Neuere Entwicklungen in der Therapie von Anorexia Nervosa

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"Extraordinary claims require extraordinary evidence."
- Carl Sagan
Collaborators

- Daniel le Grange, Ph.D
- W. Stewart Agras, MD
- Helena Kraemer, Ph.D
- Booil Jo, Ph.D
- Susan Bryson, MS
- Judy Beenhakker, MS
- Subjects and therapists
Adolescent AN Treatment Studies

Uncontrolled Studies
- Minuchin et al (1978)
- Dare (1983)
- Martin (1984)
- Mayer (1994)
- Herscovici & Bay (1996)
- Le Grange & Gelman (1998)
- Lock & Le Grange (2001)
- Wallin & Kronwall (2002)
- Le Grange et al (2005)

Controlled Studies
- Russell et al (1987)
- Eisler et al (1997)
- Le Grange et al (1992)
- Eisler et al (2007)
- Robin et al (1994)
- Gowers et al (2007)*
- Lock et al. (2010)
“The patients should be fed at regular intervals, and surrounded by persons who would have moral control over them; relatives and friends being generally the worst attendants.”

Sir William Gull
(1816-1890)
“It is necessary to separate both children and adults from their father and mother, whose influence, as experience teaches, is particularly pernicious”

Jean Martin Charcot
(1825-1893)
But just how well does this work?
Hospitalization for Adolescent AN

Crisp et al 1991

Gowers et al 2007

Baseline One Year

Assessment only

Inpatient

Outpatient (family and individual)

Outpatient (group)

Baseline Year 1 Year 2

Specialized

General

Inpatient
What about outpatient treatments?
• “excessive concern with the body and its size, and the rigid control over eating, are late symptoms in the development of youngsters who have been engaged in a desperate fight against feeling enslaved and exploited, not competent to lead a life of their own.”
“The avoidant position in anorexia nervosa is therefore a profoundly psychosomatic one, rooted in the seemingly miraculous and certainly unique capacity to reverse pubertal process and hence all of its social and psychological impacts.”
Family-Based Treatment

- Developed at the Maudsley Hospital in London in the 1980s
- Refined at the Stanford University and The University of Chicago
- Takes key strategies or interventions from a variety of Schools of Family Therapy
  - Minuchin – Structural Family Therapy
  - Selvini-Palazzoli – Milan School
  - Haley – Strategic Family Therapy
  - White – Narrative Therapy
Family-Based Treatment

- Theoretically agnostic – no assumptions about the origin of the disorder, focus on what can be done
- Parents are a resource with no blame directed to either the parents or the ill adolescent
- Siblings play supportive role and protected from the job assigned to the parents
- FBT is a team approach, i.e., primary therapist, child & adolescent psychiatrist, pediatrician
Three Phases of FBT

**Phase 1**  
(Sessions 1-10)  
• Parents in charge of weight restoration

**Phase 2**  
(Sessions 11-16)  
• Parents hand control over eating back to the adolescent

**Phase 3**  
(Sessions 17-20)  
• Discuss adolescent developmental issues
TREATMENT MANUAL
for
Anorexia Nervosa
A Family-Based Approach

JAMES LOCK
DANIEL LE GRANGE
W. STEWART AGRAS
CHRISTOPHER DARE
RCT Comparing FBT to Individual Therapy

(Lock, Le Grange et al 2010)
Rationale

• Two of the predominant models for treating adolescent AN are
  – Family-Based Treatment (FBT), a family therapy aimed at symptom management by parents early in treatment
  – Adolescent Focused Therapy (AFT) a primarily individual therapy aimed at promoting self-efficacy, self-esteem, and self-management of eating problems.
Design

Hypothesis: FBT is more effective than AFT in promoting full remission and partial remission; Medication use will moderate outcome

Randomized 121 medically stable adolescents with AN (excluding amenorrhea requirement) with parents or guardian to either FBT or AFT. Two month medication on stable dose still meeting entry criteria.

12 months of treatment (24 contact hours/ 24-1 hour sessions in FBT and 32- 45 minute sessions in AFT including collaterals with parents alone)

Primary Outcomes: Full Remission and Partial Remission

Independent assessments of weight, EDE at BL, EOT, 6 and 12 month follow-up
Ineligible = 156
Did not meet weight threshold = 80
Did not like treatments = 56
Unknown = 20

331 Screened by Telephone
Declined = 54
Lived too far away = 24
Refused randomization = 9
Out of age range = 9
Medical or Psychiatric Exclusion = 7
Unknown = 5

175 Screened by Interview

121 RANDOMIZED

AFT (N = 60)
Received intervention = 58
Did not receive intervention (fewer than 6 sessions) = 2

EOT: Assessed = 52;
Refused = 7; not reached = 1
6 Mos FU: Assessed = 46:
Refused = 13; not reached = 1
12 Mos FU: Assessed = 49;
Refused = 10; not reached = 1

ITT mixed effects modeling used all available data
Full remission = 54
Partial remission = 55

FBT (N = 61)
Received intervention = 53
Did not receive intervention (fewer than 6 sessions) = 8

EOT: Assessed = 51;
Refused = 6; not reached = 4
6 Mos FU: Assessed = 43;
Refused = 6; not reached = 2
12 Mos FU: Assessed = 44;
Refused = 14; not reached = 3

ITT mixed effects modeling used all available data
Full remission = 51
Partial remission = 52
Outcome—Clinically Significant

Primary Outcome: Full Remission (weight to 95% IBW weight for height and age according to CDC norms and EDE 1SD with community norms)

--weight threshold approximates weight needed for return to full physical health in young adolescents and to address growth, bone health, and hormonal function

--EDE threshold is in the normal range for community sample and addresses minimization common in adolescent AN
Outcome—Clinically Significant

• Secondary Outcome is partial remission defined as weight greater than 85% IBW age for height using CDC norms.
  – This threshold approximates common cut point for good/intermediate outcome in many studies using Morgan Russell Outcome Criteria.
<table>
<thead>
<tr>
<th></th>
<th>Chicago</th>
<th>Stanford</th>
<th>TOTAL</th>
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<tbody>
<tr>
<td></td>
<td>AFT</td>
<td>FBT</td>
<td>AFT</td>
</tr>
<tr>
<td>Age¹</td>
<td>14.7(1.6)</td>
<td>14.4(1.8)</td>
<td>14.8(1.4)</td>
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<tr>
<td>Comorbidity</td>
<td>31%</td>
<td>12%</td>
<td>32%</td>
</tr>
<tr>
<td>Duration of illness (in months)</td>
<td>8.9(7.8)</td>
<td>11.6(8.5)</td>
<td>11.6(9.5)</td>
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<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
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<tr>
<td>Asian</td>
<td>0 (0%)</td>
<td>1(3%)</td>
<td>6(19%)</td>
</tr>
<tr>
<td>Black</td>
<td>0 (0%)</td>
<td>0(0%)</td>
<td>1(3%)</td>
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<tr>
<td>Caucasian</td>
<td>27(93%)</td>
<td>27(84%)</td>
<td>20(64%)</td>
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<tr>
<td>Hispanic</td>
<td>1(3%)</td>
<td>3(9%)</td>
<td>2(6%)</td>
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<tr>
<td>Other</td>
<td>1(3%)</td>
<td>1(3%)</td>
<td>2(6%)</td>
</tr>
<tr>
<td>% minority</td>
<td>2 (7%)</td>
<td>5(16%)</td>
<td>11(35%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% male</td>
<td>10%</td>
<td>12%</td>
<td>3%</td>
</tr>
<tr>
<td>Intact family</td>
<td>79%</td>
<td>94%</td>
<td>74%</td>
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<tr>
<td>Medication use</td>
<td>31%</td>
<td>28%</td>
<td>6%</td>
</tr>
<tr>
<td>Parent education (years)</td>
<td>17.8(2.6)</td>
<td>16.3(2.6)</td>
<td>16.1(3.3)</td>
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<tr>
<td>Previous Hospitalizations</td>
<td>24%</td>
<td>19%</td>
<td>71%</td>
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<tr>
<td>Sample Size</td>
<td>29</td>
<td>32</td>
<td>31</td>
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<tr>
<td>Measure</td>
<td>Baseline Adjusted Estimated Mean and Standard Error</td>
<td>Baseline Adjusted Mean Difference (FBT-AFT) and 95 % Confidence Intervals</td>
<td>T-values</td>
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<td>-------------------------------</td>
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<tr>
<td></td>
<td>AFT</td>
<td>FBT</td>
<td></td>
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<tr>
<td><strong>BMI percentile for age and gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End of Treatment</td>
<td>23.4(2.8)</td>
<td>31.4(2.8)</td>
<td>8.0(0.1,15.9)</td>
</tr>
<tr>
<td>6 month F/U</td>
<td>29.1(3.4)</td>
<td>31.4 (3.5)</td>
<td>2.3 (-7.4,12.0)</td>
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<td>12 month F/U</td>
<td>29.0(3.4)</td>
<td>32.2(3.4)</td>
<td>3.2(-6.4,12.8)</td>
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<tr>
<td><strong>EDE</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>End of Treatment</td>
<td>1.20(0.15)</td>
<td>0.71(0.16)</td>
<td>-0.49(-0.93,-0.06)</td>
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<td>6 month F/U</td>
<td>1.01(0.16)</td>
<td>0.78(0.17)</td>
<td>-0.24 (-0.70, 0.22)</td>
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<td>12 month F/U</td>
<td>1.04(0.16)</td>
<td>0.79(0.16)</td>
<td>-0.25(-0.69,0.19)</td>
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</tbody>
</table>
Maintenance of Remission

- Relapse from full remission at post treatment was 10% for FBT and 45% for AFT by 12 month follow-up.
- Relapse from partial remission at post treatment was 17% for FBT and 6% from AFT by 12 month follow-up.
- The percent of participants that were partially remitted who later achieved full remission from AFT was 19% and from FBT was 25%.
Other Findings

Dropout, though low in both treatments, no differences between the two groups.

By 3 months 38% (N = 23) of FBT participants had reached 95% IBW vs 20% (N = 12) in AFT F(1,105)=5.5 p=.021

Hospitalization rates during treatment were 18% in FBT and 31% in AFT
How much FBT is needed?
Stanford Dosage Study

- 86 adolescents with AN
- Long-term FBT
- Short-term FBT

Lock et al. (2005)
Moderators of Outcome
Moderators of Treatment Outcome

Change in BMI by Treatment and YBC TOTAL

- Long term Low YBC n=21
- Long term High YBC n=19
- Short term Low YBC n=15
- Short term High YBC n=24
Moderators of Treatment Outcome

Change in Global EDE by family status
Family Criticism

- Separated vs Conjoined FBT compared in two studies controlling for family criticism
  - No differences overall in outcomes (most did well)
  - Family criticism moderated outcome; those with higher levels of criticism did better with separated FBT in both studies
  - 2 year (Le Grange) and 5 year (Eisler) follow-up showed similar pattern
    (Le Grange 1992; Eisler et al 2000)
Moderators of Remission

- Patients with higher EDE scores did better in FBT
- Patients with higher YBC-ED scores did better in FBT
- Patients with binge purge subtype did better in FBT
YBC-ED

(a) Low YBC

(b) High YBC

Legend:
- △: FBT observed
- ▲: FBT estimated
- ○: AFT observed
- ●: AFT estimated

Cure Rate

Baseline EOT 6mF 12mF
EDE Score

(a) Low EDE

(b) High EDE

- Δ: FBT observed
- ▲: FBT estimated
- ○: AFT observed
- ●: AFT estimated

Y-axis: Cure Rate
X-axis: Baseline, EOT, 6mF, 12mF
Binge-Purge sub-type

(a) Non-purger

(b) Purger

- FBT observed
- FBT estimated
- AFT observed
- AFT estimated
How do patients treated with FBT do over time?
Weight Chart for Patients in Subgroup 1 (Five Year Follow-up)

Stanford Dosage Study

48 Month Follow-up

Lock et al. (2006)
Long-term Follow-up in FBT

- Eisler et al. (1997)
- Lock et al. (2006)
- Eisler et al. (2007)
Patient and Family Satisfaction
Patient Satisfaction

• Therapeutic rapport on 5-point scale
  (mother = 4.71; father = 4.19; adolescent = 4.18)

• Success of treatment on 5-point scale
  (mother = 4.40; father = 4.10; adolescent = 3.97)

Therapeutic Alliance

- Therapeutic alliances were strong for both adolescents and parents were strong throughout treatment
- Early patient therapeutic alliance (bond) predicted early weight gain
- Early parental therapeutic alliance predicted staying in treatment
- Early weight gain predicted end of treatment EDE scores and therapeutic alliance
- Late parental alliance predicted overall weight gain

Dissemination Studies
Chicago Case Series

BMI

* t(44)-8.153, p<.001

Outcome

Le Grange et al. (2005)
Columbia Open Trial

Tx Response

- 75% completed full course of treatment
- 67% menstruating by end of treatment
- %IBW changed from 81.9 to 94.1 (p=.000)
- Sign changes in EDE Res, EC, binge/purge, and BDI

Loeb et al. (2007)
Canadian Study (Couturier et al, 2010)

- 14 Adolescents Treated Using Manual:
  Effectiveness

  - Weight – 86% were above 85% at final session, 57% were above 95%
  - Psychological symptoms – 54% were within 2 sd of normal on the EDE
  - Menses – 8/9 regained menstrual function,
    Two continued to have BP behaviours

- Fidelity – “Considerable – 5/7 or more” 72% of the time in phase I, 47% in phase II, and 54% in phase III

- Acceptability - high
Brazilian Study (Turkiewicz, et al, 2010)

11 adolescents with AN offered FBT
9 (82%) agreed (12-17 years, mean 14.64)
78% completed treatment (11 sessions over 6 months)
Mean BMI 16.39 baseline, 19.0 at end of treatment; 86% reached target weight at EOT
6 month follow-up mean BMI 20.8; no patients met criteria for an eating disorder
Status of Current Knowledge

- FBT for children and adolescent AN patients with short duration illness is effective
- FBT is more effective than psychodynamic developmentally oriented individual therapy
- Most patients respond favorably after relatively few outpatient treatment session
- The beneficial effects of FBT are sustained at 4-5 year follow-up
- Pilot studies suggest that FBT can be disseminated
Arthur Schopenhauer once said:

"All truth passes through three stages: First, it is ridiculed, second it is violently opposed, and third, it is accepted as self-evident."
What we don’t know: research directions

- FBT vs. Strategic Family Therapy (NIH)
- FBT post medical stabilization vs. long term hospital for adolescent AN (Westmead Children’s Hospital, Sydney, Australia)
- FBT for sub-syndromal AN (Mt. Sinai Hospital)(NIH)
- Multi-family Group FBT vs. FBT (Maudsley Hospital, London)
- FBT vs. Family FBT (Duke University) (NIH)
- Prevention of AN (pilot) using FBT, Germany (Jacobi)