

# Dissociation between cognitive-behavioral and emotional-psychophysiological aspects in Eating Disorders and its pre-post treatment stability

Carlo Pruneti<sup>1</sup>, Sara Guidotti<sup>1</sup>, Rene M. Lento<sup>2</sup>, Nicolò Renda<sup>1</sup>

<sup>1</sup> Clinical Psychology, Clinical Psychophysiology and Clinical Neuropsychology Labs., Department of Medicine and Surgery, University of Parma, Parma, Italy; <sup>2</sup> Graduate School of Psychology, Boston College, Boston, USA

## SUMMARY

### Objective

The present work aims to assess the effectiveness of an integrate treatment in a group of patients with Eating Disorders (EDs).

### Methods

15 women with an ED, who underwent a multidisciplinary treatment, were subdivided into two groups (Anorexia Nervosa and Bulimia Nervosa). Participants were evaluated by: Symptom Questionnaire (SQ) and Psychophysiological Profile (PPP). Administration was repeated six months after the start of treatment and at treatment termination.

### Results

Elevated levels of anxiety, depression, somatic symptoms and hostility at the diagnostic phase and low levels of physiological reactivity were observed. A significant reduction in patient-reported depressive symptoms was detected within six months following the onset of treatment. Progressive improvement of anxiety and hostility was observed in the medium-long term. At the physiological level, an increase in skin conductance values was observed during the stress phase in the medium-long term.

### Discussion

A partial desynchronization emerged between patients' physiological and cognitive responses.

**Key words:** eating disorders, integrated treatment, dissociation, emotion regulation, clinical psychophysiology

## Introduction

Although the use of an integrated treatment approach for various psychopathologies <sup>1</sup> is gradually spreading in clinical settings, the majority of current empirical researches still tends to focus attention exclusively on the effectiveness of a single psychoactive element utilized in the treatment. Secondly, the interest seems to be addressed on specific clinical population, or to focus on the comparison of the observable effects following the psychotherapeutic treatment of different theoretical and methodological matrices. Research on the therapeutic effectiveness of various interventions also raises a series of methodological problems related both to the choice of instruments used to assess a symptom's course and to differing operational definitions of clinical improvement <sup>2,3</sup>.

The present study therefore endeavored to match an "outcome" research model aimed at analyzing the results of a treatment, to a "process" research model aimed at investigating how the recovery process manifests itself over time <sup>4-6</sup>. This goal was accomplished in accordance with a multi-dimensional approach, through the utilization of both a subjective

Received: December 27, 2021

Accepted: January 22, 2022

### Correspondence

Sara Guidotti

Clinical Psychology, Clinical Psychophysiology and Clinical Neuropsychology Labs., Department of Medicine and Surgery, University of Parma, via Volturno 39, 43126 Parma, Italy. E-mail: sara.guidotti@unipr.it

**How to cite this article:** Pruneti C, Guidotti S, Lento RM, et al. Dissociation between cognitive-behavioral and emotional-psychophysiological aspects in Eating Disorders and its pre-post treatment stability. Journal of Psychopathology 2022;28:30-38. <https://doi.org/10.36148/2284-0249-451>

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patient self-report measure and objective physiological indexes<sup>7-12</sup>. In addition, this study sought to verify the presence of the noted phenomenon of “fractionation”, or division of different response channels (e.g., cognitive, emotional, physical), which are not necessarily associated to a significant change in the other aspects of the syndrome, e.g. the physiological one<sup>11,13-17</sup>.

In fact, clinical research has repeatedly highlighted how this aspect is easily found in patients with Eating Disorders (ED)<sup>1</sup>. Some reactions as the presence of negative emotion, difficulty in regulating emotions<sup>18</sup>, as well as interceptive difficulties<sup>19</sup> and alexithymia<sup>20</sup>, are very often associated with both Anorexia Nervosa (AN) and Bulimia Nervosa (BN)<sup>4,5</sup>.

In addition, alexithymia and emotional dysregulation have been identified as comorbidities that can greatly interfere with the treatment of ED and persist even after symptoms remission<sup>14</sup>. Furthermore, the stability of these factors, and the strong connection with the stable personality traits and the constitutional provisions, is highlight.

Specifically, individuals with BN and the AN-binge/purge (AN-BP) subtype have been shown to have greater amount of negative urgency, impulsivity, and novelty seeking<sup>21-24</sup>, while AN-R is characterized by a more hyper controlled, anxious, reward insensitive and rigid temperament<sup>23,25,26</sup>.

Finally, the observation regarding the difficulty of generalizing empirical results, obtained in the experimental studies, to the clinical reality has become acknowledged<sup>20,27,28</sup>. The samples used in empirical studies are often unrepresentative of the situations that therapists find themselves confronted within their active practices. Hence, the sample considered in the present article does not constitute an “experimental” group as much as a true and proper “clinical” sample, as it is comprised of patients treated in an outpatient context and not selected “a priori” in relation to specific variables.

The principal aim of the present study was to assess the effectiveness of a multidimensional treatment approach in a clinical population that (a) satisfies the current international criteria for ED diagnoses, as indicated in the latest version of DSM<sup>1</sup>, and (b) concurrently underwent both a cognitive-behavioral psychotherapy (CBT), and a controlled psychopharmacological support treatment. The therapeutic effects investigated are therefore attributable to an Integrated Therapy (IT) that is the combination of two interventions, both psychological and pharmacological.

## ED and pharmacological treatments

While there is proven efficacy of antidepressant therapy for the short-term treatment of AN and BN, many studies support the role of psychotherapy, particularly CBT, in the treatment of these disorders<sup>29-31</sup>. Numerous papers have

examined the combination of pharmacotherapy and psychotherapy. These studies used different antidepressants and different psychotherapeutic modalities, starting from nutritional counselling up to group and individual psychotherapy<sup>29-32</sup>. Overall, CBT was more effective than antidepressant medication alone, and the combination of the two was still superior to the drug alone<sup>33</sup>. However, it is unclear how much benefit comes from adding the drug to effective psychological treatment. Some studies have found that adding the antidepressant to psychotherapy does not further reduce binge eating or purging, while this combination nevertheless appears to improve symptoms such as anxiety, depressed mood and dietary restriction<sup>29-31,34</sup>. Some authors have also compared the association of a drug with CBT or with individual supportive psychotherapy, comparing the effect of combining the drug with the two different types of psychotherapy. The addition of some antidepressants seems, in some cases, to increase the effectiveness of both CBT on binge eating and depressive symptoms. However, the combination of the drug with CBT has shown greater efficacy than both treatment with the drug alone. It should be emphasized that the long-term benefits of short-term treatment protocols have only been demonstrated for psychotherapy and not for drug alone. Some studies also highlight the possibility that certain personality traits and anger levels may influence adherence to treatment and the drop-out rate<sup>33,34</sup>. However, SSRIs, in particular fluoxetine, have some utility in the treatment of BN alone, but the results are much discussed and more research is needed. Pharmacological studies have not yet uniquely identified active ingredients capable of bring about a consistent and lasting improvement in the symptoms of AN. Therefore, there are no drugs approved by the FDA or AIFA for the treatment of AN<sup>30-32</sup>.

## Methods

### Sample

All subjects of this research completed an informed consent and received a description of the results of the test administered; all the data have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Patient's anonymity was preserved and the obtained data were used exclusively for scientific purposes.

The sample was comprised of 15 women between the ages of 15 and 23-years-old ( $M = 16.6$ ;  $SD = \pm 5.13$ ) who were suffering from an ED according to the DSM-5 criteria<sup>1</sup>, not directly attributable to a specific medical condition or endogenous pathology. The exclusion criteria were severe psychiatric (i.e., psychotic symptoms, bipolar disorder and severe personality disorders) or medical comorbidities, neurological trauma or disorder, or drug addiction.

The total sample was recruited from a Clinical Psychology section of a Child Neuro-Psychiatric Centre at the St. Chiara University Hospital in Pisa (Italy). No drugs treatment were administered at the time of first consultation, with the exception of one subject who continued fluoxetine therapy, who was previously prescribed at a dose of 20 mg/3/die. In the period prior to taking charge of the patient at the clinical psychology outpatient clinic, some general practitioner and two psychiatrist had prescribed some psych drugs. Anxiolytic therapies, with both benzodiazepines and SSRIs were prescribed, generally with a very low compliance, but neither antipsychotic nor tricyclic. All subjects were subdivided into two groups, depending on whether the patients' predominant symptoms adhered to the criteria proposed by the DSM-5<sup>1</sup> for the diagnosis of AN or BN. This subdivision was conducted specifically in reference to the symptoms and the psychopathological characteristics reported by the patients at the time of their initial intakes by a mental health professional. Thus, the subdivision omitted patients' possible successive migrations toward conduct considered more typical of other psychopathological sub-profiles. For example, the conversion of the patient with a diagnosis of AN, Restricted-type to that of AN Purging-type was observed. To that end, any presence of being marked underweight ( $BN I \leq 17.5$ ) and of amenorrhea were considered to be particularly significant, and this made it possible to identify a group of AN patients (AN,  $n = 9$ ) and a group of BN patients (BN,  $n = 6$ ) (Tab. I).

All of the patients underwent a cognitive-behavioral psychotherapeutic treatment as well as a pharmacological regime, considered appropriate for each case based on the prevalent symptomatology. The integrated intervention lasted for no less than one year, but duration varied from patient to patient. Overall, in the cases in which the patient was particularly impaired, the therapy was prolonged until approximately two years after the end of the initial four-session evaluation phase.

### Materials and procedure

The Symptom Questionnaire<sup>35-37</sup> was administered to the entire sample during the initial diagnostic phase

(*phase 1*). The SQ is a tool made to evaluate the patient's current state that enables an assessment (a) of the subjective level of suffering experienced by the patient in the past week and (b) of the different, often interconnected, components of the same clinical profile. The questionnaire is composed of 92 dichotomous items, organized in four scales that assess anxiety (A), depression (D), somatic symptoms (S), and hostility (H). During administration of the questionnaire, patients are asked to respond to items because of how they felt in the past week. The SQ has been demonstrated to have excellent test-retest reliability, which, according to researchers, is due to the high consistency of the responses shown by the patients whose clinical profile remained invariable<sup>35</sup>. Such observations render this instrument as particularly adequate, not only for the initial assessment of the patients' complex clinical profiles, but, also, for monitoring the course of their self-reported symptoms overtime. The SQ was newly re-administered to each patient at a six-month follow up after the onset of therapy (*phase 2*) and upon termination (*phase 3*). Specifically, the therapeutic intervention terminated once the patient's weight was stabilized and any compensatory behaviors (e.g., abuse of laxatives or induced vomiting) were eliminated.

In association with the SQ, a Psychophysiological Profile (PPP)<sup>38</sup> was carried out for each of the three treatment phases (diagnostic phase; six-month follow up; termination). The purposes of the PPP administration were to gather information on the possible presence and consistency of a psychophysiological impairment, as well as to verify the concordance of the psychophysiological results with the patients' verbal reports of symptoms. The PPP is a psychophysiological evaluation structured in three phases: "rest" or baseline, stress, and recovery. In the baseline phase (*phase b*; 6 minutes), each patient is instructed to close his/her eyes and to remain still and relaxed. In the "stress" phase (*phase s*; 4 minutes), the patient is presented a mental task (MAT) consisting of subtracting the number 13 from the number 1007 and continuing to subtract 13 from each successive result that is obtained. "Recovery" phase (*phase r*; 6 minutes) in when the patient is instructed to relax again. Five physiological parameters are recorded during each phase: skin conductance (or Galvanic Skin Response, GSR), Heart Rate (HR) Inter Beat Interval (IBI), Heart Rate Variability (HRV), Peripheral Temperature (PT), and electrical potential of the forehead muscles (surface Electromyogram, sEMG).

### Data analysis

The SPSS.14 software was utilized to process all statistical analysis.

The following descriptive statistics were computed:

- the median scores for the four clinical scales of the SQ administered in the three different treatment

**TABLE I.** Description of the characteristics of the sample (age and type of Eating Disorder).

Sample characteristics		
<b>N. Subjects</b>		15
<b>AGE</b>	Range	15-23
	Mean (SD)	16.6 ( $\pm$ 5.13)
<b>ED</b>	AN Freq. %	60%
	BN Freq %	40%

phases (*phases 1, 2, 3*) for the total sample and for the two subgroups (AN, BN);

- the mean and the standard deviation for each psychophysiological parameter recorded for each of the PPP's three phases (*phase b, s, r*) in the three different treatment phases (*phase 1, 2, 3*) for the total sample and for the two subgroups (AN, BN).

One of the purpose of this study was identify possible significant differences in the psychopathological characteristics of the two subgroups (AN, BN); for this, considering the small sample size, the following non-parametric statistical analyzes were conducted:

- a Mann-Whitney U test comparison of the AN and BN subgroups' scores on the four clinical scales of the SQ that were administered during the initial diagnostic phase (*phase 1*);
- a Mann-Whitney U test comparison of the AN and BN subgroups' values for the five physiological parameters for the three phases of the PPP recorded during the initial diagnostic phase (*phase 1*).

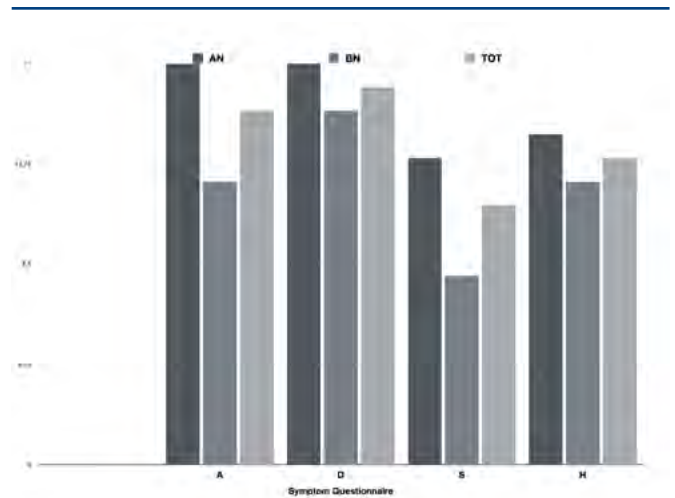
In order to assess the course of patients' self-reported symptoms and any changes in their autonomic disposition during treatment, the following analyses were conducted:

- a comparison among the scores obtained for each clinical scale of the SQ for the total sample in the three treatment phases (*phases 1, 2, 3*), using the Friedman and Wilcoxon test;
- for each physiological parameter, a comparison among the values recorded during the three treatment phases (*phases 1, 2, 3*) with each phase of the PPP (*phase's b, s, r*) of the total sample, using the Friedman and Wilcoxon statistical test.

## Results

The descriptive analyses computed from total sample's SQ scores during the diagnostic phase (*phase 1*) reveal that, from a clinical point of view, the values for all of the scales appear to be significant. Patients reported elevated levels of anxiety (scale A), depression (scale D), hostility (scale H), and somatic symptoms (scale S) (Fig. 1). However, the Mann-Whitney U test did not find statistically significant differences in scores for the two subgroups (AN and BN).

The descriptive analyses computed from the total sample's PPP values recorded during diagnostic phase (*phase 1*), show moderately high baseline values in muscle tension (sEMG > 4  $\mu$ V) and rather low baseline values in skin conductance (GSR < 6  $\mu$ S). On the other hand, baseline peripheral temperature (PT), and heart rate (HR) values did not seem to be particularly indicative. During the stress phase, a meager activation was observed in all of the patients, especially in GSR. The temperature appeared to be nearly constant for the entire profile and showed no variations during the mental stress task (MAT)



**FIGURE 1.** SQ: median scores obtained for the SQ sub-scales for the total sample and for the two subgroups, AN and BN.

administration. As for the last phase of the PPP, after the elimination of the stress stimulus, the recovery was rather meager, especially regarding the heart rate level. Overall, the mean values reported for the sample denote a generally low level of reactivity (Tab. II).

From the statistical analyses conducted using the Mann-Whitney U test, there are no statistically significant differences that emerged between the two subgroups, AN and BN, for any of the psychophysiological parameters recorded.

Concerning the course of the SQ self-reported symptoms, statistically significant reductions in anxiety, depression, and hostility levels were observed for the total sample (Fig. 2).

The median scores obtained from the SQ scales at the three-treatment assessment points have been calculated. Specifically regarding the depressive symptoms, improvement was already progressive and constant within the short-term (within six months of treatment onset). Significant differences were observed between the scale D scores obtained in the first and second SQ administrations (*phases 1-2*;  $p < .02$ ), between the second and third administrations (*phases 2-3*;  $p < .05$ ), and between the first and last administrations (*phases 1-3*;  $p < .05$ ). Significant reductions in self-reported anxiety and hostility levels were observed only in the medium-long term (more than six months after treatment onset; scale A: *phases 2-3*,  $p < .01$ ; *phases 1-3*,  $p < .005$ ; scale H: *phases 2-3*,  $p < .02$ , *phases 1-3*,  $p < .002$ ). No statistically significant differences were found between the scale S (somatic symptom) scores obtained during the three treatment assessment periods; nevertheless a progressive decrease in these scores was observable (Tab. III).

TABLE II.

Psychophysiological Profile (PPP): mean values obtained for the total sample (TOT) and for the two subgroups on four physiological parameters of the three PPP phases (b: baseline; s: stress; r: recovery).

	AN		BN		TOT	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
sEMG b ( $\mu$ V)	5	2	4	1	4	2
sEMG s	5.4	1.9	5.2	.8	5.4	1.5
sEMG r	4.8	1.9	4.2	.5	4.6	1.5
GSR b ( $\mu$ S)	2.4	1.8	4.1	2.1	3.0	2.0
GSR s	3.0	1.9	5.8	3.4	4.0	2.8
GSR r	2.7	1.8	5.0	2.8	3.5	2.4
PT b ( $^{\circ}$ C)	30.8	2.2	31.5	3.3	31.1	2.5
PT s	30.71	2.14	31.51	3.36	30.99	2.54
PTr	30.77	2.17	31.29	3.53	30.96	2.61
HR b (bpm)	68	15	68	9	68	13
HR s	72	16	73	10	73	13
HR r	71	15	68	7	70	12

Abbreviations: sEMG: surface Electromyography; GSR: Galvanic Skin Response; PT: Peripheral Temperature; HR: Heart Rate

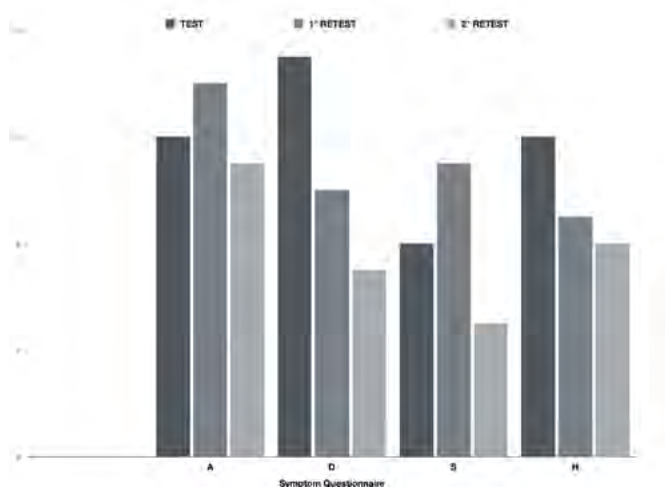


FIGURE 2. SQ: median scores obtained for the total sample at the three treatment assessment points (diagnostic phase, six-month follow up, termination).

The mean values for each physiological parameter recorded in each PPP phase during the three treatment assessment points have been evaluated. As for the treatment's effectiveness regarding the autonomic disposition of the patients, statistical analyses revealed a significant difference among GSR values recorded during the stress phases ( $p < .02$ ) (Tab. IV). In particular, it

TABLE III.

Comparison of scores obtained from the SQ scales for the total sample during the three treatment assessment phases (diagnostic phase, six-month follow up, termination); non parametric Friedman and Wilcoxon test

	Friedman	1-2	1-3	2-3
A	< .002	n.s.	< .005	< .01
D	< .001	< .02	< .001	< .05
S	n.s.	n.s.	n.s.	n.s.
H	< .005	n.s.	< .005	< .02
TOT	< .005	< .05	< .002	< .01

Abbreviations: A: Anxiety; D: Depression; S: Somatic Symptoms; H: Hostility

was possible to identify an increase in GSR levels (activation) during stress-induction. Such an increase, however, is only observable after several months of therapy. Statistically significant differences emerged only when comparing the PPP carried out at the six-month follow-up to that recorded at termination (*phases 2-3*), and when comparing the PPP carried out at the diagnostic phase to that recorded at termination (*phases 1-3*).

## Discussion

Overall, the results of the present study seem to confirm the most recent experimental research regarding the ef-

**TABLE IV.** Comparison of GSR values for the total sample during the three treatment assessment points (diagnostic phase, six-month follow-up, termination) for every phase of the PPP (rest/baseline, stress, recovery); non parametric Friedman and Wilcoxon test.

	Friedman	1-2	1-3	2-3
Rest/Baseline	n.s.			
Stress	< .05	n.s.	< .02	< .02
Recovery	n.s.			

fectiveness of CBT in the treatment of ED when it is used in adjunct to pharmacological treatment<sup>39,40</sup>. Moreover, analyzing how the “recovery” process unfolds, it was possible to observe significantly reduced levels of self-reported depression within six months of therapy onset as well as decreased anxiety and hostility scores within the first year. This short-term cognitive-level improvement was observed to occur gradually and progressively and was also found to extend to long-term.

At the physiological level, the only index that showed significant improvement involved skin conductance (GSR) reactivity in the stress phase. Furthermore, such change was found only in the medium-long term (more than six months after the onset of treatment). Indeed, meager physiological reactivity during the stress phase and the low GSR levels have frequently been observed in depressed patients, in addition to patients suffering from an ED<sup>9,41</sup>. Therefore, it was possible to observe a partial discordance in patients’ responses to the treatment: patients’ self-perceived improvement preceded any changes observable at the physiological level. The patients examined in this study showed an improvement in mood that seemed to precede the improvements revealed through “objective” measures. This finding can be explained, in part, as being consistent with organic impairments induced by fasting and purging behaviors. Often, it is necessary to establish a period of rehabilitation and normalization of eating behaviors before one can observe a normal reestablishment of the patient’s physiological functioning.

Similar results were found by Lachish and colleagues<sup>42</sup> investigating the efficiency of cardiac function in anorexic patients. Using HR and HRV, as parameters for the comparison between AN and controls, a significant difference was highlighted at the beginning and at the end of the treatment; furthermore after 24 and 36 months from the remission of symptoms and weight restoration an improvement has been described. This indicates a shift of sympatho-vagal balance, toward vagal tone predominance, and a reduced sympathetic tone<sup>42</sup>. It additionally reflects a physiological adaptation to prolonged low energy state<sup>43-45</sup>.

In a recent review<sup>43</sup> the time required for recovery of cardiac function was highlighted: bradycardia and HRV increase can be observed up to 2 years after symptom remission<sup>46</sup> as well as after 7 or even 10 years<sup>46-48</sup>.

However, the data also seems to confirm the possibility that clinical indices coming from different channels (cognitive, physiological, behavioral) are relatively independent. Furthermore, the tendency frequently found in patients suffering from EDs shows a little “ego dystonic awareness”, which means they have difficulty recognizing their emotional states and biological needs<sup>4,5,14,15,20,28,49,50</sup>.

In fact, alexithymia has been shown to be a stable trait in ED patients resulting in a predisposing and perpetuating factor: failure to recognize emotions and needs arising from one’s body allows for the maintenance of a low BMI<sup>22</sup>. As a stable factor, alexithymia persists even after the reduction of depression and anxiety<sup>51</sup>, ED behaviors<sup>4</sup>, and can negatively affect the outcome of therapy<sup>52</sup>. It has been hypothesized that AN patients with alexithymia symptoms have greater difficulty in learning new specific strategies to effectively deal with negative emotions without the use of ED behaviors.

In fact, these behaviors in restricted AN (e.g. restriction/hunger) and BN (e.g., bingeing and elimination behaviors) usually function as maladaptive strategies to regulate or compensate for deficits in emotion regulation<sup>22,26</sup>. Furthermore, some experimental research demonstrates a tendency for females suffering from EDs to “exhibit” intense emotional reactions on the behavioral and verbal levels, despite experiencing little physiological activation<sup>8,9,13,53</sup>.

Although the literature contains recent studies aimed at studying the emotional-psychophysiological aspects in ED, there is no research that has taken into consideration other psychophysiological parameters than HR and HRV<sup>42,43,46-48</sup>.

In the present study, for the first time, these parameters were measured together with GSR, an indicator so far little studied<sup>8,9,13,53-57</sup>. In fact, it is interesting to note that this parameter is the only one that manifests reactivity after the treatment. Particularly, GSR represents the efficiency of cognitive functionality and so reflects the motivational activation and the attentional processes<sup>7</sup>. In light of this, the greater physiological reactivity found in this study following the therapeutic intervention may be, at least partially, interpreted as reflecting the patients’ learning of new cognitive strategies for processing and managing their emotional experiences.

Another aspect that could explain an increase in the GSR parameter is the remission of depressive symptoms: usually, the low GSR reflects the presence of cognitive deficits, such as difficulty concentrating<sup>8,9</sup>. However, further studies need to be conducted: it would be

useful to verify if GSR could be an indicator of improved cognitive impairment in patients with ED<sup>54</sup>. To date, there are few studies in the literature that analyze the stress response in patients with ED taking into account skin conductance, and, of these studies, many of the results are controversial<sup>8,9,13,53-57</sup>, probably also due to the different emotional and stressful stimuli selected by the authors to evaluate autonomic reactivity.

In addition, monitoring the effects of any form of psychotherapy raises a number of problems relative to the measurement criteria, decisions regarding when to carry out assessments, and possible generalization of the obtained results<sup>2</sup>. It is by now evident that the effects of treatment often do not involve only variables explicitly considered by the clinician, but much more global issues affecting the individual. Measurement of therapeutic change obtained with the various assessment tools also requires special attention in regard to the interpretation of the data collected “before and after”<sup>2,3</sup>. In testing the effectiveness of a treatment, it can be useful to consider the differences between the values collected at different times or to assess the mean change obtained from patients belonging to the same diagnostic category. Although this, it is essential not to neglect the possible influence of patients’ initial levels of subjective suffering, as well as the many other variables that can notably differentiate between apparently similar psychopathological dispositions.

Experimental research has ample clarity between different diagnostic categories and this allows for the creation of homogeneous groups of patients who are similar in terms of pathological features. Despite this, each individual’s clinical profile can still hide its own idiosyncratic maintenance factors behind nosological definitions. These idiosyncrasies are explained by the specific personal history of the patient, the relationship between the patient and his/her “environment”, the meanings that the patient cognitively attaches to events, and stable traits of personality<sup>2,27,28,41</sup>. Therefore, concerning the effectiveness assessments of different interventions, it becomes crucial to reconcile and integrate a more normative vision of the results with a more subjective vision that focuses on the peculiarities of the individual. This holds true both in the study of individual cases and in investigations of actual clinical populations<sup>8,9,27,28</sup>.

Thus, in addition to the initial diagnostic phase, a thorough investigation also becomes necessary in the assessment of the therapeutic effects. Such an investigation does not focus only on the detection of single symptoms and the most salient dysfunctional characteristics, but aims to gather a true “configuration” of qualitatively different responses<sup>8,9</sup>. The adoption of a multidimensional model of care makes it necessary to reformulate the concepts “recovery” or “remission” in order to consider all levels of analysis and their possible discordance. In fact, once

accepted that there are frequent “splits” in individuals’ responses, and that there is a need for a holistic investigation of each clinical case, the importance of assessing the true “result” of an intervention is greatly enhanced by the possibility of studying its “process”<sup>4-6</sup>. In other words, the collection of various indices throughout the duration of therapy is, in itself, an excellent tool for monitoring the therapy’s validity, as well as for providing important information about which aspects (i.e., cognitive, behavioral, physiological) respond best to treatment.

Consequently, one can deduce that there is very importance of emphasizing a treatment, psychological pharmacological integrated or less does not dwell only on a general disorder profile or on self-reported symptoms. The previously mentioned discordance, between cognitive-affective, physiological and behavioral levels<sup>11,13-17,55</sup>, necessarily prompts the clinician to continue to monitor treatment until there is not just the absence of symptoms, but also an objective assurance that the therapeutic changes have stabilized.

Ultimately, these considerations suggest, at least in part, the need to “relativize” the concept of improvement and to consider new methodological pathways for studying different therapeutic interventions’ effects. This concept only underlines the importance, even in the psychiatric, psychotherapeutic and clinical fields in general, of the need to obtain clinical evidence of the goodness of the treatment and the efficacy of the treatment itself as it is administered.

### Limitation

The main limitation of this study is the small sample. This study could be replicated by involving a larger number of participants. This could favor possible comparisons between male and female gender as well as comparisons between the various subtypes that characterize the spectrum of eating disorders, namely AN with restrictions, AN with binges, and BN.

Further factors, such as co-morbidities present, could also be considered by distinguishing any associations with anxiety, depressive, or obsessive disorder.

Furthermore, the evaluation of the emotional aspects could be enriched by tests and questionnaires aimed at investigating alexithymia and the capacity for emotional self-regulation; for example, the Toronto Alexithymia Scale (TAS)<sup>52</sup> and the Difficulties in Emotion Regulation Scale (DERS)<sup>53</sup> could prove useful for possible comparisons with the objective data derived from the PPP.

Further tools could also be used for the evaluation of the psychophysiological structure. For instance, it is known that mineral and electrolyte alterations affect the function of the ANS and contribute to disturbances of the cardiac autonomic function. Therefore, their dosages could be useful to understand and better describe the organic compromise as well as the slowness in psycho-

physical recovery even after the remission of symptoms. Finally, further studies may also examine the value of HRV, considering that in recent literature it is repeatedly reported as a very useful parameter for the diagnostic setting and for the description of some psychophysiological impairment.

In this light, the effectiveness of a combination of therapy like the CBT, less or more integrated with the psychopharmacological one, and biofeedback training may be evaluated in order to improve treatment outcomes, and try to obtain a good and healthy mind-body integration.

### Acknowledgements

The Authors thank Gabriella Coscioni for the revision of the English manuscript.

### Conflict of interest statement

The Authors declare no conflict of interest.

### Funding

This research did not receive any specific grant from

funding agencies in the public, commercial, or not-for-profit sectors.

### Authors' contributions

CP and RL took care of carrying out the research. CP, SG and NR wrote the paper and took care of the corrections.

All Authors read and approved the final version of the manuscript.

### Ethical consideration

This study was approved by the Institutional Ethics Committee of the University of Pisa.

The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki.

Written informed consent was obtained from each participant/patient for study participation and data publication.

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