



Adolescent Anorexia Nervosa: Cognitive performance after weight recovery

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ABSTRACT

Objective: Although there is no definitive consensus on the impairment of neuropsychological functions, most studies of adults with Anorexia Nervosa (AN) find impaired functioning in cognitive domains such as visual-spatial abilities. The objective of this study is to assess the cognitive functions in adolescents with AN before and after weight recovery and to explore the relationship between cognitive performance and menstruation.

Methods: Twenty-five female adolescents with AN were assessed by a neuropsychological battery while underweight and then following six months of treatment and weight recovery. Twenty-six healthy female subjects of a similar age were also evaluated at both time points.

Results: Underweight patients with AN showed worse cognitive performance than control subjects in immediate recall, organization and time taken to copy the Rey's Complex Figure Test (RCFT). After weight recovery, AN patients presented significant improvements in all tests, and differences between patients and controls disappeared. Patients with AN and persistence of amenorrhea at follow-up ($n = 8$) performed worse on Block Design, delayed recall of Visual Reproduction and Stroop Test than patients with resumed menstruation ($n = 14$) and the control group, though the two AN groups were similar in body mass index, age and psychopathological scale scores.

Conclusion: Weight recovery improves cognitive functioning in adolescents with AN. The normalization of neuropsychological performance is better in patients who have recovered at least one menstrual cycle. The normalization of hormonal function seems to be essential for the normalization of cognitive performance, even in adolescents with a very short recovery time.

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Introduction

Many studies have found cognitive inefficiencies in patients with Anorexia Nervosa (AN) [1,2]. Although there is no definitive consensus on the impairment of neuropsychological functions, general studies suggest that patients with AN present alterations in cognitive domains such as visual-spatial abilities [2,5] and executive functions [6]. Patients with AN show weakness in central coherence, resulting in superior detail processing and a weakness in global integration [7]. Several authors have found difficulties in cognitive flexibility [8–10] and set-shifting abilities that lead to rigidity [7]. Some studies have compared cognitive performance before and after weight recovery in AN patients. When AN patients achieve weight restoration, improvements in tasks of attention

[2,3] and psychomotor speed [4,6] tasks have been observed. Nevertheless, almost all follow-up studies have found that alterations persist after refeeding, especially in immediate memory [3,4], delayed memory [11], motor tasks [3], visual-spatial abilities [2] and executive functions such as cognitive flexibility [12,13] and problem-solving abilities [6]. These characteristics are also found in some relatives of patients with AN [14,15]. In the light of these findings, some authors have proposed that impairment in functions such as set-shifting or central coherence may be a stable trait of the illness rather than a state, conforming an endophenotype of the disorder [7–10,16].

The majority of these studies have been conducted in adult patients with a long duration of the disorder. Little is known about cognition in adolescent patients, in whom time of evolution of AN and time of starvation are shorter, although some studies in this population have also recorded difficulties in visual-spatial abilities [17–19]. To our knowledge, few follow-up studies have assessed cognitive performance exclusively in adolescent patients with AN before and after weight

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restoration. Schmidt et al. [20] evaluated reaction time and concentration in 52 adolescent inpatients with AN, finding improvement in all cognitive measures over the course of inpatient treatment. Grunwald et al. [21] found that the haptic abilities of 10 adolescents with AN improved with refeeding. Pieters et al. [22] compared drawing and copying tasks in 17 patients versus 17 healthy controls, and reported that the AN group had shorter reaction times on tasks after weight restoration. Hatch et al. [23] found that the AN group ($n = 37$) was significantly faster on attention and executive function tasks, exhibited superior verbal fluency and working memory and a superior ability to inhibit well-learned responses than controls ($n = 45$). However, Sarrar et al. [24] found subtle deficits in cognitive flexibility in 30 AN patients compared with 28 control subjects. After weight gain, adolescents with AN improved relative to their baseline values but did not reach control values. Finally, Bühren et al. [25] compared set-shifting abilities in 28 female adolescents with AN before and after weight rehabilitation and 27 healthy controls. They found no set-shifting inefficiencies in adolescent patients with AN and proposed that the shorter duration of illness and the incomplete maturation of the prefrontal cortices compared to adult patients with AN contributed to the explanation of these findings.

Neuropsychological follow-up studies with AN patients have been carried out after weight restoration. Although weight is one indicator of biological recovery from the condition [26], menstrual function may remain abnormal in some weight-recovered patients [27,28]. Some authors have studied the relation between hormones and cognitive functioning across the female life span, in moments such as pregnancy, post-partum or menopause, and report relationships between estrogens and impairment in some cognitive functions such as verbal memory [29]. To our knowledge, only two studies have studied the relationship between menstrual function and cognitive performance in AN, and their results are conflicting. Chui et al. [30] found that adult subjects with a history of adolescent-onset AN and persistent amenorrhea or irregular menses had lower scores on a variety of domains: verbal ability, thinking ability, cognitive efficiency, working memory, oral language, broad reading, written language and math than participants with regular menses or using oral contraceptives. Also, Bühren et al. [31] found subtle memory impairments in AN adolescents before and after weight recovery and a positive correlation between verbal learning inefficiency and starvation-induced estrogen deficits after weight recovery.

In summary, in comparison with studies with adult AN patients, not all studies with adolescents with AN show impairment in cognitive performance after refeeding. In fact the results are conflicting: while some studies find persistence of cognitive inefficiencies after refeeding [24], the majority show no differences between patients and controls [22,23,25]. The main aim of this study is to describe the cognitive performance of adolescents with AN at the moment of diagnosis and after six months of treatment and refeeding. Our second objective is to study the influence of menstruation on the neuropsychological functioning in these patients. We hypothesized that adolescents with AN will show more cognitive impairments similar to those reported in adult patients – visual memory, visual-spatial ability and executive function – while they are underweight than healthy controls. We expected that functions such as velocity would improve after refeeding, but that functions related to visual-spatial abilities would remain below control group levels in the second assessment. We also expected to find subtle cognitive inefficiencies in relation to persistent amenorrhea after six months of treatment.

Method

Participants

Twenty-five patients who met the DSM-IV-TR diagnostic criteria for AN were recruited consecutively at the Department of Child and Adolescent Psychiatry and Psychology at the Hospital Clinic in Barcelona.

The patients were adolescents aged between 11 and 18 years. All were in an acute phase of the disorder with a body mass index (BMI) lower than 17.5 kg/m^2 in the first assessment. Length of illness ranged between 4 and 20 months (mean = 12.26, SD = 8.1). Patients and their parents were interviewed with a semi-structured interview following DSM-IV-TR criteria used in clinical practice at our department to investigate current psychopathology and developmental history. The control group comprised 26 female volunteers of similar age recruited from several secondary schools in Barcelona. Control subjects and their parents were interviewed using the Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS-PL) to assess current and past psychopathology [32]. Exclusion criteria in both groups were the presence of psychiatric disorder (other than AN in the patient group), history of neurological impairment or estimated low intellectual level (Standard Score below 5 on the Vocabulary subtest of the WISC-R).

Patients and control subjects were evaluated by two trained psychologists (EL and SA) using a comprehensive neuropsychological battery with pen and paper tests. A second complete evaluation was carried out in both groups after six months. During this time, AN patients followed our department's treatment program. Treatment at our unit is based on a multidisciplinary approach combining biological management, nutritional rehabilitation, a standardized behavioral program which aims to improve eating patterns and weight, individual and group cognitive treatment, and individual and group parent counseling. Only patients who respond well to treatment are seen as outpatients: when physical risk is high, psychopathology intense or cooperation in the outpatient setting very poor, inpatient treatment is indicated. During hospitalization all patients receive a complete diet of about 1250 calories per day during the first days which is increased progressively to 2500 calories per day, but they do not receive vitamin supplements or any hormonal replacement therapy. After discharge, the vast majority of patients follow a Day Hospital program which includes weight and eating control, nutritional counseling, and body image and social skills group therapy for an average of three months. After the Day Hospital program, outpatient follow-up is indicated to control weight maintenance and general outcome. In the first assessment all patients were receiving treatment in hospitalization or Day Hospital because outpatient treatment was not possible due to the severity of disorder. In this program, patients usually regain near normal weight within six months. This is one of the first objectives of the treatment, even if patients are not totally recovered.

All patients, controls and parents gave written informed consent to participate in the study. The procedures were approved by our hospital's Ethical Committee.

Psychopathological assessment

Validated Spanish versions of the following psychopathological scales were administered: the Eating Attitudes Test (EAT-40) [33], a questionnaire for evaluating eating attitudes and symptoms, the Children's Depression Inventory (CDI) [34], used to assess severity of depressive symptoms, and the Leyton Obsessional Inventory–Child Version (LOI-CV) [35] to assess the severity and interference of obsessive–compulsive symptoms.

The State and Trait Anxiety Inventory for Children (STAIC) [36] evaluates the level of anxiety at the moment of evaluation (STAIC State) and anxiety as a general trait (STAIC Trait).

Neuropsychological tests

Neuropsychological assessment in children and adolescents is difficult because these patients present different developmental levels. A battery with internationally validated tests [37] was designed by our team (S.A.) on the basis of the literature available on cognitive performance in AN. The tests with the best psychometric properties for assessing each cognitive function were selected, but some of them

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