Comorbid personality disorders in Chronic Fatigue Syndrome patients: a marker of psychopathological severity

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Introduction. This study was designed to evaluate the presence of personality disorders (PDs) in Chronic Fatigue Syndrome (CFS) patients and to determine their influence on the severity of the associated psychopathology.

Methods. 132 CFS patients were assessed using SCID-I, Personality Diagnostic Questionnaire-4+ (PDQ-4+) with its Clinical Significance Scale, and Fatigue Impact Scale. The Beck Depression Inventory, Buss-Durkee Hostility Inventory and the State-Trait Anxiety Inventory were also administered.

Results. 48.5% patients presented PDs, being the most frequent the Obsessive-Compulsive and Avoidant ones. Patients with PDs had more depressive symptoms. Irritability, resentment, suspicion and guilt were the symptoms related with PDQ-4+ total score.

Conclusions. According to these results, PDs may be frequent in CFS patients. This comorbidity is associated with a complex clinical profile, secondary to more severe psychiatric symptoms.

Keywords: Personality disorders, Psychopatology, Chronic Fatigue Syndrome

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Trastornos de personalidad comórbidos en pacientes con Síndrome de Fatiga Crónica: un marcador de gravedad psicopatológica

Introducción. Este estudio se diseñó para evaluar la presencia Trastornos de Personalidad (TP) en pacientes con Síndrome de Fatiga Crónica (SFC) y determinar la severidad psicopatológica asociada.

Método. Se evaluaron 132 pacientes con SFC mediante la SCID-I, el Cuestionario de Personalidad PDQ-4+, la Escala de Significación Clínica, y la Escala de Impacto de Fatiga. También se administraron el Inventario de Depresión de Beck, el Inventario de Hostilidad Buss-Durkee y el Cuestionario de Ansiedad Estado-Rasgo.

Resultados. El 48,5% de los pacientes presentaban TP, siendo los más frecuentes el Obsesivo-Compulsivo y el trastorno por Evitación. Pacientes con TP tenían más síntomas depresivos. Irritabilidad, resentimiento, suspicacia y culpa eran los síntomas más relacionados con la puntuación total del PDQ-4+.

Conclusiones. Según nuestros resultados, los TP pueden ser frecuentes en pacientes con SFC. Esta comorbilidad está asociada con un perfil clínico complejo, secundario a síntomas psiquiátricos más graves.

Palabras clave: Trastornos de personalidad, Psicopatología, Síndrome Fatiga Crónica

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INTRODUCTION

Chronic Fatigue Syndrome (CFS) is a medically unexplained illness associated with an important public health impact[1]. CFS patients suffer from different symptoms, being disabling chronic fatigue the principal one. Different studies have proposed several etiological factors, but its exact pathophysiology is unknown, given that research has been unable to find convincing evidence[2].

One line of research has been the influence of psychiatric and psychological factors on CFS development and prognosis. Following this trend, some studies that have focused on previous personality features of CFS patients, have suggested that previous maladaptive personality could be considered a risk factor for developing CFS (predisposing factor) and a condition contributing to its psychiatric morbidity (perpetuating and prognosis factor)[3-6]. However, this relationship has not been fully understood yet.

Although, some studies have evaluated different personality features in CFS patients, only a small number of them have examined the presence of personality disorders (PDs) considering a categorical perspective and using objective assessment instruments based on the DSM classification[3-7]. In this line, Nater et al.[3] and Ciccone et al.[4] used the Personality Diagnostic Questionnaire-4+ self-report (PDQ-4+) in order to assess the Axis II according to DSM-IV; while Johnson et al.[6] used the previous version of this instrument. Henderson and Tannock[5] employed the Structured Clinical Interview for DSM-III-R Diagnosis (SCID-II) and Courjaret et al.[7], the Assessment of DSM Personality disorders IV (ADP-IV) questionnaire. These studies have reported an overall prevalence of PDs in CFS ranging from 12% to almost 40%[4-7]. Regarding to PDs types, four studies found Obsessive-Compulsive Personality Disorder (OCPD) to be the most common[3-5,7]. However, in a previous study, it had been described that Histrionic (23%) and Borderline (17%) PDs were the most common in CFS[6]. These results concurred with the conclusions of a previous study of Pepper and cols. in which Dependent (11%), Histrionic (13%) and Obsessive-Compulsive (16%) PDs were the most frequently present in CFS patients[8]. Thus, all of these studies indicate that PDs seem relatively prevalent in CFS patients, although none has found sufficient evidence to establish a specific personality type.

Since PDs might contribute to the severity of CFS by means of a more complex psychopathological profile associated to the CFS symptoms[4]. However, there are limited published studies evaluating the relationship between PD presence and comorbid psychopathology in CFS patients[3]. Previous studies from primary and tertiary care clinics, have found high rates of current and lifetime psychiatric disorders in CFS patients, being the most frequent, mood and anxiety disorders[9,10]. In this line, Nater et al. (2009) demonstrated that almost 60% of people with CFS, fulfilled the criteria for at least one current psychiatric diagnosis and almost 90% had at least one lifetime psychiatric condition[9]. Besides, it has been suggested that around a third part of CFS patients are depressed at the time of diagnoses[11,12]. None of the studies that have evaluated psychopathological symptoms in CFS, have taken into account the influence of PDs, leaving a gap in the literature regarding the effect of this variable on the CFS psychopathological profile of these patients.

Based on this empirical background, our hypothesis was that CFS patients with premorbid PD, would exhibit more severe psychopathological symptoms at the time of the evaluation than CFS patients without PDs. To test this hypothesis, two objectives were proposed: (1) to investigate the presence of a PD in a sample of adult CFS patients, using standardized validated instruments, and (2) to compare differences in comorbid psychiatry symptoms, focusing on anxiety, depression and hostility, between CFS patients with and without a PD.

METHOD

Participants

It was an observational cross-sectional study, including 132 patients referred to the Department of Internal Medicine at the University Hospital in Barcelona. CFS diagnosis was established according to the Centre for Disease Control (CDC) criteria[1]. Inclusion criteria were being older than 18 years, having a CFS diagnosis according to CDC criteria, to complete the clinical assessment and to sign informed consent to participate. The exclusion criterion was the presence of severe unstable somatic disorders and learning disabilities. The study was approved by the Ethics Committee of the hospital research institute. All patients provided written informed consent for participation.

The initial sample consisted of 138 patients; however, 6 patients were excluded due to drop-outs, making the final sample size of 132 patients. A total of 121 (91.7%) patients from the final sample were women. The mean age of the participants at the time of evaluation was 47.7 years (*SD*=9.10). Regarding education and employment, 85 (64.4%) had studies up to primary Spanish level and only 36 (27.3%) were in an employment at the time of the study. Finally, in terms of marital status, 98 (74.2%) were married or cohabiting with a partner.

Procedure

Prior to psychiatric assessment, patients underwent an extensive clinical history and physical examination, com-

pleted by physicians with experience in CFS at the Internal Medicine Department. In order to exclude other fatigue causes, general analytic parameters, urinalysis and serological test were carried out, according to our diagnostic protocol[13]. After verifying CFS diagnosis, participants were referred to the Department of Psychiatry, in order to complete a comprehensive assessment.

After an initial screening, the psychopathological evaluation was carried out in 4 sessions by a psychiatrist and a clinical psychologist, who interviewed the patient, recorded sociodemographic and clinical data, conducted a psychopathological examination, applied the Structured Clinical Interview for DSM IV (SCID-I)[14] and administered the questionnaires.

Instruments

Personality Diagnostic Questionnaire-4+ (PDQ-4+)[15] is a 99-item self-report, true/false questionnaire, designed to assess the 10 PDs included in DSM-IV diagnostic criteria for axis II disorders. The PDQ total score provides an index of overall personality disturbance and is calculated by summing up all the pathological responses (total score ≥ 30 indicates that the respondent likely has a personality disturbance). Clinical Significance Scale is a brief structured interview, that is applied following the self-report section and it is used to confirm or not the diagnosis of each individual PD, according to the DSM-IV criteria. Spanish version of PDQ-4+ has proven suitable psychometric properties[16]. Anxiety was assessed with the Spanish version of the State-Trait Anxiety Inventory (STAI)[17]. STAI assesses Anxiety-State (temporary and transient anxiety status that results from situational stress) and Anxiety-Trait (predisposition enduring and permanent to react with anxiety in stressful situations). Depression was assessed with the Spanish version of the Beck Depression Inventory (BDI)[18]. A Spanish version of the Buss-Durkee Hostility Inventory (BDHI)[19] was used to evaluate hostility. The scale includes five subscales designed to measure aggressiveness: Assault, Indirect Hostility, Irritability, Negativism, and Verbal Aggression. The subscales composing the hostility dimension were: Resentment and Suspicion. An additional scale is Guilt. Total scores ≥ 27 indicate more aggressive/hostility or culpability. Severity of fatigue was assessed with the Spanish version of the Fatigue Impact Scale (FIS)[20]. Higher scores (range 0-160) indicate greater functional impairment.

Data analysis

Statistical analyses were performed with the SPSS version 17.0. Data analysis was performed in two steps: bivariate analysis and multivariate. In the bivariate analysis we evaluated the associations between different variables and PD presence. Between-group differences for quantitative variables were assessed with the independent *t*-test, and expressed as the 95% confidence interval (*CI*) of the mean difference. Effect size measures (Cohen's *d*) relating to the difference between patients with and without any PD were determined. The chi-square test (χ^2) or Fisher exact test were used to assess differences in categorical variables, determining the odds ratio (*OR*) and 95% *CI*. In order to reduce the presence of possible false positives effects, Bonferroni corrections were performed.

RESULTS

Sixty-four (48.5%) patients presented a PDs diagnosis according of the PDQ-4+ self-report and Clinical Significance Scale. PDQ-4+ total score comparing patients with and without any PD were 31.5 (*SD*=11.12) and 19.1 (*SD*=12.93), respectively (*t*=5.94; *p*<0.001; *CI*: 8.77 to 17.11). There were no differences between CFS patients with and without any PD in any of the demographic characteristics (Table 1).

Both groups of patients had similar age at CFS onset [PD: 33.6 (*SD*=10.45), no PD: 37.1 (*SD*=10.34); *t*=-1.93; *p*=0.06] and at CFS diagnoses [PD: 41.9 (*SD*=8.40), no PD: 42.5 (*SD*=8.58); *t*=-0.39; *p*=0.70]. The impact of fatigue, was also similar with respect to the FIS scores [PD: 131.2 (*SD*=20.61), no PD: 130.1 (*SD*=21.39); *t*=-0.29; *p*=0.77].

The mean PD number within those with any PD was 1.59 (*SD*=0.97, range: 1-5). Of the 64 patients meeting the criteria of a PD, 23 (35.9%) had more than one PD. The most frequent PDs were those from the Cluster C being the most prevalent, Obsessive-Compulsive followed by Avoidant and Depressive types (Table 2).

Regarding to the presence of any past Axis I DSM-IV disorder (SCID I), the most frequent diagnosis for total sample were mood (57.6%) and anxiety disorders (36.4%). CFS patients with any PD had more previous recurrent depressive episodes and Obsessive-Compulsive disorder; however, these differences were not statistically significant (Table 3).

Table 3 presents the scores for the different self-report psychiatric scales. The group of patients with PD reported more severe psychiatric symptoms than the group without PD. More specifically, patients CFS-PD had significantly higher mean scores than CFS-non PD in the BDHI total score and in five of its subscales: two scales of aggressiveness (Irritability, and Negativism), two of hostility (Resentment, and Suspicion) and of Guilt. The differences were not statistically significant for the BDI, STAI-Trait and STAI-State questionnaires.

Table 1 Demographic characteristics

	PD (n=64)	No PD (n=68)	χ^2	p
Age, years, mean (SD)	47.48 (8.86)	47.90 (9.38)	-0.26	0.80
Female, n (%)	58 (90.63)	63 (92.65)	0.42	0.68
Level of education				
Primary or less, n (%)	19 (29.69)	28 (41.18)	1.37	0.17
Secondary, n (%)	29 (45.31)	31 (45.59)	0.03	0.97
High (university), n (%)	16 (25.00)	9 (13.24)	1.72	0.09
Occupation				
Employed, n (%)	19 (29.69)	17 (25.00)	0.60	0.55
Unemployed, n (%)	4 (6.25)	5 (7.35)	0.07	0.80
Housewife/ studying, n (%)	41 (64.06)	45 (66.18)	0.06	0.80
Civil status				
Single, n (%)	5 (7.81)	10 (14.71)	1.24	0.21
Married or partner, n (%)	51 (79.69)	47 (69.12)	1.38	0.17

Table 2 PDs prevalence and descriptive data for the PDQ-4+ and Clinical Significance Scale

	Patients with PD n (%)	Number of PDQ4+ criteria in patients with any PD Mean (SD)	Number of PDQ4+ criteria in patients without any PD Mean (SD)	t	p	Cohen's d
CLUSTER A:	5 (3.78)	-	-	-	-	-
Paranoid	5 (3.78)	2.25 (1.75)	1.16 (1.39)	3.95	<0.001	0.69
Schizoid	0 (0.00)	2.69 (1.67)	1.72 (1.44)	3.56	0.001	0.62
Schizotypal	0 (0.00)	2.88 (1.77)	1.74 (1.79)	3.68	<0.001	0.64
CLUSTER B:	6 (4.55)	-	-	-	-	-
Histrionic	2 (1.52)	1.97 (1.46)	1.32 (0.98)	3.00	0.003	0.52
Narcissistic	1 (0.76)	1.69 (1.30)	0.94 (1.13)	3.53	0.001	0.62
Borderline	4 (3.03)	2.59 (1.73)	1.63 (1.74)	3.18	0.002	0.55
Antisocial	0 (0.00)	0.58 (0.87)	0.34 (0.56)	1.87	0.06	0.33
CLUSTER C:	40 (30.30)	-	-	-	-	-
Avoidant	23 (17.42)	3.61 (1.77)	1.93 (1.75)	5.50	<0.001	0.95
Dependent	2 (1.52)	1.86 (1.94)	1.15 (1.51)	2.36	0.02	0.41
Obsessive-compulsive	43 (32.60)	4.52 (1.45)	2.54 (1.56)	7.52	<0.001	1.31
APPENDIX:	22 (16.67)	-	-	-	-	-
Negativistic	2 (1.52)	1.98 (1.27)	1.49 (1.40)	2.13	0.04	0.37
Depressive	20 (15.15)	4.42 (1.78)	2.87 (2.06)	4.63	<0.001	0.81

DISCUSSION AND CONCLUSIONS

According to the reported results, PDs may be frequent in CFS patients and its presence is associated with a more complex clinical profile secondary to more frequent and severe psychiatric symptoms. To our knowledge, although some studies have evaluated PDs presence in CFS patients using the PDQ-4+, it is the first study that systematically applies the Clinical Significance Scale section of the instrument[4]. Clinical Significance Scale allows more rigorous

Table 3 Comparison of the psychopathological profile between CFS patients with and without any PD

Prior psychiatric disorders	PD (n=64)	No PD (n=68)	χ^2	p	OR	95% CI
Depression disorder (one episode), n (%)	10 (15.63)	19 (27.94)	1.70	0.09	0.48	0.20 to 1.13
Depression disorder (more than one episode), n (%)	19 (29.69)	10 (14.71)	2.07	0.04	2.45	1.04 to 5.78
Dysthimia, n (%)	20 (31.25)	13 (19.12)	1.60	0.11	1.92	0.86 to 4.29
Panic attacks, n (%)	8 (12.50)	8 (11.76)	0.13	0.90	1.07	0.38 to 3.05
Generalized anxiety disorder, n (%)	15 (23.44)	13 (19.12)	0.60	0.55	1.30	0.56 to 2.99
Obsessive compulsive disorder, n (%)	12 (18.75)	4 (5.88)	2.26	0.02	3.69	1.12 to 12.13
Post-traumatic stress disorder, n (%)	6 (9.38)	5 (7.35)	0.42	0.68	1.30	0.38 to 4.50
Psychopathological profile	**PD (n=64)**	**No PD (n=68)**	**t**	**p**	**Cohen's d**	**95% CI**
STAI-State, mean (SD)	33.11 (13.95)	31.09 (14.78)	0.81	0.42	0.14	-2.94 to 6.97
STAI-Trait, mean (SD)	34.92 (11.57)	31.56 (12.57)	1.59	0.11	0.28	-0.81 to 7.53
BDI, mean (SD)	24.53 (9.23)	20.24 (10.60)	2.48	0.02	0.43	0.87 to 7.73
BDHI total score, mean (SD)	33.41 (10.42)	25.69 (9.82)	4.38	<0.001	0.76	4.23 to 11.20
BDHI Assault, mean (SD)	1.44 (1.57)	1.26 (1.23)	0.71	0.48	0.13	-0.31 to 0.66
BDHI Indirect Hostility, mean (SD)	4.19 (1.52)	3.53 (1.52)	2.49	0.02	0.43	0.13 to 1.18
BDHI Irritability, mean (SD)	6.05 (2.45)	4.50 (2.50)	3.59	<0.001	0.63	0.69 to 2.40
BDHI Negativism, mean (SD)	2.19 (1.51)	1.37 (1.36)	3.28	0.001	0.57	0.33 to 1.31
BDHI Resentment, mean (SD)	2.95 (1.63)	1.75 (1.46)	4.48	<0.001	0.78	0.67 to 1.74
BDHI Suspicion, mean (SD)	4.25 (2.30)	2.99 (1.74)	3.56	0.001	0.62	0.56 to 1.97
BDHI Verbal Aggression, mean (SD)	6.88 (2.93)	6.34 (2.56)	1.12	0.26	0.20	-0.41 to 1.48
BDHI Guilt, mean (SD)	4.39 (2.05)	3.22 (1.79)	3.49	0.001	0.61	0.51 to 1.83

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; FIS, Fatigue Impact Scale; STAI, State-Trait Anxiety Inventory; BDI, Beck Depression Inventory; BDHI, Buss-Durkee Hostility Inventory

diagnosis approaches and prevents misdiagnosis secondary to premorbid illness state idealization. According to the categorical approach of this instrument, 48.5% of the CFS patients met the criteria for PDs. This findings is consistent with previous published studies[4-6] using same criteria for PD[4] or the same instrument[5,6]. However, it differs from the lower prevalence observed in studies with others diagnostic measures[7] and others samples[21]. Thus, differences in the prevalence of comorbidity in PD might be a function of the diagnostic procedures and populations studied. Interestingly, we found the most frequent PDs were those from Cluster C, being OCPD the most common one. This finding concurs with previous results although our reported prevalence is the highest amongst them[4,5,7].

OCPD is also one of the most prevalent PDs in the community and outpatient samples. However, the observed prevalence in our sample is much higher than previously reported in community samples and outpatient groups[21,22]. Other PDs, including Avoidant and Borderline PDs, were

also found to be higher in our sample when comparing to the general population[22]. Our reported prevalence of Borderline PD is lower than the described in other CFS samples[6] and others psychiatric samples[21]. Also, this result is not consistent with the studies suggesting that emotional instability could be predictive of a later diagnosis of CFS[23]. However, some authors have pointed out that this personality alteration might be merely a consequence of the illness itself[24]. Unfortunately, these hypotheses have been poorly explored. Different diagnostic approaches (categorical and dimensional) should be taken into consideration to assess the presence of BPD and emotional instability in CFS patients.

Our results could also be understood within the frame of previous reports, where premorbid personality features of CFS patients were evaluated, without considering the diagnosis of a PD. It has been reported that these patients describe themselves as perfectionists, reporting high standards for work performance, responsibility and marked achievement orientation[25]. Catastrophic beliefs, neuroticism, high conscientiousness, emotional control and low self-esteem have also been described in CFS[26]. All these personality variables point to cluster C personality traits[2,23,27].

Although OCPD has been largely recognized, we know little about its comorbidity in general population. It has been described that individuals with OCPD have higher comorbidity with many psychiatric disorders compared to general population, and anxiety and mood disorders would be the most frequent in OCPD women[28]. In our results, we observed those CFS-PDs presented higher rates of previous psychopathological disorders and more severe anxiety, depression and hostility symptoms at the time of evaluation. Significant differences in depression and hostility were found. Regarding anxiety, although the CFS-PD group had higher severity of anxiety symptoms, the differences were not significant. In generally, this result concurs with previous studies suggesting a close association between CFS and psychiatric disorders[4,29]. However, previous reports had not considered the role of PDs on psychiatric comorbidity in CFS. According to our results, it may be considered that PDs act as a psychopathological symptoms perpetuation factor in CFS patients by reinforcing the concept that they are associated with a poorer outcome. Similarly, our results make it necessary to consider the presence of clinically anxious with regard not only to the presence of PD, but also to chronic disease. Additionally, our results suggest that anxious symptoms may be more related to the chronic disease evolution than to the PD presence.

The nature of the relationship between psychiatric disorders and CFS is still a controversial issue despite the great research interest[30]. Some authors have suggested that they may act as independent risk factors for each other[31]. This frequent association could be understood as a psychological reaction to the illness functional consequences. For instance, according to the literature, CFS patients tend to exhibit maladaptive perfectionism, high self-criticism and emotional control and report high standards for work performance and responsibility[2,23,27]. All of these goals may be frustrated by the illness symptoms. From a neurobiological perspective, we could hypothesize that the considerable association between these symptoms stems from a biological origin. Some authors have argued that one of the pathophysiologic mechanisms underlying CFS may include disturbances of the neurobiological stress system, which in some vulnerable patients would lose their capacity to adapt to all kind of stressors[32]. PDs are associated with maladaptive responses to psychosocial demands leading the patient into a chronic stress situation. Therefore, these observations suggest that premorbid personality may be a CFS predisposing factor, leading to a failure of the stress system functioning in some vulnerable patients. The retrospective acquisition of the personality data in our study does not let us know if PD presence was prior to CFS. Therefore, it is necessary to develop further studies in order to confirm these explicative models.

As far as we know, although different studies have evaluated the association between depression and CFS, little is known about the clinical characteristics of this disorder in CFS. According to our results, patients with CFS and PDs may present more suspicion, resentment, irritability and guilt. These symptoms are not the most common ones in general population with depressive episodes and could reflect an atypical presentation of depression in CFS patients with PDs.

The main limitations of this study should be noted. The sample was recruited from a tertiary centre and, as a consequence, the results may be biased, presenting a more severe clinical profile. Additionally, the use of a self-reported instrument may have over diagnosed the PD frequency. Further studies using other diagnosis instruments should be developed. Another limitation is the lack of a control group. Although, it would had been interesting to explore differences between both groups, the nature of this study was descriptive with its main aim focusing on presence of PDs in a sample of CFS patients as well as comparing their psychopathologic clinical profile with CFS without PDs. To minimize this limitation, prospective studies with healthy people should be developed. Also, given the size and heterogeneity PDs found in the sample, it is difficult to generalize the results. Future research should consider these limitations to study the influence of specific PD and its associated psychopathology in CFS.

In conclusion, our findings support the idea that CFS aetiology may be evaluated with a multifactorial model, which takes into account biological and psychological

factors. PDs, especially OCPD, may be more common in CFS patients than in general population. This comorbidity is related with a more severe clinical profile, secondary to more frequent and severe psychiatric symptoms, especially depressive and hostility. The close relationship between CFS, PDs and psychopathology may determine a CFS subtype with specific predisposing and perpetuating factors. Future research is needed to confirm these results and improve the knowledge of different possible clinical profiles of CFS patients that may need different therapeutic approaches.

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