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The neural basis of self-body size perception in Anorexia Nervosa: An Activation Likelihood Estimate (ALE) meta-analysis

Master thesis Neuropsychology

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Abstract

AN patients show distorted self-body size perception that expresses itself in inaccurate representations of their body size and shape. This distortion is caused by primed processing of perceptual information, leading to an overestimated body image and an overestimated body schema. Different brain regions play a role in processes relevant to self-body size perception. Regarding this study, reduced activation within regions of the PPC, like the precuneus and IPL, the MFG, and the RSC was expected in AN compared to HC. Other-body size perception was included as an additional variable to test the assumption that distorted body-size perception is limited to the own body in AN. In the present study, an ALE meta-analysis was conducted. In total, 15 fMRI-studies were included, 11 studies regarding self-body size perception, and eight studies regarding other-body size perception. Cluster analyses, contrast analyses, and conjunction analyses were conducted by using BrainMap GingerALE. Results showed no difference in activation during self-body size perception between AN and HC. During other-body size perception, AN patients showed increased activation in the right SPL/precuneus. This ALE meta-analysis provided evidence that neural activation in AN and HC might be similar during self-body size perception. However, AN patients might experience problems in processing other female bodies. Still, further research will be necessary to investigate the neural basis of self-body size perception in AN more closely. Especially, neural processes during proprioception and interoception, the vestibular system as well as resting-state functional connectivity should be explored in AN.

Keywords: Anorexia nervosa, healthy controls, self-body size perception, other-body size perception, ALE meta-analysis

Introduction

Anorexia nervosa (AN) is a severe illness since it has a mortality rate 12 times higher than any other cause of death in young women (Frank et al., 2019). Individuals with AN often experience problems perceiving their body weight and shape correctly, which encourages a restriction of energy intake and causes a lack of recognition of the seriousness of their low body weight. Additionally, distorted body size perception is one of the most persistent symptoms in AN and its severity is crucial for treatment success and relapse (Cornelissen et al., 2017). A more extensive investigation of the underlying neural mechanisms involved in body size perception might contribute to improving existing treatment options in AN.

The perception of one's own body is a multisensory process (Blanke, 2012) since it requires neural processing and integration of various bodily internal and external signals (Riva, 2018). Therefore, an entirely different sensory input is processed during self-body perception compared to other-body perception (Kilteni et al., 2015). Other-body perception is limited to visual perception (Kilteni et al., 2015), whereas self-body perception is also mediated by perceptual information, influenced by internal information like proprioceptive, interoceptive, tactile, and vestibular input, and recalibrated through stored implicit and explicit body representations (Riva, 2018). Perceptual body information relates to the awareness of the own body through the senses (Riva, 2018). Proprioception is defined as the sense of the position of the own body parts in space, whereas interoception is the sense of the physiological condition of the own body. The vestibular system is responsible for the sense of body motion and position of the body. However, AN patients exhibit a distorted self-body size perception (Miyake et al., 2010) that expresses itself in inaccurate representations of their body size and shape (Keizer et al., 2012). This impairment can be traced back to distorted mental body representations (Keizer et al., 2012), which hold information about features of the own body, body parts, position of the body in space, and the integration of this input into a whole (Dijkerman & de Haan, 2007; Serino & Haggard, 2010). Mental body representations can be divided into a perceptual aspect, the body image, and an action-related aspect, the body schema (Keizer et al., 2013). Regarding the body image, AN patients seem to retrieve inaccurate information about their body size from their memory (Keizer et al., 2012). This body memory holds body-independent, allocentric, long-term stored representations about how the own body usually looks like (Dakanalis et al., 2016). Specifically, these allocentric representations hold information about the own body size and shape as it is remembered to be (Longo et al., 2010). In general, the body memory gets updated by body-dependent, egocentric, real-time perceptual representations about the current state of the own body

(Dakanalis et al., 2016; Serino et al., 2015). To compare information of the egocentric, perceptual input to information retrieved from the body memory, sensory information of both systems needs to be coded into a common reference frame (Riva & Gaudio, 2018; van der Stoep et al., 2017). However, this multisensory integration process is impaired in AN, preventing the body memory to be updated by egocentric, perceptual input (Serino et al., 2015). Therefore, the body memory is locked to negative concepts such as “I am fat” even after weight loss (Keizer et al., 2012; Riva & Dakanalis, 2018). Ultimately, this causes primed processing of further egocentric, perceptual experiences (Gaudio et al., 2014; Riva et al., 2015) like visual, interoceptive, proprioceptive, and tactile input (Riva & Dakanalis, 2018). Particularly, in AN primed processing of perceptual bodily information results in an overestimated body image, which forms the perceptual aspect of mental body representations (Keizer et al., 2012; Keizer et al., 2013). Consequently, distorted representations of a larger body size than the actual one and overestimation of horizontal tactile distances in areas that are known to put on weight like the abdomen (Keizer et al., 2012) and thighs (Spitoni et al., 2015) are the results. Also, altered gastric interoception regarding hunger and satiety affects the feeling of gastric fullness in AN (Kerr et al., 2016; Perez et al., 2013). Additionally, an overestimated body image also seems to cause an overestimated body schema in AN (Gadsby, 2017; Keizer et al., 2013). The body schema is an unconscious, sensorimotor representation of the own body and involved in motor control and motor imagery. Normally, it relies on visual, proprioceptive (Berlucchi & Aglioti, 2010), and somatosensory information (de Vignemont, 2010) of the body image. However, in AN overestimated perceptual information about the own body size unconsciously affects postural movements in space and judgments about the ability to move around in space (Guardia et al., 2010; Keizer et al., 2013). This results in motor planning and movements that align with a larger body size than the actual one.

These deficits in self-body size perception can be linked to neural differences distinctive to AN (Gaudio, & Quattrocchi, 2012; Uher et al., 2003). Initially, the visual input of bodies is processed in the extrastriate body area (EBA) and the fusiform body area (FBA) (Esposito et al., 2018). However, self-body size perception is a complex process of multisensory integration that relies on higher-order processing involving frontal and parietal regions (Brooks et al., 2017; Gaudio et al., 2018). The parietal cortex is linked to processing and multisensory integration of bodily information which leads to updates regarding one’s own body size representations (Zopf et al., 2016). Especially within the posterior parietal regions, the precuneus and the inferior parietal lobe (IPL) seem to be associated with processing allocentric and egocentric input regarding one’s own body. In general, the posterior parietal cortex (PPC) is related to multisensory integration of egocentric input, which is important for updating and maintaining a body schema (Prevosto et al., 2011; Schwoebel & Coslett, 2005). The precuneus is an important region for self-reference (Lou et al., 2005), mental self-representation, and manipulation of mental images (Cavanna & Trimble, 2006) and involved in egocentric processing (Riva & Gaudio, 2012; Zaehle et al., 2007). The IPL, responsible for self-body identification (Hodzic et al., 2009) is linked to egocentric perceptual processing as well as allocentric long-term processing (Riva & Gaudio, 2012; Zaehle et al., 2007). In addition, the hippocampal formation seems to be involved in allocentric long-term memory processes (Zaehle et al., 2007; Feigenbaum & Morris, 2004), like the body memory. The retrosplenial cortex (RSC) is involved in hippocampal-dependent, allocentric memory retrieval (Mitchell et al., 2018), and together with the PPC responsible for the translation between egocentric and allocentric input about the own body (Riva & Dakanalis, 2018). For higher-order somatosensory perception such as tactile distance estimation, the temporo-parieto-occipital junction (TPOJ) was identified (Spitoni et al., 2010). Furthermore, the frontal cortex and insula seem to be involved in self-recognition and self-awareness (Philippi et al., 2012). Especially, the middle frontal gyrus (MFG) is crucial for spatial working memory and updating spatial representations (Tanaka et al., 2005) of visual images of the own body (Peelen & Downing, 2007). Finally, the insula plays a crucial role in processing self-related information (Devue et al., 2007) as it is involved in interoceptive awareness like gastric fullness (Kerr et al., 2016; Mohr et al., 2010). In addition, Moseley et al. (2012) suggested a connection between the PPC and the insular cortex, which is responsible for integrating peripersonal sensory information with egocentric and allocentric bodily information.

Evidence reveals a lack of activation in multiple brain regions mentioned above in AN compared to healthy controls (HC) (Favaro et al., 2012; Mohr et al., 2010; Sachdev et al., 2008; Vocks et al., 2010; Zhu et al., 2012). This supports the idea of distorted processing and multisensory integration of bodily information in AN.

In summary, evidence of prior studies demonstrates that a large neural network is involved in self-body size perception, which seems to show a different activation pattern in AN compared to HC (Favaro et al., 2012; Sachdev et a., 2008; Vocks et al., 2010). Still, research on this topic is scarce, and insight provided by previous studies is often insufficient and conflicting regarding the involvement of specific brain regions in self-body size perception. This study aims to investigate the role of the frontal-parietal network in AN more closely since literature indicates its implication in self-body size perception (Gaudio et al., 2018; Riva & Dakanalis, 2018). However, other regions relevant to body size perception, like the EBA, FBA (Esposito et al., 2018), hippocampal formation (Zaehle et al., 2007), TPOJ (Spitoni et al., 2010), and insula (Devue et al., 2007) will also be considered. A meta-analysis on fMRI studies might lead to more evident results about how the neural basis of self-body size perception differs in AN compared to HC. Based on previous literature, reduced activation within the PPC, especially within the precuneus and the IPL, the RSC, and the MFG is expected during self-body size perception in AN compared to HC. Other-body size perception is included as an additional variable since deficits in body size perception in AN are assumed to be limited to the own body (Castellini et al., 2013; Favaro et al., 2012). Therefore, activation patterns in the brain during other-body size perception are expected to be the same in AN and HC.

Methods

Search strategy

In this meta-analysis, neuroimaging data of existing fMRI studies regarding self- and/or other-body size perception in AN and HC were included. The fMRI studies were identified through the databases ‘Scopus’ and ‘PubMed’. Search terms were a combination of the following keywords: “anorexia nervosa” AND (“fMRI” OR “brain activation” OR “neural activity”) AND (“body representation” OR “body image” OR “body perception”) for both databases. All searches were conducted in November 2020. No restriction date was set for the data search.

Article selection

The eligibility of the fMRI studies was determined based on inclusion criteria. The criteria were selected to include as many fMRI studies as possible, while maintaining maximum comparability between the studies. This was achieved by creating inclusion criteria regarding domains (demographic data; testing paradigm; neuroimaging data) that were considered important to maintain maximum comparability. Per domain, multiple inclusion criteria were established. Ultimately, fMRI studies that fulfilled all criteria of each domain were included in the meta-analysis, see Table 1.

Demographic data

- AN patients and/or HC are used as a participant sample
- AN patients are diagnosed according to the criteria of the DSM-IV-TR/DSM-5 or ICD-10
- Female AN patients or female HC are used as participants
- The participant sample does not consist of a general eating disorder group without specifications regarding the type of eating disorder

Testing paradigm

- The applied task measures self- and/or other-body size perception
- The participant sample does not receive cognitive therapy for body size perception unless neuroimaging data regarding body size perception from before the treatment are available
- No resting-state fMRI

Neuroimaging data

- Neuroimaging data are reported separately for AN, HC, and other types of eating disorders that may be included in the study
- Neuroimaging data of mixed-gender samples are reported separately for men and women
- Neuroimaging data are reported in Montreal Neurological Institute (MNI) template or Talairach space
- Neuroimaging data are not reported only after group comparison (AN vs. HC)

Data extraction

Per study relevant information regarding the name of the author(s), publication year, number of participants, gender of participants (female; male), participant condition (AN; HC), type of AN (AN; AN-Restricted type (AN-R); AN-Binge eating/Purging type (AN-BP)), testing paradigm procedure, type of testing paradigm (self; other), brain imaging technique (fMRI), number of reported foci, coordinates of brain activation (x,y,z) and the type of brain template (MNI; Talairach) was obtained and placed in a Word document. Information about the testing paradigm was used to determine the degree of involvement of the different body image components (perceptive; affective; cognitive) based on the criteria used by Gaudio and Quattrocchi (2012). The perceptive component was considered primary when the task included recognition of one’s own or others’ body images, viewing line drawings of bodies, or estimating body size (e.g., viewing images of a body or judging the weight of bodies). The affective component was rated primary when the task elicited feelings towards the body in terms of body dissatisfaction (e.g., selecting the most unpleasant image from a set of fatter and normal images of the own body). The cognitive component was considered primary when the task relied on beliefs concerning body shape and appearance as well as the mental representation of one’s own body (e.g., judging what body image represents an acceptable body size). Per study, only the coordinates of activation that passed the inclusion criteria of neuroimaging data were extracted since several studies reported additional coordinates of activation that did not apply to this study (e. g., coordinates of activation from male participants). The included studies differed in their report of coordinates of activation, as the number of participant conditions (HC; AN; AN-R; AN-BP) and testing paradigms (self; other;

combined) varied per study. The coordinates of activation per participant condition and testing paradigm were considered as separate experiments (e.g., a study that investigated self- and other-body size perception in HC, AN-R and AN-BP was considered as having six separate experiments). Therefore, some studies provide data for multiple conditions of the meta-analysis, see Table 1.

Table 1

All Studies Included in the ALE Meta-analysis Regarding Self-Body Size Perception and Other-Body Size Perception

Study	Number of subjects	Index Condition	Control Condition	Degree of involvement of body image component			Number of foci
				Perceptive	Affective	Cognitive	
Self-body size perception							
Female healthy controls (HC)							
Burke et al. (2019)	15 HC	Own body image (2 s)	Scrambled baseline image (2 s)	++	-	+	12
		Own body image (0.5 s)	Scrambled baseline image (0.5 s)	++	-	+	4
Castellini et al. (2013)	19 HC	Distorted oversized own body image	Image of houses	++	-	-	6
		Distorted undersized own body image	Image of houses	++	-	-	10
		Real own body image	Image of houses	++	-	-	6
Friederich et al. (2007)	18 HC	Other female body image	Interior image	+	++	+	5
Kurosaki et al. (2006)	11 HC	Distorted oversized own body image	Real own body image	+	++	+	8
		Distorted undersized own body image	Real own body image	+	++	+	9
Miyake et al. (2010)	11 HC	Distorted oversized own body image	Real own body image	+	++	+	9

		Distorted undersized own body image	Real own body image	+	++	+	4
Sachdev et al. (2008)	10 HC	Real own body image	Neutral stimuli	++	+	+	8
Suda et al. (2013)	15 HC	Body checking images	Control images	+	++	++	5
Via et al. (2018)	20 HC	Real own body image	Other female body image	++	-	-	16
Wagner et al. (2003)	10 HC	Distorted oversized own body image	Neutral stimuli	+	++	+	13
Female Anorexia nervosa patients (AN; AN-R; AN-BP)							
Castellini et al. (2013)	18 AN-R	Distorted oversized own body image	Image of houses	++	-	-	13
		Distorted undersized own body image	Image of houses	++	-	-	12
		Real own body image	Image of houses	++	-	-	7
Friederich et al. (2010)	17 AN	Body-shape images of slim fashion models	Control images	+	++	+	17
Miyake et al. (2010)	11 AN-R	Distorted oversized own body image	Real own body image	+	++	+	2
		Distorted undersized own body image	Real own body image	+	++	+	4
	11 AN-BP	Distorted oversized own body image	Real own body image	+	++	+	6
		Distorted undersized own body image	Real own body image	+	++	+	3
Sachdev et al. (2008)	10 AN	Real own body image	Neutral stimuli	++	+	+	0

Seeger et al. (2002)	3 AN	Distorted oversized own body image	Neutral images and distorted oversized images of other female body	+	++	+	3
Suda et al. (2013)	20 AN	Body checking images	Control images	+	++	++	2
Via et al. (2018)	20 AN	Real own body image	Other female body image	++	-	-	28
Wagner et al. (2003)	13 AN	Distorted oversized own body image	Neutral stimuli	+	++	+	11
Other-body size perception *Female healthy controls (HC)*							
Burke et al. (2019)	15 HC	Other female body image (2 s)	Scrambled baseline image (2 s)	++	-	+	9
		Other female body image (0.5 s)	Scrambled baseline image (0.5 s)	++	-	+	16
		Other female body image (2 s)	Own body image (2 s)	++	-	+	0
		Other female body image (0.5 s)	Own body image (0.5 s)	++	-	+	13
Miyake et al. (2010)	11 HC	Distorted oversized other female body image	Real other female body image	+	++	+	3
		Distorted undersized other female body image	Real other female body image	+	++	+	1
Sachdev et al. (2008)	10 HC	Other female body image	Neutral stimuli	++	+	+	8
Suchan et al. (2010)	15 HC	Other female body image	Neutral stimuli	++	-	+	15
Suchan et al. (2013)	15 HC	Other female body image	Neutral stimuli	++	-	+	10
Schweitzer et al. (2018)	24 HC	Other female body image	Scrambled images	++	-	-	9
Uher et al. (2005)	18 HC	Line drawings of undersized, oversized, and normal-sized	Neutral stimuli	++	++	+	8

		female body image					
Via et al. (2018)	20 HC	Other female body image	Own body image	++	-	-	27
Female Anorexia nervosa patients (AN; AN-R; AN-BP)							
Miyake et al. (2010)	11 AN-R	Distorted oversized other female body image	Real other female body image	+	++	+	5
		Distorted undersized other female body image	Real other female body image	+	++	+	0
	11 AN-BP	Distorted oversized other female body image	Real other female body image	+	++	+	3
		Distorted undersized other female body image	Real other female body image	+	++	+	0
Sachdev et al. (2008)	10 AN	Other female body image	Neutral stimuli	++	+	+	8
Suchan et al. (2010)	15 AN	Other female body image	Neutral stimuli	++	-	+	9
Suchan et al. (2013)	10 AN	Other female body image	Neutral stimuli	++	-	+	17
Schweitzer et al. (2018)	20 AN	Other female body image	Scrambled images	++	-	-	7
Uher et al. (2005)	13 AN	Line drawings of undersized, oversized, and normal-sized female body image	Neutral stimuli	++	++	+	6
Via et al. (2018)	20 AN	Other female body image	Own body image	++	-	-	19

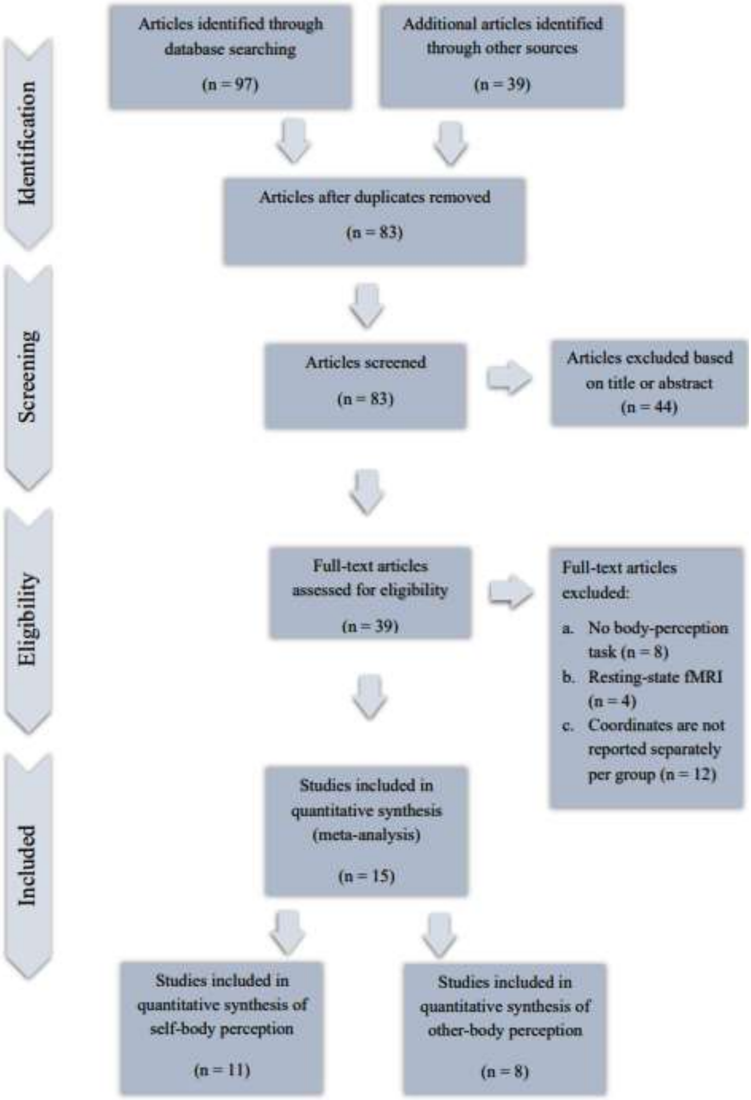
Note. Degree of body image component involvement: ++ = primary involvement; + = secondary involvement; - = no involvement.

Selection procedure

The Preferred Reporting Items for Systematic Review and Meta-analysis Protocols (PRISMA) flowchart by Moher et al. (2009) was applied for systematic identification of eligible papers, see Figure 1. First papers were identified through a databases search, see Search strategy. The identification of papers was completed by an additional screening of the reference lists of papers that underwent full-text assessment and by a manual search for eligible studies. An additional screening process was conducted by removing duplicates of papers that were multiply identified by the different search term combinations. The relevance of a paper's further investigation was determined based on its title and/or abstract. At this point, all irrelevant papers were removed, and the eligibility of the remaining papers was accessed by full-text evaluations. Papers in which the title or abstract contained ambiguous information regarding the paper's relevance for this meta-analysis, underwent a full-text evaluation as well. During this stage, the full text and supplementary material of the remaining papers were assessed to determine their eligibility for inclusion in the quantitative synthesis. This selection process was based on several inclusion criteria, see Article selection, and papers that passed this process were included in the meta-analysis.

Figure 1

PRISMA Flowchart of the Selection Procedure Regarding the Inclusion of Eligible Studies



Activation Likelihood Estimate (ALE) meta-analysis

Single condition analysis

To investigate the neural base of self- and other-body size perception in AN and HC an ALE meta-analysis was exploited, to determine the above-chance convergence of activation probabilities between the included experiments of the studies (Eickhoff et al., 2009). To conduct the meta-analysis BrainMap GingerALE, version 3.0.2, was used. The instructions of Fox et al (2013) were followed, which are based on previous research by Eickhoff et al. (2009), Eickhoff et al. (2011), Eickhoff et al., (2012), and Turkeltaub et al. (2012). Per study, separate worksheets were created for each group (AN; HC) and condition (self; other). Since the file is formatted like GingerALE is expecting, it included the applied reference space (Talairach). For each study, the first author name, publication year, experiment name, and the sample size were reported. The coordinates of activation (x,y,z) were reported in three columns. All non-coordinate data started with "//" and the document was saved as a text file (.txt). Coordinates of activation that were reported in MNI space were transformed into Talairach coordinates as recommended by Fox et al. (2013). The GingerALE, ICBM2TAL transformation was used to accommodates the spatial discrepancy between Talairach and MNI coordinates by transforming the MNI coordinates into Talairach space (Laird et al., 2010). The transformed coordinates of each study were attached to the corresponding worksheets, resulting in four separate conditions (AN-self; AN-other; HC-self; HC-other).

By using the BrainMap GingerALE software ultimately four separate ALE maps were generated that contained significant regions of activation that were consistent across the included studies (Eickhoff et al. 2009). First, per experiment, all reported foci were modelled as Gaussian distributions, whereas the width of the distribution depended on the spatial uncertainty associated with each focus. This spatial uncertainty depended on the sample size of the studies as smaller sample sizes have more spatial uncertainty and larger kernels than studies with large sample sizes (Acar et al., 2018). For each experiment, a modelled activation (MA) map, which contains 3D images of each focus, was calculated. Each MA map contained the probability of activation being located at an exact position based on the reported coordinates of the experiment. Then, the union of the MA maps of all experiments of a condition created the conditions' ALE maps. For each focus of an ALE map, an ALE value was calculated, which increases as more studies reported activation within the focus' voxel range (Acar et al., 2018). To enable spatial inference on the ALE scores, the differentiation between true convergence of foci and random clustering (e.g., noise) was tested by a permutation procedure (Nichols & Hayasaka, 2003). The *P*-value of each coordinate of activation was generated by 1,000 permutations (Eickhoff et al., 2012). The cluster-level family-wise error (FEW) was set at $p < 0.05$ for multiple comparisons with a cluster-forming threshold of $p < 0.001$, uncorrected (Eickhoff et al., 2012; Eickhoff et al., 2016; Roberts et al., 2020). The four ALE maps were separately overlaid onto a Talairach template utilized by the Multi-Image Analysis GUI (MANGO) software.

Conjunction and contrast analysis

Possible significant similarities and differences in activation between and within HC and AN regarding self- and other-body size perception were analysed by exploiting a contrast analysis in GingerALE. In this study four contrast analyses were conducted: AN vs. HC on self-body size perception, AN vs. HC on other-body size perception, self-body size perception vs. other-body-perception within AN, and self-body size perception vs. other-body-perception within HC. The contrast analyses identified areas of significant unique activation between the two included conditions. The conjunction analyses located areas of significant common activation of the two conditions. Per contrast analysis, a pooled analysis regarding the two included conditions was conducted. Two thresholded ALE images, separately for each condition, and a thresholded ALE image of the pooled analysis were included to conduct the contrast analyses. For the analyses, the *P*-value was set to $p < 0.01$ with a permutation threshold of 1,000 and a minimum cluster volume of 200mm³ (Garrigan et al., 2017).

Results

Self-body size perception

Healthy controls

To investigate self-body size perception in HC, 14 separate experiments from nine papers were included in the ALE meta-analysis. Pooled data of the nine studies resulted in a total of 115 foci and a total number of 204 subjects. The ALE meta-analysis showed six significant clusters of activation, see Table 2 and Figure 2.

Table 2

Cluster Analysis of Self-Body Size Perception in HC

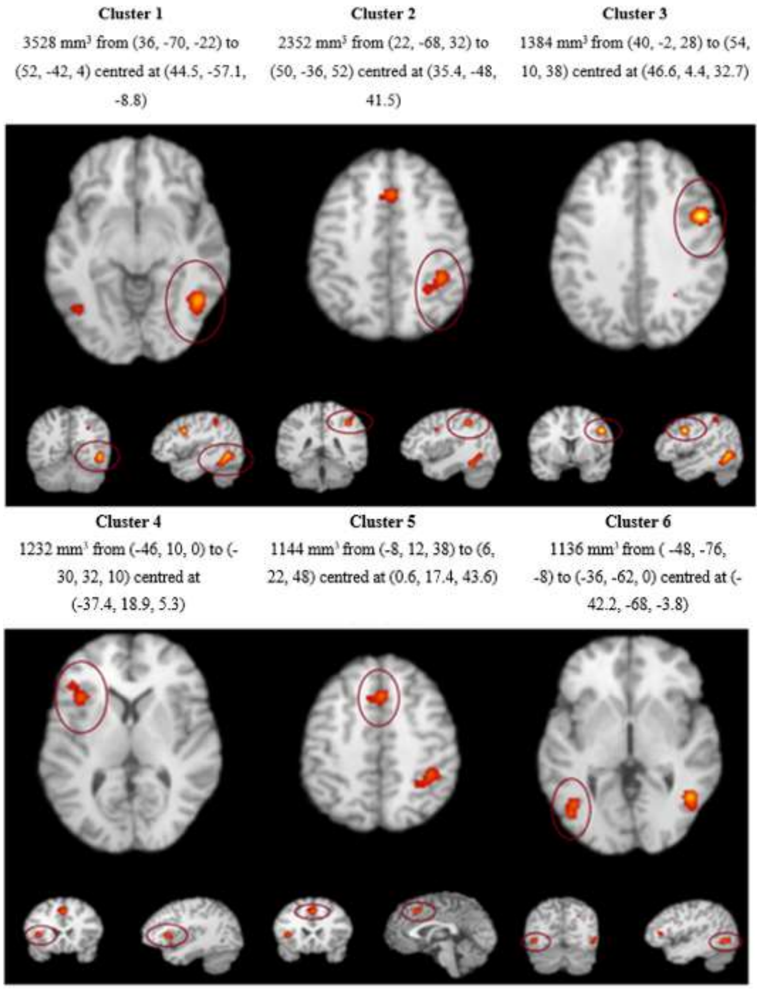
Cluster	Brain region	Voxel peak coordinates			Cluster size (mm^3)	ALE value
		X	Y	Z		
1	Fusiform gyrus/ Culmen/ Inferior temporal lobe/ Middle temporal lobe/ Middle occipital gyrus R	46	-60	-4	3528	0.025420958

2	Inferior parietal lobe/ Precuneus/ Superior parietal lobe R	40	-42	42	2352	0.017441723
		28	-54	36		0.013752752
		24	-64	36		0.012025515
		48	-38	48		0.011034333
3	Precentral gyrus/ Inferior frontal gyrus/ Middle frontal gyrus R	46	4	32	1384	0.028098496
4	Insula/ Inferior frontal gyrus/ Glaustrum L	-36	18	6	1232	0.015400488
		-42	26	8		0.011927958
5	Medial frontal gyrus/ Cingulate gyrus/ Superior frontal gyrus R/L	2	18	42	1144	0.016803652
6	Inferior occipital gyrus/ Middle occipital gyrus/ Inferior temporal gyrus L	-42	-66	-4	1136	0.016811881
		-42	-72	-4		0.01519644

Note. Cluster-level FWE $p < .05$; Threshold permutation 1,000; $p < .001$, uncorrected.

Figure 2

Significant Clusters of Activation during Self-Body Size Perception in HC



Note. Images are overlaid onto Colin 2 x 2 x 2 template in MANGO. The brain images show an axial, sagittal, and coronal view of activation.

Anorexia Nervosa

To investigate self-body size perception in AN, 12 separate experiments from seven papers were included in the ALE meta-analysis. Pooled data of the seven studies resulted in a total of 108 foci and a total number of 171 subjects. The ALE meta-analysis showed five significant clusters of activation, see Table 3 and Figure 3.

Table 3

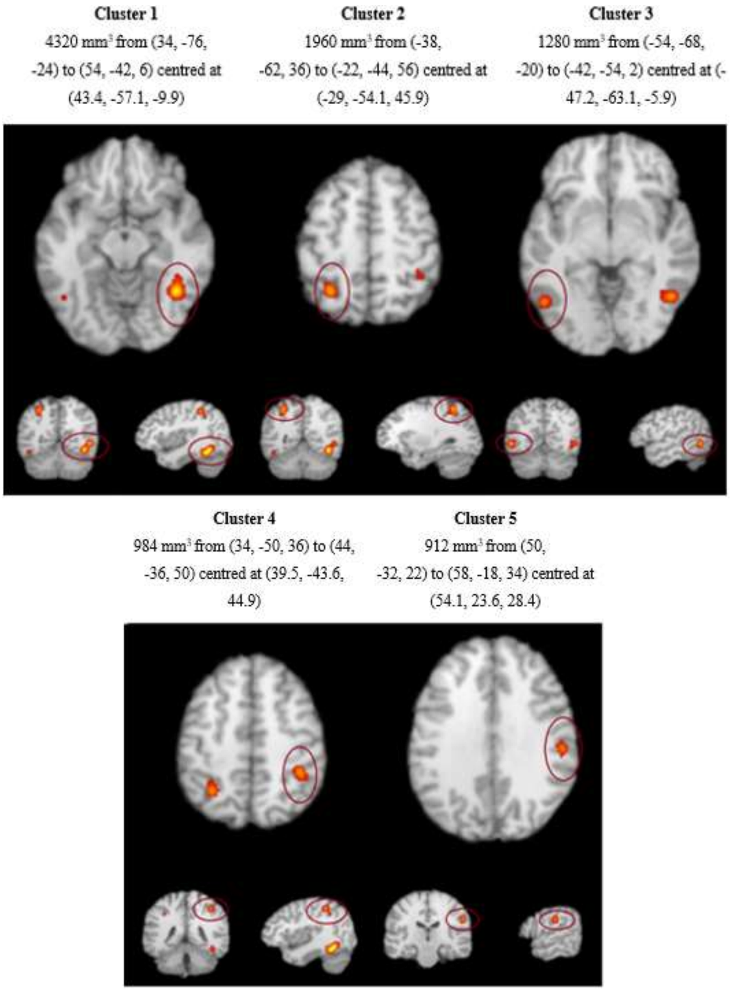
Clusters Analysis of Self-Body Size Perception in AN

Cluster	Brain region	Voxel peak coordinates			Cluster size (mm^3)	ALE value
		X	Y	Z		
1	Fusiform gyrus/ Culmen/ Inferior Temporal gyrus/ Declive/ Middle Temporal gyrus/ Middle occipital gyrus R	40	-56	-14	4320	0.024326235
		48	-60	-2		0.023221174
		50	-70	2		0.01736071
2	Superior parietal lobe/ Precuneus/ Inferior parietal lobe L	-28	-56	50	1960	0.0191293
		-32	-50	42		0.0121562695
3	Inferior temporal gyrus/ Fusiform gyrus/ Middle occipital gyrus/ Declive/ Middle temporal gyrus L	-48	-64	-4	1280	0.018810842
		-44	-58	-16		0.011539851
4	Inferior parietal lobe R	38	-42	46	984	0.017589984
5	Postcentral gyrus/ Inferior parietal lobe R	54	-24	30	912	0.017243195
		54	-32	26		0.00906805

Note. Cluster-level FWE $p < .05$; Threshold permutation 1,000; $p < .001$, uncorrected.

Figure 3

Significant Clusters of Activation during Self-Body Size Perception in AN



Note. Images are overlaid onto Colin 2 x 2 x 2 template in MANGO. The brain images show an axial, sagittal, and coronal view of activation.

Contrast analysis

A contrast analysis was conducted to assess differences in brain activation between AN and HC during self-body size perception. No significant contrast clusters were found between AN and HC.

Conjunction analysis

A conjunction analysis was exploited to assess commonalities in brain activation in both AN and HC during self-body size perception. Three significant common clusters were found, see Table 4 and Figure 4.

Table 4

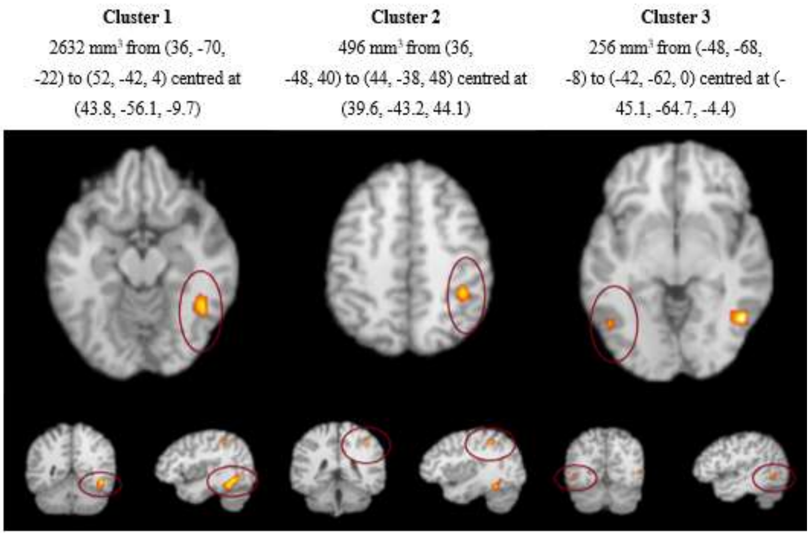
Conjunction Cluster Analysis of Self-Body Size Perception in AN and HC

Cluster	Brain region	Voxel peak coordinates			Cluster size (mm^3)	ALE value
		X	Y	Z		
1	Fusiform gyrus/ Culmen/ Inferior temporal gyrus/ Middle temporal gyrus R	48	-60	-4	2632	0.021915609
		44	-56	-12		0.01743725
		48	-68	0		0.011038791
2	Inferior parietal lobe R	40	-42	44	496	0.015072044
3	Middle occipital gyrus/ Inferior temporal gyrus L	-46	-64	-6	256	0.0119705405
		-44	-64	-2		0.011256053

Note. Conjunction and contrast analysis using $p < 0.01$; Threshold permutation 1,000; minimum volume = 200 mm^3 .

Figure 4

Significant Common Clusters of Activation during Self-Body Size Perception in AN and HC



Note. Images are overlaid onto Colin 2 x 2 x 2 template in MANGO. The brain images show an axial, sagittal, and coronal view of activation.

Other-body size perception

Healthy controls

To investigate other-body size perception in HC, 11 separate experiments from eight papers were included in the ALE meta-analysis. Pooled data of the eight studies resulted in a total of 119 foci and a total number of 169 subjects. The ALE meta-analysis showed five significant clusters of activation, see Table 5 and Figure 5.

Table 5

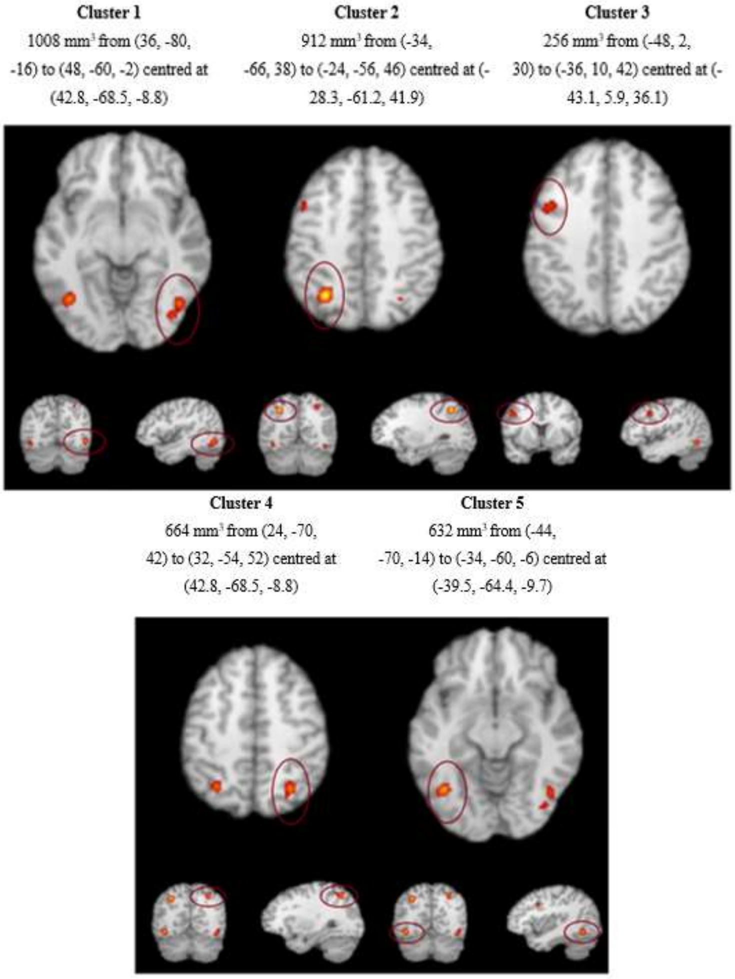
Cluster Analysis of Other-Body Size Perception in HC

Cluster	Brain region	Voxel peak coordinates			Cluster size (mm^3)	ALE value
		X	Y	Z		
1	Fusiform gyrus/ Inferior occipital gyrus/ Declive/ Middle occipital gyrus R	46	-68	-6	1008	0.015128084
		42	-62	-14		0.012901524
		40	-76	-8		0.011939297
2	Superior parietal lobe/ precuneus/ inferior parietal lobe L	-28	-62	42	912	0.02208934
3	Precentral gyrus/ middle frontal gyrus/ inferior frontal gyrus L	-42	6	34	760	0.011797157
4	Superior parietal lobe/ precuneus R	30	-64	46	664	0.015015515
5	Fusiform gyrus/ Declive L	-40	-64	-10	632	0.01679484

Note. Cluster-level FWE $p < .05$; Threshold permutation 1,000; $p < .001$, uncorrected.

Figure 5

Significant Clusters of Activation during Other-Body Size Perception in HC



Note. Images are overlaid onto Colin 2 x 2 x 2 template in MANGO. The brain images show an axial, sagittal, and coronal view of activation.

Anorexia Nervosa

To investigate other-body size perception in AN, eight separate experiments from seven papers were included in the ALE meta-analysis. Pooled data of the seven studies resulted in a total of 74 foci and a total number of 110 subjects. The ALE meta-analysis showed four significant clusters of activation, see Table 6 and Figure 6.

Table 6

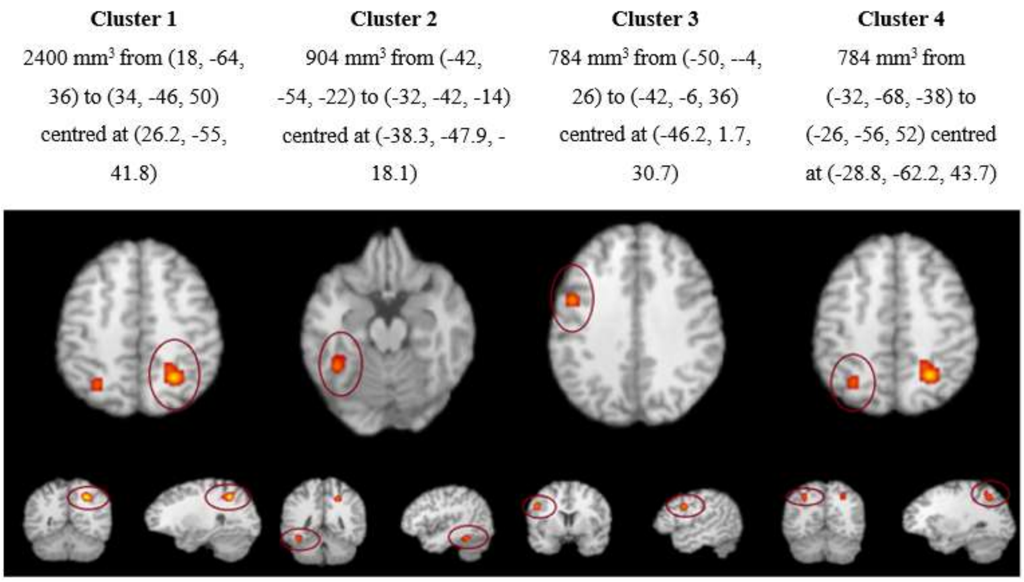
Cluster Analysis of Other-Body Size Perception in AN

Cluster	Brain region	Voxel peak coordinates			Cluster size (mm^3)	ALE value
		X	Y	Z		
1	Superior parietal lobe/ precuneus R	26	-56	42	2400	0.024262615
		22	-50	42		0.016255502
2	Culmen/ Fusiform gyrus/ Declive L	-38	-50	-18	904	0.015242107
3	Precentral gryrus/ Inferior frontal gyrus/ Middle frontal gyrus L	-46	2	30	784	0.017199472
4	Superior parietal lobe/ Precuneus L	-30	-64	42	784	0.01409754

Note. Cluster-level FWE $p < .05$; Threshold permutation 1,000; $p < .001$, uncorrected.

Figure 6

Significant Clusters of Activation during Other-Body Size Perception in AN



Note. Images are overlaid onto Colin 2 x 2 x 2 template in MANGO. The brain images show an axial, sagittal, and coronal view of activation.

Contrast analysis

A contrast analysis was conducted to assess differences in brain activation between AN and HC regarding other-body size perception. No significant contrast clusters were found for HC > AN. One significant contrast cluster was found for AN > HC, see Table 7 and Figure 7.

Table 7

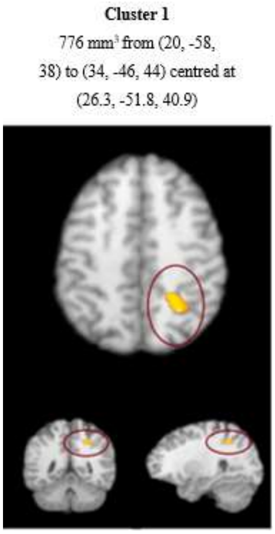
Contrast Cluster Analysis of Other-Body Size Perception between AN > HC

Cluster	Brain region	Voxel peak coordinates			Cluster size (mm^3)
		X	Y	Z	
1	Superior Parietal	28	-58	42	776
	lobe/ Precuneus R	24.3	-48.8	40.5	

Note. Conjunction and contrast analysis using $p < 0.01$; Threshold permutation 1,000; minimum volume = 200 mm^3 .

Figure 7

Significant Contrast Cluster of Activation during Other-Body Size Perception between AN and HC



Note. Images are overlaid onto Colin 2 x 2 x 2 template in MANGO. The brain images show an axial, sagittal, and coronal view of activation.

Conjunction analysis

A conjunction analysis was exploited to assess commonalities in brain activation in both AN and HC during other-body size perception. Three significant common clusters were found, see Table 8 and Figure 8.

Table 8

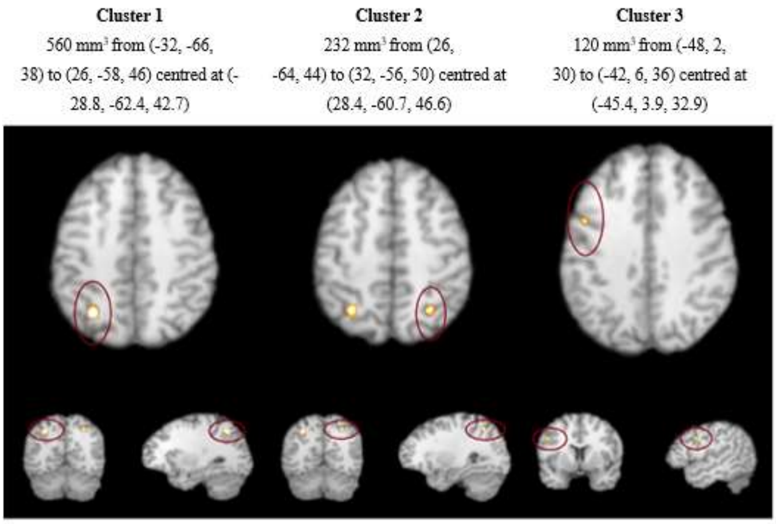
Conjunction Analysis of Other-Body Size Perception in AN and HC

Cluster	Brain region	Voxel peak coordinates			Cluster size (mm^3)	ALE value
		X	Y	Z		
1	Superior parietal lobe/ Precuneus L	-30	-64	42	560	0.01409754
2	Superior parietal lobe/ Precuneus R	28	-60	46	232	0.011972826
3	Inferior frontal gyrus/ Precentral gyrus/ Middle frontal gyrus L	-46	4	34	120	0.010632668

Note. Conjunction and contrast analysis using $p < 0.01$; Threshold permutation 1,000; minimum volume = 200 mm^3 .

Figure 8

Significant Common Clusters of Activation during Other-Body Size Perception in AN and HC



Note. Images are overlaid onto Colin 2 x 2 x 2 template in MANGO. The brain images show an axial, sagittal, and coronal view of activation.

Contrast and conjunction analysis within HC

Contrast analysis

A contrast analysis was conducted to assess differences in brain activation between other-body size perception and self-body size perception within HC. No significant contrast clusters were found between self-body size perception and other-body size perception.

Conjunction analysis

A conjunction analysis was exploited to assess commonalities in brain activation regarding other-body size perception and self-body size perception within HC. One significant common cluster was found, see Table 9 and Figure 9.

Table 9

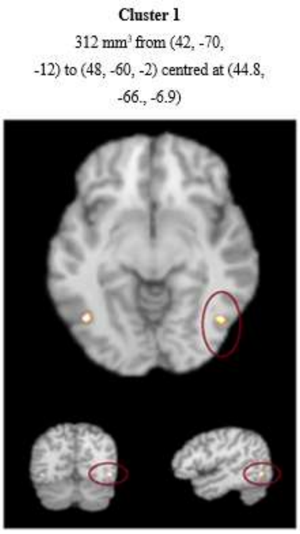
Conjunction Cluster Analysis of Self-Body Size Perception and Other-Body Size Perception in HC

Cluster	Brain region	Voxel peak coordinates			Cluster size (mm^3)	ALE value
		X	Y	Z		
1	Fusiform gyrus R	44	-66	-6	312	0.013058954

Note. Conjunction and contrast analysis using $p < 0.01$; Threshold permutation 1,000; minimum volume = 200 mm^3 .

Figure 9

Significant Common Cluster of Activation during Self-Body Size Perception and Other-Body Size Perception in HC



Note. Images are overlaid onto Colin 2 x 2 x 2 template in MANGO. The brain images show an axial, sagittal, and coronal view of activation.

Contrast and conjunction analysis within AN

Contrast analysis

A contrast analysis was conducted to assess differences in brain activation between other-body size perception and self-body size perception within AN. No significant contrast clusters were found regarding self-body size perception > other-body size perception. One significant contrast cluster was found regarding other-body size perception > self-body size perception, see Table 10 and Figure 10.

Table 10

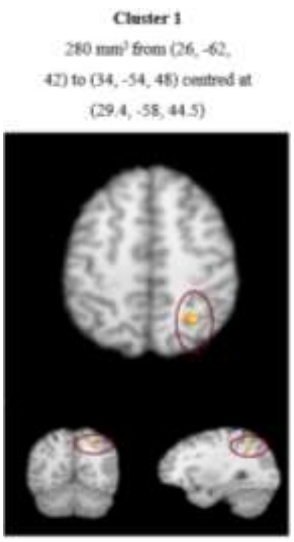
Contrast Cluster Analysis between Other-Body Size Perception > Self-Body Size Perception in AN

Cluster	Brain region	Voxel peak coordinates			Cluster size (mm³)
		X	Y	Y	
1	Superior parietal lobe R	32	-60	45	280
		28	-58	46	
		28	-54	44	

Note. Conjunction and contrast analysis using $p < 0.01$; Threshold permutation 1,000; minimum volume = 200 mm^3 .

Figure 10

Significant Contrast Cluster of Activation during Self-Body Size Perception and Other-Body Size Perception in AN



Note. Images are overlaid onto Colin 2 x 2 x 2 template in MANGO. The brain images show an axial, sagittal, and coronal view of activation.

Conjunction analysis

A conjunction analysis was exploited to assess commonalities in brain activation regarding other-body size perception and self-body size perception within. One significant common cluster was found, see Table 11 and Figure 11.

Table 11

Conjunction Cluster Analysis of Self-Body Size Perception and Other-Body Size Perception in AN

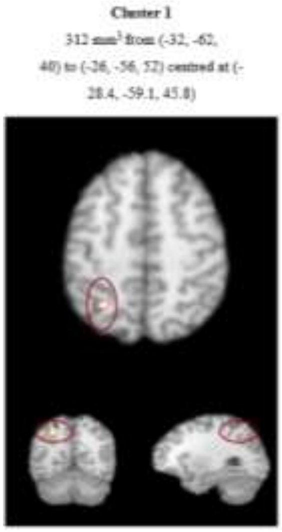
Cluster	Brain region	Voxel peak coordinates			Cluster size (mm³)	ALE value
		X	Y	Y		

1	Superior parietal lobe/ Precuneus L	-28	-60	44	312	0.012862321

Note. Conjunction and contrast analysis performed using $p < 0.01$; Threshold permutation 1,000; minimum volume = 200 mm^3 .

Figure 11

Significant Common Cluster of Activation during Self-Body Size Perception and Other-Body Size Perception in AN



Note. Images are overlaid onto Colin 2 x 2 x 2 template in MANGO. The brain images show an axial, sagittal, and coronal view of activation.

Discussion

This study investigated neural activation during self and other-body size perception in AN patients and HC. During self-body size perception reduced activation in the precuneus, the IPL, the RSC, and the MFG was expected in AN compared to HC. During other-body size perception same neural activation was expected in both groups. During self-body size perception, no differences in brain activation were found, whereas common brain activity was registered in the right fusiform gyrus (FFG), the right temporal gyrus, the middle temporal gyrus, the IPL, the left middle occipital gyrus, and the left inferior temporal gyrus. During other-body size perception, AN patients showed increased brain activation in the right SPL/precuneus compared to HC, whereas HC did not exhibit increased brain activation during other-body size perception compared to AN. Also, common brain activation in the left SPL/precuneus, the right SPL/precuneus, the left inferior frontal gyrus, the left precentral gyrus, and the left MFG was found during other-body size perception in both AN and HC. In HC, no difference in brain activation was found between self and other-body size perception, whereas common activation was found in the right FFG. In AN, increased brain activation was found in the right SPL during other-body size perception compared to self-body size perception, whereas common activation was found in the left SPL/precuneus. Based on these results both hypotheses were rejected.

The most striking finding of this study was the lack of difference in brain activation in the parietal and frontal regions between AN and HC during self-body size perception. This might suggest that brain activation during self-body size perception in AN is less deviant than previously presumed. Body image dissatisfaction is a predominant phenomenon amongst women in Western society and often associated with perceiving oneself as being too fat (Kostanski et al., 2004). Wagner et al. (2003) suggest that, like AN patients, healthy women are concerned about their appearance as well. Therefore, they pay more attention to evaluate their own body. As a result, healthy women show greater overestimation of their body size and are more sensitive to changes in their body size compared to men (Aleong & Paus, 2010). Therefore, brain activation between HC and AN during self-body size perception tasks might be similar. Still, it does not explain why AN patients show distorted self-body size perception.

A different neural explanation might come from resting-state fMRI (rs-fMRI) studies. According to McFadden et al. (2014) and Scaife et al. (2017) AN patients show reduced resting-state functional connectivity (rsFC) in the salience network (SN), the default mode network (DMN), and brain networks involved in somatosensory processing compared to HC. The SN is relevant for salient processing external and internal from the own body (Geisler et al., 2016). Reduced rsFC in the SN, especially between the insula and the thalamus, might explain the impaired integration of visuospatial and homeostatic input in AN patients, contributing to distorted self-body size perception. The default mode network (DMN) is involved in internally oriented cognition such as self-referential- and self-evaluative processing, mentalizing, interoception, body memory recall, self-judgment, including the evaluation of one’s own body (Davey et al., 2010; McFadden et al., 2014; Via et al., 2018). Normally, brain areas of the DMN are synchronously active during resting periods compared to tasks. The main DMN nodes include the precuneus, the RSC, the IPL, the hippocampal formation, the lateral temporal cortex, the insula, and the medial prefrontal cortex (De Havas et al., 2012; Via et al., 2018). During resting-state these regions show correlated signal fluctuations suggesting functional connectivity (Greicius et al., 2003). However, reduced DMN connectivity, as found in AN (McFadden et al., 2014), indicates less connectivity. Since most of the brain regions of the DMN seem to be involved in self-body size perception, reduced integration of bodily information during rest might cause distorted self-body size perception in AN. As the connectivity of the DMN gets reduced during task performance (Via et al., 2018), it might explain why AN patients and HC showed similar neural activation during body size perception tasks. Therefore, the differences in neural activation, responsible for distorted self-body size perception in AN, probably arise during rest.

Another explanation why no difference in brain activation was found during self-body size perception might be due to reduced hemispheric connectivity in processing bodily information in AN. According to Aleong and Paus (2010), women exhibit selective brain activation in the right EBA and right FBA when looking at human bodies compared to men (Downing et al., 2007). Mohr et al. (2007) found that women show an increased bias in identifying body sizes as fatter than they are when presenting the body images either only to the left visual field or right visual field. However, this bias disappears when the body image is presented to the central visual field. This might suggest that correct body size perception relies on the integration of visual input from both hemispheres. However, according to Nickel et al. (2019), AN patients show reduced white matter structure in the body of corpus callosum (CC), caused by myelin loss due to malnutrition. The body of the CC facilitates inter-hemispheric communication of frontal, and parietal regions and is involved in perceptual, motor, and cognitive functions. However, reduced white matter integrity in the CC seems to affect inter-hemispheric communication. In specific, Canna et al. (2017) suggest that reduced inter-hemispheric functional connectivity in the precuneus and insula causes alterations in self-awareness processing and interoceptive awareness in AN. This indicates that reduced inter-hemispheric connectivity might be a contributing factor to distorted higher-order processing regarding self-body size perception in AN.

Common activation within the fusiform gyrus, the IPL, and the inferior temporal gyrus/ middle occipital gyrus in AN patients and HC can be explained by sensory processing of body stimuli. The FBA, located in the fusiform gyrus, the EBA, located in the inferior temporal sulcus (Amoruso et al., 2011), and the IPL are involved in body detection (Hodzic et al., 2009). The FBA and the IPL are also involved in body identification. Additionally, the IPL is responsible for the distinction between the own body and other bodies. Common activation confirms that body detection, identification, and distinction is similar in AN and HC and that distorted self-body size perception occurs on a higher level of processing.

Regarding other-body size perception, AN patients exhibit increased activation of the right superior parietal lobe (SPL)/precuneus compared to HC. The precuneus is assumed to be involved in reflective self-awareness (Cavanna, 2007) and self-referential processing such as describing one’s personality and physical appearance (Kircher et al., 2000) but also in self-other body evaluation, perspective-taking, and theory of mind (Via et al., 2018). However, the increased activation in the precuneus might be an indication that AN patients have an increased tendency of comparing themselves to bodies of other women through self-referential processes. Ultimately, this leads to maladaptive self-other body evaluations (Via et al., 2018).

Another reason for increased activation in the precuneus might come from structural brain imaging studies. Multiple studies reported grey matter reduction in the precuneus in AN (Joos et al., 2010; Titova et al., 2013), with a disease duration less than a year (Gaudio et al., 2011), longer than a year (Joos et al., 2010) but also in females who recovered from AN for over 5 years (Joos et al., 2011). Increased functional activation in the precuneus might be a sign of a compensatory process for more efficient neural processing due to reduced volume (Soloveva et al., 2018). Since AN patients have more difficulties in processing and understanding information from other people during body image processes, they must rely on compensatory strategies during other-body size perception (Via et al., 2018). However, AN patients also show lower identification with their own bodies (Mölbert et al., 2017). If increased activation of the precuneus is indeed a compensatory strategy during body size perception, it seems interesting that increased activation of the precuneus only arises during other-body size perception and not during self-body size perception. Therefore, lack of activation in the precuneus might contribute to distorted self-body size perception in AN.

Compared to self-body size perception, common activation in AN and HC in various frontal regions during other-body size perception might explain distorted self-body size perception in AN as well. As previously mentioned, the MFG is involved in short-term maintenance, processing, and updating of body images (Favaro et al., 2012). During other-body size perception HC and AN patients exhibited common brain activation in the MFG, which suggests that AN patients process and update body images of other women comparable to HC. However, as HC show significant activation in the MFG during self-body size perception as well, AN patients do not. Also, no common activation in the MFG during self-body size perception was found for AN and HC. This might indicate that AN patients have problems with processing and updating their body images. Therefore, the MFG might be involved in distorted self-body size perception in AN.

Additionally, the right SPL/precuneus showing common and different activation during other-body size perception between AN and HC is contradictive. However, the contrast activation that was found in the SPL is more anteriorly compared to the common activation in the SPL. Wang et al. (2015) identified five subregions in the SPL. The two anterior subregions are involved in action processes and visually guided visuomotor functions. The three posterior subregions are primarily associated with visual perception, spatial cognition, reasoning, working memory, and visuospatial attention (Wang et al., 2015; Wu et al., 2016). Additionally, the anterior region of the precuneus is associated with self-centered mental imagery, whereas posterior region of the precuneus subserves episodic memory retrieval due to connections to the RSC (Cavanna, & Trimble, 2006). As previously mentioned, AN patients show increased precuneus activation during other-body size perception probably due to increased self-other comparison through self-referential processes (Via et al., 2018). Since the anterior region of the precuneus is involved in self-referential processing (Cavanna, & Trimble, 2006), it might explain why increased activation in AN during other-body size perception was limited to the anterior part of the SPL/precuneus. Additionally, the posterior SPL and precuneus seem to be involved in cognitive functions relevant for general visual task performance, like visual and spatial perception (Calhoun et al., 2001), and attention (Wilder et al., 2009). This might account for the common activation found in the posterior regions the SPL/precuneus in AN and HC. However, additional research might be necessary to investigate the role of the SPL/precuneus in other-body size perception for more conclusive results.

Still, some limitations of the study need to be addressed. First, the number of studies and experiments involved in each analysis might have led to underpowered results. Eickhoff et al. (2016) recommend at least 20 experiments per ALE-analysis when using a cluster-level FWE thresholding to create valid and decent power. For contrast analysis, GingerALE recommends at least 25 experiments for valid power. In this study, the number of experiments for single analyses varied between 8-14 experiments, whereas contrast analysis included 19-26 experiments. Results of analyses that include less than 20 experiments are most likely driven by an individual experiment and only have sufficient power to detect effects that are extremely obvious (Eickhoff et al., 2016). The results might have differed or might have been more conclusive if more studies would have been available to include in the meta-analysis.

Another issue that might have affected the outcomes of the meta-analysis is the possibility of publication biases, which occurs when the results of published and unpublished studies significantly differ (Acar et al., 2018). As statistically significant findings are more likely to get published than studies with non-significant results, non-significant results often remain hidden. This might have influenced the outcome of the meta-analysis by overestimating the effects of neural impairments on distorted self-body size perception in AN, as no contra-evidence is available to consider.

Furthermore, regarding the methodology of the studies, the type of used stimuli is very limited regarding the concept of body size perception. All studies used visual information to measure body size perception, which makes comparison very straight forward. However, as previously mentioned self-body perception incorporates more than visual perception of the own body. Interoceptive, proprioceptive, and vestibular information also contributes to the concept of self-body perception (Riva, 2018) but are not included in any of the studies. Therefore, a great amount of information might be missing that could contribute to a better understanding of the neural basis of distorted self-body size perception in AN.

Another critical point must be made regarding the methodology of the included studies, as the measured type of body perception (perceptual; affective; cognitive) varied between the experiments (See Methods, Table 2). According to Gaudio and Quattrocchi (2012), the perceptive component seems to be related to the precuneus and the IPL, the affective component seems to be mainly related to the prefrontal cortex, the insula, and the amygdala, whereas the cognitive component has been weakly explored. Even though all studies measure one or more components of body size perception the different brain regions involved in each component reduce comparability. Therefore, results regarding the involvement of frontal and parietal regions in self-body size perception might have been less conclusive.

Also, a reason why no increased activation during self-body size perception was found, might be caused by the choice of the researchers to show only images of headless bodies during the own body conditions. This could have reduced the sense of self-reference during self-body size perception tasks (Via et al., 2018).

Conclusion

In summary, this study provided evidence that neural activation in the precuneus, the IPL, the MFG, and the RSC seems to be similar in AN and HC during self-body size perception. However, during other-body size perception, AN patients show increased activation in the right SPL/precuneus compared to HC. Still, the exact involvement of different brain structures and brain networks in self- and other-body size perception remains unclear. Previous studies mainly reported contradictory results, which could be explained by different methodological approaches used to investigate body size perception. Regarding self-body size perception, experiments exclusively involved visual stimuli, which seems insufficient to measure the multisensory concept of self-body size perception. Therefore, interpretations regarding self-body size perception must be made with caution. Further research will be necessary to investigate the neural basis of self-body size perception more closely by exploring proprioception, interoception, and the vestibular system as well. Also, rsFC might provide information to disentangle the concept of distorted self-body size perception in AN. Therefore, both rsFC and task-related neural activation could provide valuable insight and information to improve knowledge and treatment options regarding distorted self-body size perception in AN.

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