<tr>
<td>Dialogue has a specific focus</td>
<td>1.39</td>
</tr>
<tr>
<td>Termination of therapy is discussed</td>
<td>1.32</td>
</tr>
<tr>
<td>Therapist is directly reassuring</td>
<td>1.29</td>
</tr>
<tr>
<td>Therapist draws attention to patient’s nonverbal behavior</td>
<td>1.27</td>
</tr>
<tr>
<td>Therapist makes interpretations referring to actual people</td>
<td>1.25</td>
</tr>
<tr>
<td>in patient’s life</td>
<td></td>
</tr>
<tr>
<td>There is discussion of body functions, physical symptoms, or</td>
<td>1.20</td>
</tr>
<tr>
<td>health</td>
<td></td>
</tr>
<tr>
<td>Therapist’s remarks are aimed at facilitating patient’s</td>
<td>1.19</td>
</tr>
<tr>
<td>speech</td>
<td></td>
</tr>
<tr>
<td>Therapist clarifies, restates, or rephrases patient’s</td>
<td>1.15</td>
</tr>
<tr>
<td>communication</td>
<td></td>
</tr>
<tr>
<td>Therapist comments on changes in patient’s mood or affect</td>
<td>1.13</td>
</tr>
<tr>
<td>Patient’s treatment goals are discussed</td>
<td>1.10</td>
</tr>
<tr>
<td>Patient’s current or recent life situation is emphasized in</td>
<td>1.09</td>
</tr>
<tr>
<td>discussion</td>
<td></td>
</tr>
<tr>
<td>Therapist adopts supportive stance</td>
<td>1.09</td>
</tr>
<tr>
<td>Patient experiences discomforting or troublesome (painful)</td>
<td>1.05</td>
</tr>
<tr>
<td>affect</td>
<td></td>
</tr>
<tr>
<td>There is discussion of scheduling of hours or fees</td>
<td>0.94</td>
</tr>
<tr>
<td>Therapist accurately perceives the therapeutic process</td>
<td>0.91</td>
</tr>
</tbody>
</table>

**a** From the Psychotherapy Process Q-Set, 100 statements describing the therapist-patient interaction during the treatment hour designed to provide a standard language for the therapeutic process and allow quantitative comparison and analysis of different forms of psychotherapy. Each statement is rated on a 9-point scale (1=least characteristic or negatively salient, 9=most characteristic or salient).

**b** Derived from ratings of the 100 Psychotherapy Process Q-Set items by 11 expert interpersonal psychotherapists.
Rating therapist-patient interactions in PT-groups of NIMH study

- 35 patients (from 47 completers) treated with CBT
- 29 patients (from 37 completers) treated with IPT
  - Data available only from 2 of 3 sites

- Audio tapes of 4th and 12th session were transcribed

- Rating of transcripts with PT Q-Sort
  - 9 Psychologists with a master degree and eclectic theoretical orientation
  - 2 Raters per transcript (Cronbach’s Alpha .82).
    If disagreement, a third rater was consulted
  - Randomized and blind allocation of transcripts to raters
Preparation and analysis of data

- Computation of profil-correlations between
  - Ideal-Q-Prototype and
  - every selected psychotherapy session (CBT or IPT)

- Coefficients are measures of how similar a therapy session was to ideal CBT or IPT prototype.

- After Fisher’s z-transformation scores are correlated with outcome measures
Average similarity of PT sessions with CBT and IPT prototypes
Correlation between similarity with prototype and outcome measures (pre-scores controlled)

<table>
<thead>
<tr>
<th>Treatment Group and Outcome Measure</th>
<th>Correlation (r)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adherence to Interpersonal Psychotherapy Prototype</td>
</tr>
<tr>
<td>Interpersonal psychotherapy group</td>
<td></td>
</tr>
<tr>
<td>23-item Hamilton Depression Rating Scale</td>
<td>0.32*</td>
</tr>
<tr>
<td>Global score on the Modified Social Adjustment Scale</td>
<td>0.27</td>
</tr>
<tr>
<td>HSCL-90</td>
<td>0.29*</td>
</tr>
<tr>
<td>Beck Depression Inventory</td>
<td>0.37*</td>
</tr>
<tr>
<td>Dysfunctional Attitudes Scale</td>
<td>0.24</td>
</tr>
<tr>
<td>Global Assessment Scale</td>
<td>0.24</td>
</tr>
<tr>
<td>Cognitive behavior therapy group</td>
<td></td>
</tr>
<tr>
<td>23-item Hamilton Depression Rating Scale</td>
<td>0.26</td>
</tr>
<tr>
<td>Global score on the Modified Social Adjustment Scale</td>
<td>0.11</td>
</tr>
<tr>
<td>HSCL-90</td>
<td>0.30</td>
</tr>
<tr>
<td>Beck Depression Inventory</td>
<td>0.41*</td>
</tr>
<tr>
<td>Dysfunctional Attitudes Scale</td>
<td>0.48**</td>
</tr>
<tr>
<td>Global Assessment Scale</td>
<td>0.22</td>
</tr>
</tbody>
</table>

\(^a\) Positive correlations reflect a favorable association with outcome. All Pearson correlations are partial correlations controlling for patient pretreatment scores.

\(^*\) \(p<0.05\)  \(^**\) \(p<0.01\)
Summary and Discussion

- Both CBT and IPT correlated higher with ideal prototype of CBT than with ideal prototype of IPT.

- The closer therapy was performed according to the CBT ideal the more patients improved.

- Results could explain similar outcomes from different therapies.

- Authors don’t report how much ideal prototypes of IPT and CBT overlap:
  - If ideal prototypes overlap, it is more likely that sessions analyzed show correlations with both prototypes.
  - However, overlap in CBT and IPT prototypes would not explain why behavior of IPT therapists correspond more to CBT prototype than to IPT prototype.
Discussion

- PT-theory specific languages for similar therapist behaviors blow differences up
- Contribution of patients underestimated
- Results show that control of therapist behaviors and their interaction with patients in RCT is insufficient
A Component Analysis of Cognitive-Behavioral Treatment for Depression

Jacobson and colleagues


Background:
Assumptions of cognitive model of depression

- Depressed people have stable cognitive schemas (core beliefs)
  - develop as consequence of early learning processes
  - Predispose towards negative interpretations of life events
    - cognitive distortions, or automatic thoughts (AT))
  - depressive symptoms
Background: Cognitive Behavioral Treatment

CBT consists of 3 progressive steps:

1. Changing overt behavior

2. Assessing and Correcting situation-specific distortions in thinking

3. Identification and modification of more stable depressive schemas and presumed cognitive structures
Background

Which components of CBT produce change?

Activation-hypothesis
- change through activation
- instigation to become active and put in contact with available sources of reinforcement -> experience pleasure
- Plays major role in early stages of CT
  - Studies showed that most change occurs during first weeks
  - Behavioral activation (BA) largely responsible for efficacy

Coping skills hypothesis.
- Clients learn to cope with depressing events and ATs associated with these events
  - BA and new set of coping skills responsible for efficacy

Cognitive restructuring hypothesis
- cognitive structures (core schemas) produce ATs
- structural changes in cognitive structures (core schemas) are necessary for improvement
Research Questions

- Which of the three treatment conditions is most efficacious?

- How treatments effect change
  - Do the treatments operate by means of different mechanisms?
  - Do the treatments differentially effect the processes that they are supposed to effect?
Expectations regarding the efficacy of components

- BA
- AT
- CT
Patients

- 151 Participants (113 women, 38 men)
  - 80% from health maintenance organizations,
  - 20% from publicities

- Inclusion criteria:
  - Depression (DSM-III-R)
  - Beck Depression Inventory (BDI): ≥ 20
  - Hamilton Rating Scale for Depression (HRSD): ≥ 14

- Exclusion criteria:
  - Other mental disorders
  - Other psychotherapeutic or medical treatments
  - Hospitalization (suicidal tendency, Psychosis)
Therapists

4 therapists provided treatment in all 3 conditions
- 7 to 20 years (M = 14.8) clinical experience,
  8 to 12 years experience with CT treatment
- 1 year extra training for BA und AT treatments
Treatment conditions

- Manual for each treatment condition
  - Based on original CT manual
  - Prescribed and proscribed interventions were specified

- 20 sessions

- Protocol adherence
  - Sessions were audiotaped
  - 20% of the sessions were checked
  - Immediate contact with therapist, when protocol violation occurred
Treatment conditions: Behavioral Activation

- Activation is the exclusive focus

- Aims of BA:
  - identify behavior problems and
  - activate people in their natural environment

- Interventions:
  - Monitoring daily activities and assessing the pleasure and mastery involved.
  - Assigning new daily activities to increase pleasure and mastery.
  - Imaginal rehearsal of activities before they are undertaken.
    - participants imagine themselves engaging in various activities with the intent of finding obstacles to the imagined pleasure or mastery expected from those events
  - Discussion of specific problems (e.g., difficulty in falling asleep) and prescription of behavior therapy techniques for dealing with them
  - Interventions to address social skills deficits such as assertiveness and communication training.
  - Proscription: work on automatic dysfunctional thoughts and underlying core beliefs or schemas
Treatment conditions: Activation and Modification of Dysfunctional Thoughts (AT)

- **Aim of AT**
  - identify and modify automatic dysfunctional thoughts

- **techniques:**
  - Identifying automatic thoughts arising in session
  - Use of Daily Thought Records
  - Examining evidence for and against automatic thoughts
  - Examining attributional biases in the way participants assess their successes and failures
  - Homework assignments in which participants assess the validity of their negative interpretations

- **AT condition permitted use of all interventions from BA condition**

- **Proscription:** work on underlying core beliefs or schemas
Treatment conditions:
Cognitive Therapy in its complete form

- **Aim of CT**
  - identification and modification of more general patterns of thought that are stable and presumably causes of cognitive distortions and negative feelings

- **techniques:**
  - "downward arrow": client explains problems -> therapist hypothesizes general concerns and core beliefs
  - explicit identification of underlying assumptions and core beliefs
  - Developing alternative assumptions or core beliefs
  - discussion of advantages and disadvantages of holding assumptions or core beliefs
  - homework to determine assumptions or core beliefs and apply other assumptions to circumstances
  - Application of techniques to modify dysfunctional thinking to core beliefs rather than situation-specific dysfunctional thinking

- Allowed use of full range of BA, AT, and CT interventions
  - Minimum of eight sessions with primary focus on assumptive work
Assessment of treatment adherence

- Protocol adherence
  - sessions were audiotaped
  - random selection of 9 clients for each condition
    - 3 tapes: early middle late session
  - Blind judges rated behaviors of therapists on 45 items
    - prohibited or prescribed
    - measuring particular intervention focused on BA, AT, CT
# Treatment adherence

## Table 2

<table>
<thead>
<tr>
<th>Rating for phase of therapy</th>
<th>Overall rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>Middle</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Items measuring BA</td>
<td></td>
</tr>
<tr>
<td>BA</td>
<td>83</td>
</tr>
<tr>
<td>AT</td>
<td>67</td>
</tr>
<tr>
<td>CT</td>
<td>112</td>
</tr>
<tr>
<td>Items measuring AT work</td>
<td></td>
</tr>
<tr>
<td>BA</td>
<td>2</td>
</tr>
<tr>
<td>AT</td>
<td>119</td>
</tr>
<tr>
<td>CT</td>
<td>139</td>
</tr>
<tr>
<td>Items measuring core schema work</td>
<td></td>
</tr>
<tr>
<td>BA</td>
<td>0</td>
</tr>
<tr>
<td>AT</td>
<td>0</td>
</tr>
<tr>
<td>CT</td>
<td>34</td>
</tr>
</tbody>
</table>

*Note.* In each condition, $n = 27$. The higher the score, the more frequently or thoroughly these interventions were made. Ratings were made on a Likert-type scale ranging from *not at all* (0) to *extensively or frequently* (6). The means here are multiplied by 10 to illuminate differences, and analyses were based on raw scores. BA = behavioral activation; AT = automatic thoughts; CT = cognitive–behavioral therapy.
Treatment adherence

Table 2
Adherence Ratings by Treatment Condition

<table>
<thead>
<tr>
<th>Type of item and condition</th>
<th>Rating for phase of therapy</th>
<th>Overall rating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early</td>
<td>Middle</td>
</tr>
<tr>
<td>Items measuring BA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BA</td>
<td>83</td>
<td>86</td>
</tr>
<tr>
<td>AT</td>
<td>67</td>
<td>52</td>
</tr>
<tr>
<td>CT</td>
<td>112</td>
<td>53</td>
</tr>
<tr>
<td>Items measuring AT work</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BA</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>AT</td>
<td>119</td>
<td>133</td>
</tr>
<tr>
<td>CT</td>
<td>139</td>
<td>100</td>
</tr>
<tr>
<td>Items measuring core schema work</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BA</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>AT</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>CT</td>
<td>34</td>
<td>60</td>
</tr>
</tbody>
</table>

Note. In each condition, n = 27. The higher the score, the more frequently or thoroughly these interventions were made. Ratings were made on a Likert-type scale ranging from not at all (0) to extensively or frequently (6). The means here are multiplied by 10 to illuminate differences, and analyses were based on raw scores. BA = behavioral activation; AT = automatic thoughts; CT = cognitive-behavioral therapy.
Assessment of treatment outcome

<table>
<thead>
<tr>
<th>Pre</th>
<th>Treatments</th>
<th>Post</th>
<th>Follow-Up:</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDI</td>
<td>BA</td>
<td>BDI</td>
<td>6, 12, 18, 24 months</td>
</tr>
<tr>
<td>HRSD</td>
<td>AT</td>
<td>HRSD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CT</td>
<td>LIFE</td>
<td></td>
</tr>
</tbody>
</table>

LIFE = Longitudinal Interval Follow-Up Evaluation to assess depression DSM-III-R

20 sessions within 16 Weeks
Criteria for clinically significant change

- **Recovered**
  - BDI ≤ 8
  - HRSD ≤ 7 and only minimal depressive symptoms in LIFE
  - > 8 weeks without depressive symptoms in LIFE

- **Improved**
  - Below DSM-III-R criteria for Major Depression, but not recovered

- **Relapse**
  - 2 weeks with DSM-III-R criteria for Major Depression
  - Additional treatment
Pre-Treatment-Differences

- Despite random assignment of patients to conditions:
  - Sig. difference in HRSD pre scores: BA: 17.4 < AT: 19.3 = CT: 19.1
  - Less previous episodes in BA (n.s.)
  - Education higher in BA (n.s.)
Post-Results BDI
Total Sample (N = 149) (Intent to Treat)

MANCOVA: no sig. differences between groups

Prä-Messung | Post-Messung | 6 Monate
---|---|---
BA | AT | CT
Post-Results HRSD
Total Sample (N = 149) (Intent to Treat)

MANCOVA: no sig. differences between groups

p < .05
Post-Results: Improved, Recovered Total Sample (N = 149) (Intent to Treat)

\[ \chi^2: \text{no sig. differences between groups} \]
Pre-Post-Follow-Up Results: BDI
(N = 131 to 139)
24 months follow up
Patients who were recovered after treatment

Table 5
Percentage of Participants Who Relapsed Through 24-Month Follow-Up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment condition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BA</td>
</tr>
<tr>
<td>Recovered (BDI &lt; 9)*</td>
<td>%</td>
</tr>
<tr>
<td>Relapsed</td>
<td>31.8</td>
</tr>
<tr>
<td>MDD or Tx</td>
<td>50.0</td>
</tr>
<tr>
<td>No relapse</td>
<td>50.0</td>
</tr>
</tbody>
</table>

MDD or Tx = participants who either returned to treatment for depression or met LIFE-II relapse criteria during follow-up (or previous follow-up evaluations); BA = behavioral activation; AT = automatic thoughts; CT = cognitive–behavioral therapy; BDI = Beck Depression Inventory;
Survival Analysis: Probability of relapse for patients who were recovered after treatment
Summary and Discussion

- No sig. differences between treatment conditions in any of the outcome measures:
  - neither post treatment
  - nor at follow ups

- Potential alternative explanations could be ruled out
  - Null-findings not due to inadequate power, power was sufficient (.8) to detect modest to moderate effects
  - therapists were rated as competent
  - treatment integrity was high

- Results have high credibility
  - contrary to hypotheses of CT model that was preferred
  - contrary to allegiance effect
    - Therapists expected CT to be most effective
    - Lower morale in BA condition
Summary and Discussion

- Absolute long term effects
  - About 60% of patients were recovered directly after treatment
  - 50% had no relapse after 2 years
    - Comparable to results of Treatment of Depression Collaborative Research Program
  - Only about 25% of patients stayed healthy
  - Depression = chronic disease
  - Relapse is likely for most patients

- Maintenance therapy and booster sessions required
Conclusions

- Results question theory of change of CT (Beck et al.)
- Exposure to naturally reinforcing contingencies might produce changes in thinking more effectively than explicite cognitive interventions
- “If BA and AT treatments are as effective as CT and also are as likely to modify the factors that are thought to be necessary for change to occur, then not only the theory but also the therapy may be in need of revision.” (Jacobson et al., 1996, p. 303).
- BA and AT are more parsimonious treatments than CT
  - more accessible to less experienced or paraprofessional therapists
- BA and AT component treatments may also be more amenable to less costly alternatives to psychotherapy
  - self-administered or
  - peer support treatments
Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the treatment of adults with major depression.

Dimidjian et al. (2006); Dobson et al. (2008)


Background: Cognitive Behavioral Treatment

- Antidepressant medications (ADMs) = standard treatment for (severe) major depression
  - Most common treatment
- Cognitive therapy (CT) = most extensively studied psychosocial treatment for depression
  - efficacy of CT in many studies,
  - but not in largest RCT (TDCRP; Elkin, 1994)
- Behavioral Activation (BA) alone was as efficacious as full CT
  - expanded BA: idiographic functional analysis to understand depressive behavior and create contextual interventions.

“The expansion of the BA component treatment is an attempt to renew focus on the purely behavioral aspects of these traditions, which were largely overlooked in recent decades.” (Dimdijan, 2006, p. 659)
Research Questions

- Goal: Replication and extension of TDCRP and the component analysis study

- How efficacious is BA in the treatment of major depression compared to
  - CT
  - ADM
  - Placebo

- Are psychosocial treatments an alternative to ADM in the treatment of moderate to severe depression?

- How enduring are effects?

- Hypotheses
  - for severely depressed participants
    - ADM > placebo
    - no differences between active treatments
  - for less severely depressed participants
    - no differences between treatments and placebo
Patients

- 241 Participants (66% women)
  - 32% from local agencies and others
  - 62% from publicities

- Inclusion criteria:
  - Depression (DSM-IV)
  - Beck Depression Inventory (BDI-II): ≥ 20
  - Hamilton Rating Scale for Depression (HRSD): ≥ 14

- Exclusion criteria:
  - Other mental disorders
    - lifetime diagnosis of psychosis, bipolar disorder, organic brain syndrome, or mental retardation, suicide risk, alcohol or drug abuse, primary diagnosis of panic disorder, obsessive–compulsive disorder, pain disorder, anorexia, or bulimia; or personality disorder
  - Unstable medical condition, any medication that would complicate the administration of paroxetine
  - Not responded favorably to either CT or paroxetine in previous year
Therapists

- BA: 2 psychologists (7 y. experience)
  - training by Jacobson
- CT: 3 psychologists (14 y. experience)
  - training by the Beck Institute
- ADM and Placebo: 5 pharmacotherapists (12 y. experience)
Treatment conditions: Behavioral Activation

- Activation is the exclusive focus

- Aims of BA:
  - Promote engagement with activities and contexts that are Reinforcing and consistent with an individual’s long-term goals
  - Change patterns of avoidance and withdrawal that prevent contact with potential reinforcers

- Interventions:
  - Monitoring daily activities and assessing the pleasure and mastery involved.
  - Exploring alternative behaviors related to achieving goals,
  - Using role-playing to address specific behavioral deficits.
  - Increased focus on the assessment and treatment of avoidance behaviors
  - Establishment or maintenance of regularized routines
  - Behavioral strategies for targeting rumination
    - including an emphasis on the function of ruminative thinking
    - moving attention away from the content of ruminative thoughts toward direct, immediate experience

- Proscription: use of specific cognitive interventions
Treatment conditions: Cognitive Therapy

- **Aim of CT**
  - identification and modification of general patterns of thought that are stable and presumably causes of cognitive distortions and negative feelings

- **Interventions targeting the following areas:**
  - behavioral dysfunction
  - Situational specific negative thinking and cognitive distortions
  - Underlying dysfunctional beliefs or cognitions assumed to be related to the participant’s

- Components were implemented in an integrative fashion, in contrast to the sequential manner used in the component analysis study

- **CT therapists used BA strategies outlined in the CT texts**
  - but not the strategies added as part of the expanded BA model
Treatment conditions: Pharmacotherapy

- Paroxetine (selective serotonin reuptake inhibitors, SSRIs)
  - most widely used and best tolerated ADM

- Medications were provided on a flexible schedule
  - maximum dose of up to 50 mg per day at the 12 week
  - If side effects occurred dose was temporarily and raised again at later

- Clinical management (protocol developed for the TDCRP)
  - develop therapeutic relationships characterized by support, reassurance, and optimism about the treatment regimen to maximize participant adherence
  - administration of the HRSD every session
  - inquiry about treatment response, side effects, and nonstudy medication
  - information, help participants to develop reasonable expectations regarding treatment, give (limited) advice
Administration of treatment conditions

- Manual for each treatment condition
  - Based on original CT manual
  - Prescribed and proscribed interventions were specified

- Psychotherapy conditions
  - Maximum of 24 sessions a 50-min over 16 weeks
  - Two weekly sessions for the first 8 weeks and
  - One weekly session for the next 8 weeks

- Pharmacotherapy conditions
  - Weekly for the first 4 weeks (30 to 45 min)
  - Thereafter biweekly meetings a 30 min.
  - Triple-blind (participants, pharmacotherapists, evaluators) in the beginning
    - At 8 weeks, blind was broken
    - Placebo participants were offered their choice of treatment
### Assessment of treatment outcome

<table>
<thead>
<tr>
<th>Pre</th>
<th>Every 2nd week during Treatment</th>
<th>Post</th>
<th>Follow-Up:</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDI</td>
<td></td>
<td>BDI</td>
<td>3, 6, 12, 13, 14, 18, 24 months</td>
</tr>
<tr>
<td>HRSD</td>
<td></td>
<td>HRSD</td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td></td>
<td>BDI</td>
<td></td>
</tr>
<tr>
<td>HRSD</td>
<td></td>
<td>HRSD</td>
<td></td>
</tr>
<tr>
<td>BA</td>
<td></td>
<td>LIFE</td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td></td>
<td>LIFE</td>
<td></td>
</tr>
<tr>
<td>ADM</td>
<td></td>
<td>LIFE</td>
<td></td>
</tr>
<tr>
<td>PLA</td>
<td></td>
<td>LIFE</td>
<td></td>
</tr>
</tbody>
</table>

**LIFE** = Longitudinal Interval Follow-Up Evaluation to assess depression DSM-IV
Assessment of treatment adherence

Completed Intake Assessment
N = 388

Excluded or Declined
N = 147

Randomized
N = 241

Cognitive Therapy
N = 45
  Refused Randomization
N = 1
  Did Not Complete
N = 5
  Completed
N = 39

Behavioral Activation
N = 43
  Refused Randomization
N = 3
  Did Not Complete
N = 4
  Completed
N = 36

Antidepressant Medication
N = 100
  Refused Randomization
N = 14
  Did Not Complete
N = 30
  Completed
N = 56

Placebo
N = 53
  Refused Randomization
N = 8
  Did Not Complete
N = 4
  Completed
N = 41
Assessment of treatment adherence

Completed Intake Assessment
N = 388

- Excluded or Declined
  N = 147

  - Cognitive Therapy
    N = 45
      - Refused Randomization
        N = 1
          - Did Not Complete
            N = 5
              - Completed
                N = 39
      - Did Not Complete
        N = 5
          - Completed
            N = 36
  - Behavioral Activation
    N = 43
    - Refused Randomization
      N = 3
    - Did Not Complete
      N = 4
    - Completed
      N = 36
  - Antidepressant Medication
    N = 100
    - Refused Randomization
      N = 14
      - Did Not Complete
        N = 30
        - Completed
          N = 56
    - Did Not Complete
      N = 4
      - Completed
        N = 41
  - Placebo
    N = 53
    - Refused Randomization
      N = 8
      - Did Not Complete
        N = 4
        - Completed
          N = 41

Attrition sig. higher in ADM than PT conditions
Differences in side effects between Paroxetine vs Placebo

- More sexual side effects:
  - anorgasmia, 17% vs 0% **
  - decreased libido, 15% vs 0% **

- Gastrointestinal distress:
  - nausea, 19% vs 6% *

- Sleep-related difficulties:
  - insomnia, 25% vs 9% *
  - somnolence, 38% vs 6% ***
  - yawning, 12% vs 0% **

- dry mouth, 17% vs 6% *

- excessive sweating, 13% vs 0% **
Mildly depressed patients (BDI)
Completers: Pre and 8 week-assessments
Severely depressed patients (BDI)
Completers: Pre- and 8 week-assessments

![Bar chart showing BDI scores for CT, BA, Paroxetine, and Placebo groups before (N = 138) and after 8 weeks (N = 103).]
Mildly depressed patients (HRSD)
Completers: Pre- and 8 week-assessments

HRSD Scores

<table>
<thead>
<tr>
<th>CT</th>
<th>BA</th>
<th>Paroxetine</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>10</td>
<td>12</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>0</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

Pre (N = 103)  8 weeks (N = 79)
n.s. Interaction
Severely depressed patients (HRSD) Completers: Pre- and 8 week-assessments

* Interaction
Improvement over time (Intent to treat) BDI

- Sig. improvement over time in all groups
- Different improvement for severely depressed patients:
  CT < (BA = ADM)
- Equal improvement for mildly depressed patients
  CT = BA = ADM
Improvement over time (Intent to treat) HRSD

- Same pattern of results as for BDI
  - Sig. improvement over time in all groups
  - Different improvement for severely depressed patients: CT < (BA = ADM)
  - Equal improvement for mildly depressed patients CT = BA = ADM
Response- (50% improvement) and remission rates (BDI ≤ 10; HRSD ≤ 7) at post treatment

**Figure 3.** Response and remission rates at posttreatment based on the Beck Depression Inventory (BDI) for the high-severity subgroup for antidepressant medication (ADM), cognitive therapy (CT), and behavioral activation (BA). Total bar represents response; lower bar represents remission.

**Figure 4.** Response and remission rates at posttreatment based on the Hamilton Rating Scale for Depression (HRSD) for the high-severity subgroup for antidepressant medication (ADM), cognitive therapy (CT), and behavioral activation (BA). Total bar represents response; lower bar represents remission.
Design of the follow up study (Dobson et al., 2008)

<table>
<thead>
<tr>
<th>only responders at Post: N = 106</th>
<th>1. year follow-up: 3, 6, 12 months</th>
<th>2. year follow-up: 13, 14, 18, 24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 w</td>
<td>BA 27</td>
<td>ADM 28</td>
</tr>
<tr>
<td></td>
<td>CT 30</td>
<td>ADM 17</td>
</tr>
<tr>
<td></td>
<td>ADM 21</td>
<td>PLA 17</td>
</tr>
</tbody>
</table>
Figure 2. Cumulative proportion of treatment responders who survived without relapse over the 2 years of follow-up (the vertical line indicates the point at which patients on continuation medication were withdrawn from medication). BA = behavioral activation; CT = cognitive therapy.
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Cummulative proportion of treatment responders (Dobson et al., 2008)

**Figure 2.** Cumulative proportion of treatment responders who survived without relapse over the 2 years of follow-up (the vertical line indicates the point at which patients on continuation medication were withdrawn from medication). BA = behavioral activation; CT = cognitive therapy.

No relapse (e.g. HRSD ≥ 14) during the whole 2 years follow up

cADM < CT *
cADM < BA #
BA = CT, n.s.
Sustained improvement of all patients initially assigned to treatment (Dobson et al., 2008, p. 474)

Sustained response = proportion of patients initially assigned, who completed and responded to acute treatment and who remained free from relapse.

![Bar chart illustrating sustained response percentages across different treatment conditions.]

*Figure 4.* Sustained improvement for all patients initially assigned to active treatment. The total percentages of each bar represent the sustained response in each treatment condition at the end of the 1st year of follow-up; the lower portion of the Prior CT and Prior BA bars represents the sustained response (i.e., sustained recovery) at the end of the 2nd year of follow-up. ADM = antidepressant medication; PLA = placebo condition; BA = behavioral activation; CT = cognitive therapy.
Sustained improvement of all patients initially assigned to treatment (Dobson et al., 2008, p. 474)

“These results indicate that brief treatment with either CT or BA is as efficacious over the long run as keeping people on ADM.” (p. 474)
Summary and Discussion

- Replication of results of TDCRP (Elikin, 1994) and Dismanteling study of Jacobson et al. (1996)
  - After 8 weeks, ADM was only better than placebo among more severely depressed patients
  - Post Treatment (after 16 weeks)
    - Among less severely depressed patients, BA was comparable to antidepressant medication, and CT.
    - Among more severely depressed patients, BA was comparable to antidepressant medication, and both significantly outperformed CT directly after treatment.
Summary and Discussion

- Longterm results
  - Difference between BA and CT were small and not significant
  - psychotherapeutic treatments were at least as efficacious as the continuation of medication
  - CT and BA were more efficacious than continuation of initial ADM treatment with placebo
  
  - Continuation with ADM was less sustainable
    - Not better than continuation with placebo
    - Risk of relapse increased, when ADM was withdrawn
Summary and Discussion

Limitations

- High Drop out rates
  - Only 56% of participants were available for Follow up
  - Highest attrition in the medication group
- For follow up comparisons power was low (only rather big effects could be detected)
- Success of blinding during follow up was not assessed
- Allegiance effects can’t be excluded (in favor of BA)
- Treatment was un flexible
  - PT was terminated after 16 weeks
  - No booster sessions were allowed
  - For ADM, no other medication was allowed
Conclusions

• Results are in contrast to the fact that ADM treatment is considered the standard of care for depression in current psychiatric guidelines for moderately and severely depressed patients.

• Critical meta analytic reviews (Kirsch et al., 2008; Kirsch, 2014) show that compared to placebo ADM has only small effects even in severely depressed patients -> “Antidepressents can be considered as active placebos” Kirsch (2014)
Conclusions

- Conclusion including literature reviews (Longmore & Worrell, 2007, Shinohara et al., 2013)
  - BA and CT produce sustainable effects
    - Skill training, change of appraisals
  - Little evidence that specific cognitive interventions significantly increase the effectiveness of therapy
  - Little empirical support for the role of cognitive change as causal in the symptomatic improvements achieved in CBT
    - CBT is often associated with rapid, early improvement in symptoms that most likely occurs before the implementation of cognitive techniques.
    - However, in the current studies BA seemed to lead to faster improvements
  - Changes in cognitive mediators (the thoughts and beliefs held by the cognitive model to underpin disorder) do not precede changes in symptoms
Take home message

- PT-Treatments contain packages of different methods
  - What is really performed in a certain psychotherapy might differ from what is theoretically expected

- Which components are really efficacious and therefore necessary for an efficacious treatment can only be revealed by systematic research
  - challenge theoretical assumptions
  - improve treatments in the long run

- Antidepressant medication only works better than placebo in more severely depressed and in the short run
  - at the cost of attrition and side effects
  - In the long run it seems to be less sustainable
References


