Neurologic Soft Signs in Borderline Personality Disorder

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Objective: Borderline personality disorder is a disabling and dramatic psychiatric condition. To date, its pathophysiology remains unclear. Scientific evidence seems to have found underlying, nonfocal, central nervous system dysfunction in borderline personality disorder. Neurologic soft signs are anomalies only evidenced by specific motor, sensory, or integrative testing when no other sign of a neurologic lesion is present. Neurologic soft signs have been proposed to be nonfocal in origin and to reflect central nervous system failure. The assessment of neurologic soft signs now appears reliable and stable. Assuming that neurologic soft signs reflect nonfocal central nervous system dysfunction, we hypothesized that patients with borderline personality disorder should have an increased frequency of neurologic soft signs, therefore enhancing the possibility of the existence in borderline personality disorder of a nonlocalized brain dysfunction.

Method: To test this hypothesis, we compared 29 neurologic soft signs in 20 drug-free patients with DSM-III-R borderline personality disorder and 20 controls, using an examination adapted from the literature on neurologic soft signs. The study was conducted from February 1991 to March 1993.

Results: Thirteen neurologic soft signs were significantly more frequent in the borderline group. Patients with borderline personality disorder showed more left side, right side, and total neurologic soft signs than controls ($p = .0001$). All patients in the borderline group exhibited at least 1 neurologic soft sign, while only 7 controls did ($p = .0001$).

Conclusion: Our hypothesis was confirmed. These results add evidence to the possibility of the existence of a nonfocal central nervous system failure in borderline personality disorder.

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The physiopathologic processes involved in borderline personality disorder remain unclear. Borderline personality disorder has been associated with several pathologic conditions such as schizophrenia,[1,2] schizoaffective disorders,[3] atypical psychoses,[3,4] and affective disorders.[2,5,6] Dysfunction of the noradrenergic and opiate,[7] serotonin,[8–10] dopamine,[11,12] and acetylcholine[13] systems has been proposed to contribute to borderline personality disorder. Epilepsy-related phenomena have also been evoked. Snyder and Pitts,[14] Cowdry and Pickar,[15] Tanahashi,[16] and De la Fuente et al.[17] have found significant abnormalities in electroencephalographic (EEG) scalp records of borderline patients. These EEG abnormalities in borderline personality disorder could illustrate a non–EEG-localizable brain dysfunction.[17,18] In addition, personalities with aggressive and impulsive behavior—2 main characteristics of borderline personality disorder—have been proposed to exhibit neurologic damage.[19–21]

The so-called neurologic "soft" signs are neurologic anomalies only evidenced by specific motor, sensory, or integrative testing when no other sign of a neurologic lesion is present. The assessment of neurologic soft signs now appears reliable[22] and stable.[23] Neurologic soft signs have been studied in several psychiatric[24–51] and risk pediatric populations.[35,52–56] Neurologic soft signs have been proposed to be nonfocal in origin and to reflect central nervous system failure.[24–26,30,35–37,43,50–52] Two previous studies[36,40] have found significantly increased neurologic soft signs in patients with borderline personality disorder. We have previously described metabolic cerebral disturbances[57,58] and a 40% incidence of diffuse slow EEG

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activity[17] in borderline personality disorder suggesting underlying brain dysfunction. The EEG study also showed no evidence of focal abnormality.

Assuming that neurologic soft signs do reflect underlying nonfocal central nervous system dysfunction, we hypothesized that patients with borderline personality disorder should have an increased frequency of neurologic soft signs compared to controls, therefore enhancing the possibility of the existence of a nonlocalized brain dysfunction in those patients, as we have already proposed. To test this hypothesis, and given the potential influence of psychotropic drugs on the results,[42,59] we compared the incidence of 29 neurologic soft signs in 20 drug-free patients with borderline personality disorder and 20 controls.

METHOD

Patients

Twenty consecutive inpatients (14 women, mean age = 32.40 years; range, 21–45) fulfilling the DSM-III-R[60] criteria for borderline personality disorder (mean = 6.8 criteria) and with a score of at least 7 (mean = 8.75) on Gunderson and colleagues' Diagnostic Interview for Borderlines (DIB)[61] were recruited. Patients were screened, using the DSM-III-R and the Schedule for Affective Disorders and Schizophrenia lifetime version (SADS-L),[62] in order to determine the existence of other present or past DSM-III-R (clinical interview) and Research Diagnostic Criteria (RDC)[63] diagnoses. Other criteria for inclusion were normal physical and neurologic standard examination findings, normal standard biological blood test values, and normal electrocardiogram results. A 24-item Hamilton Rating Scale for Depression (HAM-D) was obtained from patients on the same day of examinations. Exclusion criteria included present DSM-III-R Axis I disturbances; history of epilepsy, encephalitis, head trauma, or other neurologic events; and inability to discontinue alcohol or psychoactive substances during the washout period.

The 20 patients underwent a washout period of at least 10 days (15 days for tricyclic antidepressants and monoamine oxidase inhibitor agents). No borderline patient had taken neuroleptics in the 2 months before the study. Patient compliance regarding the use of any recreational drug, medication, or alcohol during the preexamination washout period was strictly verified by repeated and unannounced plasma screenings. All 20 patients had borderline personality disorder as the main diagnosis. All patients were aware of the objectives of the study, and all gave informed consent.

Twenty age- and sex-matched healthy volunteers (14 women and 6 men, mean age = 35.45 years; range, 24–44) were recruited through announcements. These controls were also screened using the DSM-III-R and the SADS-L.

Table 1. Clinical Features in 20 Patients With Borderline Personality Disorder and 20 Controls

Variable	Borderline Personality Disorder	Controls[a]
Age, mean ± SD, y	32.40 ± 6.90	35.45 ± 5.79
Women, N	14	14
Lifetime prevalence of drug/alcohol abuse, N	11	
DSM-III-R, mean ± SD score	6.8	
DIB, mean ± SD score	8.75	

[a]The controls did not exhibit lifetime prevalence of drug/alcohol abuse, and they did not score on the diagnostic DSM-III-R and DIB tools.
Abbreviations: DIB = Diagnostic Interview for Borderlines; DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised.

The study was conducted between February 1991 and March 1993.

Neurologic Soft Signs

Twenty-nine neurologic soft signs were assessed by a trained physician with an adapted examination derived from the literature as described by Quitkin et al.[30] and later adapted by Gardner et al.[36] The examinations were done in a place that was different from the inpatient unit. Neurologic soft signs were always assessed by the same trained clinician who was blind to the psychiatric or control status of the subject.

Statistical Analysis

As neurologic soft signs were distributed normally in the borderline group but not in the control group, we used the nonparametric Mann-Whitney U test to assess differences between groups. When a neurologic soft sign showed a statistical difference between groups, in the group showing more individuals with that sign (always patients with borderline personality disorder), the possible influence on the amount of that neurologic soft sign of sex, age, intensity of depressive symptoms (HAM-D), and antecedents of drug and alcohol abuse were assessed using t tests for the continuous parameters and χ^2 tests for the categorical ones.

RESULTS

Age was not statistically different between groups ($t = 1.51$, $df = 38$, $p = .1$). Clinical features are shown in Table 1.

As displayed in Table 2, neurologic soft signs were present in both groups. Mann-Whitney test showed statistical differences between groups ($U = 12.50$, $Z = –5.18$, $p = .0001$). All patients in the borderline group exhibited at least 1 neurologic soft sign, and 7 individuals in the control group did ($U = 70$, $Z = –4.33$, $p = .0001$). Thirteen neurologic soft signs were significantly more frequent in the borderline group. Borderline personality disorder patients

Table 2. Distribution of Neurologic Soft Signs in 20 Patients With Borderline Personality Disorder and 20 Controls[a]

Neurologic Soft Sign[b]	Borderline Personality Disorder (N)	Controls (N)	U	Z	p
Speech	10	2	120	–2.72	**.006**
Left-right confusion	7	2	150	–1.86	.06
Hopping left	6	0	140	–2.62	**.009**
Hopping right	5	0	150	–2.36	**.01**
Gait	2	0	180	–1.43	.15
Running	5	0	150	–2.36	**.01**
Adventitious overflow	7	0	130	–2.87	**.004**
Finger-thumb opposition, left	5	2	170	–1.23	.21
Finger-thumb opposition, right	6	1	150	–2.05	**.04**
Finger-thumb mirror, left	5	0	150	–2.36	**.01**
Finger-thumb mirror, right	5	1	170	–1.74	.08
Pronation-supination, left	4	0	160	–2.08	**.03**
Pronation-supination, right	3	1	180	–1.04	.29
Pronation-supination, right, left, left	4	0	160	–2.08	**.03**
Pronation-supination, right, left, right	2	1	190	–0.59	.55
Pronation-supination, mirror left	5	0	150	–2.36	**.01**
Pronation-supination, mirror right	5	0	150	–2.36	**.01**
Foot taps left	1	0	190	–1.00	.31
Foot taps right	3	0	170	–1.77	.07
Foot taps right, left, left	3	0	170	–1.77	.07
Foot taps right, left, right	2	0	180	–1.43	.15
Foot taps mirror left	3	0	170	–1.77	.07
Foot taps mirror right	1	0	190	–1.00	.31
Face-hand simultaneous touch	5	0	150	–2.36	**.01**
Stereognosia left	0	0	200	0	1.00
Stereognosia right	0	0	200	0	1.00
Agraphesthesia left	2	1	190	–0.59	.55
Agraphesthesia right	0	1	190	–1.00	.31
Tandem walking	7	1	140	–2.34	**.01**
Left side neurologic soft signs	38	3	40.50	–4.64	**.0001**
Right side neurologic soft signs	32	5	54.50	–4.21	**.0001**
Total neurologic soft signs	113	13	12.50	–5.18	**.0001**
At least 1 neurologic soft sign	20	7	70	–4.33	**.0001**

[a]Neurologic soft signs reaching significant ($p < .05$) differences between groups are shown in bold.
[b]Mann-Whitney U test: borderline personality disorder vs. control (U = 12.50; Z = –5.18; p = .0001).

showed more left side, right side, and total neurologic soft signs than controls (left side: N = 38 vs. N = 3, U = 40.50, Z = –4.64, p = .0001; right side: N = 32 vs. N = 5, U = 54.50, Z = –4.21, p = .0001; total neurologic soft signs: N = 113 vs. N = 13, U = 12.50, Z = –5.18, p = .0001.

Age, sex, intensity of depressive symptoms, and a past history of drug or alcohol abuse failed to show any statistically significant effect on the number of neurologic soft signs in the borderline group except for age on the number of left side neurologic soft signs: patients with more left side neurologic soft signs were older (33.71 ± 6.46 vs. 25.00 ± 4.58 years; t = –2.21, df = 18, p = .04). In the borderline group, there were not more left than right neurologic soft signs (left: N = 38; right: N = 32; t = 1.24, df = 19, p = .23).

DISCUSSION

We found more neurologic soft signs in a group of drug- and treatment-free borderline personality disorder patients compared to controls. Consequently, our hypothesis was confirmed.

This study was prospective; the researcher was blind to the subject condition, and all examinations were performed after rigorously controlled washout and admission criteria review. On the other hand, our work has as a limitation the relative small number of patients.

Our present results are in accord with the 2 previous studies on neurologic soft signs in borderline personality disorder.[36,40] Gardner et al.[36] excluded alcohol and drug abuse patients from the study and observed a drug washout period of 2 weeks, but the raters were aware of the patients' diagnoses. Stein et al.[40] were blind to the subjects' diagnoses but not all their patients were free of treatment, and, while they described that 90% of patients had positive histories of substance abuse, nothing was specified for drug and alcohol at the time of examinations.

As a whole, neurologic soft signs were not lateralized. As illustrated in Table 2, contralateral differences were significant between groups for only 4 signs.

Keenan et al.[64] suggested a relationship between alcohol abuse and the occurrence of neurologic soft signs. We failed to detect any significant effect of past history of drug or alcohol abuse on the number of neurologic soft

signs in our borderline group, but, unlike the Keenan et al. patients, our group was completely abstinent from alcohol.

Psychotropic medication has been proposed both to contribute to the prevalence of neurologic soft signs[42] and to have no link to it.[49,59] The high incidence of neurologic soft signs found in our study might not be a consequence of concomitant medication or drug use as no patient had taken neuroleptics in the 2 months before the examination and the drug washout was verified by unannounced plasma screenings.

There is now scientific evidence of brain dysfunction in the borderline syndrome. Besides the EEG and neurologic soft sign publications, Drake et al.[65] have found altered responses on auditory evoked potentials, suggesting differences in limbic system function in patients with borderline personality disorder. Structural brain abnormalities have been suggested by computed tomography (CT) scan[66–68] and magnetic nuclear resonance[69] studies. We have previously described metabolic cerebral disturbances as relative hypometabolism in the dorsolateral part of the frontal cortex, the anterior cingulate cortex, and the basal ganglia and the thalamus[57,58] and a 40% incidence of diffuse slow EEG activity[17] in borderline personality disorder suggesting underlying brain harm. All these findings along with our present results seem to indicate underlying brain dysfunction, without evidence of focal abnormality, as a substrate for borderline patients.

Gray matter volume loss has been found in the left amygdala of women with borderline personality disorder.[69] Dazzan et al.[51] more recently suggested that neurologic soft signs are associated with gray matter volume changes and that they may represent a perturbed corticosubcortical connectivity. Our results showing neurologic soft signs in borderline personality disorder might, therefore, reflect the existence of gray matter troubles in this disorder.

A high proportion of neurologic soft signs has been described in other psychiatric conditions including schizophrenia[27,37,44,59,70]; offspring of mothers with schizophrenia[56]; childhood hyperactivity and attention deficit disorder[71]; anxiety and affective disorder in children, adolescents,[35] and adults[38]; obsessive-compulsive disorder[39,41,72]; and posttraumatic stress disorder.[46,47] Neurologic soft signs have also been proposed to predict cognitive and psychiatric problems in hearing-impaired children,[53] female adolescents,[35] and low-birthweight children.[52,54] Beyond all those findings, we should not forget that all of them may be nonspecific and that the symptoms in pathologies such as borderline personality disorder might be purely epiphenomenological as it is possible that all brain disorders are characterized by both neurologic and psychiatric symptoms.[73] In that case, the goal would be to determine which brain disorder or disorders explain the borderline personality disorder symptoms.

To date, we have no treatment of choice in borderline personality disorder, which causes enormous suffering and continues to be a life-threatening condition. Advances in the knowledge of the pathophysiologic substrate of this condition are important as they would help to find efficacious treatments.

From a nosological and formal point of view, the future classifications of mental disorders (DSM-V)[74] will probably need to include not only clinical and epidemiologic criteria but also biological evidence, in order to definitely differentiate personality disorders from normal personality. If confirmed by other independent studies, the existence of neurologic soft signs in borderline personality disorder could be an aid to the diagnosis of this entity and a proof that borderline personality disorder is not merely an "extreme variant" of the maladaptive variants of personality within the normal population as proposed by some,[75] because the normal population do not show neurologic soft signs, CT scan or EEG alterations, or metabolic cerebral disturbances.

Finally, more research on the underlying mechanisms of borderline personality disorder seems warranted because the more we know about the pathophysiology of this condition, the closer we will be to finding an effective treatment for these patients.

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