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Psychopathological alterations and neuroimaging findings with discriminant value in eating behavior disorders

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Introduction. The difficulties encountered in regards to defining the diagnosis of patients with an Eating Behavior Disorder (EBD) have favored the use of multidimensional models. This study has aimed to identify which psychopathological and neurobiological variables could have a discriminating capacity regarding the different EBD diagnostic subtypes.

Methods. A total of 42 patients with an EBD diagnosis (11 Restrictive Anorexia (R-AN), 10 Purgative Anorexia (P-AN), 7 Non-purgative Bulimia (NP-BN), 14 Purgative Bulimia (P-BN)), according to DSM-IV criteria, were selected from those who came for treatment in the Ciudad Real General Hospital Eating Disorder Unit. Twelve healthy controls were also included. All of the subjects underwent a brain SPECT to measure regional cerebral blood flow (rCBF) in baseline situation (rest). A second one was performed after a visual neutral stimulus (sight of a calm sea) and another one after confronting them with their own corporal image, filmed two weeks before. A battery of questionnaires was administered to evaluate general and eating psychopathology.

Results. Patients with NP-BN showed less eating and general psychopathology. Furthermore, unlike patients with R-AN and P-BN, they did not experience an increase of the rCBF when confronted with their own body image. Discriminant variables were body dissatisfaction measured with the BSQ, BMI; BITE scores, ideal silhouette scores, and temporal right hyperactivation when they were shown their own body image.

Conclusions. The subgroup of patients diagnosed with NP-BN showed less emotional alteration and less emotional response when they were shown their own body image than the rest of patients with EBD. These differences might have implications from the therapeutic, prognostic or even taxonomic viewpoint.

Key words:
Eating disorders, brain SPECT, neurofunction, diagnostic subtypes, anorexia nervosa, bulimia nervosa.

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Alteraciones psicopatológicas y hallazgos de neuroimagen con valor discriminante en los trastornos de la conducta alimentaria

Objetivos. Las dificultades en la delimitación diagnóstica de las pacientes con un Trastorno de la Conducta Alimentaria (TCA) ha favorecido la consideración de modelos multidimensionales. El objetivo del presente trabajo es identificar qué variables psicopatológicas y neurobiológicas podrían tener capacidad discriminante entre los distintos subtipos diagnósticos de TCA.

Métodos. Seleccionamos 42 pacientes diagnosticadas de un TCA según criterios DSM-IV entre las que acudieron para recibir tratamiento en la Unidad de Trastornos Alimentarios del Hospital General de Ciudad Real: 11 Anorexia Restrictiva (AR), 10 Anorexia Purgativa (AP), 7 Bulimia no Purgativa (BNP), 14 Bulimia Purgativa (BP). Incluimos 12 controles sanos. En todas ellas realizamos un SPECT cerebral para medir el flujo sanguíneo regional cerebral (rCBF) en situación basal (reposo), otro tras estímulo visual neutro (vista del mar en calma) y otro tras confrontarlos con su propia imagen corporal filmada dos semanas antes. Les administramos una batería de cuestionarios para evaluar psicopatología general y alimentaria.

Resultados. Las pacientes con BNP presentaban menor psicopatología alimentaria y general, así mismo, a diferencia de las pacientes con AR y BP, no experimentaron incremento del rCBF al confrontarlas con su propia imagen corporal. Las variables discriminantes fueron: insatisfacción corporal, IMC, puntuaciones del BITE, pun-

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tuaciones sobre la silueta ideal, e hiperactivación temporal derecha al exponerlas a la propia imagen.

Conclusiones. El subgrupo de pacientes diagnosticadas de BNP presentaba menor alteración emocional y menor respuesta emocional frente a su propia imagen que el resto de pacientes con TCA. Estas diferencias podrían tener implicaciones terapéuticas, pronósticas e incluso taxonómicas.

Palabras clave:
Trastornos de la Conducta Alimentaria, SPECT Cerebral, Neurofunción, subtipos diagnósticos, Anorexia nerviosa, Bulimia.

INTRODUCTION

The instability regarding the diagnostic subtype in patients with Eating Behavior disorder (hereinafter EBD) is a frequent clinical observation. In fact, the first description of Bulimia Nervosa (BN) referred to this as an "ominous" variable of Anorexia Nervosa (AN) and up to 25% of the patients with Bulimia had previous criteria of Restrictive Anorexia (R-AN). Migration from one diagnosis to another has been reported in half of the cases and only one third maintain their original diagnoses after 30 months.[1] Small changes in weight may lead to a change in diagnoses. Another manifestation of the limitation of the classification of eating disorders is that the diagnosis of Eating Disorder Not Otherwise Specified (EDNOS) is the one used the most both in the clinical context with a prevalence of 50 to 70% in every case of EBD[2] as well as in epidemiological studies in general population.[3] This situation may imply that a 14-year-old girl who has all of the criteria for AN except for absence of amenorrhea may have the same diagnosis of EDNOS as a 46-year old male with compulsive eating episodes without compensatory maneuvers. This reveals the high heterogeneity of this diagnosis and limitation of the current systems of diagnostic classifications. However, this variability in the psychopathological compression of different diagnostic categories of EBD contrasts with its stability in the evolution to other psychiatric disorders, independently of its frequent comorbidity with mood or anxiety state disorders or with axis II alterations. The above suggests the presence of some common mechanisms for all eating disorders and other mechanisms that could be specific to each diagnostic subgroup.[4] In this sense, the work performed by Vaz et al.[5] indicates that those patients with BN who have a previous background of AN continue to have differential psychopathological traits in relationship to patients diagnosed of bulimia who do not have these criteria in the beginning, for example, greater body in satisfaction, lower ideal weight, lower frequency of vomiting and higher frequency of fasting behaviors and of methods to control weight. This was true even though both groups met the same diagnostic criteria according to the DSM-IV. Therefore, these same authors find that the previous backgrounds of anorexia nervosa in patients who currently have criteria for bulimia nervosa is associated to a worse prognosis.[6]

Table 1 Mean Age and Body Mass Index (BMI) of the patients and controls

		Mean	Confidence interval for the mean at 95%	
			Lower limit	Upper limit
Age	R-AN	27.10	20.48	33.72
	P-AN	28.38	22.87	33.88
	P-BN	30.69	25.29	36.10
	NP-BN	34.71	28.01	41.42
	Control	20.58**	18.88	22.29
	Total	27.74	25.34	30.14
BMI	R-AN	18.10	17.03	19.16
	P-AN	17.67	16.24	19.10
	P-BN	22.92*	20.55	25.29
	NP-BN	33.20**	25.29	41.10
	Control	21.52	20.38	22.66
	Total	22.22	20.45	23.98

Single Factor Analysis of Variance. * p< 0.05; ** p < 0.01

An interesting work developed in our country described BN as a multidimensional disorder that emerges from the interaction of two large groups of clinical manifestations, some related with eating symptoms and others with some dysfunctional personality traits, depressive symptoms being associated to the latter.[7] Knowing the relevance that both the biological aspects (genetic, temperament) as well as environmental aspects (social of familial pressure, traumatic events or special bibliographic situations) can have in the psychopathological expression of the different diagnostic subtypes has special clinical interest. This is because it would make it possible to identify early those subjects with a greater risk of evolving to other more serious pictures (e.g. Restrictive Anorexia -R-AN- that evolves to Purgative Anorexia - P-AN) and possibly prevent their appearance during the treatment. In addition, identifying the specific neuropsychological characteristics of each one of these diagnostic subgroups not only would give greater importance to the biological factors in the predisposition to develop a diagnostic subtype versus environmental aspects but also would facilitate the identification of possible cognitive functions that do not follow an appropriate maturative process and that could be an object of rehabilitation. This aspect has already been previously indicated by other authors in relationship to other clinical pictures that also begin, principally, in adolescents, such as borderline personality disorder.[8]

Table 2 Eating psychopathology and results of the Silhouette Test and in the Body Shape Questionnaire (BSQ)

		Media	Intervalo de confianza para la media al 95%	
			Límite inferior	Límite superior
EAT	R-AN	44.89	22.35	67.43
	P-AN	65.25	51.16	79.34
	P-BN	42.92	28.55	57.28
	NP-BN	23.86**	8.26	39.46
	CONTROL	6.17***	4.05	8.28
BITE symptoms	R-AN	6.13	2.89	9.36
	P-AN	13.63*	10.00	17.25
	P-BN	21.77***	18.18	25.35
	NP-BN	16.00**	8.40	23.60
	CONTROL	5.18	1.77	8.59
BITE severity	R-AN	3.63	-0.47	7.72
	P-AN	7.88**	5.14	10.61
	P-BN	8.62***	6.27	10.96
	NP-BN	3.17	0.48	5.86
	CONTROL	0.82	0.16	1.48
Sum BITE	R-AN	9.75	3.59	15.91
	P-AN	21.50**	16.23	26.77
	P-BN	30.38***	25.28	35.49
	NP-BN	19.17*	9.58	28.75
	CONTROL	6.00	2.12	9.88
BSQ	R-AN	119.33***	89.71	148.96
	P-AN	156.38**	126.38	186.37
	P-BN	140.54***	115.78	165.30
	NP-BN	141.14**	112.99	169.29
	CONTROL	69.08	48.11	90.06
Ideal Silhouette	R-AN	-4.80***	-5.91	-3.69
	P-AN	-4.88***	-5.57	-4.18
	P-BN	-3.69**	-4.36	-3.02
	NP-BN	-1.00	-3.00	1.00
		-0.92	-1.91	0.08
Real Silhouette	R-AN	-1.30	-2.13	-0.47
	P-AN	-1.88	-3.39	-0.36
	P-BN	1.08	-0.17	2.32
	NP-BN	4.00***	1.80	6.20
	CONTROL	0.33	0.02	0.65
Dissatisfaction	R-AN	6.00**	3.39	8.61
	P-AN	7.13**	4.50	9.75
	P-BN	5.62	4.10	7.13
	NP-BN	5.86	4.13	7.58
	CONTROL	1.17	0.32	2.02
Distortion Silhouette	R-AN	2.30	-0.20	4.80
	P-AN	4.13***	0.89	7.36
	P-BN	0.85	-0.17	1.86
	NP-BN	0.86	-0.50	2.21
		0.08	-1.14	1.31

Single factor ANOVA. * p< 0.05; ** p< 0.01; *** p< 0.001

The progress undergone by functional neuroimaging tests in recent years has made it possible for some clinical and psychopathological characteristics to be related with a specific anatomical and neurophysiological correlate.[9] In this sense, would it be possible to find biological markers having the trait that would consolidate the diagnostic grouping of these clinical subtypes? This study has aimed to identify if a group of psychopathological and neurobiological variables could have discriminant capacity between the different diagnostic subtypes of patients with EBD, including a control group.

METHODOLOGY

A total of 42 patients diagnosed of an EBD according to the DSM-IV criteria were selected from those who came for treatment in the Eating Disorders Unit of the Hospital General de Ciudad Real: 11 Restrictive Anorexia (R-AN), 10 Purgative Anorexia (P-AN), 7 Non-Purgative Bulimia (NP-BN), 14 Purgative Bulimia (P-BN). Twelve healthy controls were included from the University School of Nursing of Ciudad Real. All of the participants underwent SPECT to measure regional cerebral blood flow (rCBF) at baseline (rest), another one after a neutral visual stimulus (viewing a calm sea) and another after showing them their own body image film 2 weeks earlier. All the subjects included in the

study agreed to participate voluntarily and those who had left laterality, other neurological or psychiatric disorders on axis I or II, or who were or had been planning to become pregnant during the days of the study were excluded. We recorded nutritional status and treatment with psychopharmaceuticals used during the days of the study.

Measurement instruments

As part of the evaluation, a battery of questionnaires were administered to evaluate general and eating psychopathology. These, which had been validated in the Spanish population, were the EAT-40 (*Eating Attitudes Test*),[10] EDI-2 (*Eating Disorders Inventory-2*),[11] BITE (*Bulimic Inventory Test Edinburgh*),[12] BSQ (*Body Shape Questionnaire*)[13] and the silhouette test.[14] We also applied other questionnaires to evaluate general psychopathology such as the BDI (Beck Depression Inventory),[15] STAI (State-Trait Anxiety Inventory),[16] the Rosenberg self-esteem scale (RSE)[17] and the Hamilton Depression Rating scale.[18]

Statistical analysis

In the first place, a Descriptive Statistics was performed to know the characteristics of the participants at baseline. The Analysis of the Variance was used to study the differences between the diagnostic subtypes in regards to the psychopathological variables and the regional cerebral blood flow pattern. After, the Discriminant Analysis was used to select those subsets of independent variables that would most discriminate the groups established by the dependent variable (diagnoses).

RESULTS

Sample description

As shown in table 1, the controls were significantly younger than the patients diagnosed of NP-BN and P-BN. The body mass index of the patients with NP-BN was significantly greater than in the rest of the patients and the controls.

Psychopathological characteristics

Tables 2 and 3 show the differences in regards to the mean scores obtained in the psychopathological variables between the different diagnostic subtypes. The following findings stand out:

Patients with NP-BN, as the controls, had significantly lower scores than the R-AN on the EAT and than the P-AN and P-BN in the Severity scores on the BITE, that is, they had less eating psychopathology.

Patients with NP-BN, as the controls, differed from the rest of the patients in regards to ideal silhouette, having significantly lower mean scores. However, the scores in the

Table 3 General psychopathology

		Mean	Confidence interview for the mean at 95%	
			Lower limit	Upper limit
BDI	R-AN	16.33***	7.53	25.14
	P-AN	21.00**	15.05	26.95
	P-BN	22.62*	17.28	27.95
	NP-BN	9.29	1.65	16.93
	CONTROL	4.42	1.35	7.49
STAI-State	R-AN	25.56	16.53	34.58
	P-AN	36.50**	23.28	49.72
	P-BN	36.08**	28.41	43.75
	NP-BN	22.00	14.41	29.59
	CONTROL	13.58	8.22	18.95
STAI-Trait	R-AN	28.78	19.96	37.60
	P-AN	41.88***	34.00	49.75
	P-BN	39.46***	32.27	46.65
	NP-BN	31.86	18.07	45.64
	CONTROL	16.92	10.62	23.22
Hamilton Depression	R-AN	4.10	0.57	7.63
	P-AN	4.43	2.17	6.68
	P-BN	5.75**	2.70	8.80
	NP-BN	3.33	-0.09	6.76
	CONTROL	0.25	-0.14	0.64
Self-esteem (RSE)	R-AN	22.33*	17.83	26.83
	P-AN	16.50***	12.36	20.64
	P-BN	20.08**	15.72	24.44
	NP-BN	27.86	22.25	33.47
	CONTROL	30.75	28.40	33.10

Single factor ANOVA: * p< 0.05; ** p< 0.01; *** p< 0.001

measurement of the real silhouette perceived by the patients with NP-BN were significantly greater than the remaining groups because of being obese. The distortion of the silhouette was greater in the P-AN than in the remaining groups and lack of satisfaction with the silhouette was greater than that of the controls in all the groups.

The patients diagnosed of P-AN and P-BN had significantly greater general psychopathology than the controls, the NP-BN being those that least differed from the controls in this aspect

Changes in regional cerebral blood flow in the right temporal level in the different diagnostic subtypes

When passing from the baseline situation to the neutral stimulus, a decrease was found in the right temporal regional cerebral blood flow in all the diagnostic groups (table 4). However, when passing the neutral stimulus to being confronted with their own body image (positive stimulus), the patients with R-AN and P-BN experienced an increase in the regional cerebral blood flow on the right temporal level (table 4 and figure 1).

Discriminant analysis

In order to select a group of variables that most differentiated the diagnostic subtypes, a discriminant analysis was carried out. In the data analysis, age, BMI, psychopathological variables measured at baseline, as well as the regional cerebral blood flow (rCBF) patterns presented by the patient and controls when confronted with their own previously filmed body image were included. The variables whose Wilks' Lambda value was the minimum value among those obtained in each one of the groups formed by the independent variables were selected, the p value being less

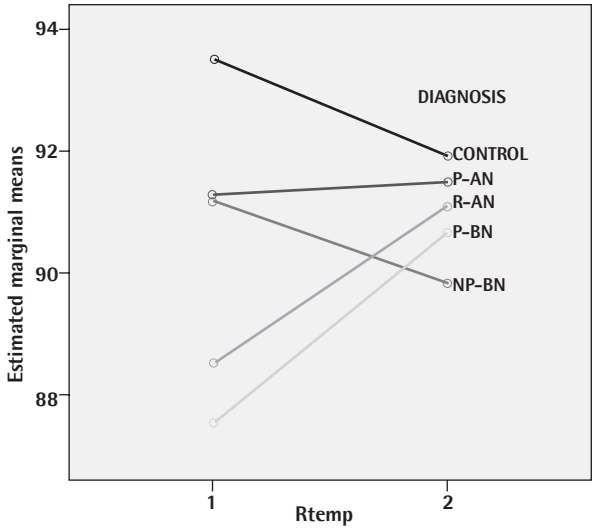

Figure 1 Estimated marginal means of Changes rCBF RTemp

Table 4 General psychopathology

Diagnosis	Changes rCBF	Mean	95% confidence interval		Changes rCBF	Mean	95% confidence interval	
			Lower limit	Upper limit			Lower limit	Upper limit
R-AN	Baseline	90.60	87.05	94.14	Neutral S	88.50	85.51	91.48
	Neutral S.	88.50	85.51	91.48	Positive S.	91.10	87.83	94.36
P-AN	Baseline	91.87	87.91	95.83	Neutral S	91.25	87.91	94.58
	Neutral S.	91.25	87.91	94.58	Positive S.	91.50	87.85	95.14
P-BN	Baseline	89.46	86.35	92.56	Neutral S	87.53	84.92	90.15
	Neutral S.	87.53	84.92	90.15	Positive S.	90.69	87.83	93.55
NP-BN	Baseline	93.66	89.094	98.23	Neutral S	91.16	87.31	95.01
	Neutral S.	91.16	87.31	95.01	Positive S.	89.83	85.62	94.04
Control	Baseline	95.58	92.35	98.81	Neutral S	93.50	90.77	96.22
	Neutral S.	93.50	90.77	96.22	Positive S.	91.91	88.93	94.89

Table 5 Summary of the canonical discriminant function -A Discriminant Analysis. Four discriminant functions were obtained

Self-values

Function	Self-value	% of variance	% accumulated	Canonic correlation
1	5.156(a)	64.1	64.1	0.915
2	2.207(a)	27.5	91.6	0.830
3	0.658(a)	8.2	99.8	0.630
4	0.019(a)	0.2	100.0	0.137

a The first 4 canonical discriminant functions were used in the analysis.

Wilks' Lambda

Contrast of the functions	Wilks' Lambda	Chi-square	gl	Sig.
1 a la 4	0.030	136.797	20	0.000
2 a la 4	0.184	65.914	12	0.000
3 a la 4	0.592	20.462	6	0.002
4	0.981	0.736	2	0.692

Standardized coefficients of the canonical discriminant functions

	Function			
	1	2	3	4
BMI	-0.179	0.890	0.261	-0.455
Sum BITE	-0.961	0.125	-0.943	-0.034
Ideal silhouette	0.720	0.272	-0.128	0.820
Right temporal	0.733	-0.250	0.380	0.146
BSQ	-0.274	-0.034	0.840	0.615

than 0.05. The discriminant variables were: scores on the BSQ, BMI, Sum of the BITE, scores on the ideal silhouette, and right temporal hyperactivation against the body image per se. Four discriminant functions whose self-values and correlation coefficient are summarized in table 5 were obtained. The percentage of correctly classified cases was 95%.

DISCUSSION

There is growing interest in the utility and validity of the current subtypes of EBD due to the upcoming publication of the DSM-V[19] and the contributions supposed by the new study instruments, such as neuroimaging. The question is relevant in relationship to the predictive validity and stability of the different diagnostic subtypes in regards to therapeutic planning.[20] During the clinical evolution, the phenomenon of transdiagnosis frequently occurs, that is, passage from R-AN to P-AN and from P-AN to P-BN[21]. This decreases the predictive validity of the diagnostic subtypes of AN[22] since there is evidence that the patients with P-AN have greater psychopathology[23] and worse prognoses.[24] In the case of the BN, differences have been pointed out between the P-BN and NP-BN in regards to prognoses.[25] Garfinkel found greater comorbidity in P-BN regarding NP-BN.[26] Our study has confirmed these differences. We have found that NP-BN significantly differentiates between the R-AN, P-AN and P-BN in finding that the latter have greater general and eating psychopathology. Some authors consider that the NP-BN is more similar to Binging Disorders, casting doubt on the utility of the P-BN as a diagnostic subtype[27] within Bulimia Nervosa.

The results of the present study have once again put into doubt the adequacy of the current categorial classification system and the inclusion of patients with NP-BN within the category of NB. The former have differential characteristics regarding P-BN and the remaining EBD analyzed, above all greater overweight, lower dissatisfaction

with the body image and lower distortion of the silhouette as well as decrease in the cerebral blood flow of the right temporal lobe in the face of the provocation tests, similar to that produced in the control population. In fact, the subset of variables having the greatest discriminant capacity found was that form by BMI, the sum of BITE, scores on the ideal silhouette, dissatisfaction with the body image measured with the BSQ and the changes in regional cerebral blood flow on the right temporal side when confronted with their body image.

Compared with the categorial consideration of the diagnoses, that have limitations such as those previously presented, there are other interesting approaches to the problem of the diagnostic heterogeneity of the EBD, such as the notion of the subphenotypes and endophenotypes.[28, 29] The term subphenotype refers to a subgroup of identifiable and measurable symptoms in the disorders and the endophenotypes are hereditary and also measurable components, that can also be present in individuals without active disease or in healthy family members.[29] From this perspective, although there is heterogeneity, the core characteristics of the disorders are clearly identifiable. Our finding that there are significant differences between the P-BN and NP-BN, both in regards to the psychopathology, as well as the different pattern of cerebral regional blood flow after the stimulus of one's own image, is consistent with the idea that there are different subphenotypes, some common and other differential ones, within the diagnostic groups of EBD. Steiger[28] has stated that approximately one third of the patients with BN have a "deregulated" pattern that not only affects appetite but also emotions. Another third are more compulsive, with periods of over-eating, and another third have fewer psychopathological alterations. In our study, patients with P-BN, as those with P-AN, have greater eating and general psychopathology than the rest of the patients. This suggests the existence of a deregulated pattern of behavior. The greatest distortion of the body image was common to patients with Anorexia Nervosa and Purgative Bulimia versus patients with NP-BN, who had less eating psychopathology and less body image distortion. The latter showed overweightness and compulsivity in intake but had less emotional deregulation. The increase in blood flow on the right temporal level when the subjects were confronted with their own filmed image has been related to the phobic emotional response.[30] According to our findings, NP-BN patients would suffer this type of response less. Therefore, there seems to be differences in regards to the core characteristics of AN (anorexia nervosa) and P-BN with regards to NP-BN.

The heterogeneity of BN (bulimia nervosa) has been and continues to be object of many works. Thus, the consideration of BN with a history of AN versus the rest of the patients with BN reveals differences in regards to the personal backgrounds of maltreatment in childhood and in regards to current eating psychopathology, the core symptoms of AN persisting.[31] The fact that NP-BN does not have the same clinical and neurobiological variables could lead us to think that there are differences regarding the etiopathogeny of the nucleus of the EBD. We understand that the identification of the common endophenotypes would be a crucial aspect for the grouping of different clinical pictures within the spectrum of the EBDs. The effect that showing patients with an eating disorder their own body image has on them and its correlate in the modification of the cerebral brain flow in the previously-mentioned regions could be a relevant and specific aspect for the diagnostic grouping of these disorders, characteristics that are not shared by the patients diagnosed of NP-BN and that could justify their exclusion.

However, it is necessary to continue identifying common endophenotypes in the eating disorders that adequately justify such separation. Our results still have to be interpreted with care, such as the different age of the controls compared to the patients with BN, that it was not possible to perform a previous washout period of the psychopharmacological treatment, and the reduced sample size. Longitudinal studies that also include biological markers to examine the differences in regards to the etiopathogeny and prognosis are necessary.

In summary, in our work, we have found a subgroup of discriminant variables between the different types of EBD, both clinical, psychopathological and neuroimaging, as is the alteration in the regional cerebral blood flow pattern when the subject is shown his/her own image. The subgroup of patients diagnosed of NP-BN had a lower emotional alteration and lower emotional response to their own image. These differences could have implications from the therapeutic, prognostic and even taxonomic point of view. Our findings would not support the inclusion of NP-BN within the clinical category of BN, but rather in one closer to other disorders, such as Binging Disorder.

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