The Challenge of Treating Adults with Anorexia Nervosa

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Overview

• Introduction
  • Available Evidence
• Outpatient therapy for patients with AN
  • MANTRA
    ➢ Development
    ➢ Research Evidence
• Interventions for carers as adjuncts to treatment
  • Overcoming Anorexia Online
  • Echo
• The way forward
Anorexia Nervosa in Adulthood

• ‘one of the most difficult psychiatric disorders to treat’ (Halmi et al., 2005)
  • Ambivalence about treatment
  • Hospitalisation generally results in weight gain, but is costly, disruptive & often followed by relapse
• ‘difficult to study’ (Fairburn et al., 2012; Watson & Bulik, 2012)
First Line Out-Patient Psychological Therapy

Very limited evidence base (n=10 trials)
• Most trials are small and have methodological problems

No leading psychological therapy
• CBT, IPT, CAT, family therapy, focal psychodynamic therapy have all been tried
• Specialist better than non-specialist treatment
• Dietary treatment alone less effective
• In pure adult samples only 20-30% of cases are recovered at 1 year, 40-50% at 5 yrs
Out-Patient Therapy for Relapse Prevention Post-Inpatient Treatment

Limited evidence base:

• Three trials
  • Individual supportive psychotherapy superior to Family Therapy (Russell et al., 1987)
  • CBT superior to nutritional therapy (Pike et al., 2003)
  • Internet-based CBT superior to TAU (Fichter et al., 2011)
17 small trials of antidepressants / antipsychotics
- 6 trials in out-patients; 9 in in-patients; 2 for relapse prevention

**Antidepressants:**
- Addition to in-patient refeeding does not improve outcome
- Fluoxetine does not reduce relapse rates

**Antipsychotics**
- **Olanzapine:**
  - Improves weight-gain a bit, reduces obsessional symptoms
Interventions for More Severe AN

Comparisons between different treatment settings:
• Day-patient services:
  • No RCT evidence in adults
• In-patient vs specialist out-patient treatment:
  • No difference between groups (BUT: hard to interpret) (Crisp et al., 1991)

Psychological therapies in intensive treatment settings
• Social skills training (Pillay et al., 1981)

Other adjuncts to inpatient regimes
• Warming vs placebo (Birmingham et al., 2004)
• Nasogastric feeding (Rigaud et al., 2007)
Conclusions

- Dearth of evidence
- “A treatment that produced enduring change would be of great value, especially if it were deliverable on an outpatient basis” (Fairburn et al., 2012)
MANTRA: Maudsley Model of Anorexia Nervosa Treatment for Adults

- Manual-based
- Trait-focused
- Drawing on neuropsychological, social cognitive & personality research
- Based on maintenance model
- Modular treatment
- Promising pilot data (Wade et al., 2011)

Schmidt & Treasure (2006)
What the person brings to AN

- **Traits/personality**
  - Anxious, Obsessional Perfectionist
  - Pro-anorexia beliefs
  - High Expressed Emotion, enabling, accommodating

- **Events/challenges /difficulties**
  - Mismatch between challenges and resources

- **Support**
  - Valued nature of AN
  - Thinking style
    - Inflexible, detail focused
  - Social & emotional mind
  - Difficulties recognising, processing & expressing emotions in close relationships

How others keep AN going
Example: Development of one of the MANTRA Treatment Modules - The Social and Emotional Mind Module
Social & emotional behaviours are intertwined

- We can have emotions outside social contexts, but it is difficult to have social interactions without emotions (Ochsner, 2008)
- Social & emotional brain overlap (e.g. Fossati, 2012)
Impairments in Socio-Emotional Processing in AN: Evidence from Experimental Studies

Emotional Processing
Recognition, Attentional Bias

Emotion Regulation & Expression

Theory of Mind

Social Problem Solving

e.g. Davies et al., 2011; Harrison et al., 2010; Oldershaw et al., 2010, 2011a,b; Sternheim et al. 2012; Renwick et al., 2013; Schober et al., submitted
Emotion Processing in AN

Basic emotion recognition

- Kessler et al: Standardised mean difference (95% CI) = -0.19 (-0.55, 0.17), % Weight = 14.1
- Mendlewicz et al: Standardised mean difference (95% CI) = -0.43 (-0.92, 0.05), % Weight = 11.4
- Zonnevyle-Bender et al: Standardised mean difference (95% CI) = -0.25 (-0.65, 0.15), % Weight = 13.1
- Zonnevyle-Bender et al: Standardised mean difference (95% CI) = -0.06 (-0.55, 0.44), % Weight = 11.1
- Kucharska-Pietura et al: Standardised mean difference (95% CI) = -0.60 (-1.12, -0.09), % Weight = 10.7
- Zonnevyle-Bender et al: Standardised mean difference (95% CI) = -0.51 (-1.02, -0.00), % Weight = 10.8
- Subtotal: Standardised mean difference (95% CI) = -0.31 (-0.50, -0.13), % Weight = 71.2

Complex emotion recognition

- Harrison et al: Standardised mean difference (95% CI) = -1.21 (-1.88, -0.53), % Weight = 8.1
- Oldershaw et al: Standardised mean difference (95% CI) = -0.55 (-0.98, -0.12), % Weight = 12.5
- Russell et al: Standardised mean difference (95% CI) = -1.41 (-2.07, -0.75), % Weight = 8.2
- Subtotal: Standardised mean difference (95% CI) = -1.01 (-1.57, -0.44), % Weight = 28.8
- Overall: Standardised mean difference (95% CI) = -0.52 (-0.77, -0.27), % Weight = 100.0

Oldershaw et al., 2011
AN Patients’ Experience of Socio-Emotional Difficulties

- Alexithymia – inability to label/describe emotions
- High levels of anger, shame and self-disgust
- Poor tolerance of emotional experience
- Poor emotion regulation
- Negative attitudes towards emotion expression
- High levels of interpersonal sensitivity and social anxiety
- Give priority to others’ feelings and needs
- Fear of negative evaluation by others
- High levels of social comparison

For review see: Arcelus et al., 2013; Oldershaw et al., submitted
### Meta-Analysis of Alexithymia in AN (Oldershaw et al., submitted)

**NOTE:** Weights are from random effects analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>SMD (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bourke et al. (1992)</td>
<td>1.93 (1.38, 2.48)</td>
<td>6.22</td>
</tr>
<tr>
<td>Schmidt et al. (1993)</td>
<td>0.91 (0.60, 1.23)</td>
<td>7.82</td>
</tr>
<tr>
<td>Cochrane et al. (1993)*</td>
<td>0.99 (0.53, 1.46)</td>
<td>6.80</td>
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<tr>
<td>Troop et al. (1995)</td>
<td>1.18 (0.78, 1.58)</td>
<td>7.27</td>
</tr>
<tr>
<td>Taylor et al. (1996)</td>
<td>1.93 (1.38, 2.48)</td>
<td>6.22</td>
</tr>
<tr>
<td>de Zwaan et al. (1996)</td>
<td>1.74 (1.10, 2.38)</td>
<td>5.63</td>
</tr>
<tr>
<td>Guttman &amp; Laporte (2002)</td>
<td>0.10 (-0.38, 0.57)</td>
<td>6.71</td>
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<tr>
<td>Zonnevylle-Bender et al. (2002)</td>
<td>1.28 (0.62, 1.94)</td>
<td>5.50</td>
</tr>
<tr>
<td>Eizaguirre et al. (2004)</td>
<td>2.05 (1.58, 2.52)</td>
<td>6.79</td>
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<tr>
<td>Zonnevylle-Bender et al. (2004a)</td>
<td>0.75 (0.34, 1.17)</td>
<td>7.16</td>
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<tr>
<td>Zonnevylle-Bender et al. (2004b)</td>
<td>0.89 (0.37, 1.40)</td>
<td>6.44</td>
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<tr>
<td>Speranza et al. (2005)</td>
<td>0.85 (0.64, 1.05)</td>
<td>8.41</td>
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<tr>
<td>Montebonacci et al. (2006)</td>
<td>1.02 (0.33, 1.72)</td>
<td>5.26</td>
</tr>
<tr>
<td>Kessler et al. (2006)</td>
<td>1.40 (1.00, 1.80)</td>
<td>7.26</td>
</tr>
<tr>
<td>Parling et al. (2010)</td>
<td>1.11 (0.61, 1.62)</td>
<td>6.51</td>
</tr>
<tr>
<td>Overall (I-squared = 79.3%, p = 0.000)</td>
<td>1.19 (0.94, 1.44)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

**NOTE:** Weights are from random effects analysis
Development of the MANTRA Module Addressing Socio-Emotional Impairments

- **Explicit** rather than **implicit** focus
  - E.g. biology/function of emotional & social mind within evolutionary framework
- Emphasis on micro- and macro-skills
  - Emotion recognition, Theory of Mind/mentalising, expression of emotions/needs in social contexts
- ‘Dissecting’ avoidance of emotional/social stimuli
  - E.g. role of beliefs, the role of skills deficits
- Increasing self-compassion

Schmidt et al., 2011
Study Design of Pilot RCT

Clinician assessment

Researcher assessment

Randomisation

MANTRA
20 weekly sessions & 4 monthly sessions

6 month Assessment

Post-treatment

12 month Follow-Up

Specialist Supportive Clinical Management
20 & 4 sessions

6 month Assessment

Post-treatment

12 month FU

Add-ons:
2 sessions with carer
4 sessions with dietician
Low weight patients:
10 extra sessions

Adult out-patients
BMI < 18.5 kgs/m²
Specialist Supportive Clinical Management (SSCM)

- Aims “to mimic outpatient treatment that could be offered to individuals with AN in usual clinical practice”.

- SSCM more effective than CBT or Interpersonal Therapy

McIntosh et al., 2005; 2006
## Baseline Data

<table>
<thead>
<tr>
<th></th>
<th>MANTRA (n=34)</th>
<th>SSCM (n=37)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>25.6 (6.9)</td>
<td>27.5 (8.7)</td>
</tr>
<tr>
<td><strong>Gender (♂ : ♀)</strong></td>
<td>♂ 3: ♀ 31</td>
<td>♂ 2 : ♀ 35</td>
</tr>
<tr>
<td><strong>Married or stable</strong></td>
<td>8.8%</td>
<td>27%</td>
</tr>
<tr>
<td><strong>relationship</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration of illness</strong></td>
<td>77.3 (70.8)</td>
<td>83.5 (73.6)</td>
</tr>
<tr>
<td><strong>(months)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Previous treatment</strong></td>
<td>50%</td>
<td>67.6%</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>16.3 (1.3)</td>
<td>16.4 (1.3)</td>
</tr>
<tr>
<td><strong>EDE Global</strong></td>
<td>3.3 (1.5)</td>
<td>3.2 (1.3)</td>
</tr>
</tbody>
</table>
Body Mass Index (BMI)

Schmidt et al., 2012 Br J Psych
BMI for Severe Group Only

BMI below 17.5 (n=54)

Pre | Post | FU
---|---|---
15.5 | 16 | 16.5
16 | 17 | 17.5
17 | | 18

MANTRA vs SSCM
Intermediate Summary. I

- Patients had a pretty chronic and severe form of the illness
- Two very different forms of treatment
  - The therapy dose was modest
- Patients in both treatments improved significantly
  - MANTRA might be better for those with a more severe illness
  - Recent study suggests SSCM effects not long-lasting (Carter et al., 2011)
- Since doing this study we have refined MANTRA
- Two large trials are now in progress in the UK and in Australia comparing MANTRA with SSCM and CBT-e
Assessed For Eligibility (n=314)

Excluded (n=172)
- Did not meet inclusion criteria (n=46)
- Met exclusion criteria (n=33)
- Refused Participation (n=73)
- Other (n=20)

Randomised into Study (n=142)

MANTRA (n=72)

SSCM (n=70)
<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td>26.2 (7.7)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>96.5% female</td>
</tr>
<tr>
<td><strong>AN or EDNOS</strong></td>
<td>75.7% and 24.3%</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>16.6 (1.2)</td>
</tr>
<tr>
<td><strong>Age of Onset</strong></td>
<td>17.7 (6.5)</td>
</tr>
<tr>
<td><strong>Duration of Illness</strong></td>
<td>8.3 (7.3)</td>
</tr>
<tr>
<td><strong>Global EDE</strong></td>
<td>3.3 (1.3)</td>
</tr>
<tr>
<td><strong>Taking Antidepressant</strong></td>
<td>38.2%</td>
</tr>
</tbody>
</table>
Qualitative Studies of Therapist & Patient Views of MANTRA:

Therapists’ Views

• I think it’s got everything in there that you’d need.....you can really tailor it, more than any other therapy.....

• I feel that the patient could drive their own care....take things from the manual that they were particularly interested in or wanted to focus on

• It’s such a great resource; I’ll just have a look at the manual and see what they say...there are so many great exercises

Patients’ Views

• It was almost tailor made to me brilliantly, so it was very good.

• I have learned a lot, ....if I am having a bad day and feeling you know, not that great, then I can think “oh what did she say about that” and look at the manual, I think that’s good

• ...it was a really interesting to just go “I’m just gonna listen to you, Mr Book, and let you guide me”

Lose et al., in preparation; Waterman-Collins et al. in preparation
One cannot think well, love well, sleep well if one has not dined well.
Overview

• Introduction
  • Available Evidence

• Outpatient therapy for patients with AN
  • MANTRA

• Interventions for carers as adjuncts to treatment
  • Overcoming Anorexia Online
  • Echo

• The way forward
How Families/Carers keep AN going

AN symptoms

Worsens how carer feels & how person with AN feels

Creates or Worsens Problems

Carers concerned and anxious

Expressed Emotion Accomodation/Enabling

Overcoming Anorexia Nervosa Online (OAO)
A web-based skills training for families

Follows a systemic CBT model
- 8 interactive online modules, e.g.:
  - Communication about AN
  - Giving meal support
  - Assessing/managing risk
  - Carers’ own needs
- Accompanying Workbooks
- With therapist guidance

Schmidt et al., 2007; Grover et al., 2010; Grover et al., 2011
Design

Assessment of carer outcomes, e.g. mood, care giving burden, Expressed Emotion

Baseline

Post treatment

Follow Up

OAO plus clinician guidance

Time (months)
### Characteristics of Carers

<table>
<thead>
<tr>
<th></th>
<th>OAO (n=34)</th>
<th>Beat (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean Age (Years)</strong></td>
<td>47.3 (8.7)</td>
<td>49.1 (6.2)</td>
</tr>
<tr>
<td><strong>Living with Patient</strong></td>
<td>78.8%</td>
<td>76.7%</td>
</tr>
<tr>
<td><strong>Relationship to Patient</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Mother</td>
<td>69.7%</td>
<td>90%</td>
</tr>
<tr>
<td>• Other</td>
<td>30.3%</td>
<td>10%</td>
</tr>
</tbody>
</table>
Other outcomes also improved (e.g. high Expressed Emotion)

90% of participants completed all modules

Most rated the intervention as highly interesting and useful

Most useful module: effective communication

Grover et al., 2011
Expert Carers Helping Others: ECHO vs ECHOc

1) Self Help Manual

2) 5 DVDs, giving information and examples of behaviour (role plays)

+/- Support by telephone (3 calls with a coach (ECHOc))

Goddard et al. (2011) Br J of Psychiatry
ECHO: Study Design

Intervention

Baseline 1
N = 178

Pre-treatment
N = 153

ECHO
N = 80

Post treatment
N = 63 (79%)

Follow up
N = 61 (73%)

ECHOc
N = 73

Post treatment
N = 57 (78%)

Follow up
N = 52 (72%)

Time (Weeks)
Carers’ symptoms: HADS

HADS total score

Baseline  Pre-intervention  Post intervention  3 month follow up

HADS total score

ECHOC
Maintaining Factors

Expressed Emotion

Accommodating and Enabling

Expressed Emotion: GLMM Estimate = -3.1 (95% CI -4.5 to -1.7), p < .001

Accommodating und Enabling GLMM Estimate = -9.1 (95% CI -13.4 to -4.8), p < .001
Intermediate Summary. II

• Both carer interventions (Online or manual & DVDs) reduce carer symptoms and improve their ability to care for the patient

• In the ECHO study additional support by phone does not improve outcomes
  • ? Too few calls
  • ? Did coaches adhere to treatment model

• We now need data on how interventions for carers impact on the patient
  • Two ongoing multi-centre studies are examining this
Overall Summary & Future Directions

• The search for improved outcomes in the treatment of adults with AN carries on
  • Large scale more definitive trials are beginning to emerge
In future greater consideration needs to be given to:
• Combination of individual psychotherapy with carers’ interventions
• Novel approaches targeting prognostically ominous symptoms (binge eating; exercise) and comorbidities (OCD, anxiety)
Novel Adjuncts to Talking Therapies in Adults with AN

- Medication: e.g. new antipsychotics (e.g. aripiprazole, Trunko et al., 2011)
- Attention Bias Modification: to reduce anxiety (Renwick et al., 2013)
- Cognitive Remediation Treatment: to reduce cognitive rigidity
- Non-Invasive Brain Stimulation (NIBS: to enhance new learning (Van den Eynde et al., 2011)
- Real time fMRI feedback
- And for the very chronic very severely ill ones…deep brain stimulation (Lipsman et al, in press)