

Neuroanatomy of Orthorexia Nervosa: Emerging Insights from Structural Neuroimaging

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Abstract

Objective

There are no published studies in the contemporary scientific literature that have directly applied neuroimaging techniques (such as fMRI, PET, or structural/functional MRI) to individuals with orthorexia nervosa (ON) to characterize brain alterations specific to this condition. Although interest in ON is increasing, a critical area of investigation concerns its phenomenological overlap with obsessive-compulsive disorder (OCD) and other feeding and eating disorders (FED). The present study aims to examine morphological brain differences in individuals with ON using high-resolution 3D T1-weighted MRI, with the goal of determining whether structural profiles observed in ON are comparable to those seen in OCD and in established eating disorder phenotypes.

Methods

Twenty-seven participants (12 females, 15 males) were enrolled in the study and underwent a comprehensive psychometric assessment including the ORTO-15, Italian-Düsseldorf Orthorexia Scale (I-DOS), Yale-Brown Obsessive Compulsive Scale (Y-BOCS), and the Multidimensional Perfectionism Scale (MPS). Participants were stratified into those exhibiting orthorexic behaviour and those without (healthy control group, HC) according to ORTO-15 scores. The imaging protocol included the acquisition of high-resolution three-dimensional T1-weighted MRI scans. Groups were compared regarding cortical and subcortical parameters in order to identify neuroanatomical differences associated with orthorexic behaviour.

Results

Morphometric analysis revealed a significant correlation between ORTO-15 score and cortical thickness (CT) in key brain regions. Specifically, lower ORTO-15 scores—indicative of greater orthorexic tendencies—were associated with a marked reduction in CT of the entorhinal cortex (EC). Conversely, an increased CT was observed in the right posterior cingulate cortex (PCC).

Discussions

The observed alterations in the EC and PCC suggest that ON may share neurobiological patterns with OCD and FED. These findings support the notion of ON as a distinct yet transdiagnostic clinical entity. However, the small sample size highlights the need for further large-scale investigations to confirm the presence and reliability of these potential neurobiological biomarkers.

1. Introduction

Orthorexia nervosa (ON) is a relatively recent psychopathological construct describing a behavioural pattern characterized by excessive, rigid, and pathological attention to foods perceived as “pure” (Bratman & Knight, 2004; Cena et al., 2019). Unlike common health-related concerns, in ON adherence to self-imposed dietary rules assumes a central and pervasive role in the individual’s cognitive organization (Cena et al., 2019; Koven & Abry, 2015). In addition, sociocultural factors, including exposure to health- and diet-related content on social media, may contribute to orthorexic symptoms; in an Italian web-based survey, greater time spent on social media was associated with more pronounced symptoms of orthorexia nervosa (Tarsitano et al., 2022).

To establish a nosological framework, a panel of forty-seven experts from fourteen countries across four continents, representing multiple disciplines, collaborated on a consensus document defining ON and its diagnostic criteria (Donini et al., 2022).

Nevertheless, in recent years, the debate has intensified regarding the appropriate nosographic classification of ON. Dietary restriction, food-related anxiety, and perfectionistic traits, like anorexia nervosa, leads some authors to consider ON more appropriately placed among eating disorders; others have emphasized its significant overlap with obsessive-compulsive disorder (OCD), particularly regarding intrusive thoughts rigidity and food preparation and selection rituals advocating its inclusion among obsessive-compulsive spectrum disorders (Koven & Abry, 2015; Horovitz & Argyrides, 2023; Donini et al., 2022; Foyster et al., 2023). Furthermore, the development of ON symptoms as a consequence of other previously diagnosed psychiatric conditions adds even greater uncertainty. (Rania M, et al. 2021).

The topic also receives much attention in the oncology field, with several studies focusing on changing eating habits, particularly towards rigid and restrictive behaviour (Guarascio et al. 2026).

Volumetric MRI and cortical thickness (CT) studies in FED have revealed alterations in volume and thickness across several brain regions, with increases or decreases varying compared to healthy controls (Vidal et al., 2021; Tose et al., 2024).

Individuals with ON exhibit intrusive thoughts related to purity, health, and contamination, accompanied by high levels of anxiety. Therefore, despite ON shares some features with FED, the most supported hypothesis situates it within the OCD spectrum. (Hanras et al., 2024).

Recent MRI studies in patients with FED have documented systematic reductions in regions critical for cognitive and emotional control, including the anterior cingulate cortex (ACC), orbitofrontal cortex (OFC), and insula, suggesting widespread gray matter alterations and neurobiological vulnerability trajectories (King et al., 2018; Tose et al., 2024). Similarly, research in OCD has highlighted alterations in fronto-striato-thalamo-cortical circuits, often most pronounced in the OFC and ACC regions implicated in cognitive rigidity, value processing, and impulse control (Piras et al., 2015).

Based on this evidence, the present study aims to advance the understanding of ON by delineating a potential morphological brain profile in individuals exhibiting behaviours and habits consistent with this

condition, using high-resolution T1-weighted volumetric MRI and integrating specific psychometric assessments with advanced morphometric analyses.

2. Methods

2.1 Participants

Twenty-seven university students (12 females and 15 males), mean age of 25.4 ± 3.4 years, were recruited at the Magna Graecia University Hospital “Renato Dulbecco” between July 2023 and January 2024.

Neurological or psychiatric disorders, current use of psychoactive medications, history of head trauma, prior brain surgery, and diagnosed eating disorders were adopted as exclusion criteria.

The study protocol was approved by the Ethics Committee of the Calabria Region and was conducted in accordance with national regulations and the principles outlined in the Declaration of Helsinki (1964). All participants provided written informed consent after receiving a comprehensive explanation of the study procedures.

2.2 Psychological variables

Participants completed several standardized psychometric instruments widely used in the literature, including the ORTO-15 Questionnaire (Donini et al., 2004) and the Italian version of the Düsseldorf Orthorexia Scale (I-DOS; Cerolini et al., 2022) to assess the propensity toward orthorexic behaviours and traits.

The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS; Goodman et al., 1989) was administered to evaluate the severity of obsessive-compulsive symptoms, while the Multidimensional Perfectionism Scale (MPS; Hewitt & Flett, 1991) was used to assess different dimensions of perfectionism.

2.3 Imaging acquisition and data processing

Participants underwent magnetic resonance imaging (MRI) using a 1.5 Tesla scanner (Philips Achieva). High-resolution three-dimensional T1-weighted sequences were acquired (slice thickness: 1.2 mm; TR: 25 ms; TE: 4.6 ms) without the administration of a contrast agent.

All MRI examinations were performed at the Neuroradiology Unit of the Magna Graecia University-Hospital “Renato Dulbecco” of Catanzaro, Italy.

Freesurfer (version 7.4.1) was used to perform cortical reconstruction and volumetric segmentation (Dale et al., 1999; Dale and Sereno, 1993; Fischl and Dale, 2000; Fischl et al., 2001; Fischl et al., 2002; Fischl et al., 2004a; Fischl et al., 1999a; Fischl et al., 1999b; Fischl et al., 2004b; Han et al., 2006; Jovicich et al., 2006; Segonne et al., 2004, Reuter et al. 2010, Reuter et al. 2012).

Cortical parcellation and subcortical segmentation are based on Desikan/Killany atlas (Desikan et al., 2006).

Default parameters values were used to process T1-weighted sequences and FWHM of 10 mm smooths participant's resampled images.

An expert neuroradiologist (E.T.) identified and fixed recon-all output images errors if any.

CT groups' statistical inference was performed using 2-sample t-test accounting for the effects of age and gender.

A general linear model (GLM) was developed to evaluate the association between CT and both body mass index (BMI) and ORTO-15 scores, adjusting for age and sex. Statistical significance was set at $p < 0.05$, with false discovery rate (FDR) correction for multiple comparisons.

A further GLM was developed to assess group differences in subcortical volumetric measures. In this model, segmented subcortical volumes were entered as dependent variables, age and total intracranial volume (TIV) as covariates, and sex and group as fixed factors.

Finally, the relationship between subcortical regions of interest (ROIs), BMI, and orthorexic symptom severity was examined using a GLM with ROI volumes as dependent variables; age, TIV, BMI, and orthorexic scores as independent variables; and sex as a factor. A threshold of $p < 0.001$ was adopted to correct for multiple comparisons across the number of ROIs analyzed.

CT analyses were performed using FreeSurfer, while statistical analyses of segmented subcortical volumes were conducted using Minitab software.

3. Results

Participants with orthorexic behaviour were identified by means of the ORTO-15 questionnaire: individuals scoring below the established cut-off (< 35) were classified as exhibiting a greater tendency toward orthorexic behaviors (Segura-Garcia et al., 2012; Dunn & Bratman, 2016; Mitrofanova et al., 2021). Accordingly, the final sample consisted of 9 individuals with ON and 18 age- and sex-matched healthy controls. Table 1 summarizes the differences between the groups across the psychometric measures.

Table 1
Groups comparison

	ORTO-15 $\geq$ 35		ORTO-15 < 35		t	p	Cohen's d
	(N = 18)		(N = 9)				
	Mean	SD	Mean	SD			
I-DOS	16,9	3,7	19,8	3,9	-1.771	0.090	-0.767
ORTO-15	39,1	2,8	31,5	2,1	6.795	< .001	2.942
Y-BOCS	5,9	4,7	11,1	4,9	-2.513	0.020	-1.088
MPS_Self oriented	59,4	10,2	65,0	13,8	-1.119	0.275	-0.485
MPS_Others oriented	61,8	8,6	62,3	7,3	-0.141	0.889	-0.061
MPS_Socially prescribed	57,5	8,0	60,0	11,2	-0.633	0.533	-0.274

Morphometric analysis revealed two significant cortical differences between the ON and control groups. Specifically, individuals in the ON group exhibited reduced CT in the left entorhinal cortex (EC), a region implicated in memory processing, spatial encoding, and emotional integration. Conversely, increased CT was observed in the right posterior cingulate gyrus (PCG), an area involved in self-referential processing, internal monitoring, and behavioural regulation (Table 2; Fig. 1).

Table 2
Coordinates of brain areas involved

Comparison	Peak MNI Coordinates (x, y, z)	$-\log_{10}$ (p-value)	Brain Area
ON > HC	11, -18, 38	4,90	Right Posterior Cingulate
ON < HC	-21, -10, -31	3,43	Left Entorhinal Cortex

Table 1. CT differences between the orthorexic group and healthy controls (FDR = 0.05)

4. Discussion

The aim of the present study was to deepen a potential morphological brain profile of individuals exhibiting Orthorexic behaviours by means of high-resolution T1-weighted volumetric.

MRI findings from the present study revealed significant differences between the group of orthorexic behaviours and healthy controls in two cortical regions: the left EC and the right PCG. Specifically, reduced CT in the left EC was observed in individuals with lower ORTO-15 scores, whereas increased CT in the right PCG was associated with lower scores on the same measure.

The left EC is a key structure located in the medial temporal lobe, positioned between the hippocampus and adjacent cortical regions such as the perirhinal and parahippocampal cortices. It plays a fundamental role in multiple cognitive functions, particularly memory processing and spatial navigation. The EC is crucial for the formation and consolidation of episodic and declarative memories and serves as an interface between the hippocampus, where information is consolidated, and the neocortex, where long-term memories are stored (Van Strien et al., 2009; Gerlei et al., 2021). Moreover, it is involved in spatial navigation through grid cells that encode spatial positioning via a regular activation network (Jacobs et al., 2013; Moon et al., 2022).

Neuroimaging studies have identified alterations in several brain regions among patients with FED, particularly within medial temporal lobe structures including the EC. These structural and functional changes have been associated with cognitive deficits and body image distortions characteristic of NED. Functional connectivity analyses have also demonstrated alterations in neural circuits involving the EC, suggesting a potential role of these networks in emotional regulation and eating behavior, domains frequently impaired in eating disorder psychopathology (Kanzawa et al., 2025). For example, Amianto et al. (2013) investigated gray matter volumetric changes in patients with anorexia nervosa (AN) and bulimia nervosa (BN), identifying abnormalities in several brain regions, including the medial temporal lobe.

Based on this evidence, the involvement of the left EC in the neurobiological profile of ON appears to align the condition with FED from a cognitive-emotional perspective. However, the concurrent alterations observed in the right PCG suggest that ON may also overlap with mechanisms typically associated with OCD, thereby supporting the conceptualization of ON as a hybrid condition sharing both eating-related and obsessive-compulsive dimensions.

Abnormalities in the Posterior Cingulate Cortex (PCC) may impair emotional regulation and contribute to dysfunctional eating behaviours (Simon et al., 2016). Recent evidence indicates that the PCC plays a role in anxiety modulation and influences cognitive processes such as information accumulation during attention-demanding tasks, potentially amplifying anxiety-related emotional responses in eating disorders (Gorka et al., 2023). Functional neuroimaging studies in OCD have demonstrated significant alterations within both the Default Mode Network (including the PCC) and fronto-striato-thalamo-cortical circuits (Zhang et al., 2022). Hou et al. (2013) reported increased functional connectivity within cortico-striatal circuits (OFC, caudate nucleus, and thalamus), alongside structural and functional abnormalities in the PCC. Such alterations may play a critical role in maintaining obsessive-compulsive symptomatology: hyperconnectivity between the OFC, implicated in decision-making and reward processing, and basal ganglia structures, key regulators of motor behaviour, supports the pathophysiology of repetitive behaviours. Additional studies have reported disrupted PCC connectivity with other regions, including the cerebellum and medial temporal cortex, suggesting a broader dysregulation affecting cognitive-emotional integration (Gürsel et al., 2018).

Overall, the findings of the present study suggest that ON should be considered a condition of clinical relevance and that individuals exhibiting orthorexic behaviours may partially share neurobiological features with both FED and OCD.

Despite the novelty of present results, several limitations should be acknowledged. The questionnaire used to assess orthorexic tendencies has limited psychometric robustness; to avoid false positives, we adopted a more restrictive cut-off to enhance validity. On the other hand, the use of a 1.5 Tesla scanner may have reduced sensitivity in detecting subtle structural differences in certain brain regions.

Future research should integrate morphological data with functional and connectivity-based neuroimaging techniques (e.g., resting-state, fMRI and diffusion tensor imaging) to provide a multimodal characterization of the neurobiological correlates of ON. Longitudinal designs would be particularly valuable in clarifying whether the observed alterations represent vulnerability markers, consequences of restrictive eating behaviours, or maintenance factors of the condition. Direct comparisons with clinically diagnosed OCD and FED samples would further delineate shared and disorder-specific neurobiological features, contributing to a more precise placement of ON within the psychopathological spectrum.

From a clinical standpoint, the identification of specific morphological alterations associated with ON may have important translational implications. The characterization of structural biomarkers could strengthen the nosological validity of ON and improve differential diagnosis. Moreover, understanding the neural circuits involved may guide more targeted therapeutic interventions. Finally, the identification of specific neurobiological correlates may enable risk stratification and personalized treatment approaches, fostering the development of brain-informed interventions and enhancing the effectiveness of early therapeutic strategies in individuals at risk for orthorexic symptomatology.

What is already known on this subject?

Orthorexia nervosa (ON) is characterized by a pathological concern with healthy eating and rigid dietary rules, but its nosological status and underlying neurobiology remain unclear. ON shows phenomenological overlap with obsessive-compulsive disorder (OCD) and feeding and eating disorders (FED), particularly with respect to obsessive thoughts, compulsive behaviors, perfectionism, and cognitive rigidity. Although neuroimaging studies have extensively investigated OCD and established FED phenotypes, no published study has directly characterized structural brain alterations in individuals exhibiting orthorexic symptomatology.

What does this study add?

This study provides the first preliminary evidence of cortical morphological differences associated with orthorexic symptomatology. Greater orthorexic tendencies, reflected by lower ORTO-15 scores, were associated with reduced cortical thickness of the entorhinal cortex and increased cortical thickness of the right posterior cingulate cortex. These findings identify brain regions potentially involved in the neurobiological phenotype of ON and provide preliminary support for its conceptualization as a distinct

but potentially transdiagnostic condition sharing neurobiological features with OCD and FED. Given the small sample size, these findings should be considered exploratory and require replication in larger, clinically characterized samples.

Declarations

Ethics Statement

The study followed all relevant ethical guidelines. All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments (or comparable ethical standards).

Consent

Informed consent has been obtained from all participants, and the investigation has been conducted according to the best principles of research with human beings.

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contribution

ET: conceptualization, writing, project administration; AM: writing, data curation; ADR: data analysis, review; MAM: editing; US review, supervision; CSG: review, supervision; MGT: conceptualization, writing, project administration. All authors read and approved the final version of the manuscript.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Figures

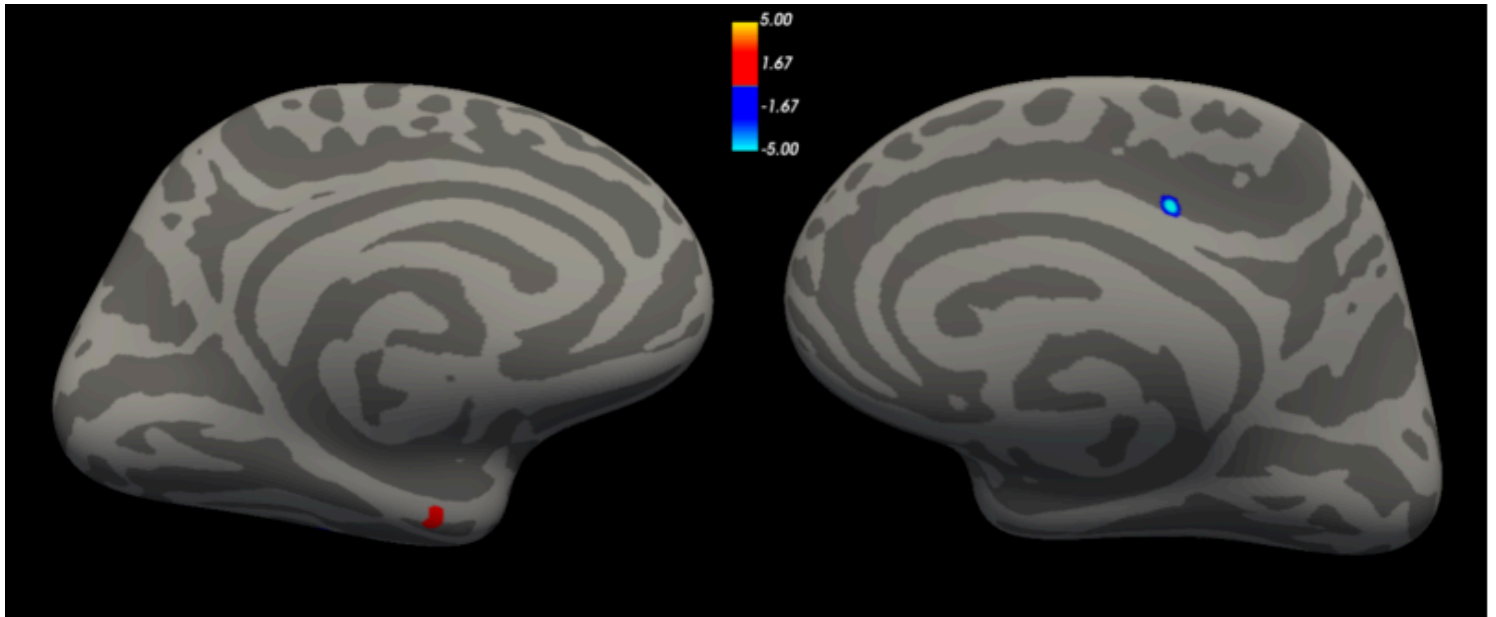


Figure 1

ON subjects showed CT reduction in left EC (A) and increase in right PCC (B), p-value of 0.001 correct for multiple comparisons.