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Does depression matter in neuropsychological performances in anorexia nervosa? A descriptive review

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ABSTRACT

Objective. This review aims to examine the impact of depressive symptoms on the assessment of cognitive flexibility, central coherence, and decision-making in individuals with anorexia nervosa (AN).

Method. An online search was carried out using PubMed and PsycInfo. Articles were selected for review if they were published in English between 1990 and 2014 and used the Wisconsin Card Sorting Test, the Trail Making Task parts A and B, the Brixton Test, the Rey-Osterrieth Complex Figure Test, and/or the Iowa Gambling Task.

Results. Sixty-two studies were included. Thirty (48%) of the studies statistically assessed the association between depression and neurocognition in AN versus healthy controls. Where significant correlations were found, it became clear that the more serious the depression, the greater the neuropsychological impairment. Only six (10%) studies examined whether increased depressive symptoms were able to eliminate the differences between individuals with AN and healthy controls, and one study found that depressive symptoms did eliminate group differences in cognitive flexibility and decision-making.

Discussion. Only a subgroup of articles on neuropsychology in AN adjusted for depression. However, given the role of depression that some articles suggest, future studies should pay closer attention to the evaluation of this potential confounder.

Keywords: anorexia nervosa; neuropsychology; depression; cognitive flexibility; central coherence; decision making.

EMPIRICAL ARTICLE

Introduction

Major depressive disorder is a frequent comorbid condition of anorexia nervosa (AN),[1, 2] and the impact of depressive symptoms on neurocognition has been acknowledged.[3] In fact, literature has reported depressed patients to have altered set-shifting[4-6] and decision-making[7] abilities. Several mechanisms may underlie such alterations, including attention, memory, emotional information, motivation, rumination, and response to failure[8].

However, the available body of evidence on the potential role of depression on neuropsychological performances of patients with eating disorders is still debated.[9, 10] Regarding AN, results are even more mixed, with studies proposing a depression-related impairment in cognitive flexibility, mainly with respect to attention[11] and serotonin dysregulation.[12] A few reviews on neuropsychological domains in AN exist,[13-18] but none of them specifically address depression-related aspects.

The main aim of this work is twofold: (1) to examine whether depressive symptoms were assessed in patients with AN in studies evaluating cognitive flexibility, central coherence, and decision-making. The latter domains were chosen given their well-established alterations[17] in AN; (2) to outline the body of evidence currently available on the effects of depression on neuropsychology in AN. In fact, where depression is present, the different performances on neuropsychology found between healthy controls (HC) and those with AN might be due to depression rather than the AN pathology.

Methods

Two independent researchers (S.B. and M.A.) carried out an online search on PubMed and PsycInfo databases. A hand search of the reference lists of all articles meeting the inclusion criteria was also performed.

The following inclusion criteria were adopted: (1) articles published between 1990 and 2014; (2) studies focusing on currently ill adults with AN; (3) works on cognitive flexibility, decision-making, and central coherence; (4) original research articles; (5) English language; (6) HC as a comparison group; (7) use of the following tests: Wisconsin Card Sorting Test (WCST), Trail Making Task parts A and B (TMT-A/-B), Brixton Test, Rey-Osterrieth Complex Figure Test (ROFT), and Iowa Gambling Task (IGT). Reviews and case reports were excluded.

To ascertain the second aim of this review, we focused on two main statistical methods: (1) correlational analyses (Pearson's or Spearman's linear correlations), and (2) statistical adjustments for depression (e.g., univariate general linear model [UGLM], multivariate analysis of variance [MANOVA], multivariate analysis of covariance [MANCOVA]). The former analyses identify a bidirectional evaluation between depression and neuropsychology. The latter instead aim to verify whether depression can explain the difference on neuropsychological performance between AN and HC.

The search keywords included the following: "eating disorders" OR "anorexia nervosa", AND "neuropsychology", OR "cognitive flexibility", OR "decision-making", OR "rigidity", OR "set-shifting", OR "central coherence", OR "Wisconsin Card Sorting Test", OR "Iowa Gambling Task", OR "Trail Making Task", OR "Brixton Test", OR "Rey-Osterrieth Complex Figure Test".

Results

In total, the initial search yielded 77 studies (72 using the online search and five with the hand search); however, 15 articles were excluded because six were reviews,[13-18] two were case reports,[19, 20] four had no HC group,[21-24] and three showed recovered individuals[25-27]. Thus, 62 studies were finally included.

Of all studies considered, 30 (48%)[1, 9, 28-55] statistically addressed the influence of depression on cognitive flexibility, central coherence, and decision-making. However, only six studies[1, 30, 36, 37, 41, 51] statistically controlled for depression, and one article[1] concluded that depression was able to erase the difference between AN and HC, concerning both cognitive flexibility and decision-making. Of 16 studies[9, 31, 32, 35, 38, 41-46, 48, 49, 53-55] on cognitive flexibility performing correlations, 14 studies[31, 32, 35, 38, 41, 42, 44-46, 48, 49, 53-55] found nonsignificant findings and two studies[9, 43] reported significant positive correlations between depression and suboptimal neurocognition. Moreover, of those papers that did not take depression statistically into account, 24 articles[56-79] did not acknowledge the lack of investigation of depression as a limitation. In addition, 29 studies[9, 29, 31, 39, 43, 46-50, 52, 55-57, 62, 63, 66-73, 79-83] were conducted on a sample of less than 30 affected participants.

Assessment *of Neuropsychological Domains*

Cognitive Flexibility

Both not computerized and adapted computerized versions of WCST[84], TMT-A/-B[85], and Brixton Test[86] have been included.

Forty-three studies[1, 9, 31, 32, 35-38, 41-46, 48, 49, 51, 53-56, 58, 60-62, 64, 67-73, 75-77, 79, 81-83, 87-89] investigated cognitive flexibility and 29 articles[1, 31, 32, 35-38, 41, 43, 44, 46, 48, 49, 51, 53, 61, 62, 67, 68, 71, 72, 75-77, 81-83, 88, 89] found significant differences between patients with AN and HC on this neuropsychological domain (Table 1).

Thirty-five studies[1, 9, 31, 32, 35-38, 41-46, 48, 49, 51, 53-55, 60,61, 67-73, 75, 79, 82, 83, 88, 89] investigated depression and 20 articles[1, 9, 31, 32, 35-38, 41-46, 48, 49, 51, 53-55] included this assessment in subsequent statistical analyses yielding significant findings in three cases[1, 9, 43] (Fig. 1a). With more detail, of 16 studies[9, 31, 32, 35, 38, 41-46, 48, 49, 53-55] performing correlations, 14 studies[31, 32, 35, 38, 41, 42, 44-46, 48, 49, 53-55] found nonsignificant findings, whereas two studies[9, 43] reported instead significant positive correlations demonstrating that the greater the depression score, the more impaired the neuropsychological performance. Five studies[1, 36, 37, 41, 51] controlled the difference between AN and HC for depression, and in one case[1], such a difference did not hold significant after statistical control.

TABLE 1. Studies on cognitive flexibility, decision-making, central coherence, and their evaluation of depression (N = 62)

Article	Sample	Mean Age (years)	Gender	Neuropsychological Domains Investigated and Main Results Comparing AN versus HC	Instrument Used to Assess Depression	Correlations Between Neuropsychological Performance and Depression in AN	Control for Depression
Abbate-Daga et al., 2011[1]	30 AN; 30 HC	24.1 AN; 24.7 HC	All females	Cognitive flexibility: ≠ Decision making: ≠	BDI	—	UGLM Depression Sig. (F and p values not available)
Adoue et al., 2014[28]	63 AN; 49 HC	24.8 AN; 30.3 HC	All females	Decision making: ≠	BDI	NS (rho and *p* values not available)	—
Arbel et al., 2013[56]	15 AN; 10 EDNOS-AN; 25 HC	23.8 AN; 23.1 HC	All females	Cognitive flexibility: =	—	—	—
Bodell et al., 2014[29]	15 AN-R; 7 AN-BP; 20 HC	25.6 AN	All females	Decision making: ≠	HDRS	NS (*r* and *p* values not available)	—
Brogan et al., 2010[80]	22 AN; 17 BN; 18 OB; 20 HC	29.1 AN; 29.9 BN; 52.1 OB; 27.7 HC	All females	Decision making: ≠	—	—	—
Castro-Fornieles et al., 2009[57]	12 AN; 9 HC	14.5 AN; 14.6 HC	AN: 91.67% females HC: 88.89% females	Central coherence: =	CDI	—	—
Cavedini et al., 2004[58]	26 AN-R; 33 AN-BP; 82 HC	21.7 AN-R; 23.4 AN-BP; 30.9 HC	AN-R: 96.1% females AN-BP: 96.6% females HC: 52.4% females	Cognitive flexibility: = Decision making: ≠	—	—	—
Cavedini et al., 2006[59]	18 AN-R; 20 AN-BP; 30 HC	23.8 AN-R; 21.5 AN-BP; 22.6 HC	All females	Decision making: ≠	—	—	—
Chan et al., 2014[30]	94 AN; 63 BN; 67 HC	25.6 AN; 26.9 BN; 25.5 HC	97% females	Decision making: =	BDI	NS (*r* and *p* values not available)	Test statistics not available Depression NS (*F* and *p* values not available)
Danner et al., 2012[31]	16 AN; 15 AN-Rec; 15 HC	25.6 AN; 24.3 AN-rec; HC 25.8	All females	Cognitive flexibility: ≠ Decision making: = Central coherence: =	BDI-II	Cognitive flexibility: WCST perseveration $r = 0.13$, $p =$ NS Decision making: IGT $r = 0.24$, $p =$ NS Central coherence: ROFT copy $r = -0.12$, $p =$ NS ROFT recall $r = 0.10$, $p =$ NS	—
Dmitrzak-Weglarz et al., 2013[60]	46 AN-R; 14 AN-BP; 45 HC	15.7 AN-R; 16.5 AN-BP; 37.7 HC	All females	Cognitive flexibility: =	BDI	—	—
Fagundo et al., 2012[61]	35 AN; 52 OB; 137 HC	28.1 AN; 40.5 OB; 24.8 HC	All females	Cognitive flexibility: ≠ Decision making: ≠	SCL-90-R	—	—
Fassino et al., 2002[62]	20 AN-R; 20 HC	23.8 AN; 23.1 HC	All females	Cognitive flexibility: ≠	—	—	—
Favaro et al., 2012[63]	29 AN; 16 AN-Rec; 26 HC	25.8 AN; 23.8 AN-Rec; 26.7 HC	All females	Central coherence: ≠	HSCL	—	—
Favaro et al., 2013[32]	73 AN-R; 93 AN-Rec; 140 HC	25.0 AN; 27.2 HC	All females	Cognitive flexibility: ≠	HSCL	Cognitive Flexibility: WCST global score $r = -0.03$, $p =$ NS	-
Fitzpatrick et al., 2012[87]	32 AN; 22 HC	14.9 AN; 15.4 HC	All females	Cognitive flexibility: =	—	—	—
Galimberti et al., 2013[81]	29 AN; 29 UR-AN; 29 HC; 29 UR-HC	24.1 AN; 43.8 UR-AN; 28.6 HC; 43.3 UR-HC	All females	Cognitive flexibility: ≠ Decision making: ≠	—	—	—
Garrido et al., 2013[33]	27 AN-R; 24 AN-BP; 20 BN; 38 HC	25.9 AN-R; 28.2 AN-BP+BN; 23.3 HC	All females	Decision making: ≠	BDI	NS (r and p-values not available)	—

TABLE 1. *Continued*

Article	Sample	Mean Age (years)	Gender	Neuropsychological Domains Investigated and Main Results Comparing AN versus HC	Instrument Used to Assess Depression	Correlations Between Neuropsychological Performance and Depression in AN	Control for Depression
Giel et al., 2013[9]	15 AN; 20 UD; 35 HC	23.9 AN; 36.3 UD; 30.2 HC	AN: 100% females UD: 60% females HC: 77%females	Cognitive flexibility: =	QIDS-SR	Cognitive Flexibility: WCST: rho = 0.33, $p = 0.006$ TMT: rho = 0.31, $p = 0.041$	—
Gillberg et al., 2007[64]	51 AN; 51 HC	24.5 AN; 24.2 HC	Not available	Cognitive flexibility: =	—	—	—
Goddard et al.,2014[82]	29 AN; 42 HC	26.2 AN; 26.4 HC	All males	Cognitive flexibility: ≠ Central coherence: ≠	DASS-21	—	—
Guillaume et al., 2010[89]	49 AN; 38 BN; 83 HC	23.3 AN; 23 BN; 28 HC	All females	Decision making: =	HDRS	—	—
Harrison et al., 2011[34]	35 AN-R; 15 AN-BP; 48 BN; 35 AN-Rec; 89 HC	27.1 ED group; 29 AN-Rec, 28.5 HC	All females	Central coherence: ≠	DASS-21	Overall ED group: NS (rho and p values not available)	—
Heled et al., 2014[65]	30 AN; 30 AN-WR; 44 HC	23.2 AN; 24.6 AN-WR; 24.5 HC	All females	Central coherence: ≠	—	—	—
Holliday et al., 2005[35]	47 AN; 47 US-AN; 47 HC	26.3 AN; 27.6 US-AN; 26.5 HC	All females	Cognitive flexibility: ≠	HADS	Overall ED group: NS (r and p values not available)	—
Jones et al., 1991[36]	30 AN; 20 AN-WR; 38 BN; 39 HC	24.4 AN; 26 AN-WR; 24.1 BN; 24.9 HC	All females	Cognitive flexibility: ≠ Central coherence: ≠	MMPI Scale 2	—	MANCOVA Depression NS $F(15, 326.16) = 1.48$ $p = 0.11$
Kanakam et al., 2013[88]	41 MZ-ED; 11 MZ-H; 12 DZ-ED; 8 DZ-H; 42 Control twins	31 MZ-ED; 54 MZ-H; 35 DZ-ED; 52 DZ-H; 45 Control twins	All females	Cognitive flexibility: ≠ Central coherence: =	DASS-21	—	—
Kim et al., 2010[37]	40 AN; 28 BN; 34 HC	22.8 AN; 23 BN; 22.6 HC	All females	Cognitive flexibility: ≠	BDI	—	MANOVA Depression NS (F and p values not available)
Kim et al., 2011[66]	22 AN; 28 BN; 26 HC	22 AN; 23 BN; 23.5	All females	Central coherence: ≠	BDI	—	—
Kingston et al., 1996[38]	46 AN; 41 HC	22.1 AN; 22 HC	All females	Cognitive flexibility: ≠ Central coherence: ≠	BDI	NS Central coherence: ROFT copy $r = -0.253$, $p =$ NS (r and p values not available)	—
Konstantakopoulos et al., 2011[67]	25 AN; 15 BN; 35 HC	28.6 AN; 27.2 BN; 24.9 HC	All females	Cognitive flexibility: ≠	HADS	—	—
Liao et al., 2009[39]	29 AN; 26 BN; 51 HC	28.5 AN; 27.8 BN; 29.4 HC	All females	Decision making: ≠	BDI	NS (r and p values not available)	—
Lopez et al., 2008[40]	42 AN; 42 HC	28.4 AN; 26.3 HC	All females	Central coherence: ≠	HADS	NS (r and p values not available)	—
Lounes et al., 2011[41]	45 AN; 49 HC	27.6 AN; 24.1 HC	All females	Cognitive flexibility: ≠	HADS	Cognitive flexibility: $r = 0.130$, $p =$ NS	MANCOVA Depression NS $F(1,80)=0.007$; $p>0.05$
Mathias and Kent, 1998[42]	34 AN; 31 HC	22 AN; 20.8 HC	All females	Cognitive flexibility: = Central coherence: ≠	BDI	Cognitive flexibility: TMT-A $r = 0.001$, $p =$ NS TMT-B $r = 0.157$, $p =$ NS Central coherence: ROFT recall $r = -0.166$, $p =$ NS ROFT copy $r = -0.354$, $p =$ NS	—

TABLE 1. *Continued*

Article	Sample	Mean Age (years)	Gender	Neuropsychological Domains Investigated and Main Results Comparing AN versus HC	Instrument Used to Assess Depression	Correlations Between Neuropsychological Performance and Depression in AN	Control for Depression
McAnarney et al., 2011[68]	24 AN; 37 HC	16.3 AN; 15.9 HC	All females	Cognitive flexibility: ≠	BDI-II	—	—
Murphy et al., 2002[69]	16 AN; 16 BN; 16 HC	22.3 AN; 22 BN; 25.3 HC	All females	Cognitive flexibility: = Central coherence: =	BDI	—	—
Murphy et al., 2004[70]	16 AN; 16 BN; 16 OCD; 16 HC	22.3 AN; 22.0 BN; 25.1 OCD; 25.3 HC	All females	Cognitive flexibility: = Central coherence: =	BDI	—	—
Nakazato et al., 2009[71]	29 AN; 18 AN Rec; 28 HC	28.3 AN; 32.2 AN-Rec; 26.9 HC	All females	Cognitive flexibility: ≠	HADS	—	—
Nakazato et al., 2010[72]	27 AN; 18 AN-Rec; 28 HC	27.7 AN; 32.2 AN-Rec; 26.9 HC	All females	Cognitive flexibility: ≠	HADS	—	—
Ohrmann et al., 2004[43]	11 AN; 12 HC	22.7 AN; 27.5 HC	All females	Cognitive flexibility: ≠	BDI; MADRS	Cognitive flexibility: WCST number of cards rho = 0.888, $p < 0.001$ WCST false category rho = 0.672, $p < 0.05$ WCST perseverations rho = 0.867, $p < 0.001$	—
Oltra-Cucarella et al., 2014[73]	12 AN; 12 AN-WR; 16 HC	21.7 AN; 22.2 AN-WR; 18.6 HC	All females	Cognitive flexibility: = Central coherence: ≠	BDI-II	—	—
Pignatti and Bernasconi, 2013[83]	23 AN; 17 BN; 20 HC	29.1 AN; 29.9 BN; 27.8 HC	All females	Cognitive flexibility: ≠	SCL-90-R	—	—
Roberts et al., 2010[44]	35 AN-R; 33 AN-BP; 30 BN; 30 AN-Rec; 30 US-AN; 20 US-BN; 88 HC	23.7 AN-R; 25.6 AN-BP; 26.4 BN; 32.1 AN-Rec; 24.2 US-AN; 27.6 US-BN; 28.4 HC	All females	Cognitive flexibility: ≠	HADS	NS (r and p values not available)	—
Roberts et al., 2013[74]	35 AN-R; 33 AN-BP; 30 BN; 30 AN-Rec; 30 US-AN; 20 US-BN; 88 HC	23.7 AN-R; 25.6 AN-BP; 26.4 BN; 32.1 AN-Rec; 24.2 US-AN; 27.6 US-BN; 28.4 HC	All females	Central coherence: ≠	HADS	—	—
Sarrar et al., 2011[45]	30 AN; 28 HC	16.2 AN; 16.7 HC	All females	Cognitive flexibility: =	DIKJ	NS (r and p values not available)	—
Sato et al., 2013[46]	15 AN; 15 HC	23 AN; 22 HC	All females	Cognitive flexibility: ≠	MMPI Scale 2	NS (r and p values not available)	—
Sherman et al., 2006[47]	18 AN; 19 HC	25.6 AN; 25.7 HC	All females	Central coherence: ≠	BDI	NS (r and p values not available)	—
Stedal et al., 2012[89]	155 AN; 66 HC	17.1 AN; 15.4 HC	AN: 95.5% females	Cognitive flexibility: ≠ Central coherence: ≠	BDI	—	—
Steinglass et al., 2006[48]	15 AN; 11 HC	24 HC; 25.6 AN	All females	Cognitive flexibility: ≠	BDI	NS (r and p values not available)	—
Szmukler et al., 1992[49]	18 AN; 18 HC	Mean age not available	All females	Cognitive flexibility: ≠	BDI	NS (r and p values not available)	—
Tapajóz P de Sampaio et al., 2013[50]	8 AN-R; 1 AN-BP; 15 EDNOS-AN; 15 BN-P; 3 BN-NP; 6 EDNOS-BN; 24 HC	24.5 AN; 24.4 BN; 25.2 HC	All females	Central coherence: ≠	BDI	NS (rho and p values not available)	—

TABLE 1. *Continued*

Article	Sample	Mean Age (years)	Gender	Neuropsychological Domains Investigated and Main Results Comparing AN versus HC	Instrument Used to Assess Depression	Correlations Between Neuropsychological Performance and Depression in AN	Control for Depression
Tchanturia et al., 2004[51]	34 AN; 19 BN; 35 HC	26.7 AN; 26.5 BN; 24.8 HC	All females	Cognitive flexibility: ≠	HADS	—	MANCOVA Depression NS [$F(4,82) = 1.40$, $p = 0.24$]
Tchanturia et al., 2004[75]	20 AN-R; 14 AN-BP; 18 AN-R Rec; 36 HC	27.2 AN; 28.4 AN-Rec; 25.9 HC	All females	Cognitive flexibility: ≠	HADS	—	—
Tchanturia et al., 2007[52]	29 AN; 14 AN-Rec; 29 HC	28.5 AN; 28.9 AN-Rec; 26.3 HC	All females	Decision making: ≠	BDI	Decision making: IGT performance $r = -0.283$, $p =$ NS	—
Tchanturia et al., 2011[76]	215 AN; 72 AN-Rec; 69 BN; 29 EDNOS; 216 HC	26.9 AN; 30.2 AN-Rec; 27.7 BN; 26.5 EDNOS; 27 HC	All females	Cognitive flexibility: ≠	—	—	—
Tchanturia et al., 2012[77]	171 AN-R; 90 AN-Rec; 82 BN; 199 HC	25.4 AN-R; 30.7 AN-Rec; 27.3 BN; 27.7 HC	All females	Cognitive flexibility: ≠	—	—	—
Tchanturia et al., 2012[78]	19 AN or sub-threshold AN male; 29 AN or sub-threshold AN female; 20 HC male; 41 HC female	27.2 AN male; 27.5 AN female; 25.4 HC male; 22.2 HC female	AN or sub-threshold AN: 60.4%	Decision making: ≠	—	—	—
Tenconi et al., 2010[53]	60 AN; 63 AN-WR; 29 AN-Rec; 28 US-AN; 120 HC	25.7 AN; 24.5 AN-WR; 30.8 AN-Rec; 27.5 US-AN; 27.4 HC	All females	Cognitive flexibility: ≠ Central coherence: ≠	HSCL	NS (r and p values not available)	—
Tokley and Kemps, 2007[79]	24 AN; 24 HC	21.8 AN; 22 HC	All females	Cognitive flexibility: =	DASS-21	—	—
Van Autreve et al., 2013[54]	31 AN-R; 20 AN-BP; 26 HC	26 AN-R; 20 AN-BP; 19 HC	All females	Cognitive flexibility: =	BDI-II	NS (r, rho and p values not available)	—
Wilsdon and Wade, 2006[55]	22 AN-R; 21 LO-HC; 20 HO-HC	27.6 AN-R; 22.6 LO-HC; 21.1 HO-HC	All females	Cognitive flexibility: =	DASS-21	Cognitive flexibility: WCST perseverative errors: $r = 0.06$, $p =$ NS WCST total errors: $r = -0.03$, $p =$ NS WCST total trials; $r = -0.02$, $p =$ NS	—

Notes: AN: anorexia nervosa; AN-BP: anorexia nervosa–binge-purging subtype; AN-R: anorexia nervosa–restricting subtype; AN-Rec: anorexia nervosa–recovered; AN-WR: anorexia nervosa–weight restored; BN: bulimia nervosa; BN-NP: bulimia nervosa–nonpurging; BN-P: bulimia nervosa–purging; EDNOS: eating disorder not otherwise specified; EDNOS-AN: eating disorder not otherwise specified–anorexia nervosa type; EDNOS-BN: eating disorder not otherwise specified–bulimia nervosa type; OB: obesity; UD: unipolar depression; OCD: obsessive-compulsive disorder; UR-AN: unaffected relatives of AN; UR-HC: unaffected relatives of HC; US-AN: unaffected sisters of AN; US-BN: unaffected sisters of BN; MZ-ED, monozygotic eating disorder probands; MZ-H: monozygotic non-eating-disorder cotwin; DZ-ED: dizygotic eating disorder probands; DZ-H: dizygotic non-eating-disorder cotwin; LO-HC: health control with low obsessionality; HO-HC: health control with high obsessionality; HC: healthy controls.

Neuropsychological domain investigated and main results comparing AN versus HC; ≠: the performance of patients with anorexia nervosa were significantly worse than healthy controls; =: no significant differences were found between patients and controls.

Instrument used to assess depression: BDI: Beck Depression Inventory; CDI: Children"s Depression Inventory; BDI-II: Beck Depression Inventory-II; SCL-90-R: Symptom Check List–90-Revised; HSCL: Hopkins Symptoms Check List; QIDS-SR: Quick Inventory of Depressive Symptomatology; DASS-21: Depression, Anxiety, and Stress Scale-21; HDRS: Hamilton Depression Rating Scale; MMPI: Minnesota Multiphasic Personality Inventory; HADS: Hospital Anxiety and Depression Scale; MADRS: Montgomery Asberg Depression Rating Scale; DIKJ: Depressionsinventar für Kinder und Jugendliche; No: depression not evaluated.

Correlations between neuropsychological performance and depression in AN: —: no correlations were performed; NS (not significant): no significant correlations were found.

Control for depression: —: depression was not investigated as a confounding variable; UGLM: univariate general linear model; MANOVA: multivariate analysis of variance; MANCOVA: multivariate analysis of covariance; Depression NS: depression was found not to reach significance; Depression Sig: depression was found to reach significance.

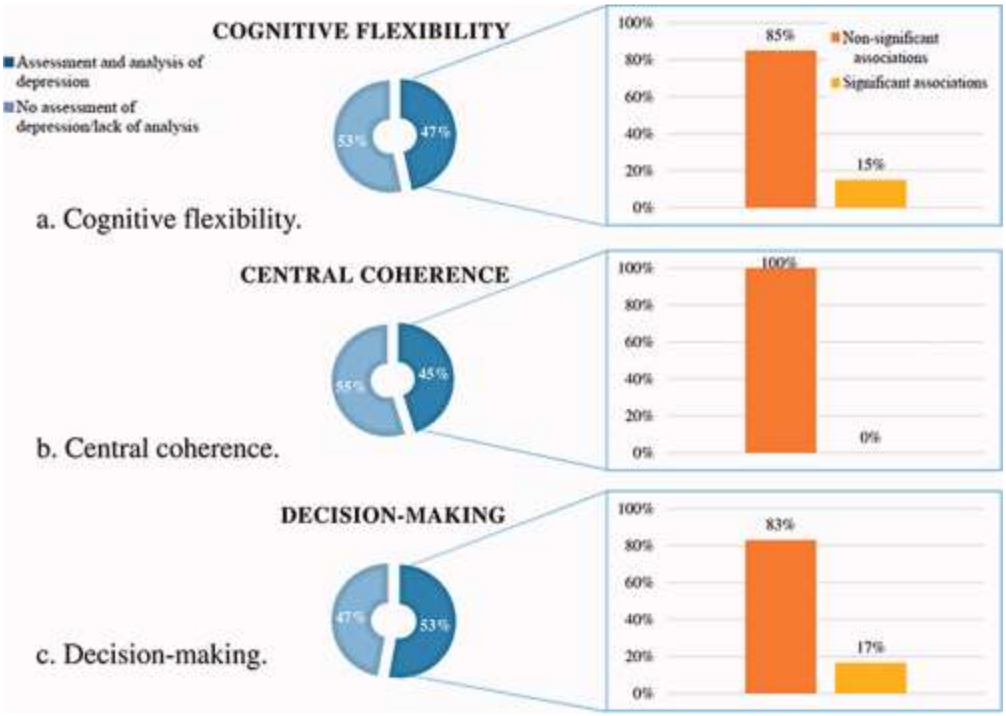

FIGURE 1. Proportion of studies on neuropsychological impairments in anorexia nervosa that took depression statistically into account and their reported presence of significant versus nonsignificant associations. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Central Coherence

Studies assessing central coherence using the ROCF[90], a test used to assess visuospatial abilities, were included. A Central Coherence Index can be computed resulting from the order of construction and style indices. The drawing style can be assessed according to the scoring systems of Savage and colleagues[91] and of Booth[92]. Of 20 articles[1, 34, 36, 38, 40, 42, 47, 50, 53, 57, 63, 65, 66, 69, 70, 73, 74, 82, 88, 89] on central coherence, 15 studies[34, 36, 38, 40, 42, 47, 50, 53, 63, 65, 66, 73, 74, 82, 89] found significant differences in global score between AN and HC on this measure (Table 1).

The vast majority of studies investigated depression (19[31, 34, 36, 38, 40, 42, 47, 50, 53, 57, 63, 66, 69, 70, 73, 74, 82, 88, 89]) with studies[31, 34, 36, 38, 40, 42, 47, 50, 53] including such data in subsequent statistical analyses. No articles reported significant findings on the role of depression using either correlations[31, 34, 38, 40, 42, 47, 50, 53] or MANCOVA[36] (Fig. 1b).

Decision-making

Fifteen studies[1, 28-31, 33, 39, 52, 58, 59, 61, 78, 80, 81, 93] investigated decision-making using the IGT[94] and 12 studies[1, 28, 29, 39, 52, 58, 59, 61, 78, 80, 81, 93] reported differences between AN and HC (Table 1).

Ten studies[1, 28-31, 33, 39, 52, 61, 93] investigated depression and 8 studies[1, 28-31, 33, 39, 52] included this assessment in subsequent statistical analysis. In one case[1], the difference between AN and HC on neurocognition was no longer significant after adjusting for depression.

Discussion

Most studies on neuropsychology in AN performed an assessment of depression using either self-report or clinician-rated instruments. However, about half of the articles included in this review statistically addressed (e.g., correlations, UGLM, MANOVA, etc.) the role of depression, and as a result, the state-of-the-art on this topic is mixed. Significant positive correlations were reported by two studies[9, 43] demonstrating that the greater the depression score, the more impaired the neuropsychological performance. Regarding depression, five studies[30, 36, 37, 41, 51] of six[1, 30, 36, 37, 41, 51] did not find depression to explain the difference between AN and HC on neuropsychology.

From a statistical standpoint, correlations can effectively identify a bidirectional association between depression and neurocognition; however, only a statistical adjustment for depression could ascertain whether the difference in the performance between AN and HC goes away. Nevertheless, only a minority of studies (i.e., 10%) used such a statistical analysis.

The plethora of instruments that have been used to assess depression hampers the generalizability of the available findings. In addition, the small sample size considered in some studies makes the statistical power of the analysis questionable.

Such methodological flaws and the scarcity of studies on this topic represent a finding in itself of great interest, given the relevant influence of depression on neurocognition[3]. This is even more important due to the fact that depressive symptoms frequently plague individuals with AN[2]. Moreover, the rationale for controlling for depression in AN has also been recently acknowledged[95] by a study showing that the adjustment for depression evened out the difference between AN and HC regarding speed of information processing and verbal fluency and overall reduced the differences with respect to a variety of neuropsychological domains[95].

Bearing in mind that only preliminary data exist, studies on cognitive flexibility seem to support the possibility of a marginal effect of depressive symptoms on this neuropsychological domain. In contrast, central coherence was consistently found not to be influenced by depression. Although one study found depression to influence decision-making[1], only eight studies[1, 28-31, 33, 39, 52] are available on the latter domain, so conclusions cannot be drawn in this regard.

Speculating on the possible reasons for the association between depression and cognitive flexibility is beyond the scope of this review. However, these findings are in line with a recent meta-analysis on depression[3] and multiple mechanisms may be involved[8]. Instead, central coherence seemed to be unrelated to depression, although the ROFC could be influenced not only by depressive symptoms but also by obsessive traits[96]. Studies on major depressive disorder showed decision-making to be impaired to different degrees in affected individuals depending on cognitive flexibility[97]. Further research is needed on this topic in AN because no definitive statements can be made yet.

Some limitations should be acknowledged: studies on recovered individuals have been excluded and differences between AN subtypes have not been considered. Also, other neuropsychological domains have not been included, as well as starvation and other psychiatric comorbidities. Still, some clinical characteristics of the sample may vary (e.g., age) or could not be evaluated because that information was not available in all articles (e.g., duration of illness and medications).

In closing, the study of the relationship between depression and neurocognition in AN is only in its infancy. However, the data seem to suggest such an association, mostly in regard to cognitive flexibility. Therefore, future studies comparing individuals affected by AN with and without comorbid major depression versus HC may shed light on this matter. The influence of depression on neuropsychological impairments in AN may have research (i.e., debate on cognition as candidate endophenotype[98]) and clinical (e.g., Cognitive Remediation Therapy[99, 100]) implications. For example, Cognitive Remediation Therapy may be tailored according to patients' needs and depending on their depressive symptoms.

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