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A process approach to verbal memory assessment: Exploratory evidence of inefficient learning in women remitted from anorexia nervosa.

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Abstract

Introduction: Anorexia nervosa (AN) is associated with deficits in set-shifting and cognitive flexibility, yet less is known about the persistence of these deficits after recovery and how they might contribute to reported difficulties organizing and learning new information. To address this question, the current study applied a process-focused approach, that accounts for errors and strategies by which a score is achieved, to investigate the relationship between verbal memory and executive function in women remitted from AN.

Method: Twenty-six women remitted from anorexia nervosa (RAN) and 25 control women (CW) aged 19–45 completed the California Verbal Learning Test, Second edition (CVLT-II) and the Wisconsin Card Sorting Test (WCST). Groups were compared on overall achievement scores, and on repetition, intrusion, and perseverative errors on both tests. Associations between learning and memory performance and WCST errors were also examined.

Results: RAN and CW groups did not differ on overall CVLT-II learning and memory performance or errors on the WCST, though the RAN group trended towards greater WCST non-perseverative and total errors. On the CVLT-II, the RAN group made significantly more repetition errors than CW ($p = 0.010$), and within-trial perseveration (WTP) errors ($p = 0.044$). For the CW group, CVLT-II learning and memory performance was negatively associated with errors on the WCST, whereas among RAN, primarily delayed memory was negatively correlated with WCST errors. Notably, for RAN, greater WCST perseverative responses were correlated with greater

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CVLT-II repetition and WTP errors, showing convergence of perseverative responding across tasks.

Conclusions: Despite similar overall learning and memory performance, difficulties with executive control seem to persist even after symptom remission in patients with AN. Results indicate an inefficient learning process in the cognitive phenotype of AN and support the use of process approaches to refine neuropsychological assessment of AN by accounting for strategy use.

Keywords

Anorexia nervosa; California Verbal Learning Test; neuropsychology; verbal learning; error analysis

Introduction

Anorexia nervosa (AN) is an eating disorder characterized by dangerously low body weight and an overconcern with weight and shape (American Psychiatric Association, 2013). Patients with AN often display rigid behaviors and cognitions in the form of preoccupation with details and a resistance to change (Tchanturia, Lloyd, & Lang, 2013). These behaviors are frequently linked to eating disorder symptoms such as food restriction and an obsession with weight and shape. Inflexibility also manifests in exercise routines, work or school performance, or in relationships with family and friends (Tchanturia et al., 2013). Cognitive inflexibility theoretically relates to neurocognitive dysfunction, and may represent predisposing traits that increase risk for developing AN (Holliday, Tchanturia, Landau, Collier, & Treasure, 2005; Kanakam, Raoult, Collier, & Treasure, 2013; Lopez, Tchanturia, Stahl, & Treasure, 2009; Roberts, Tchanturia, & Treasure, 2013; Tchanturia, Morris, Surguladze, & Treasure, 2002; Teconi et al., 2010). This may manifest in the form of set-shifting deficits i.e. the inability to shift attention between one task and another (Roberts, Tchanturia, Stahl, Southgate, & Treasure, 2007) and a detail-focused processing style, often called weak central coherence, which includes difficulties with understanding the context or seeing “the bigger picture” (Lang, Lopez, Stahl, Tchanturia, & Treasure, 2014; Lang & Tchanturia, 2014; Lopez, Tchanturia, Stahl, & Treasure, 2008). Less is known about the persistence of deficits after recovery, or if altered cognitive function causes difficulties with organizing and learning new information. Some studies have found that patients remitted from AN show impaired central coherence (Tenconi et al., 2010; Weinbach, Perry, Sher, Lock, & Henik, 2017), set-shifting deficits (Danner et al., 2012; Lindner, Fichter, & Quadflieg, 2014; Roberts, Tchanturia, & Treasure, 2010; Tchanturia et al., 2004; Tchanturia et al., 2002; Teconi et al., 2010) and verbal memory difficulties (Bentz et al., 2017). On the other hand, other studies have not confirmed these findings and report no dissimilarities between remitted patients and healthy controls in terms of central coherence (Danner et al., 2012; Lang et al., 2016; Lindner, Fichter, & Quadflieg, 2013), set-shifting (Gillberg, Rastam, Wentz, & Gillberg, 2007; Nakazato et al., 2010) and verbal memory (Gillberg et al., 2007).

One of the limitations of previous studies is that the vast majority of conclusions are based on global, or overall, achievement scores. Neuropsychologists have cautioned against this approach, emphasizing that individuals can arrive at a similar solution, or total achievement score, by employing different processes which could reflect different functions of the central nervous system (Kaplan, 1990; Werner, 1937). It has been suggested that patients with AN compensate for their cognitive deficits by employing different, potentially more demanding, strategies to achieve the same total score as healthy controls (Stedal, 2012). These process-related challenges go undetected by standard total score analyses. The process approach is a specific methodology which was first described in the late 1980s (Kaplan, 1988). It is based on analyzing the process a participant undertakes to reach a solution, instead of solely focusing on total achievement scores. Analyses of a participant's error scores are often included in the process approach. By investigating incorrect answers on a test, it is possible to learn more about how the participant arrived at the derived answer (Milberg, Hebben, & Kaplan, 2009) and error analyses have been described as "*the best behavioral windows into brain function and dysfunction"* (Delis, Kramer, Kaplan & Ober, 2000, p. 41). This approach may prove beneficial by increasing our understanding of brain-behavior relationships, and scores obtained from process analyses can be used for making diagnoses, recommending therapeutic interventions, monitoring recovery and investigating the effect of a given intervention (Kaplan, 1990). For this reason, it has been proposed that process scores, which are generated by monitoring the behaviors used to solve the task, provide more useful information than total achievement scores (Kaplan, 1990).

In studies of AN, the process approach has predominantly been used in studies of visual memory (Lang et al., 2016). The findings from this research have revealed an association between strategy use for copying a complex figure, and the total achievement score on a measure of visual memory (Sherman et al., 2006). In comparison to healthy controls, patients with AN seem to apply an inefficient strategy when copying a complex figure, which is associated with impaired visual memory (Sherman et al., 2006). It has been suggested that this impairment may result from a specific processing style or a perceptual bias for details, or that it could be due to inefficient higher level cognitive abilities – collectively referred to as *executive function* (Miyake, Friedman, Rettinger, Shah, & Hegarty, 2001; Oltra-Cucarella et al., 2015). Thus, if the visual memory impairment seen in patients with AN is due to a more generalized difficulty with higher level cognitive abilities, we would expect to see difficulties on other tasks which benefit from the organization of complex materials. Verbal learning and memory is one such area which can be influenced by higher level cognitive abilities (Tremont, Halpert, Javorsky, & Stern, 2000). Previous studies have shown impaired verbal memory functioning in patients with AN (Bayless et al., 2002; Chui et al., 2008; Kingston, Szmukler, Andrewes, Tress, & Desmond, 1996; Weider, Indredavik, Lydersen, & Hestad, 2014) for both immediate (Bayless et al., 2002; Hamsher, Halmi, & Benton, 1981; Jones, Duncan, Brouwers, & Mirsky, 1991; Kingston et al., 1996; Mathias & Kent, 1998; Moser et al., 2003; Oltra-Cucarella et al., 2015) and delayed (Bayless et al., 2002; Jones et al., 1991; Mathias & Kent, 1998; Oltra-Cucarella et al., 2014) verbal recall. Oltra-Cucarella and colleagues (2015) suggested that verbal recall scores could be associated with basic cognitive abilities, such as speed of information processing and cognitive inhibition. In addition, executive dysfunction specifically related to perseverative behavior can be detected by performing error analyses of serial list learning tasks, such as the California Verbal Learning Test (Davis, Price, Kaplan, & Libon, 2002).

Difficulties with cognitive flexibility and elevated preservative errors have been shown in patients both recovered and currently suffering from AN when employing a commonly used measure of cognitive flexibility, the Wisconsin Card Sorting Test (Abbate-Daga et al., 2011; Tchanturia et al., 2012; Westwood, Stahl, Mandy, & Tchanturia, 2016). In addition, Abbate-Daga and colleagues (2011) revealed that patients with AN also display cognitive rigidity in verbal domains. However, to our knowledge, no previous studies have employed a process approach to explore the relationship between cognitive flexibility, verbal learning and memory in patients remitted from AN. The application of error analyses to the performance of recovered patients is advantageous because this approach controls for the immediate effects of malnutrition that can confound neuropsychological studies of patients currently suffering from AN. Assessments of remitted patients also provide an alternative method for exploring potential trait alterations and is proposed as a suitable alternative to prospective studies (Nikendei et al., 2010).

The aim of the current study was to apply a process-focused neuropsychological approach to explore the relationship between cognitive flexibility and verbal memory in women remitted from AN. We expected that participants with remittent AN would show impaired verbal memory performance and display more errors and perseverations on a verbal learning task compared to healthy controls. We also expected verbal learning and memory performance to be significantly associated with cognitive flexibility in both groups.

Method

Participants

Women with a history of AN (RAN; N = 26) and healthy control women (CW; N = 25) were included as a part of a larger study. All participants were aged 19–45 years old, and right-handed. RAN participants had a history of DSM-IV diagnosis for AN with an onset of illness greater than 4 years prior to participation. Remittance was defined as having maintained a stable weight of 90% - 120% ideal body weight (IBW), regular menstrual cycles, and having no clinically significant symptoms for the 12 months prior to study. Most participants were Caucasian (84.3%), and 7.8% identified as Hispanic. Participants were recruited through flyer and online advertisements through the University of California, San Diego.

Exclusion criteria for the RAN group included: (a) restrictive eating or disorder-related behaviors within 12 months of study participation, (b) alcohol or substance abuse/dependence within the previous 3 months, (c) current severe psychopathology that might require inpatient hospitalization, (d) use of psychoactive medication or antidepressants within three months of the time of testing, and (e) presence of major neurological or medical disorders. The CW group had no stigmata suggestive of an eating disorder or any psychiatric, medical, or neurological illness. They had maintained an IBW between 90% and 120% since menarche.

Participants were screened for initial inclusion/exclusion criteria and then invited to complete self-report questionnaires online. Upon passing this stage of screening, participants were evaluated for inclusion/exclusion criteria using structured interviews conducted by doctoral-level psychologists. Participants were assessed using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) (First, Gibbon, Spitzer, & Williams, 1996) for the first half of the study and the MINI-International Neuropsychiatric Interview Plus (MINI) (Sheehan et al., 1998) in combination with Module H of the SCID for the second half of the study. The MINI has been validated against the much longer SCID and is a more time-efficient alternative to the SCID (Sheehan et al., 1998), which prompted the change in assessment. There were no differences on clinical self-report measures between participants assessed with the full SCID and those who completed the MINI.

The study was conducted according to the Institutional Review Board regulations of the University of California, San Diego. Written informed consent was obtained from all participants.

Procedure

Measures—Demographic variables included age, body mass index (BMI; kg/m^2), education, and lowest ever BMI (nadir BMI). Participants also completed the following measures:

Eating Disorder Inventory - Second Version (EDI-2) (Garner, 1991).: The EDI-2 is a self-report questionnaire that evaluates behaviors and cognitions common to anorexia and bulimia nervosa, with strong reliability, while subscales have shown fair-to-good internal consistency (Cronbach's α ranging from 0.73 (asceticism) to 0.93 (bulimia)(Thiel & Paul, 2006) and good construct validity (van Strien & Ouwens, 2003). The EDI-2 comprises eight subscales measuring (1) drive for thinness, (2) bulimia, (3) body dissatisfaction, (4) ineffectiveness, (5) perfectionism, (6) interpersonal distrust, (7) interoceptive awareness, (8) maturity fears, (9) asceticism, (10) impulse regulation, and (11) social insecurity.

Beck Depression Inventory II (BDI-II) (Beck, Steer, & Brown, 1996).: The BDI-II is a widely used measure of depression, with high reliability, adequate convergent validity, and strong internal consistency (Cronbach's alpha = 0.86 among psychiatric outpatients, 0.81 among a non-psychiatric sample, 0.86 in a sample of participants at risk for or with current eating disorders (Byrne, Eichen, Fitzsimmons-Craft, Taylor, & Wilfley, 2016). Twenty-one items are scored 0–3; higher scores indicate more severe depression.

State-Trait Anxiety Inventory (STAI) (Spielberg, Gorsuch, & Lushene, 1983).: This self-report questionnaire is a reliable, valid, and internally consistent measure (Cronbach's alpha = 0.86–0.95) of anxiety severity (Spielberg et al., 1983). Each of the two subscales (State Anxiety and Trait Anxiety) contains 20 items on a 4-point rating scale, with higher scores indicating greater anxiety.

California Verbal Learning Test – Second Edition (CVLT-II) (Delis, Kramer, Kaplan, & Ober, 2000).: The CVLT-II is a test of verbal learning and memory, in which participants are required to learn a 16-item word list over five trials and to recall it after short and long delays, with and without semantic cues. Performance on the CVLT-II was assessed using Total Recall from Trials 1–5 (learning performance), Short Delay and Long Delay Free and Cued Recall (memory performance), Semantic and Serial Clustering scores (learning strategy), Repetition Errors and Intrusion Errors. In addition, Trans- and Within-trial errors were calculated to further refine examination of perseverative errors as recommended in the study by Davis et al., (Davis et al., 2002). Clustering strategy refers to one's learning strategy and indicates whether the performance is based on regrouping the target words based on categories (semantic clustering) or by recalling the target words in the order in which they were presented (serial clustering). Trans-trial Perseverations (TTP) are scored when initial Intrusion Errors are repeated on subsequent learning trials, and are thought to reflect difficulties with semantic processing of the items. Within-trial Perseverations (WTP) are scored when a response, correct or incorrect, is repeated within each individual learning trial. Thus, WTP include perseverations on both non-target and correct target words on each free recall learning trial (Davis et al., 2002) and are thought to be strongly associated with executive function.

Wisconsin Card Sorting Test (WCST, Computer version 4) (Heaton, 1993).: The WCST is a traditional measure of visuospatial cognitive flexibility and was chosen as it has been used in a number of studies of AN (e.g. (Harper, Brodrick, Van Enkevort, & McAdams, 2017; Lang, Stahl, Espie, Treasure, & Tchanturia, 2014; Roberts, Tchanturia, & Treasure, 2016)). It is a standardized test of set-shifting, sustained attention, rule maintenance, and response to feedback. Participants completed a computerized version of the task, which requires participants to match a stimulus card to one of four comparison cards. Matching rules can be based on color, number, or shape, and the rule changes unpredictably over the course of the task. Participants are given feedback after each trial on whether they correctly matched the card. Performance on the WCST was assessed using response and error analysis (total errors, perseverative responses, perseverative errors, non-perseverative errors).

Wechsler Abbreviated Scale of Intelligence (WASI-II) (Wechsler, 1999).: The WASI is a brief measure of intelligence based on four subscales designed to measure verbal knowledge, visual information processing, spatial and nonverbal reasoning. This test assesses a variety of cognitive functions and has been shown to be a valid measure of general intelligence in a psychiatric population (Hays, Reas, & Shaw, 2002).

Analyses—All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0. Groups were compared on demographic variables using one-way ANOVAs, and neuropsychological variables of interest using four multivariate analyses of variance. These analyses controlled for age and education, as well as BDI-II and STAI Trait scores, as depression and anxiety differed between groups (described below) and have both been shown to impact executive function in eating disorders (Abbate-Daga et al., 2015; Ely, Wierenga, & Kaye, 2016). These MANCOVAs compared groups on 1) learning and memory performance as measured by the CVLT-II, 2) errors on the CVLT-II, 3) errors on the WCST, and 4) clustering strategies. Partial eta squared was also calculated as a measure of effect size. Pairwise comparisons were based on estimated marginal means and a Bonferroni adjustment for multiple comparisons was employed during the analyses, within SPSS. Relationships between CVLT-II and WCST performance were explored using Pearson's partial correlations, controlling for age and education. The distributions of Trans-trial perseverations on the CVLT-II and Non-perseverative errors on the WCST were not normally distributed, however log-transformation did not change the results of correlation analyses and as such non-transformed data is reported here. Distributions for all other variables were normal (George & Mallery, 2010). Given correlational analyses were exploratory, no adjustment was made for multiple comparisons. Scores for a given measure were considered outliers and removed from analysis if they were greater than 3 standard deviations from the mean. Only one outlier was omitted from comparisons involving CVLT-II WTP, Repetition and Intrusion errors, WCST Perseverative Responses and Perseverative Errors. In comparisons involving CVLT-II TTP, 2 CW outliers and 1 RAN outlier was removed. The respective Ns are noted in Table 2.

Results

Descriptive variables

Groups did not differ significantly on age, BMI, education, or WASI IQ (Table 1). There was a significant expected difference between groups in lowest-ever BMI ($F(1,51) = 217.3$, $p < 0.001$), with RAN reporting a significantly lower nadir BMI than CW. RAN participants had been remitted for an average of 6.66 years, with an average duration of illness of 5.84 years. Additional information regarding the RAN group is included in Table 1. The RAN group also scored significantly higher on the BDI ($F(1, 52) = 7.98$, $p = 0.007$), the STAI State ($F(1, 52) = 5.74$, $p = 0.02$) and the STAI Trait ($F(1, 52) = 7.13$, $p = 0.01$), and EDI-2 Drive for Thinness subscale ($F(1, 52) = 9.41$, $p = 0.004$), but there were no significant differences between the groups on any of the other EDI-2 subscales. Nadir BMI was correlated with Short Delay Free Recall performance on the CVLT-II among CW ($r = 0.427$, $p = 0.037$) but no other performance or error variables, and not with any performance or error variables among RAN. Race and ethnicity of participants did not differ between groups.

Neuropsychological Assessments

Group differences—Group comparison analyses (Table 2) revealed that groups did not differ in their learning and memory performance on the CVLT-II (Pillai's Trace = 0.009, $p = 0.996$), as measured by Trials 1–5 Total Recall, Short Delay Free and Cued Recall performance, or Long Delay Free and Cued Recall performance. MANCOVA revealed a significant difference between groups on CVLT-II errors (Pillai's Trace = 0.202, $p = 0.046$) with RAN demonstrating significantly more Repetition Errors ($F(1,50) = 7.27$, $p = 0.01$) and WTP errors ($F(1, 50) = 4.28$, $p = 0.044$) than CW. Differences between groups on Intrusion Errors and TTP were non-significant. Clustering strategy scores did not differ between groups (Pillai's Trace = 0.118, $p = 0.248$). Comparison of groups on the WCST revealed no significant differences (Pillai's Trace = 0.111, $p = 0.283$) though pairwise comparisons reached trend-level, with RAN showing greater error rates than CW.

Exploratory correlational analyses—Association between verbal learning and cognitive flexibility: Both groups demonstrated negative associations between CVLT-II learning and memory performance variables and errors on the WCST. Among CW, WCST errors were negatively related to Trials 1–5 Total Recall, Short and Long Delay Free Recall, and Short and Long Delay Cued Recall (Table 3a). In other words, greater WCST errors were associated with fewer words recalled across all learning and memory trials. Among

RAN, greater WCST errors were associated with Trials 1–5 Total Recall, Long Delay Free Recall, and Short and Long Delay Cued Recall (Table 3b).

Association between error performance on the CVLT-II and WCST: A comparison of error performance between tests revealed no associations between error types in the CW group (Table 3a). Among the RAN group, Perseverative Responses on the WCST were significantly correlated with CVLT-II Repetition Errors ($r = 0.460$, $p = 0.024$) and WTP ($r = 0.439$, $p = 0.032$) (Table 3b). According to Evans' (Evans, 1996) guide for strength of correlations, these associations can be considered moderate. In addition, WCST Perseverative Errors showed a weak relationship with CVLT-II Repetition Errors ($r = 0.375$, $p = 0.071$), and with WTP ($r = 0.360$, $p = 0.084$) for RAN participants, suggesting convergence between perseverative responses across tests.

Examination of learning strategy revealed that learning and memory performance on the CVLT-II was related to clustering strategies in both groups. As expected, among CW, greater use of a semantic clustering strategy was associated with greater free and cued recall at short and long delays (Table 4a). Among RAN, semantic clustering was positively correlated with Short Delay Free and Cued recall, as well as Trials 1–5 Total Recall, and a moderate and weak correlation with Long Delay Free and Cued recall, respectively (Table 4b). In the RAN group, greater semantic clustering was associated with fewer CVLT-II Repetition Errors ($r = -0.490$, $p = 0.015$) and WTP errors ($r = -0.468$, $p = 0.021$), indicating less perseveration, while bidirectional serial clustering scores were not related to any type of CVLT-II error. Use of a serial clustering strategy revealed a weak association, with fewer Repetition Errors ($r = -0.393$, $p = 0.064$) and WTP errors in CW ($r = -0.394$, $p = 0.063$), whereas a semantic clustering strategy was not linked with CVLT-II errors.

Discussion

The aim of the current study was to employ a process-oriented neuropsychological approach to investigate verbal learning and memory in women with a history of AN. The investigation of remitted patients avoids confounding effects from malnutrition and could also provide information regarding potential cognitive endophenotypes of AN. Overall, the results indicate that participants remitted from AN do not show impaired verbal memory when comparing CVLT-II total recall scores to healthy controls. However, the remitted patient group displays significantly more errors when performing the learning and memory task and in contrast to our hypothesis, only some aspects of verbal memory were associated with cognitive flexibility in the RAN group.

When comparing total output scores on the CVLT-II, the RAN group performed equivalently to CW subjects. However, by investigating the process scores of the CVLT-II, we found that the RAN group made significantly more repetitions of the source words (Total repetition errors) and perseverative responses within trials (WTP), but not of confabulated words (intrusion errors) or perseverations across trials (TTP). The total output memory scores on the CVLT-II are not negatively impacted by repeating a previously said word, nor is it specified in the instructions that the participants should avoid saying a word previously named. The finding that the RAN group made significantly more repetition errors and WTP errors can be interpreted as either an inability to inhibit a previous response, i.e. an indication of perseverative tendencies, or as a difficulty with remembering whether the examiner or the examinee was the last person to say the word (Delis et al., 2000). The RAN group's repetition errors and WTPs are both correlated with perseverative responses on the WCST. These findings could indicate that the CVLT-II errors are due to a tendency for a type of double-checking strategy, rather than difficulties with remembering whether the word has previously been said or not. Patients with AN are often described as having personality traits related to perfectionism, obsessions and anxiety (Kaye, Wierenga, Bailer, Simmons, & Bischoff-Grethe, 2013). The repetition of words on the CVLT-II could reflect these traits. It is possible that the elevated error scores on the CVLT-II reflect a form of perseverative checking behavior, where the RAN participants repeat words they have already said to ensure that they have not missed any words and as a form of self-reassurance. This finding is in line with previous studies demonstrating difficulties with cognitive flexibility in patients both currently suffering and recovered from AN (Tchanturia et al., 2004).

Previous studies have shown a strong relationship between executive functioning and memory capacities, and there seems to be a high degree of overlap between verbal memory and executive functioning, i.e. individuals who perform well on tasks of executive functioning also do better on memory measures (Bryson, Whelahan, & Bell, 2001; Duff, Schoenberg, Scott, & Adams, 2005; Tremont et al., 2000). For verbal memory, it has been suggested that impaired delayed recall scores in AN are a reflection of executive functioning rather than memory deficits (Oltra-Cucarella et al., 2015). Comparable with the findings by Duff and colleagues (2005), we found both short term and long term verbal memory were strongly related to cognitive flexibility in the CW group. Thus, the results from the CW group showing that better cognitive flexibility skills are associated with better learning and memory recall on the CVLT-II confirm previous studies demonstrating a shared variance of up to 55% for cognitive flexibility and verbal memory (Duff et al., 2005). It also supports findings from research comparing participants with different levels of executive dysfunction (Brooks, Weaver, & Scialfa, 2006; Tremont et al., 2000). The results from these experiments show that cognitive flexibility has an impact on both the acquisition and short-delay retrieval of verbal information. Conversely, although the findings from the CW group in the current study are in line with these previous studies, the results from the RAN group are not. Instead, overall CVLT-II learning and short-term memory performance appears somewhat independent of cognitive flexibility in women remitted from AN, although perseverative responses on each task are associated. This discovery is noteworthy as it is in contrast to the CW group, as well as outcomes from previous studies on the relationship between executive function and verbal memory. Interestingly, a similar pattern has been demonstrated in patients currently suffering from AN. Oltra-Cocarella and colleagues (2015) explored the influence of speed of information processing (SIP) and inhibition on delayed verbal recall. The authors found that 91% of the variance in delayed recall could be accounted for by speed of information processing, inhibition, and immediate recall (Oltra-Cucarella et al., 2015). The authors propose that delayed recall in AN could be influenced by basic cognitive abilities, and in line with the current study, cognitive flexibility was related to delayed memory, independent of immediate recall.

This finding could indicate some differences in the way verbal material is encoded in women remitted from AN compared to healthy controls. To allow for optimal learning and recall, list learning tasks like the CVLT-II require participants to rely on their ability to organize and structure the material. Consequently, it has been suggested that the CVLT-II is more closely tied to executive abilities than other verbal memory tasks, as the performance can be improved by semantically organizing the words (Tremont et al., 2000; Vanderploeg, Schinka, & Retzlaff, 1994). This organization of words belonging to the same category is usually referred to as semantic clustering (Bousfield, 1953; Bousfield & Sedgewick, 1944) and is considered a reflection of whether the participant has actively organized the list of words in terms of their mutual semantic features. This strategy is thought to aid in the encoding into, and retrieval from, long-term memory (Delis, 1989). Conversely, when participants recall words in the same order in which they are presented, it is referred to as serial-clustering. For most people, this is a more ineffective learning strategy, and it is often reflective of a “stimulus-bound” form of recall, where the participant adheres to the order in which the list was presented in a rigid manner and thereby fails to reorganize the words semantically (Delis et al., 2000). The current study confirms previous findings that organizing words in terms of semantic features is associated with a beneficial outcome in memory performance in both the RAN and CW group (Tremont et al., 2000; Vanderploeg et al., 1994). However, only for the RAN group is semantic clustering also associated with learning performance, fewer repetition errors and WTPs. Thus, the remitted patients who apply a more advantageous strategy by clustering the words into semantic categories, also learn better, make fewer repetition errors and exhibit less within trial perseverations, all indicative of better cognitive flexibility.

Strengths and limitations

Studies like the current are important as they greatly enhance our ability to understand the process behind a patient’s poor, or superior, neurocognitive test performance. By including error scores in the analyses of verbal memory performance, we were able to demonstrate that RAN participants more often repeat a previously stated word, possibly due to a perseverative response style, as revealed by the association with WCST. The findings should, however, be interpreted in light of their limitations. First, the correlation analyses were not corrected for multiple comparisons, which could lead to reporting significant findings that have occurred by chance, i.e. a Type I error. However, the literature on performing multiple-testing correction presents conflicting viewpoints and it has been advised that data from exploratory studies should be analyzed without adjusting for multiplicity (Bender & Lange, 2001). Second, the two groups differed on two measures of psychopathology whereby the RAN group scored statistically significantly higher on measures of depression and anxiety. Nevertheless, this difference was less than two points on the BDI and approximately four points for the STAI scales, a difference which is usually not considered clinically significant. In addition, the groups were comparable in terms of their other psychometric measures, including their EDI scores which is a good indication of full recovery in the RAN group. Differences between groups may be less evident because we used a remitted sample rather than testing ill subjects. However, the finding that cognitive flexibility and the encoding of verbal material may be disturbed even after weight restoration and symptom remittance is clinically important. Future research would benefit from examining these phenomena in patients currently ill with AN, and might also wish to include measures of other executive components, such as planning. Some caution should also be taken when debating whether or not the current findings are reflective of an endophenotype. The evidence is limited as to whether or not cognitive difficulties are present in children and adolescents with AN, indicating that cognitive inflexibility might not be a vulnerability factor, but rather a central part of the illness at a later stage (Lang, Stahl, et al., 2014; Shott et al., 2012). Lastly, participants were predominantly Caucasian, and as a result these findings may not be applicable to a more diverse sample.

Conclusion

The findings from the present study add to the scarce literature employing a process approach to investigate cognitive functioning in women remitted from AN. Participants with remitted AN had a tendency for increased perseverative responses. In contrast to the control group, their verbal learning strategy seemed less dependent on cognitive flexibility. Future studies of patients with AN, both currently ill and remitted, should put emphasis on the documentation of strategy use in neuropsychological assessments. This will allow for analysis of factors involved in test performance and would considerably increase our understanding of cognitive functioning in patients with AN.

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Table 1.

Group comparison, descriptive variables

	CW		RAN			
	N	**Mean (*SD*)/ N (*%*)**	**N**	**Mean (*SD*)/ N (*%*)**	***F*/χ^2**	***p***
Age (years)	25	25.02 *(6.2)*	26	27.07 *(7.04)*	1.02	0.32
Education	25	15.64 *(1.25)*	25	16.32 *(1.97)*	2.12	0.15
WASI Full Scale IQ	18	111.94 *(10.42)*	21	112.43 *(11.63)*	0.02	0.89
BMI	25	22.12 *(1.86)*	26	21.91 *(1.69)*	0.18	0.67
Nadir BMI[1]	25	20.42 *(1.24)*	26	14.76 *(1.46)*	217.3	<**.001**
Age of onset of AN			26	14.81 (2.94)		
Age of remission			25	20.79 (5.11)		
Duration of illness (years)			25	5.84 (5.22)		
Time since remission (years)			25	6.66 (5.44)		
BDI-II	24	0.29 (*0.46*)	25	1.44 (*1.94*)	7.98	**0.007**
STAI State	25	24.40 (*3.51*)	26	28.31 (*7.39*)	5.74	**0.02**
STAI Trait	25	24.56 (*4.41*)	26	28.27 (*5.44*)	7.13	**0.01**
EDI-2 Drive for thinness	23	0.044 (0.21)	25	0.97 (*1.43*)	9.41	**0.004**
EDI-2 Bulimia	25	0.12 (*.60*)	25	0.00 (*.00*)	1.00	0.32
EDI-2 Body Dissatisfaction	24	0.92 (*2.19*)	25	2.12 (*2.76*)	2.85	0.098
Race					2.56	0.11
Caucasian	19	76%	24	92.30%		
Asian	6	24%	2	7.70%		
African American	0	-	0	-		
Native American/Alaskan Native	0	-	0	-		
Other	0	-	0	-		
Ethnicity					1.17	0.28
Hispanic	3	12%	1	3.85%		
Non-Hispanic	22	88%	25	96.15%		

Note. CW, control women; RAN, remitted anorexia nervosa; SD, Standard Deviation; BMI, Body mass index; WASI, Wechsler abbreviated scale of intelligence; BDI, Beck depression inventory; STAI, State trait anxiety inventory; EDI-2, Eating disorders inventory – second version; 1self-reported, P < 0.05 in bold.

Table 2.

Group comparison, California verbal learning test-II (CVLT-II) and Wisconsin card sorting test (WCST), controlling for age, education, BDI-II score and STAI score

	Pillai's Trace (p)		CW		RAN				
			N	Mean (*SD*)	N	Mean (*SD*)	*F*	*PES*	*P*[a]
CVLT-II									
		Trials 1–5 Total recall	25	59.12 (9)	26	58.69 (8.97)	0.05	0.00	0.819
		Short delay free recall	25	12.36 (3.05)	26	12.38 (2.84)	0.02	0.00	0.902
	0.009 (.996)	Short delay cued recall	25	13.44 (2.22)	26	13.23 (1.77)	0.03	0.00	0.861
		Long delay free recall	25	12.72 (2.78)	26	12.85 (2.13)	0.01	0.00	0.924
		Long delay cued recall	25	13.28 (2.34)	26	13.31 (2.19)	0.00	0.00	0.991
		Total repetition errors	**25**	**5.64 (4.20)**	**25**	**8.92 (5.96)**	**7.27**	**0.14**	**0.010**
		Total intrusion errors	25	3.16 (2.58)	25	2.60 (3.25)	0.84	0.02	0.365
	0.202 (0.046)	**Within trial preservations**	**25**	**4.72 (3.45)**	**25**	**6.48 (4.42)**	**4.28**	**0.09**	**0.044**
		Trans trial perseverations	23	0.39 (0.72)	25	0.24 (0.60)	0.01	0.00	0.940
WCST									
		Total errors	25	16.96 (13.65)	26	27.12 (22.97)	3.24	0.07	0.079
	0.111 (0.283)	Perseverative responses	25	9.44 (8.13)	25	12.84 (9.18)	3.63	0.08	0.063
		Perseverative errors	25	8.72 (7.04)	25	11.60 (7.59)	3.30	0.07	0.076
		Non-perseverative errors	25	8.24 (7.08)	26	14.54 (14.76)	2.87	0.06	0.097
CVLT-II Clustering									
		Raw Semantic Clustering	25	2.06 (1.84)	26	1.24 (2.73)	1.124	0.024	0.295
		Standard Semantic Clustering	25	0.57 (1.05)	26	0.06 (1.64)	0.829	0.018	0.367
	0.118 (0.248)	Raw Serial Clustering Bidirectional	25	0.58 (1.01)	26	0.86 (1.18)	0.001	0.00	0.977
		Standard Serial Clustering Bidirectional	25	−0.29 (0.93)	26	0.03 (1.02)	0.128	0.003	0.722

Note. CW, control women; RAN, remitted anorexia nervosa; PES, Partial Eta Squared; SD, Standard deviation; p < 0.05 in bold.

[a]Based on estimated marginal means; Bonferroni adjustment for multiple comparisons

Table 3a.

Partial correlations between California verbal learning test-II (CVLT-II) and Wisconsin card sorting test (WCST), healthy control women.

		CVLT-II								
		Learning and Memory Performance					Errors			
		Trials 1–5 total recall	Short delay free recall	Short delay cued recall	Long delay free recall	Long delay cued recall	Total repetition errors	Total intrusion errors	WTP	TTP
WCST Errors	Total errors	**−0.477***	**−0.717*****	**−0.541****	**−0.518***	**−0.667****	−0.095	0.154	0.019	0.227
	Perseverative responses	**−0.557****	**−0.726*****	**−0.614****	**−0.558****	**−0.683*****	−0.050	0.127	0.054	0.134
	Perseverative errors	**−0.539****	**−0.723*****	**−0.582****	**−0.548****	**−0.661****	−0.093	0.105	0.011	0.155
	Non-perseverative errors	−0.389	**−0.674*****	**−0.471***	**−0.462***	**−0.639****	−0.092	0.196	0.026	0.288

Note: Age and education included as covariates. TTP, Trans trial perseverative errors; WTP, Within-trial perseverative errors,

* p<.05;

** p<.01;

*** p<.001

Table 3b.

Partial correlations between California verbal learning test-II (CVLT-II) and Wisconsin card sorting test (WCST), women remitted from Anorexia Nervosa.

		CVLT-II								
		Learning and Memory Performance					Errors			
		Trials 1–5 total recall	Short delay free recall	Short delay cued recall	Long delay free recall	Long delay cued recall	Total repetition errors	Total intrusion errors	WTP	TTP
WCST Errors	Total errors	**−0.415***	−0.339	**−0.404***	**−0.603****	**−0.5***	0.253	−0.033	0.201	0.001
	Perseverative responses	−0.25	−0.2	−0.381	**−0.583****	**−0.543****	**0.46***	0.136	**0.439***	0.055
	Perseverative errors	−0.271	−0.23	−0.397	**−0.581****	**−0.539****	0.375	0.132	0.36	0.045
	Non-perseverative errors	**−0.414***	−0.342	−0.327	**−0.518***	−0.385	0.116	−0.161	0.045	−0.042

Note: Age and education included as covariates. TTP, Trans trial perseverative errors; WTP, Within-trial perseverative errors,

* p<.05;

** p<.01;

*** p<.001

Table 4a.

Partial correlations between California verbal learning test-II (CVLT-II) performance and clustering strategies, healthy control women.

		CVLT-II								
		Learning and Memory Performance					Errors			
		Trials 1–5 total recall	Short delay free recall	Short delay cued recall	Long delay free recall	Long delay cued recall	Total repetition errors	Total intrusion errors	WTP	TTP
CVLT-II Clustering Strategies	Raw Semantic Clustering	.409	**0.469***[*]	**0.55**[**]	**0.514**[*]	**0.464**[*]	0.115	0.003	0.048	0.007
	Raw Serial Clust. Bidirectional	0.052	−0.037	−0.049	−0.047	0.037	−0.393	−0.011	−0.394	0.04

Note: Age and education included as covariates. TTP, Trans trial perseverative errors; WTP, Within-trial perseverative errors,

[*] p<.05;

[**] p<.01;

[***] p<.001

Table 4b.

Partial correlations between California verbal learning test-II (CVLT-II) performance and clustering strategies, women remitted from Anorexia Nervosa.

		CVLT-II								
		Learning and Memory Performance					Errors			
		Trials 1–5 total recall	Short delay free recall	Short delay cued recall	Long delay free recall	Long delay cued recall	Total repetition errors	Total intrusion errors	WTP	TTP
CVLT-II Clustering Strategies	Raw Semantic Clustering	**0.635****	**0.417***	**0.42***	0.402	0.378	**−0.49***	−0.159	**−0.468***	−0.211
	Raw Serial Clust. Bidirectional	−0.125	−0.001	−0.03	0.06	−0.002	0.29	−0.007	0.196	0.026

Note: Age and education included as covariates. TTP, Trans trial perseverative errors; WTP, Within-trial perseverative errors,

* p<.05;

** p<.01;

*** p<.001