Neuropsychology and anorexia nervosa. Cognitive and radiological findings

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Abstract
Introduction: Research into neuropsychological impairments present in the patients suffering from anorexia nervosa (AN) has advanced considerably, in the past decades. It now provides neuropsychologists with a wide field of knowledge of the changes found in the cerebral and cognitive capabilities of these patients, as well as their reversible or static features, thereby yielding a characteristic profile of neuropsychological impairment in AN.
Development: We present a review updated to December 2010 of the results delivered by studies of both morphological and cognitive changes, providing us with an updated theoretical and practical framework for conducting future research.
Conclusions: The studies to date show morphological and functional cerebral changes in the patients diagnosed with AN, but have yet to clarify whether these changes occur after the onset of the disease or if, as more recent research shows, they are one of its causes and could be the basis for a tendency towards developing anorexic symptomatology. Later studies show a neuropsychological network with impairments in the prefrontal and right parietal cortices as a characteristic feature, meaning that those capacities and their related cerebral areas would play major role in the onset and development of the illness. These studies have completely changed classic theories about AN.

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PALABRAS CLAVE
Alteraciones cognitivas; Anorexia nerviosa;
Introduction

Beginning in the early 1980s and throughout more than a decade, multidisciplinary teams studied cognitive impairments in patients diagnosed with eating disorders (EDs) in order to gain a better understanding of the consequences of typical food-related behaviours in patients with either anorexia nervosa (AN) (both the restrictive and purgative forms), or bulimia nervosa (binge-eating disorders).\(^1\)\textsuperscript{–}\textsuperscript{6}\n
In the 1990s and after turn of the 21st century, these studies have advanced considerably and saw the rise of research groups which added to the available body of knowledge, refined research, and created neuropsychological, neurobiological, functional and metabolic models to explain the aetiopathogenesis of EDs. Researchers from the fields of neurology, molecular biology, and radiology\(^7\)\textsuperscript{–}\textsuperscript{27} improved the methodology and incorporated medical technology capable of providing empirical data to the study of the cognitive functions. With the aim of analysing the changes that typify these patients, researchers have performed neuroimaging tests such as a positron emission tomography (PET), single-photon emission computed tomography (SPECT), and even functional magnetic resonance imaging (fMRI). These scans measure cognitive processes and show which cerebral areas have functional impairments in this population.

The objective of this study is to provide an updated review of findings from the study of cognitive impairments in AN as of November 2010, including radiological findings. This article gives an overview of the results from different fields of science responsible for studying brain function without focusing on any single aspect of the manifestations of this disorder.\(^15\) To this end, we performed a literature search using the PubMed, ScienceDirect, MEDLINE and Cochrane Library databases, using terms related to our topic, such as ‘anorexia nervosa’, ‘neuropsychology of eating disorders’, ‘mental flexibility in eating disorders’ or ‘cerebral function and structure in anorexia nervosa’.

Analysis

AN is characterised by relentless insistence on thinness and an excessive refusal to maintain body weight within normal limits, according to the person’s age and body type. It is also accompanied by intense fear of gaining weight or becoming obese.\(^28\) The main numerical criterion for establishing a diagnosis of ED is weight under 85% of that recommended for the subject based on age and height. Patients affected by this disorder have distorted perceptions of their image and body size and also estimate their weight and size erroneously.

Another fundamental criterion for diagnosing ED is the presence of amenorrhea in postmenarcheal females.

The DSM-IV-TR recognises 2 clinical subtypes of anorexia: restrictive and the purgative AN. Patients with the first subtype aim to reach the desired weight by drastically restricting ingested food, strictly controlling the types of food they eat, and limiting caloric intake. They also engage in excessive physical exercise. Patients in the purgative subtype do not restrict food intake as much. They attempt to lose weight by using purgative techniques such as vomiting or laxative abuse. Less than half of all patients recover completely and a third of them only experience partial remission (they continue to suffer with at least 1 of the symptoms of the eating disorder).\(^29\)\textsuperscript{–}\textsuperscript{33} According to a large body of evidence in the literature, the function of the central nervous system (CNS) undergoes changes in patients with AN compared to control subjects.\(^34\)\textsuperscript{,}\textsuperscript{35} For that reason, functional changes in the CNS in these patients have been researched exhaustively and from within different theoretical frameworks in
order to understand the onset and course of the disorder, continuation, and prior dysfunctions that may trigger it. Researchers have found huge variations when measuring patients’ neuropsychological abilities, such as attention (and its different currently accepted subtypes), working memory, long-term learning, autobiographical memory, processing speed, psychomotor speed, behaviour planning, impulsiveness, problem solving, haptic skills, skin conductance, and information processing.

**Neuropsychological findings**

At present, the onset of cognitive impairments in patients with AN is a controversial subject. Some authors state that cognitive deficits occur in specific cerebral regions or result from a decrease in either the total cerebral metabolic rate, in blood perfusion, or in the normal function of certain neurotransmitters. Other studies expanded the debate on the scope of cerebral dysfunction by providing data suggesting that 1 cerebral hemisphere was more affected than the other, and researchers completed in-depth analyses of cognitive capacities that are thought to be specific to concrete areas of each cerebral hemisphere.

**Initial theories**

In 1984, Kinsbourne and Bemporad hypothesised that there was evidence of dysfunction in the right hemispheres of adolescent female AN patients, especially in the parietal cortex. They concluded that this dysfunction might be related to the girls’ erroneous perception of their own bodies (which they called ‘distorted body image’). Based on this premise, researchers began carrying out studies on abilities thought to be localised in the right hemisphere. Pendleton-Jones, Duncan, Bradley and Rovet all researched AN, and their results varied considerably. While there seemed to be differences in evoked potentials related to a specific cognitive-perceptual event, other researchers found no differences between anorexic patients and control subjects on cognitive tasks intended to measure performance by the right hemisphere.

At a later date, Laessle, Pendleton-Jones, Small, Madero and Szmukler found abnormalities in perceptive tasks which could not be explained by impairments in the right hemisphere alone.

In 1996, Kingston et al. found that visuospatial capacities and short-term memory were deficient in both the acute phase of AN and the period following weight gain. This contradicted findings from neuromaging tests that showed recovery following weight gain.

In 1999, after 12 sessions of surgery, Lauer et al. found abnormalities in attention-related tasks, but not in memory and problem-solving tasks. Similar results have been observed in other studies, such as those carried out by Touyz et al., Laessle et al., Pendleton-Jones et al., and Szmukler et al.

In 2001, in a study of haptic perception in patients with AN and control subjects, Grunwald et al. found changes in perceptual processing and somatosensory integration, as well as in short-term memory and selective attention.

**New theories**

Since the turn of the 21st century, studies about abnormalities in adolescents with ED have become focused on neural networks research and the most typical neuropsychological profiles of patients diagnosed with AN. In 2003, Halmi et al. suggested that AN could be a form of obsessive–compulsive disorder (OCD). Since that time, research groups have focused on evaluating the differences between young anorexic girls and healthy subjects by performing tasks related to executive functions. Their studies therefore revolve around the problem solving process, cognitive flexibility, changes in criteria, and types of information processing.

In 2004, Cavedini et al. found that during the acute phase of the disorder the sample of patients with AN delivered abnormal results on the IGT (Iowa Gambling Task), but not on other cognitive tests. They concluded that impaired decision-making is not merely a non-specific example of the negative effects of malnutrition, but rather that neither nutritional state, severity of the symptoms, general cognitive impairment, nor the mood disorders found in other studies of AN patients is responsible for abnormal performance on the IGT, as there was no relationship between execution of the task and the variables listed above. These impairments were specific to the frontal dysfunctions commonly found in patients with AN and observed using neuroimaging techniques.

This resulted in a new hypothesis and line of research supported by a number of other authors. It stated that general abnormalities in decision-making, cognitive flexibility, criteria, or information processing styles were probably not a direct consequence of malnutrition or an indirect result of cerebral morphological impairments, but rather premorbid symptoms of a tendency towards AN. This tendency could then worsen upon the appearance of the different biological (biochemical, morphological, functional, and endocrine) consequences typically found in anorexia-type eating disorders. Although other authors have found results that contradict Cavedini’s, their samples differed in the areas of symptom severity or control over emotional variables, and those differences may have influenced results.

In 2004, Tchanturia et al. researched cognitive flexibility in patients with AN and found 4 specific factors: simple alternation, mental flexibility, perseveration, and perceptual shift. Patients with AN performed more poorly than control subjects on simple alternation and perceptual shift tasks. An interesting fact about that study is that researchers checked for variations in scores between the 2 AN subgroups (restrictive and purgative) and found no significant differences.

In 2006, Steinglass et al. found cognitive flexibility problems in patients with AN, although other cognitive functions were normal. More specifically, AN patients experienced difficulty with set shifting tasks and were less able to adapt to changes in rules. These authors concluded that the presence of cognitive problems in subjects of normal weight and without attention deficit disorder suggests that neuropsychological disorders which are not attributable to low weight alone may be present in AN. This supports the hypothesis that abnormalities may exist prior to onset of the disorder rather than merely resulting from it.
In 2007, Tchanturia et al. demonstrated that AN patient scores on the IGT did not improve over time. This study, which used skin conductance measures, concluded that according to the somatic marker hypothesis, deficient decision-making ability could be due to lack of sensitivity and/or failure to generate peripheral alarm responses.

In 2008, the same authors used the Haptic Illusion Task which revealed abnormal results for a task involving estimating the weight of different balls. They concluded that these results could have to do with changes in the right parietal cortex and/or the prefrontal cortex.

According to Jacobi et al., there are links between deficiencies in criteria-changing ability and cognitive flexibility in AN and obsessive-compulsive personality traits (preoccupation with details, lists and order; perfectionism; inflexible and rigid mind-set), all of which are significant predisposing factors in the complex aetiology of AN. Following these observations, Southgate et al. carried out a study that measured how AN patients performed on a test that distinguishes between different information processing styles. In line with prior studies demonstrating that anorexic patients performed better on tasks requiring local information processing (e.g. the Embedded Figures Test) than on tasks requiring more global processing (e.g. puzzles, Rey-Osterrieth complex figure test, Bender-Gestalt test), these researchers used the Matching Familiar Figures Test (MFFT). The test revealed that AN patients performed better on a task consisting of presenting six possible options and asking the subject to find the only figure identical to the model. Patients with AN answered more rapidly and precisely than control subjects. The authors concluded that their good performance on this task reflects weak central coherence, that is, a bias towards processing details rather than the Gestalt or whole view of the image. As they did not find an association between the variables and body mass index (BMI), the authors suggested that data could not be said to result from the subject’s physical condition. In fact, the good performances by subjects with AN and low body weight were revealing, since food deprivation and dieting have been associated with cognitive deficits.

In 2008, Chui et al. found abnormal results in neuropsychological tests performed on AN patients compared to healthy subjects, even 6 years after diagnosis and with a mean BMI of 21.8. They detected impairments in verbal abilities, cognitive efficiency, reading, mathematics, and long-term verbal memory. For the first time, this study compared patients with and without amenorrhea and found that patients with amenorrhea or irregular menstruation did not present significantly higher levels of cerebrospinal fluid in the lateral ventricles or in their temporal horns. However, they scored significantly lower than control subjects in the areas of verbal ability, cognitive efficiency, oral language, mathematics, reading, and long-term memory.

Neuroimaging findings

The different studies including neuroradiological tests have revealed data indicative of functional changes in large regions of the brain (e.g., frontal cortex, parietal cortex), and specific cerebral areas (e.g., caudate nucleus, thalamus, lateral inferior frontal cortex) in patients with acute ED compared to control subjects, subjects with other psychiatric disorders, or subjects diagnosed with AN who meet specific criteria for being considered in recovery or remission.

Positron emission tomography

The first studies with PET and SPECT presented significant methodological flaws such as very small sample size and control groups containing only males or very elderly subjects. As a result, conclusions from these studies cannot be compared with those from other studies in young female populations.

According to functional neuroimaging studies in patients with AN, the parietal cortex (PC) is the area of the brain most affected by the disorder. Parietal activity decreases prior to treatment and weight gain, and it increases after treatment. Some authors observed decreased perfusion and metabolism in the superior frontal and dorsolateral prefrontal cortex (PET) in patients with very low body weight, which seemed to revert after weight gain. At the same time, they discovered increases in metabolism in the caudate nucleus and lateral inferior frontal cortex, thalamus and putamen, which persisted after weight gain.

Single-photon emission computed tomography

Whereas some authors observed that patients with very low body weights presented decreased perfusion and metabolism in frontal regions (SPECT) that seem to revert after weight gain, other authors found such decreases in the orbitofrontal (SPECT) and right prefrontal dorsolateral cortex (SPECT) after weight gain, which contradicts prior findings. The fact that these abnormalities do not revert after weight gain shows that rather than being caused by malnutrition, they underlie the disorder.

Lesions and dysfunctions of the right hemisphere seem either to play a more important role in the onset of the disorder or else show increased susceptibility to the consequences resulting from malnutrition and the typical behaviours of subjects with AN. Nevertheless, this is a very controversial topic given that lateralisation of this cerebral pathology has not been demonstrated by all the studies, as most of them focus on assessing concrete areas of the brain.

Functional magnetic resonance imaging

In a study of how AN patients process images of themselves and of other people, Sachdev’s group found differences in the activation of the medial frontal gyrus, precuneus, and occipital regions of acute-phase AN patients compared to a control group. In studies comparing satiated or hungry patients with control subjects, researchers observed that satiated patients presented less PC activity (Brodmann area [BA]40) than control subjects during a challenge test with food drawings. Nevertheless, when patients were hungry, activity in the primary area and the associative area of the
occipital cortex (BA 17 and 18) was lower than in control subjects.  
In addition, researchers have also found changes in cerebral activation in the anterior cingulate gyrus and the left insula.  
Data gathered from patients in long-term recovery showed hyperactivity in the medial prefrontal cortex (BA 8, 9, 10, and 32) and the cerebellum, as well as hypoactivity in the PC (BA 7 and 40) and occipital cortex (BA 18). Moreover, other researchers  
found that in the presence of symptom-inducing stimuli, activity in the insula, anterior cingulate cortex, and ventral and dorsal striatum was significantly decreased in recovered AN patients compared to control subjects. 

The ventromedial prefrontal cortex is linked to rewarding stimuli, such as good tastes or smells, while the ventrolateral frontal cortex assesses punitive stimuli and whether or not behaviour should be changed.  
With the help of studies offering structural images of the brain and others using computed tomography scans, researchers have reached a consensus regarding the decrease in cerebral volume and the dilation of the cerebral ventricles, with an increase in cerebrospinal fluid volume (CSF). These changes seem to revert, at least partially, after weight gain.

**Discussion**

Studies on the neuropsychological abilities of AN patients have revealed the wide variety of deficits that may appear in this disorder. As studies multiply, theories develop, assessment techniques improve, and knowledge increases, researchers are beginning to assess the disorder from another angle. While conclusions from earlier studies stated that AN patients showed reversible morphological changes and overall neuropsychological impairments that significantly impacted information processing speed, attention capacities,  
and verbal memory, we now observe that these changes are predisposing factors for the disorder rather than results of its effect. Researchers have changed approaches and now concentrate more on studying neuropsychological abilities specific to the right hemisphere and prefrontal cortex, according to theories by Halmi et al.  
and the links between AN and OCD. This new angle is supported by neuroimaging findings that show specific alterations in the frontal areas and the neuropsychological abilities localised there: cognitive flexibility, impulsiveness, problem solving, perseveration, and change of criteria. Researchers also point to the detail-oriented information processing style which, along with changes in the parietal and the occipital cortex, could explain patients’ behaviour when confronted with food-related variables, causing such changes to be identified as predisposing factors rather than results of the malnutrition that characterises AN patients.  

There is still considerable work to be done with regard to analysing neuropsychological changes in patients diagnosed with AN. This is particularly true in Spain, where only a few groups have studied this disorder in a systematic and exhaustive way. As our field of knowledge on the subject increases, we will be able to provide better care, and with the help of neuropsychological treatment, the percentage of remissions and recoveries may increase. Over the years, clinical neuropsychology has evolved to constitute a basic tool for the identification, prevention, and management of eating disorders. It acts as a complement to classic clinical psychology and neuroimaging tests by allowing early identification of typical symptoms of AN in these patients. As a result, doctors can take action in the initial stages of the disorder in order to prevent patients’ body weights from reaching unhealthy levels.

**Conflicts of interest**

The authors have no conflicts of interest to declare.

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