Received: 1 December 2017 | Revised: 11 April 2018 | Accepted: 11 April 2018

DOI: 10.1002/eat.22876

ORIGINAL ARTICLE

International Journal of EATING DISORDERS

The acceptability, feasibility, and possible benefits of a neurobiologically-informed 5-day multifamily treatment for adults with anorexia nervosa

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Funding information
National Eating Disorders Association (NEDA); the Global Foundation for Eating Disorders (GFED) and the Price Foundation

Abstract

Objective: Novel treatments for adults with anorexia nervosa (AN) are lacking. Recent scientific advances have identified neurobiologically-driven temperament contributors to AN symptoms that may guide development of more effective treatments. This preliminary study evaluates the acceptability, feasibility and possible benefits of a multicenter open trial of an intensive 5-day neurobiologically-informed multifamily treatment for adults with AN and their supports (SU). The temperament-focused treatment combines psychoeducation of AN neurobiology and SU involvement to develop skills to manage traits contributing to disease chronicity.

Method: Fifty-four adults with AN and at least one SU ($n = 73$) received the 5-day treatment. Acceptability, feasibility, and attrition were measured post-treatment. Clinical outcome (BMI, eating disorder psychopathology, family function) was assessed post-treatment and at >3-month follow-up.

Results: The treatment had low attrition, with only one drop-out. Patients and SU rated the intervention as highly acceptable, and clinicians reported good feasibility. At post-treatment, patients demonstrated significantly increased BMI, reduced eating disorder psychopathology, and improved family function. Benefits were maintained in the 39 patients who completed follow-up assessment, with 62% reporting full or partial remission.

Discussion: Preliminary results are promising and suggest this novel treatment is feasible and acceptable. To establish treatment efficacy, fully-powered randomized controlled trials are necessary.

KEYWORDS
anorexia nervosa, intensive multifamily treatment, open trial, temperament based treatment

1 | INTRODUCTION

Anorexia nervosa (AN) is a serious psychiatric disorder that is difficult to treat and is associated with significant medical and psychological complications. Treatment efficacy in adults is limited, with no treatment showing superiority (NICE, 2017). Approximately 50% of patients develop a persistent, relapsing, and remitting course (Hay, Touyz, & Sud, 2012; Steinhausen, 2002). As such, identifying efficacious treatments for adults with AN is imperative (Hay et al., 2012; Watson & Bulik, 2013). Unfortunately, the etiology of AN is poorly understood, hindering the ability of treatments to target underlying mechanisms.

Accumulating behavioral and neuroimaging evidence supports a neurobiologically-based temperament that impacts the development and maintenance of AN—characterized by anxiety, reward insensitivity, perfectionism, altered interoceptive awareness, harm avoidance, and cognitive inflexibility (Fassino, Piero, Gramaglia & Abbate-Daga, 2004; Harrison, O'Brien, Lopez, & Treasure, 2010; Lilenfeld, 2011)—that is related to altered insula and fronto-striatal neural circuit function (Berner et al., 2017; DeGuzman, Shott, Yang, Riederer, & Frank, 2017;

Kerr et al., 2016; Oberndorfer et al., 2013; Wierenga et al., 2015). In addition to predating AN, mild to modest amounts of these traits often persist after recovery (Wagner et al., 2006), suggesting those who recover might do so by effectively managing these traits. This personality and behavior profile establishes a framework to guide development of therapies designed to directly target trait-related symptoms specific to AN. Yet, to date only a few therapies, such as Maudsley model of anorexia nervosa treatment for adults (MANTRA) (Schmidt et al., 2013), are based on such an empirically supported understanding of AN, and none are administered in an intensive multifamily format with neurobiological psychoeducation and skills training.

To address this need and respond to the recent call that treatments for AN not remain "brainless" (Schmidt & Campbell, 2013), we developed an intensive 5-day multifamily treatment for adult AN (formerly called intensive temperament based therapy and neurobiologically enhanced with family eating disorder trait response treatment [NEWFED-TR]) (Kaye et al., 2015; Knatz, Wierenga, Murray, Hill, & Kaye, 2015). The treatment includes psychoeducation to emphasize the key role of neurobiological factors in the development of AN, teaching the patient and Support (SU) age-appropriate skills to manage disorder-related temperament (see Supporting Information for details, including the schedule of treatment modules and activities). We previously demonstrated clinical effects following a 1-week intervention for adolescent AN (Marzola et al., 2015; Rockwell, Boutelle, Trunko, Jacobs, & Kaye, 2011). This intensive format was adapted for adults while incorporating different interventions specific to adult AN (Hill, 2017; Hill, Peck, Wierenga, & Kaye, 2016) (see Supporting Information). The 5-day treatment leverages SU participation based on considerable data showing that AN-focused family therapy (FT-AN) is the most effective approach in treating adolescents with AN (Eisler, Grange, & Lock, 2015; Lock, 2015; NICE, 2017), with multifamily therapy showing improved efficacy over single-family therapy (Eisler et al., 2016). In adult AN, family therapy has evidenced superiority to treatment as usual and efficacy equal to other specialist eating disorder (ED) therapies (Dare, Eisler, Russell, Treasure, & Dodge, 2001), with considerable evidence that family interventions in adult mental health can be enhanced by using a multifamily treatment format (Lemmens, Eisler, Buysse, Heene, & Demyttenaere, 2009; McFarlane, 2016; Miller, Solomon, Ryan, & Keitner, 2004), and is feasible in adult AN (Dimitropoulos, Farquhar, Freeman, Colton, & Olmsted, 2015; Tantillo, 2006).

To our knowledge, an intensive (e.g., ~40 h) multifamily treatment format has not been implemented for adult AN. Thus, this preliminary study evaluated the feasibility and acceptability of an intensive, multifamily, temperament-focused treatment for adult AN, and secondarily explored changes in clinical outcome (e.g., self-reported ED symptoms, family function).

2 | METHODS

2.1 | Participants

Participants were recruited via advertisements on our clinic websites. Sixty-two adults were assessed for eligibility, of which seven met DSM-IV-TR (American Psychiatric Association, 2000) criteria for bulimia nervosa (BN) or subthreshold BN and were excluded (see Supporting Information for additional exclusionary criteria). Fifty-five adult women met criteria for broadly defined AN (e.g., including DSM-IV-TR AN, AN in partial remission, and Eating Disorder Not Otherwise Specified, restricting type) as determined by consensus diagnosis and based on Module H of the Structured Clinical Interview for DSM-IV (First, Gibbon, Spitzer, & Williams, 1996) administered by trained clinicians. Patients selected their participating SU ($n = 73$): parents (36 mothers, 17 fathers), significant others (2 boyfriends, 2 fiances, 5 husbands, 2 partners, 1 wife), other family members (4 sisters, 1 cousin, and 1 nanny), and friends (2). 39 patients were accompanied by 1 SU, 14 patients by 2 SU, and 2 patients by three SU.

The study conforms to the standards of the Declaration of Helsinki and the protocol was reviewed and approved by the Institutional Review Board of the University of California San Diego, which covered The Center for Balanced Living as a secondary site. All AN and SU participants provided written informed consent.

2.2 | Measures

2.2.1 | Feasibility

Qualitative feedback was gathered from study clinicians, patients, SU, and the multidisciplinary team regarding the program's practical implementation and the ease of adapting the intensive multifamily format to an adult population. This included an assessment of clinician willingness to recruit participants, staff time required, participant ability to engage with the activities, and estimation of follow-up rates.

2.2.2 | Acceptability

An 18-item Patient and SU Satisfaction Questionnaire developed by our team was used to assess patient and SU liking and any concerns related to the 5-day treatment (patient $\alpha = 0.92$; SU $\alpha = 0.88$). The measure also included an open-ended question to elicit qualitative feedback. Daily attendance was recorded and a daily feedback form was administered to participants to track dropout and evaluation of experiential activities.

2.2.3 | Clinical measures

Staff measured patients' height and gown weight immediately prior to and following 5-day treatment. Measurements were converted to body mass index (BMI; kg/m^2), and ideal body weight (%IBW) was calculated for sex and height using the 1959 Metropolitan Life Insurance table. Participants completed self-report assessments at entry, immediately post-treatment, and at follow-up (>3 months), including the Eating Disorder Examination Questionnaire (EDE-Q) (Fairburn & Beglin, 1994) with parent version (P-EDEQ; (Loeb, 2008) modified for SU, McMaster Family Assessment Device (FAD) (Epstein, Baldwin, & Bishop, 1983), and Spielberger State-Trait Anxiety Inventory (STAI) (Spielberger, Gorsuch, & Lushene, 1970). Cronbach's alphas for all measures within the present study were strong ($\alpha = .88–.97$). Secondary measures are reported in the Supporting Information.

2.3 | Exploratory outcome classification

Patients who completed assessments at pretreatment, post-treatment, and follow-up were classified as fully remitted, partially remitted, or poor outcome according to criteria set forth by (Bardone-Cone et al., 2016) (see Supporting Information for details).

2.4 | Statistical analysis

Parametric and nonparametric tests were selected as appropriate. Measures with missing values were excluded from analysis; missing values occurred on <1% of all self-reported items. Within-subject changes in clinical measures between pre- and post-treatment were analyzed using paired sample *t* tests. These analyses were repeated for SU responses, weighted for number of SU per patient. McNemar's exact tests were used to compare good (partial or full remission) vs. poor outcome classification of patients between pretreatment, post-treatment, and follow-up. Lastly, we examined whether treatment location predicted outcome and follow-up assessment completion using linear and logistic regression analyses (see Supporting Information for details of additional statistical analysis of follow-up data).

3 | RESULTS

3.1 | Feasibility

At each site, the treatment included an intake coordinator, three clinicians, a dietician, a physician, and a clinical administrative assistant. Including preparation, actual sessions, communicating with other treatment providers, discharge planning, and note writing, 80 h of staff time were required. This was perceived as feasible by the two administering programs, considering that up to 6 patients' and 6–15 SUs attendance equated to 13 h of staff time per patient for the entire intervention.

3.2 | Attrition and acceptability

One patient necessitated a higher level of care after attending one day of the 5-day program, resulting in an attrition rate of 1.8%. Patient and SU acceptability ratings were strong across the 18 questions (Table 1), and 88% of patients and 95% of SU reported treatment met their expectations. Objective and qualitative feedback indicated that patients and SU particularly liked the neurobiology psychoeducation (97%), activities (98%), group format (100%), and behavioral contracting (89%). Of treatment completers ($n = 54$), 7% of patients ($n = 4$), and 8% of SU ($n = 6$) did not complete clinical outcome assessments at post-treatment. Of post-treatment assessment completers ($n = 50$), 22% of patients did not complete follow-up self-report assessments ($n = 11$) and an additional 24% of patients ($n = 12$) completed neither follow-up self-report nor weight assessments. The primary reason provided for not completing follow-up assessments was that patients were doing better and thought the questions would be triggering. Sixty-nine percent of SU did not complete follow-up assessments.

3.3 | Patient characteristics pre- and post- 5-day treatment

Table 2 includes patient characteristics of the 50 women (primarily Caucasian, 84.6%) who completed assessments pre- and post-treatment at the University of California, San Diego ($n = 17$) or at The Center for Balanced Living, Columbus OH ($n = 33$). Immediately after 5-day treatment, there was a significant increase in BMI ($p = .001$, $d = 0.10$, 95% CI = −0.68–0.46), though this likely does not represent a clinically meaningful change. Patients also reported significant reductions in EDE-Q Global score ($p = .014$, $d = 0.27$, 95% CI = −0.15–0.69), state anxiety ($p < .001$, $d = 0.68$, 95% CI = −2.87–4.09), and improvements in FAD General Family Function ($p = .005$, $d = 0.36$, 95% CI = 0.20–0.51) (Table 2); see Supporting Information for follow-up data results.

3.4 | Support ratings post 5-day treatment

Data from 67 SU who completed pre- and post-treatment assessments, weighted to reflect 50 unique patients, revealed significant improvements in observed ED symptoms of their loved one (EDE-Q Global score [observer modified], $p < .00$, $d = 0.72$, 95% CI = 0.30–1.08), and general family function (FAD, $p < .01$, $d = 0.54$, 95% CI = 0.43–0.64) (Supporting Information Table 2; see Supporting Information for follow-up data).

3.5 | Patient outcome classification

At post-treatment, 31% of patients were classified as fully remitted (10%, $n = 4$) or partially remitted (21%, $n = 8$), while 69% reported a poor outcome. At follow-up, 62% of patients achieved either full remission (31%, $n = 12$) or partial remission (31%, $n = 12$), while 38% ($n = 15$) reported a poor outcome (Supporting Information Table 3 and Figure 2). A significant difference was found for the proportion of individuals with good outcome (i.e., full or partial remission) at pretreatment versus follow-up ($p < .001$) and at post-treatment versus follow-up ($p = .004$), but not at pre- versus post-treatment ($p = .125$). No associations were found between treatment site and outcome or failure to complete follow-up assessments ($ps > .05$).

4 | DISCUSSION

This study represents the first step in evaluating the feasibility, acceptability, and possible benefits of an intensive 5-day neurobiologically-informed intervention for adult AN that enlists SU involvement through multifamily neurobiologically based psychoeducation and skills-training, aimed at managing traits that contribute to AN. Consistent with previous findings in a smaller sample (Hill, 2017), the treatment is feasible, has low attrition and high acceptability. Among treatment completers, findings indicate increased BMI, reduced ED symptoms, reduced state anxiety, and improved family function post-treatment. Exploratory results indicate that 62% of patients who completed follow-up assessments achieved full or partial remission (aka, good outcome) at follow-up. No differences in outcome were detected between treatment sites.

TABLE 1 Acceptability ratings post-treatment

	Pt (*N* = 45)	SU (*N* = 67)
1. I would recommend the 5-day program to others	4.5	4.8
2. I would prefer additional group treatment sessions or exercises	3.6	3.9
3. I would be willing to participate in additional group treatment sessions or exercises	4.1	4.5
4. I enjoyed the learning about the neurobiology of eating disorders through the group exercises (e.g., nondominant hand writing exercise, brain wave)	4.7	4.8
5. The exercises on neurobiology improved my understanding about my eating disorder	4.8	4.8
6. I enjoyed the activities for learning/practicing effective communication with my Support(s)/loved one	4.5	4.7
7. I feel that my Support(s) are equipped with more/better tools for supporting me through recovery/I feel that I am equipped with more/better tools for supporting my loved one through recovery	4.6	4.7
8. I feel that I am better able to communicate with my Support(s)/loved one about my/her eating disorder	4.5	4.6
9. I enjoyed working on developing a contract/treatment plan with my Support(s)/loved one	3.8	4.6
10. I am more confident about my Support(s)'/my ability to support me/my loved one through recovery	4.4	4.6
11. I feel that my Support(s)'/my role in my/my loved one's treatment has been clarified	4.3	4.5
12. My relationship with my Support(s)/loved one has improved as a result of this treatment	4.3	4.2
13. I believe my experience from this treatment will be helpful in decreasing the likelihood that I/my loved one will engage in behaviors such as restricting, over-exercising, purging, etc	4.4	4.4
14. I believe this treatment will be helpful in either decreasing my/my loved one's anxiety and/or other negative emotions or improving my/my loved one's ability to cope with these emotions	4.0	4.4
15. I enjoyed interacting with other patients and their Supports in the group	4.7	4.7
16. I learned skills and ideas from the other Supports and patients that I can now apply to myself/to working with my loved one in treatment	4.4	4.6
17. I felt supported by the other group members	4.5	4.7
18. I plan to continue to have my Support(s) involved in my treatment/I plan to continue my involvement in my loved one's treatment	4.5	4.8
Mean (SD)	4.4 (.31)	4.6 (.26)

	Yes (%)		Somewhat (%)		No (%)	
	Pt	SU	Pt	SU	Pt	SU
19. Did this treatment meet your expectations?	**88.4**	**95.4**	11.6	3.1	0	1.5

Note. Pt = patient; SU = support.
Acceptability ratings based on a 5-point Likert scale with higher ratings indicating greater acceptability for questions 1–18. Values associated with Question 19 indicate the percentage of respondents who felt that the treatment met expectations.

However, 22–46% of patients and 69% of SU failed to complete follow-up assessments, indicating suboptimal acceptability of ongoing study participation following treatment.

Future studies are needed to establish the efficacy and explore potential mechanisms of this neurobiologically-informed multifamily intervention. The neurobiological focus may have imparted benefits, as another trait-focused treatment (MANTRA) has shown efficacy (Byrne et al., 2017; Schmidt et al., 2013). The intensive nature of treatment may also have conferred benefits. Treatment models for anxiety indicate that intense, repeated, and focused *in vivo* practice is key to altering biologically-driven avoidance behaviors by maximizing learning through massed practice and allowing close monitoring of compliance (Abramowitz, Foa, & Franklin, 2003; Gallo, Chan, Buzzell, Whitton, & Pincus, 2012; Storch et al., 2007). The contribution of other treatment components (e.g., multifamily format, behavioral contracting, dietary involvement) to outcome requires further study.

Despite these promising findings, this study has several limitations. These preliminary results are from an open trial with treatment-seeking patients who have active SU, resulting in a possible selection bias that may reflect particularly motivated AN (and/or SU) who are mild/moderately ill. As such, findings may not be representative of more resistant, severely underweight AN who lack social support, and clinical

TABLE 2 Patient clinical variables at pre- and post-5-day treatment

	Pretreatment (n = 50) Mean (SD)	Post-treatment (n = 50) Mean (SD)	p	Cohen's d	95% CI
Age (years)	24.5 (8.8)				
Illness duration (years)	9.1 (8.6)				
BMI (kg/m^2)	18.1 (2.1)	18.3 (2.0)	0.001	−0.10	−0.68-0.46
IBW (%)	83.1 (9.2)	84.1 (8.9)	0.001	−0.11	−2.66-2.36
EDE-Q Global Score	3.5 (1.5)	3.1 (1.5)	0.014	0.27	−0.15-0.69
FAD general family function	2.2 (.59)	2.0 (.53)	0.005	0.36	0.20-0.51
STAI state	56.2 (12.8)	47.8 (12.3)	<0.001	0.68	−2.87-4.09
STAI trait	55.3 (10.3)	53.4 (10.0)	0.26	0.19	−2.67-2.96
	***n* (%)**				
ED diagnosis					
AN-R	26 (52%)				
AN-BP	12 (24%)				
EDNOS-restricting type	2 (4%)				
AN-partial remission	10 (20%)				
Comorbid diagnoses					
Major depressive disorder	14 (28%)				
Generalized anxiety disorder	21 (42%)				
Panic disorder	7 (14%)				
Social phobia	13 (26%)				
Obsessive–compulsive disorder	5 (10%)				
Post-traumatic stress disorder	4 (8%)				

Note. BMI = body mass index; EDE-Q = Eating Disorder Examination-Questionnaire; FAD = McMaster Family Assessment Device; IBW = ideal body weight; STAI = Spielberger State Trait Anxiety Inventory.
Paired sample t tests were used to assess statistical significance for within-subject differences in continuous variables over time. Lower scores reflect decreased symptoms (EDE-Q, STAI) and improved family function (FAD). The EDE-Q was modified for the post-treatment evaluation to assess ED symptoms over the past 7 days. The Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998), a structured clinical interview designed to assess the presence of DSM-IV psychiatric disorders in adults, was used to assess current comorbid psychiatric diagnoses.

outcomes must be interpreted with caution. There was no experimental control of treatment between post-treatment and follow-up assessment, and service utilization data were not collected, rendering it difficult to attribute follow-up benefits solely to this 5-day treatment. Another significant limitation is the relatively poor follow-up assessment compliance. However, the difference in BMI from post-treatment to follow-up indicates that patients continued to gain weight, which may be attributable to continued application of skills learned during treatment or to responsiveness to other interventions after the 5-day treatment. Notably, this 5-day treatment may increase effectiveness of subsequent treatment by serving as a primer and motivating patients and their SU to engage in longer-term care. Moreover, our finding that individuals lost to follow-up were less chronic leads to the notion that this may be a promising treatment for long-standing AN. Fully-powered randomized controlled trials with longer follow-up periods will be needed to firmly establish the efficacy of this treatment.

5 | CONCLUSION

This preliminary study investigated an innovative SU-involved and neurobiologically-guided program delivered via an intense 5-day multifamily format. Findings suggest this is a feasible, acceptable and potentially effective approach to reduce AN symptoms. This study begins to address the critical need to develop and test neurobiologically-targeted treatments for adults with AN.

ACKNOWLEDGMENTS

Support provided by the National Eating Disorders Association (NEDA) to CEW and LH, the Global Foundation for Eating Disorders (GFED) and the Price Foundation.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

How to cite this article: Wierenga CE, Hill L, Knatz Peck S, et al. The acceptability, feasibility, and possible benefits of a neurobiologically-informed 5-day multifamily treatment for adults with anorexia nervosa. *Int J Eat Disord*. 2018;00:1–7. https://doi.org/10.1002/eat.22876

Supplementary Table 1. Treatment Schedule

5-day Treatment Schedule Registration & pre-testing occur on Sunday. If coming from out of town, make arrangements to arrive no later than Saturday before the treatment week.										
TIME	Monday		Tuesday		Wednesday		Thursday		Friday	
Varies	8:00 AM Medical Check-in		8:00 AM Medical Check-in		8:30 AM Medical Check-in		8:30 AM Medical Check-in		8:00 AM Medical Check-in	
9 AM	Interactive Breakfast & 10 Minute Movement		Interactive Breakfast & 10 Minute Movement		Interactive Breakfast & 10 Minute Movement		Interactive Breakfast & 10 Minute Movement		Interactive Breakfast & 10 Minute Movement	
10 AM	Multi-Family Input: Introductions and Jep-EDardy		Multi-Family Input: Self-Critique – What worked? What didn't What would you do differently? & Medication Management		Multi-Family Input: Patients as experts teach Carers two tools		Multi-Family Input: Pharmacological/Biological ED Q&A		Multi-Family Input: Q&A among Patients & Carers	
11:30 AM	Restroom & Interactive Snack		Restroom & Interactive Snack		Restroom & Interactive Snack		Restroom & Interactive Snack		Restroom & Interactive Snack	
12 PM	Neurobiology Psychoeducation & Telephone Tool Developed by Laura Hill, Ph.D.		Neurobiology Psychoeducation & Anxiety Wave Tool Developed by Laura Hill, Ph.D.		Neurobiology Psychoeducation & Land Mine Tool Developed by Laura Hill, Ph.D.		Neurobiology Psychoeducation & Wire-Rewire Tool Developed by Laura Hill, Ph.D.		Neurobiology Psychoeducation & Brain Wave Tool Developed by Laura Hill, Ph.D.	
1 PM	Restroom, Interactive Lunch & 10 Minute Movement		Restroom, Interactive Lunch & 10 Minute Movement		Restroom, Interactive Lunch & 10 Minute Movement		Restroom, Interactive Lunch & 10 Minute Movement		Restroom, Interactive Lunch & 10 Minute Movement	
2 PM You will begin in one group and then rotate to the other	*Patient Session with Their Carers:* ED Behavior Agreement-Honesty Agreement	Nutrition Consult	*Patient Session with Their Carers:* ED Behavior Agreement-Prioritize Goals, Goals' Objective & Repair Formation	Nutrition Consult	*Patient Session with Their Carers:* ED Behavior Agreement-Goals' Objective & Repair Formation	Nutrition Consult	*Patient Session with Their Carers:* ED Behavior Agreement-Goals' Objective & Repair Formation	Nutrition Consult	*Patient Session with Their Carers:* ED Behavior Agreement-Completion and Signing	Nutrition Consult
3:30 PM Patient & Carer split into two groups	*Patient Toolbox:* Dialectical Model-Active Listening & Honesty Dialectics	*Carer Toolbox:* Dialectical Model-Active Listening & Honesty Dialectics	*Patient Toolbox:* L&P* Stop, Reboot, Reroute; Plan & Structure Tool	*Carer Toolbox:* L&P* Stop, Reboot, Reroute; Validation & Planning	*Patient Toolbox:* L&P* Act Intentionally & The Non-Negotiable	*Carer Toolbox:* L&P* The Non-Negotiable or "Hold the Line"	*Patient Toolbox:* L&P* Distraction & Grounding Tools	*Carer Toolbox:* L&P* Honest with Self & Others & Validation	*Patient Toolbox:* L&P* WW_D & WWID4_	*Carer Toolbox:* L&P* Planning Ahead & Time Out Tools
4:30 PM	Restroom, Interactive Snack & Daily Feedback: Non-Dominant Hand Activity		Restroom, Interactive Snack & Daily Feedback		Restroom, Interactive Snack & Daily Feedback		Restroom, Interactive Snack & Daily Feedback		Restroom, Interactive Snack & Daily Feedback; The Gauntlet, Ending with "Centered Activity"	
5 PM	*See section 3 in your manual L&P=Learn & Practice								5:00-6:00 PM Post-Testing Please Note: Some participants often do not finish until 7:00 PM	

Note: Treatment modules are color-coded and are aimed at targeting neurobiologically-mediated temperament constructs in AN (e.g., anxiety, cognitive inflexibility, altered sensitivity to reward/punishment, altered interoceptive awareness), delivered interactively to both patient and SU. Each module is formatted to deliver: 1) Neurobiological psychoeducation that integrates research findings into treatment tools (e.g., experiential exercises), aimed at increasing insight of the biological nature of the illness and reducing blame (in light blue); 2) Separate patient and

SU neurobiological skills training and practice consisting of teaching skills to address deficits and facilitate constructive methods for using temperament (in yellow and blue); 3) SU support enlistment consisting of teaching SU effective response and management strategies in a multifamily format (in purple); 4) Behavioral contracting (in green); and 5) Dietary training/meal planning to address the brain-basis of restriction and underweight status (in pink). Red cells indicate snacks or meals administered; Orange cells indicate medical check-in. Unless otherwise noted, groups include patients and Supports.

Supplementary Table 2. Support data at pre- and post- 5-day treatment

	Pre-Treatment (n=67*)	Post-Treatment (n=67*)			
	Mean (SD)	Mean (SD)	p	Cohen's *d*	95% CI
PEDE-Q Global Score	3.4 (1.5)	2.4 (1.3)	<0.001	0.72	0.30-1.08
FAD General Family Function	2.0 (.38)	1.8 (.37)	0.009	0.54	0.43-0.64

* Support data were weighted so each patient (n=50) is equally represented. PEDE-Q, Eating Disorder Examination-Questionnaire (Parent modified); FAD, McMaster Family Assessment Device.

Supplementary Table 3. Lost case analysis

	Completed Follow-up (n=39, 78%)	Lost to Follow-up (n=11, 22%)	
	Mean (SD)	Mean (SD)	p
Age at entry (years)	25.8 (9.3)	19.6 (2.4)	0.02
BMI at entry (kg/m^2)	18.0 (2.2)	18.6 (1.5)	0.33
IBW (%)	82.5 (9.7)	85.3 (7.0)	0.32
Illness Duration (yrs)	10.4 (9.2)	4.7 (2.8)	0.03
	n (%)	n (%)	p
ED Diagnosis			
AN-R	20 (51)	6 (55)	1.0
AN-BP	12 (30)	0 (0)	0.32
EDNOS-restricting type	1 (2)	1 (9)	0.40
AN-partial remission	6 (15)	4 (36)	0.20
Major Depressive Disorder	12 (31)	2 (18)	0.27
Generalized Anxiety Disorder	17 (44)	4 (36)	1.0

Note: Mann–Whitney–Wilcoxon tests and Fisher's exact tests were used to assess between group differences on continuous and categorical variables, respectively.

Supplementary Table 4. Patient clinical variables at pre- and post-treatment and follow-up for those who completed follow-up assessments

	1. Pre-Treatment	2. Post-Treatment	3. Follow-up					
	Mean (SD)	Mean (SD)	Mean (SD)	F	df	p	η^2	pairwise p
Length of BMI follow-up (days) (n=39)			228.0 (177.7)					
Length of EDE-Q follow-up (days) (n=28)			142.4 (81.5)					
BMI (kg/m^2) (n=39)	18.0 (2.2)	18.2 (2.1)	19.6 (2.0)	26.6	(1.1, 41.7)	<0.001	0.41	1 vs 2 = 0.05 1 vs 3 = <0.001 2 vs 3 = <0.001
%IBW (n=39)	82.5 (9.7)	83.4 (9.5)	89.6 (9.6)	24.5	(1.1, 42.8)	<0.001	0.39	1 vs 2 = 0.06 1 vs 3 = <0.001 2 vs 3 = <0.001
EDE-Q Global Score (n=28)	4.1 (1.3)	3.4 (1.4)	3.0 (1.5)	8.4	(2, 54)	0.001	0.24	1 vs 2 = 0.02 1 vs 3 = 0.002 2 vs 3 = 0.54
	n (%)	n (%)	n (%)					
Outcome								
Full remission	1 (2)	4 (10)	8 (21)					
Partial remission	7 (18)	8 (21)	16 (41)					
Poor outcome	31 (80)	27 (69)	15 (38)					
Dichotomous outcome								
Good	8 (21)	12 (31)	24 (62)					
Poor	31 (79)	27 (69)	15 (38)					

Note: Repeated measures analysis of variance with Bonferroni corrected pairwise comparisons were used to assess statistical significance for continuous variables. Lower scores reflect decreased symptoms. BMI, body mass index; Eating Disorder Examination-Questionnaire.

Supplementary Table 5. Support report at pre- and post-treatment and follow-up for those who completed follow-up assessments

	1. Pre-Treatment	2. Post-Treatment	3. Follow-up					
	Mean (SD)	Mean (SD)	Mean (SD)	F	df	p	η^2	pairwise p
Length of follow-up (days) (n=*21)			142.4 (81.5)					
PEDE-Q Global Score (n=*19)	3.6 (1.6)	2.9 (1.4)	2.7 (1.8)	3.4	(2, 28)	0.05	.19	1 vs 2 = 0.21 1 vs 3 = 0.019 2 vs 3 = 1.0
FAD General Family Function (*n=21)	1.9 (.35)	1.8 (.32)	1.8 (.23)	.40	(2, 32)	0.67	.02	1 vs 2 = 1.0 1 vs 3 = 1.0 2 vs 3 = 1.0

* Support data were weighted so each patient is equally represented (FAD, n=17 patients; PEDE-Q n=15 patients). *Note:* Repeated measures analysis of variance with Bonferroni corrected pairwise comparisons were used to assess statistical significance for within-subject continuous variables. Lower scores on the EDE-Q and FAD reflect decreased symptoms and improved family function. PEDE-Q, Eating Disorder Examination-Questionnaire (Parent modified); FAD, McMaster Family Assessment Device.

Supplementary Material

Methods

Treatment

Similar to multifamily interventions used successfully in treatment of adults with other psychiatric disordersn (Gelin, Cook-Darzens and Hendrick, 2017), the current treatment includes psychoeducation to emphasize the key role of neurobiological factors in the development of the illness, teaching the Support(s) (SU) age-appropriate skills to manage disorder-related temperament features and actively engaging multifamily groups to generate hope, reduce stigmatization and encourage practical constructive ways to respond to difficulties arising from the illness. The 5-day program maintains the FT-AN emphasis on weight restoration through meals with SU, and recognizes that the that patients and SU need to negotiate what kind of meal support is going to be most helpful because adults need both autonomy and needed support to manage through illness provoked ambivalence about change. Modifications are particularly focused on reducing dietary restriction and developing skills to shape food intake per dietary recommendations prescribed by program dietitians. Some examples include: 1) implementing a pre-meal routine to distract patients from negative internal states linked to anticipating the effects of eating, and reducing anxiety surrounding exposure to food, 2) increasing predictability and certainty around food while maintaining caloric-sufficiency to reduce anxiety and increase weight (e.g., fixed meal plan with increased calories over time), 3) meal coaching and time-limited post-meal movement to redirect the patient when anxiety or obsessions occur to reduce food refusal and improve support function, and 4) implementing an individually agreed behavioral contract (“agreement”) to achieve compliance with weight restoration (Hill, 2017a, 2017b; Knatz-Peck, 2016). The behavioral agreement serves as a motivation system and highly structured agreement that actively establishes how to manage eating disorder symptoms and traits for a 3-month period, and that outlines: 1) specific

guidelines for recovery and associated target behaviors (e.g., number of meals needed, meal times), 2) contingencies for target behaviors, and 3) roles of SU to help shape target behaviors. SU are taught basic behavioral principles and tools to help sustain AN recovery and to consistently maintain compliance with the contract (Knatz-Peck, 2016). See (Hill, 2017b; Kaye *et al.*, 2015; Knatz *et al.*, 2015) for more detail.

Participant exclusionary criteria

The following additional criteria were used to exclude participants: 1) medical instability as determined by study physician; 2) developmental, intellectual or psychotic disorder, 3) diagnosis of alcohol or drug abuse or dependence in the 3 months prior to the study, or 4) missing SU assessments.

Secondary Measures

Temperament: Temperament was assessed pre- and post- 5-day treatment with the following self-report assessments. The Temperament and Character Inventory (TCI) (Cloninger, Przybeck, Svrakic and Wetzel, 1994) Harm Avoidance subscale measures inflexibility, anxiety and inhibition (Frank *et al.*, 2012; Klump *et al.*, 2004; Krug *et al.*, 2011; Wagner *et al.*, 2006; Zerwas *et al.*, 2013). The Intolerance of Uncertainty Scale (IUS) (Buhr and Dugas, 2002) measures negative perceptions of uncertainty. The Sensitivity to Punishment Sensitivity to Reward Questionnaire (SPSRQ) (Torrubia, Avila, Molto and Caseras, 2001) assesses individual sensitivity to reward and punishment as related to Gray's original Reinforcement Sensitivity Theory (Gray, 1970). The Multidimensional Assessment of Interoceptive Awareness (MAIA) (Mehling *et al.*, 2012) measures interoceptive body awareness (Brown *et al.*, 2017). The Toronto Alexithymia Scale (TAS) (Bagby, Parker and Taylor, 1994) assesses difficulty with understanding, processing, and describing emotions. Cronbach's alpha for all measures within the present study was strong (α=.88-.97), with the exception of the SPSRQ (α=.75).

Exploratory outcome classification

Patients who completed assessments at pre-treatment, post-treatment, and follow-up were classified as fully remitted, partially remitted, or poor outcome according to the criteria set forth by (Bardone-Cone *et al.*, 2016) with a slight modification to how binge/purge behaviors were assessed and classified given our available data. Thus we categorized outcome as follows: (i) Full remission: a BMI of at least 18.5 kg/m^2, scores within 1 SD of age-matched community norms on all the subscales of the EDE-Q (Mond, Hay and Owen, 2006), and absence of binge/purging behaviors (as assessed per EDE-Q items 15-18) in the previous 28 days. (ii) Partial remission: a BMI of at least 18.5 kg/m^2 but with at least one subscale score on the EDE-Q above one SD of age-matched norms and/or binge–purging symptoms occurring less than once per week. (iii) Poor outcome: failure to achieve a BMI of 18.5 kg/m^2 or presence of binge–purging episodes during the previous 28 days with a frequency of once a week or more. Participants who did not complete the EDE-Q at follow-up were conservatively classified as partially remitted (n=5) or poor outcome (n=2) based on BMI (all denied binge/purge behaviors).

Statistical analysis of follow-up data

Preliminary lost case analysis evaluated any differences in pre-treatment variables between those who completed follow-up assessments and those who declined to complete the assessments using Mann–Whitney–Wilcoxon test and Fisher's exact test to test between group differences on continuous and categorical variables, respectively. For participants who completed follow-up assessments, changes in BMI, %IBW, and EDE-Q scores between pre-treatment, post-treatment and follow-up were analyzed with repeated measures Analysis of Variance (ANOVAs). These analyses were repeated to compare SU reports of changes in their loved one's ED symptoms and family function, weighted for number of supports per participant. Lastly, we examined the following baseline variables as possible predictors of outcome (good, poor): age, baseline BMI, duration of illness, subtype of AN, and length of follow-up using logistic regression analyses. Exploratory logistic regression analyses examined temperament traits, AN symptoms, and family function as additional possible predictors of outcome.

Follow-up data results

AN lost case analyses

The lost case analyses suggested assessment completers had more long-standing AN. Individuals who completed follow-up assessment (n=39) tended to be older (p=0.02) and have a greater duration of illness (p=0.03) than those who declined to participate in follow-up assessment (n=11). The groups did not differ on BMI or %IBW at study entry or on diagnostic subtypes (Supplementary Table 3).

AN patient characteristics at follow-up

Height and weight data were available for 39 participants (78%) at follow-up (25 staff measured, 14 self-reported; mean length of follow-up = 228.0 days, range = 79-742 days). Twenty-eight participants (56%) also completed the EDE-Q at follow-up (mean length of follow-up = 142.4 days, range = 75-500 days) (Supplementary Table 4). At follow-up, mean BMI was 19.6 kg/m^2, representing a significant and meaningful increase in weight ($p<0.001$, $\eta^2=.41$) across the 3 time points, with significant differences between pre-treatment and follow-up ($p<0.001$) and between post-treatment and follow-up ($p<0.001$). Mean %IBW at follow-up was 89.6%, representing a statistically significant increase ($p<0.001$, $\eta^2=.39$) across the three time points, with significant differences between pre-treatment and follow-up ($p<0.001$) and between post-treatment and follow-up ($p<0.001$). Participants also endorsed a significant decrease in ED symptoms on the Restraint ($p<0.001$, $\eta^2=.27$), Eating Concern ($p<0.001$, $\eta^2=.34$) and Global ($p=0.001$, $\eta^2=.24$) EDE-Q subscales across the three time points.

Relationship between clinical variables and outcome in AN

Binary logistic regressions for good vs poor outcome indicated a higher age (OR=0.854, 95% CI =0.758-0.963, p=0.010) and longer illness duration (OR=0.857, 95% CI=0.763-0.964, p=0.010) were associated with greater likelihood of a good outcome. In contrast, no associations were found between outcome and BMI at baseline, treatment location, diagnostic subtype, and length

of follow-up (ps>0.05). Exploratory analyses revealed that patient report of improved Communication (OR=0.143, 95% CI=0.025-0.817, p=0.029) and Affective Involvement (OR=0.142, 95% CI=0.029-0.709, p=0.017) on the FAD from pre- to post- 5-day treatment was associated with greater likelihood of a good outcome. No other predictors of outcome were significant.

Support ratings at follow-up

Data from 21 SU who completed follow-up assessments indicated a significant decrease in ED symptoms on the Restraint (p=0.007) and Eating Concern (p=0.010) subscales of the PEDE-Q, and improvement in Problem Solving (p=0.007) on the FAD across the three time points (Supplementary Table 5).

Figure Legend

Supplementary Figure 1. Open trial flow diagram showing patient flow through the study.

Supplementary Figure 2. Distribution of outcome categorization over time for patients who completed follow-up assessment (n=39).

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