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Neuropsychological and cognitive correlates of recovery in anorexia nervosa

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Abstract

Objective—To identify clinical or cognitive measures either predictive of illness trajectory or altered with sustained weight-recovery in adult women with anorexia nervosa.

Methods—Participants were recruited from prior studies of women with anorexia nervosa (AN-C) and in weight-recovery following anorexia nervosa (AN-WR). Participants completed a neuropsychological battery at baseline and clinical assessments at both baseline and follow up. Groups based on clinical outcome (continued eating disorder, AN-CC; newly in recovery, AN-CR; sustained weight-recovery, AN-WR) were compared using one-way ANOVAs with Bonferroni-corrected post hoc comparisons.

Results—AN-CC had poorer neuropsychological function and self-competence at baseline than AN-CR. AN-CR showed changes in depression and externalizing bias, a measure of self-related attributions. AN-WR differed from both AN-CC and AN-CR at baseline in externalizing bias, but only from AN-CC at outcome.

Discussion—Neuropsychological function when recently ill may be a prognostic factor, while externalizing bias may provide a clinical target for recovery.

Keywords

anorexia nervosa; self-perception; cognitive rigidity; attribution bias

INTRODUCTION

Anorexia nervosa (AN) is a serious mental illness marked by distortions in self-perception and an inability to maintain body weight. During the disease, many medical, neurological and psychiatric abnormalities are observed (Keski-Rahkonen & Mustelin, 2016; Reville, O'Connor, & Frampton, 2016; Westmoreland, Krantz, & Mehler, 2016). AN includes not

only the expected cognitive and behavioral distortions surrounding food and body size, but has also been associated with differences in neuropsychological functioning (Westwood, Stahl, Mandy, & Tchanturia, 2016), self-esteem (Collin et al., 2016), emotional processing (Lavender et al., 2015; Westwood, Kerr-Gaffney, Stahl, & Tchanturia, 2017), and interpersonal function (Tchanturia et al., 2013).

For adults with AN, there are no measures available early in presentation that predict either the immediate course of treatment or the long-term course and severity of a particular individual's illness (Dechartres et al., 2011; Sly, Morgan, Mountford, & Lacey, 2013). Because nearly half of all patients hospitalized from AN, both adult and child, have relapses leading to further hospitalization (Keel & Brown, 2010; Steinhausen, 2002), identification of factors associated with positive and negative outcomes may allow better treatments targeted to the anticipated illness trajectory. Most studies examining the course of disease have focused on understanding the expression of the clinical symptoms most closely associated with the disease (Steinhausen, 2009), specifically BMI (Bodell, Racine, & Wildes, 2016; Kastner et al., 2015; Madden et al., 2015; Wild et al., 2016) and measures of ED behaviors (Gianini et al., 2016; Lavender et al., 2011; Rigaud, Pennacchio, Bizeul, Reveillard, & Verges, 2011; Zerwas et al., 2013) and ED cognitions (Keel, Dorer, Franko, Jackson, & Herzog, 2005; Lock et al., 2013).

Fewer studies have considered how neurocognitive and psychological characteristics associated with adult AN relate to the progression of the disease. Keifer et al. (2010) found that estimated premorbid cognitive function and AN subtype predicted neuropsychological improvement following treatment but did not examine neuropsychological function in relation to illness trajectory. A recent study by Steward et al. (2016) related function to illness state, assessing decision making using the Iowa Gambling Task at treatment admission and at one-year follow-up. Those with AN performed more poorly at admission than healthy controls; at follow up, those in remission showed improved performance while patients with partial or no remission showed no improvement. AN outcome groups performed equally poorly at baseline, suggesting that impaired decision making may be a disease state.

Another neurocognitive factor related to AN is set-shifting, the ability to observe and respond to changes in rules (Roberts, Tchanturia, Stahl, & Treasure, 2007). Tchanturia et al. (2004) examined set-shifting longitudinally, and found that set-shifting deficits in AN persisted after weight recovery and were associated with premorbid childhood rigidity, but prognosis was not evaluated based on the deficits. Another study found that more problems in set shifting predicted a more severe and prolonged illness but neither disease duration nor BMI history predicted set-shifting difficulty (Filoteo et al., 2014). Weak central coherence, a cognitive style with global processing difficulties but superior local processing (attention to detail), has also been proposed as a characteristic of AN (Lang, Lopez, Stahl, Tchanturia, & Treasure, 2014). Finally, using fMRI to evaluate both set-shifting and central coherence, regional brain activation associated with set-shifting, but not central coherence, predicted treatment response (Garrett et al., 2014). Neuropsychological deficits may hinder or complicate clinical progress by making it more difficult for individuals to develop and

implement new cognitive and behavioral patterns. These studies suggest neuropsychological function in the illness may be an important measure of prognosis.

Another avenue of research has suggested that differences in self-perception and interpersonal behaviors may be important in disease progression. Interpersonal difficulties identified in AN include failures to recognize and respond appropriately to social cues as well as a cognitive bias to attribute negative, but not positive, interpersonal interactions to oneself (a negative externalizing bias) (Dalglish et al., 2003; Mansfield & Wade, 2000; McAdams, Lohrenz, & Montague, 2015; Morrison, Waller, & Lawson, 2006). Other problems related to positive interpersonal behaviors have been observed in AN, including low self-esteem (Bardone-Cone, Schaeffer, et al., 2010) and recognition of positive interpersonal interactions (Ambwani et al., 2016). Self-perceived low social rank predicts an increase in AN symptoms (Troop, Andrews, Hiskey, & Treasure, 2014). Social emotional difficulties and poor work and social adjustment have been associated with illness severity (Harrison, Tchanturia, Naumann, & Treasure, 2012; Tchanturia et al., 2013). Similarly, short-term follow-up studies have indicated social impairment predicts a more chronic course (Herzog et al., 1993; Strober, Freeman, & Morrell, 1997).

Here, we determined long-term clinical outcomes for women with AN, using participants from previous cross-sectional studies (Acevedo, Valencia, Lutter, & McAdams, 2015; McAdams et al., 2016; McAdams et al., 2015). These studies had included neuropsychological assessments of set-shifting and central coherence, as well as measures of body-perception, eating behaviors, self-esteem, alexithymia, and interpersonal attribution biases. Participants with anorexia nervosa had previously been recruited as either currently-ill or in long-term weight recovery; here we re-assessed the clinical status of these participants 2 - 6 years after original measures, identifying those remaining ill, those recently in recovery, and those in sustained recovery. Neuropsychological assessments were performed only at baseline; we hypothesized that set-shifting would be a positive prognostic factor in recovery. Clinical symptoms and self-report assessments were completed at both baseline and follow-up. We hypothesized that participants who recovered would show an increased externalizing bias, decreasing the number of self-attributed negative events relative to the number self-attributed positive events. We also hypothesized that those who recovered will show improved self-esteem and reduced eating disorder symptoms.

METHODS

Participants

A total of 46 women ages 20–61 ($M = 30.26$, $SD = 8.61$) were recruited for follow up from 55 eligible participants from three previous studies examining currently-ill (AN-C) and weight-recovered (AN-WR) women with AN (Acevedo et al., 2015; McAdams et al., 2016; McAdams et al., 2015). Women in the AN-C group had met DSM-IV criteria for AN within the previous six months and women in the AN-WR group had maintained a BMI > 19 for at least 12 months but had met DSM-IV criteria for AN in their lifetime. Participants completed follow up assessments an average of 46 months after initial data collection (minimum: 20 months, maximum: 72 months). The variation in follow up period was due to differences in initial enrollment, participant availability, and funding.

Participants provided written informed consent approved by the UT Southwestern Institutional Review Board. All participants completed the Structured Clinical Interview for DSM-IV (First, Spitzer, Miriam, & Williams, 2002) upon initial enrollment to confirm current or past AN and comorbid diagnoses. Follow up self-reports were collected and managed using REDCap electronic data capture tools hosted at UT Southwestern (Harris et al., 2009), where participants provided digital consent upon beginning their surveys.

Outcome Groups

After completing follow up, participants were designated as still ill (AN-CC), in recovery from a baseline ill status (AN-CR), or sustaining weight recovery (AN-WR). Recovery was defined as maintaining a BMI > 19 for at least 12 months; this matched the enrollment criteria utilized for AN-WR in the original studies. In addition, participants in recovery could not have participated in intensive outpatient, partial hospital, residential, or inpatient treatment for at least 12 months, and reported no medical complications of their eating disorder during the prior 12 months.

Neuropsychological Assessments, Completed at Baseline Only

Wechsler Abbreviated Scale of Intelligence (WASI)—The two subtest version of the WASI (vocabulary and matrix reasoning) provided an estimate of intelligence level (Wechsler, 1999).

Wisconsin Card Sorting Test (WCST)—The 64-run digital version of the WCST tests participants' cognitive flexibility and set-shifting capabilities when facing changing reinforcement. Participants must match stimulus cards to the correct card deck; they are told if their match is correct but are not given instructions on how to match. Matching rules change throughout the task (Kongs, Thompson, Iverson, & Heaton, 2000). We examined total score, perseverative and non-perseverative errors, and conceptual-level responses. Total score and number of errors assessed general performance and broad executive function, number of perseverative errors assessed difficulties switching to a new rule (set-shifting deficits), and number of conceptual-level responses assessed flexibility and concept formation.

Trail Making Test (TMT)—The TMT is a timed test that asks participants to accurately connect a series of circles as quickly as possible. In TMT-A, they must connect 25 numbers in order (i.e. 1-2-3, etc.). In TMT-B, they must alternate between numbers and letters (i.e. 1-A-2-B, etc.). The TMT assesses several aspects of executive function including cognitive flexibility, set shifting, visual search, and psychomotor speed (*Army Individual Test Battery*, 1944). The outcome of interest for this study was time to complete TMT-B as a measure of set-shifting (Kortte, Horner, & Windham, 2002; Sánchez-Cubillo et al., 2009).

Rey-Osterrieth Complex Figure Test (RCFT)—The RCFT was used to assess perception and cognitive style. Participants were asked to copy a complex line drawing while the test administrator noted the order of image component completion (Lezak, Howieson, & Loring, 2004). For this study, we used the copy of the figure as an assessment of central coherence using a scoring system developed by Booth (2006). This system,

previously utilized in eating disorders, provides scores for order of construction (whether a participant began with large image elements or smaller details), style (whether image components were fragmented or drawn continuously), and central coherence (the sum of construction and style indices) (Harrison et al., 2012; Lang et al., 2014).

Self-Report Assessments, Completed at Both Baseline and Outcome

Eating Attitudes Test (EAT)—The 26 item version of the EAT is a valid and reliable measure for rating frequency of eating and exercise related behaviors and concerns in both clinical and non-clinical samples ($\alpha = .90$ in AN samples) (Garner, Olmsted, Bohr, & Garfinkel, 1982).

Body Shape Questionnaire (BSQ)—This 34-item validated questionnaire measures concerns about body shape and weight ($\alpha = .88$) (Cooper, Taylor, Cooper, & Fairburn, 1987; Rosen, Jones, Ramirez, & Waxman, 1996).

Toronto Alexithymia Scale-20 (TAS)—The TAS is a validated measure that assesses difficulty in describing emotions, identifying emotions, and the tendency to focus attention externally or minimize emotions ($\alpha = .81$) (Bagby, Parker, & Taylor, 1994).

Self-Liking and Self-Competence Scale (SLSC)—This validated multi-dimensional self-esteem scale ranks degree of agreement or disagreement with positive and negative self-appraisal statements, yielding a self-liking score ($\alpha = .90$) and a self-competence score ($\alpha = .83$) from two 8-item subscales (Mar, DeYoung, Higgins, & Peterson, 2006; Tarafodi & Swann, 2001).

Internal, Personal, and Situational Attributions Questionnaire (IPSAQ)—This 32 question validated assessment examines automatic interpretations of sixteen positive and sixteen negative interpersonal situations. The IPSAQ yields externalizing bias (the extent to which an individual attributes positive social exchanges versus negative exchanges to themselves), negative personalizing bias (the extent to which an individual attributes negative exchanges to another person relative to the situation), and positive personalizing bias (the extent to which an individual attributes positive exchanges to another person relative to the situation) scores. Subscale reliability coefficients range from .61 to .76 (Kinderman & Bentall, 1996). The subscale of interest for this study was the externalizing bias, which is the number of positive situations minus the number of negative situations that a person attributes to themselves. A positive score indicates a tendency to attribute more positive interactions to oneself while externalizing blame for negative interactions; a negative score indicates a tendency to attribute more negative than positive interactions to oneself.

Clinician Assessments, Completed at Both Baseline and Outcome

Structured clinician assessments of depression [Quick Inventory of Depression Symptoms, QIDS-CR (Rush et al., 2003), $\alpha = .85$ (Trivedi et al., 2004)] and anxiety symptoms [Structured Interview for Hamilton Anxiety Scale, SIGH-A, $\alpha = .82$ (Shear et al., 2001)], treatment history, and current height and weight measurements were completed during an in-

person or phone interview with a physician. Weight and height were measured for all participants at baseline; participants who completed follow up in person had weight and height measured but participants who completed the interview by phone provided a current weight and height verified by a third party (e.g. current medical provider).

Statistical Analysis

Statistical analyses were conducted using the IBM Statistical Package for Social Sciences (SPSS; v.23). Outcome group demographics (age, onset age, BMI, follow-up period), neuropsychological measures (WASI, TMT, WCST, RCFT), and clinical measures (EAT, BSQ, TAS, SLSC, IPSAQ, QIDS, SIGH-A) were first compared using one-way ANOVAs followed by post hoc Bonferroni comparisons. For all significant findings, one-way ANCOVAs considered whether the relationship between participant group and cognitive performance was influenced by depression, anxiety, or BMI at intake. Participant group was entered in the general linear model as a fixed factor, and depression, anxiety, and BMI were entered as covariates for each neuropsychological assessment.¹

One-way ANCOVAs were also used to examine whether anxiety and depression influenced relationships between participant group and measures relating to self and other perception (SLSC, IPSAQ). Participant group was entered in the general linear model as a fixed factor, and baseline depression and anxiety were entered as covariates for baseline self-liking, self-competence, and externalizing bias. The process was repeated for follow up measures, controlling for follow up depression and anxiety. Because we hypothesized that improved externalizing bias would be associated with recovery, we also assessed within group changes in externalizing bias with two-tailed, paired samples t-tests. See Figure 1 for a depiction of study design.

RESULTS

Clinical Outcomes

28 of the women in the AN-C group and 18 women in the AN-WR group completed follow up. Clinical assessments were completed over the phone for 20 participants (8 AN-CC, 4 AN-CR, 8 AN-WR) and in the office for 26 participants (10 AN-CC, 7 AN-CR, 9 AN-WR). Eight of the original AN-C group and one of the AN-WR group did not respond to phone/email outreach or were unable to complete follow-up; these subjects did not differ from the completers in age, BMI, or eating disorder symptoms at baseline.

For the AN-C group, 17 participants remained ill (AN-CC) and 11 achieved recovery from a baseline ill status (AN-CR), a recovery rate of 39%. All 18 of the AN-WR group that participated remained weight-recovered at follow up (AN-WR). There was no difference in the distributions of subtypes of AN by group (AN binge-purge/restricting, AN-CC 9/8, AN-CR 5/6, AN-WR 11/7; $X^2(2, N = 46) = 0.67, p = .71, V = 0.12$).

¹One AN-WR participant was identified as an outlier and excluded for analysis of neuropsychological assessment.

Demographic Comparisons

Groups did not differ in age, follow-up period, or lowest BMI (Table 1). There were effects of group related to age of illness onset (AN-WR < AN-CR, $p = 0.02$), baseline BMI (AN-WR > AN-CC & AN-CR, $p < 0.001$), and follow up BMI (AN-CC < AN-CR & AN-WR, $p < 0.001$).

Neuropsychological Differences at Baseline

Neuropsychological differences across groups were observed for the TMT-B and the WCST but not the RCFT nor WASI (Table 2). All group differences were retained after controlling for depression, anxiety, and BMI. On TMT-B, AN-CR was faster than both AN-CC ($p = 0.04$) and AN-WR ($p = 0.04$). For the WCST, there was a marginal effect of group for the entire task, with the post-hoc suggesting that AN-CC was marginally worse than AN-CR ($p = .03$). There were effects of group on overall errors (AN-CC > AN-CR, $p = 0.01$), non-perseverative errors (AN-CC > AN-CR, $p = 0.02$), and number of conceptual level responses (AN-CC < AN-CR, $p = 0.02$). Neither AN-CC nor AN-CR differed significantly from AN-WR on the WCST.

Psychological Symptoms at Baseline and Outcomes

There were no effects of group at baseline or follow-up for the BSQ, TAS, self-liking component of SLSC, IPSAQ positive personalizing bias, IPSAQ negative personalizing bias, or SIGH-A (Table 3). There were effects of group on the baseline EAT (AN-WR < AN-CC, $p = 0.004$; AN-WR < AN-CR, $p = 0.005$), but the AN-CC and AN-CR did not differ from each other in eating disorder symptoms (EAT, BSQ) at either time point. There was an effect of group related to depression at follow up (QIDS, AN-CR < AN-CC, $p = 0.01$).

For the self-competence component of the SLSC, there were trending group differences both at baseline (AN-CC < AN-WR, $p = 0.03$) and at follow-up (AN-CC < AN-CR, $p = 0.08$); after controlling for depression and anxiety, the effect of group on baseline self-competence was marginally significant ($F(2, 41) = 2.89$, $p = .07$, $\eta^2 = .005$; AN-CC < AN-WR, $p = 0.02$), with no effect at follow-up.

For the externalizing bias of the IPSAQ, there were group differences at both baseline (AN-WR > AN-CC, $p = 0.01$) and at follow-up (AN-WR > AN-CC, $p = 0.02$). The AN-CR group did not differ from either the AN-CC or AN-WR group at either time. After controlling for depression and anxiety, group differences related the externalizing bias at baseline in the AN-CR group also emerged ($F(2, 41) = 4.61$, $p = 0.02$, $\eta^2 = .14$; AN-WR > AN-CC, $p = 0.01$; AN-WR > AN-CR, $p = 0.03$) with little change in the effects observed at follow up ($F(2, 41) = 3.12$, $p = 0.06$, $\eta^2 = .12$; AN-WR > AN-CC, $p = 0.02$). Within groups, AN-CR showed a trend-level increase in externalizing bias between time points ($M = 2.82$, $SD = 4.96$, $t(10) = 1.89$, $p = 0.09$, $d = 0.57$) while AN-CC and AN-WR did not ($M = 0.12$, $SD = 4.41$, $t(16) = 0.06$, $p = .96$, $d = .01$; $M = 0.00$, $SD = 5.37$, $t(17) = 0.00$, $p = 1.00$, $d = 0.00$) (Figure 2).

DISCUSSION

This study examined the course of disease in adult women with AN, assessing neuropsychological function, clinical symptoms, and measures related to self-perception. Four key findings were obtained. First, neuropsychological function of the currently-ill women and the self-competence measure of self-esteem were the only measures at baseline related to clinical outcome. Second, self-reports of anxiety, alexithymia, body-shape perception, and the eating attitudes test measured both at baseline and at follow-up were not related to the clinical outcome. Third, changes in depression, as well as the externalizing bias were observed in women recently achieving recovery but not the other groups. Finally, we found a recovery rate of 39%, consistent with literature reports of 37-73% (Berkman, Lohr, & Bulik, 2007; Eddy et al., 2016; Steinhausen, 2002).

The neuropsychological measures at baseline differed for AN-CC and AN-CR. Specifically, the AN-CC performed worse than AN-CR on both TMT-B and the WCST, suggesting that neuropsychological function when recently ill may be an important predictor of the immediate ability to recover. Neuropsychological differences were not as consistent with AN-WR, which performed more poorly than AN-CC on TMT-B but did not differ from AN-CC or AN-CR on WCST. This is inconsistent with previous studies that indicate that those in recovery perform better on the WCST than those that are currently ill (Tchanturia et al., 2012). However, for the AN-WR, we do not have neuropsychological measures collected during their illness. In sum, consideration of baseline neuropsychological function in currently ill individuals may be an important prognostic indicator. While we did observe poorer overall WCST performance and more overall errors in the AN-CC group compared to the AN-CR group, we did not observe a difference in perseverative errors as a measure of set-shifting ability. The higher number of overall errors was accounted for by non-perseverative errors, which may indicate difficulty with attention or working memory. Despite not demonstrating differences in set-shifting ability on the WCST, AN-CC may have had more deficits in flexibility and concept formation as indicated by a lower conceptual-level response score. Reduced performance on the WCST and TMT-B is consistent with prior research indicating that cognitive flexibility, but not central coherence, is a predictor of treatment response and clinical outcome (Garrett et al., 2014).

Consistent with prior work examining symptoms in bulimia nervosa (Bardone, Perez, Abramson, & Joiner, 2003), the self-competence component of self-esteem, an assessment of one's perception of one's ability to be successful in life, was also predictive of outcome. We hypothesize that both cognitive control and self-competence may be related to one's ability to respond to current therapeutic interventions in AN.

While central coherence was not identified as a predictor of outcome in Garrett et al. or in the present study, it may be still be associated with the recovery process. Lang et al. (2016) recently observed that those with current AN had poorer global processing than both those recovered from AN and healthy controls but that those recovered from AN did not differ from healthy controls. This suggests that central coherence may be impacted by nutritional state and improve with recovery. It is surprising then that we did not find differences between AN-WR and either of the currently ill groups. However, the currently ill

participants in Lang et al. were included at a lower BMI threshold than participants in the present study, which may partially explain why we did not find baseline group differences.

Importantly, we also found that eating disorder clinical symptom reports (EAT and BSQ) and anxiety symptoms (SIGHA), measured both at baseline and at the 2-year follow up, were not related to clinical outcome. Surprisingly, both baseline ill groups showed reductions in overall eating disorder symptomatology over time, but these did not differ across groups. We hypothesize that patients currently ill may have low insight and deny symptoms, and those currently in treatment programs may show transient changes in symptoms. Conversely, those that achieve sustained weight-recovery may be more aware of eating disorder thoughts, but have developed skills to prevent the behaviors (Schoen et al., 2012; Starzomska & Tadeusiewicz, 2016; Viglione, Muratori, Maestro, Brunori, & Picchi, 2006). In sum, assessments of eating disorder cognitions may not accurately reflect severity and impact of AN on life function and may not be sensitive or early measures to identify progress in treatment.

The primary motivation for this study were the differences in externalizing bias, a measure of self-blame versus self-promotion, previously reported in comparisons of currently-ill and weight-recovered women with AN (McAdams et al., 2015). Here in a larger sample, after controlling for depression and anxiety, both AN-CC and AN-CR showed more negative externalizing biases than AN-WR at baseline. However, at follow-up, only AN-CC continued to differ from AN-WR, suggesting that a more negative externalizing bias is associated with disease state and prognosis. AN-CR also had trending within group changes in externalizing bias while AN-CC and AN-WR did not. In concert, these data support a hypothesis that development of a positive externalizing bias may be important target for recovery in AN. This is exciting because attributional biases are known to change during cognitive behavioral therapy for depression, and furthermore these changes are persistent and independent of other depressive symptoms (Jarrett, Vittengl, Doyle, & Clark, 2007; Rubenstein, Freed, Shapero, Fauber, & Alloy, 2016; Wang, Zhang, Li, Zhang, & Zhang, 2011). This provides a potentially new, accessible therapeutic target in evaluation and treatment of AN.

Limitations

There are many limitations to this study. First, only clinical and self-report information but not the neuropsychological tests were completed at follow-up, preventing analysis of how changes in neuropsychological function might relate to clinical and cognitive symptoms. Second, the longitudinal component of this study was not planned at the initial enrollment of subjects, resulting in variability in the timing of the follow-up measures relative to the baseline across subjects and groups. Third, measurement of eating disorder symptomatology (but not outcome) was primarily based on self-reports. Fourth, after dividing into the three groups, the sample size of each group remains small. It is possible that small sample size impacted findings, especially with regards to the findings that clinical scales were not associated with recovery and that AN-WR did not demonstrate better neuropsychological performance than either of the initially ill groups. Additionally, the groups only included women, and findings may not be generalizable to men or nonbinary individuals.

Another challenge in studying adult AN is the definition of recovery; we utilized objective criteria based on weight and level of care utilized during preceding 12 months. Some subjects in the AN-CC group considered themselves recovered, despite low BMIs or experiencing medical complications related to AN, and were not in treatment. For example, three were very involved in fitness activities and perceived themselves to be healthy despite BMIs of 17-18. Both weight and behavioral recovery have been shown to precede psychological recovery (Bardone-Cone, Harney, et al., 2010; Darcy et al., 2010; Strober et al., 1997), these results, particularly the lack of differences in the clinical symptom scales, support this idea.

Another factor that is both a limitation and a strength is that at baseline, none of women were assessed during inpatient, residential or partial hospital treatment; all were appropriate for outpatient or intensive outpatient treatment. One subject was in partial hospital treatment at follow-up. Thus, the neuropsychological performance and self-reports were completed during relatively stable stages of illness, compared to the rapid changes in body mass and eating disorder symptoms observed during the course of a hospital or residential treatment of an ED (Born et al., 2015; Stroe-Kunold et al., 2016). This differs from many studies of AN that often measure factors at the beginning of treatment, when the subjects are severely malnourished (Collin et al., 2016; Keifer et al., 2010; Steward et al., 2016). Findings need to be corroborated using larger sample sizes and a longitudinal design with consistent and planned follow up points to improve our understanding of the trajectories for change and recovery in adult AN.

Conclusion

Consistent with literature (Eddy et al., 2016), recovery from AN may require years. Nevertheless, all participants weight-recovered at baseline continued to demonstrate sustained recovery, demonstrating that AN is not always a chronic illness. Recovery from AN may include changes that are both directly (BMI) and indirectly (depression and externalizing bias) related to clinical symptoms expressed during the disease (BSQ and EAT). Depression and the interpersonal attributional bias related to self-perception, the externalizing bias, emerge as two factors that change with recovery and may thus serve as specific clinical targets important during treatment. Conversely, anxiety, eating symptoms, and alexithymia were not related to illness or recovery at either baseline or follow-up, and may not change early in recovery. Neuropsychological function and the self-competence component of self-esteem should be further evaluated as potential predictors of course of illness in adult AN. Future studies to more clearly determine the process and predictors of change in women with AN during the course of recovery are needed, such studies should recognize that evaluation of recovery requires years.

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Figure 1.
Mixed design longitudinal study flow chart. Large arrows indicate areas of statistical comparison.

Figure 2.

Externalizing bias scores on the Internal, Personal, and Situational Attribution Questionnaire (IPSAQ) at baseline and follow-up for each group. AN-CC = women remaining ill with anorexia nervosa, n = 17; AN-CR = women recently recovered from anorexia nervosa, n = 11; AN-WR = women sustaining recovery from anorexia nervosa, n = 18. Data are mean ± SEM. * Significant difference (p < 0.05) between this group and the AN-WR measured at same time.

Participant Characteristics

Table 1

Measure	Participant Group						Statistical Comparisons		
	AN-CC (<i>n</i> = 17)		AN-CR (<i>n</i> = 11)		AN-WR (<i>n</i> = 18)		<i>F</i>	<i>p</i>	<i>η</i> ²
	Mean(<i>SD</i>)	Range	Mean(<i>SD</i>)	Range	Mean(<i>SD</i>)	Range			
Age (years)	28.2(7.47)	20–49	28.8(6.24)	21–42	33.2(10.65)	23–61	1.62	0.21	0.07
ED Onset Age	16.3(3.10)	12–23	19.3(7.78)	11–38	14.1(3.30)	9.5–22	4.01	0.03 [*]	0.16
Follow-Up Period (months)	41.1(17.04)	20–72	40.9(16.22)	25–62	38.1(11.36)	21–62	0.07	0.93	0.003
Lowest BMI	14.60(2.05)	10.5–17.2	15.72(1.61)	13.3–17.5	15.82(1.44)	13.3–17.6	1.97	0.15	0.08
BMI at Baseline	17.54(1.52)	14.6–20.4	18.39(1.08)	17.2–20.4	22.84(2.69)	19.2–28.5	36.38	<.001 ^{*,^}	0.63
BMI at Follow-Up	17.78(1.52) ^a	14.4–19.6	21.05(1.56)	19.1–24.1	23.37(3.66)	19.3–32.9	20.86	<.001 ^{^,‡}	0.50

AN-CC = women remaining ill with anorexia nervosa; AN-CR = women recently recovered from anorexia nervosa; AN-WR = women sustaining recovery from anorexia nervosa. ED = eating disorder; BMI = body mass index.

^a BMI not provided for one participant who was currently involved in treatment, AN-CC *n* = 16

^{*} AN-CR differs from AN-WR (*p* < 0.05)

[^] AN-CC differs from AN-WR (*p* < 0.05)

[‡] AN-CC differs from AN-CR (*p* < 0.05)

Table 2

Neuropsychological Assessment

Measure	Participant Group						Statistical Comparisons		
	AN-CC (<i>n</i> = 17)		AN-CR (<i>n</i> = 11)		AN-WR (<i>n</i> = 16)				
	Mean(SD)	Range	Mean(SD)	Range	Mean(SD)	Range	<i>F</i>	<i>p</i>	<i>N²</i>
Intelligence (WASI)	121.2(8.12)	107–133	118.6(9.35)	99–131	122.0(10.01)	99–137	0.49	0.62	0.02
TMT-A (Seconds)	26.36(7.76)	11.90–44.55	20.24(6.55)	10.90–34.40	28.33(13.33)	10.60–64.00	2.25	0.12	0.10
TMT-B (Seconds)	45.33(9.85)	25.00–58.00	35.25(8.64)	22.20–50.10	45.92(13.68)	23.10–83.00	3.57	0.04 ^{*,†}	0.15
TMT B:A	1.81(0.48)	1.04–2.51	1.85(0.63)	1.23–3.43	1.77(0.45)	1.15–2.69	0.09	0.92	0.004
Wisconsin Card Sort	51.3(4.52) ^a	44–57	54.8(2.36)	51–58	52.1(4.41)	42–58	2.64	0.08 [‡]	0.12
Total Errors	13.3(4.41) ^a	7–20	9.2(2.36)	6–13	11.9(4.41)	6–22	3.50	0.04 [‡]	0.15
Non Perseverative Errors	7.3(2.49) ^a	3–10	4.0(2.00)	1–7	6.4(4.15)	2–17	3.63	0.04 [‡]	0.15
Perseverative Errors	6.1(3.04) ^a	2–14	5.2(1.25)	4–8	5.5(1.51)	4–9	0.58	0.56	0.03
Perseverative Resp.	6.3(3.52) ^a	2–16	5.4(1.75)	4–10	5.8(1.95)	4–10	0.45	0.64	0.02
Conceptual-level Resp.	47.5(6.58) ^a	39–57	53.0(3.55)	47–58	49.9(6.12)	35–58	2.95	0.06 [‡]	0.13
RCFT Order	2.39(0.43) ^b	1.66–3.00	2.08(0.79) ^b	0.50–3.30	2.21(0.79) ^b	0.50–3.00	0.62	0.55	0.03
RCFT Style	1.79(0.22) ^b	1.33–2.00	1.56(0.48) ^b	0.58–2.00	1.61(0.43) ^b	0.50–2.00	1.27	0.29	0.07
RCFT Coherence	1.61(0.17) ^b	1.25–1.83	1.41(0.47) ^b	0.44–2.00	1.46(0.46) ^b	0.36–1.91	1.00	0.38	0.05

AN-CC = women remaining ill with anorexia nervosa; AN-CR = women recently recovered from anorexia nervosa; AN-WR = women sustaining recovery from anorexia nervosa. One AN-WR participant did not complete neuropsychological assessment; one AN-WR participant was identified as an outlier and removed from analysis. WASI = Wechsler Abbreviated Scale of Intelligence; TMT = Trail Making Test; RCFT = Rey-Osterrieth Complex Figure Test

^a *n*=16

^b The RCFT was not completed by the earliest participants at baseline due to protocol change. AN-CC *n*=15; AN-CR *n*=9; AN-WR *n*=15

^{*} AN-CR differs from AN-WR (*p* < 0.05) after controlling for anxiety, depression, and BMI

[‡] AN-CC differs from AN-CR (*p* < 0.05) after controlling for anxiety, depression, and BMI

Table 3

Clinical Measures at Baseline and Follow Up

Measure	Participant Group						Statistical Comparisons		
	AN-CC (n = 17)		AN-CR (n = 11)		AN-WR (n = 18)		F	p	η^2
	Mean(SD)	Range	Mean(SD)	Range	Mean(SD)	Range			
Eating Attitudes Test	33.5(19.23)	1-66	35.6(14.82)	14-64	16.1(8.62)	0-33	8.41	0.001 ^{*,^}	0.28
	24.3(16.71)	2-64	18.0(14.18)	3-42	17.2(15.23)	1-47	1.03	0.37	0.05
Body Shape Questionnaire	125.5(42.65)	59-196	127.2(31.97)	73-170	111.1(31.36)	54-189	0.87	0.43	0.04
	95.0(44.13)	39-192	88.4(35.99)	44-154	107.1(45.18)	56-186	0.72	0.49	0.03
Toronto Alexithymia Survey	54.1(12.28)	25-72	56.8(13.05)	33-75	50.8(10.76)	30-71	0.92	0.41	0.04
	51.8(16.12)	24-77	47.4(12.25)	26-70	46.8(12.34)	31-71	0.63	0.54	0.03
Self-Liking	16.7(6.19)	9-32	16.0(4.75)	9-24	18.1(5.47)	8-29	0.55	0.58	0.03
	18.4(8.38)	8-32	23.9(7.42)	17-39	19.7(5.55)	13-29	2.06	0.14	0.09
Self-Competence	20.5(4.95)	8-27	23.1(6.07)	16-37	24.7(3.61)	20-31	3.39	0.04 [^]	0.14
	19.7(6.03)	8-30	24.8(6.21)	15-37	23.2(5.09)	14-33	3.05	0.06	0.12
IPSAQ Externalizing Bias	-3.41(5.52)	-14-6	-2.18(5.74)	-11-9	1.72(4.07)	-5-8	4.83	0.01 ^{*,^}	0.18
	-3.35(6.21)	-15-6	0.64(5.52)	-8-9	1.72(4.92)	-9-10	3.88	0.03 [^]	0.15
IPSAQ Positive Personalizing Bias	0.58(0.31)	0-1	0.46(0.28)	0.13-1	0.43(0.26)	0.00-0.86	1.36	0.27	0.06
	0.48(0.27)	0-0.93	0.48(0.29)	0-1	0.47(0.30)	0.00-0.92	0.01	0.99	0.001
IPSAQ Negative Personalizing Bias	0.67(0.39)	0-1	0.68(0.23)	0.33-1	0.72(0.24)	0.15-1.00	0.13	0.88	0.01
	0.41(0.29)	0-0.90	0.53(0.26)	0.17-1	0.57(0.20)	0.17-0.92	1.85	0.17	0.08
Quick Inventory of Depression	6.8(5.62)	0-16	6.2(5.21)	0-16	5.6(5.11)	0-17	0.23	0.80	0.01
	6.8(4.10)	0-15	2.6(2.16)	0-8	5.6(3.53)	2-14	4.86	0.01 [^]	0.18
Structured Clinical Interview for Anxiety	8.1(7.78)	0-25	11.2(8.60)	0-29	8.3(6.58)	0-20	0.66	0.52	0.03
	8.9(7.37)	0-21	4.9(3.21)	1-13	7.6(3.38)	0-13	1.96	0.15	0.08

For each measure, top value corresponds to baseline and bottom value corresponds to follow up. AN-CC = women remaining ill with anorexia nervosa; AN-CR = women recently recovered from anorexia nervosa; AN-WR = women sustaining recovery from anorexia nervosa. IPSAQ = Internal, Personal, and Situational Attributions Questionnaire.

* AN-CR differs from AN-WR ($p < 0.05$) after controlling for anxiety and depression.

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AN-CC differs from AN-WR($p < 0.05$) after controlling for anxiety and depression.

AN-CC differs from AN-CR ($p < 0.05$) after controlling for anxiety and depression (for Quick Inventory of Depression, $p < 0.05$ with no covariates included in the model).