

Neurologic Soft Signs in Chronic Posttraumatic Stress Disorder

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Background: Subtle neurologic impairment has been reported in several mental disorders. The goals of the present study were to evaluate neurologic status in patients of both sexes with chronic posttraumatic stress disorder (PTSD) from different traumatic experiences.

Methods: Twenty-one adult women who were sexually abused as children (12 with PTSD, 9 without) and 38 male Vietnam War combat veterans (23 with PTSD, 15 without) underwent examination for 41 neurologic soft signs, which were scored by the examiner as well as a blind rater observing videotapes. Subject history was obtained with special attention to neurodevelopmental problems. Psychometrics included the Wender Utah Rating Scale for symptoms of childhood attention-deficit/hyperactivity disorder and the Michigan Alcoholism Screening Test. Veterans also completed the Combat Exposure Scale and subtests of the Wechsler Adult Intelligence Scale–Revised.

Results: Average neurologic soft sign scores (interrater

reliability = 0.74) of women with PTSD owing to sexual abuse in childhood (mean [SD], 0.77 [0.32]) and veteran men (0.72 [0.20]) with combat-related PTSD were comparable and significantly ($P < .001$) higher than those of women sexually abused as children (0.42 [0.10]) and combat veteran men (0.43 [0.17]) without PTSD. This effect could not be explained by a history of alcoholism or head injury. Subjects with PTSD reported more neurodevelopmental problems and more childhood attention-deficit/hyperactivity disorder symptoms and had lower IQs, all of which were significantly correlated with neurologic soft signs.

Conclusion: Neurologic compromise is evident from subject history and findings from physical examination in both women and men with chronic PTSD who had experienced different kinds of traumatic events in childhood and adulthood.

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NEUROLOGIC soft signs (NSSs) reflect subtle abnormalities of language, motor coordination, perception, and other central nervous system functions.^{1,2} Neurologic soft signs are nonspecific indicators of impairment that typically do not allow localization of central nervous system lesions. An increased incidence of NSSs has been found in patients with mental disorders, including those with schizophrenia,^{1,3-10} obsessive-compulsive disorder (OCD),¹¹⁻¹⁷ and social phobia.^{18,19} Neurologic soft signs have also been reported as sequelae of child abuse.²⁰⁻²²

In a preliminary study,²³ we reported more NSSs in a sample of male Vietnam War veterans with chronic combat-related posttraumatic stress disorder (PTSD) compared with a sample of male Vietnam War combat veterans without PTSD. We also reported more frequent childhood learning problems and enuresis in subjects with PTSD. That study involved only 1 gender and 1 type of trauma.

However, as currently understood, PTSD is a unified diagnostic concept that reflects a potential psychiatric outcome resulting from exposure to a variety of emotionally traumatic events. The goal of this study is to extend our preliminary observations from male combat veterans to adult women exposed to childhood sexual abuse (CSA) while at the same time attempting to replicate our previous findings in a new sample of male Vietnam War veterans. We hypothesized that subjects with chronic PTSD would demonstrate increased NSSs and compromised neurodevelopmental histories, regardless of gender or the nature of the trauma.

Our previous study²³ also had methodological limitations. First, NSSs were only scored by the examiner. This did not allow assessment of interrater reliability. In the present study, a second blind rater scored the NSSs from videotapes. Second, the previous study scored NSSs only regarding presence or absence. In the present investigation, the severity of NSSs was scored on an ordinal scale using an improved protocol.

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SUBJECTS AND METHODS

SUBJECTS

A convenience sample of 59 paid subjects was recruited from the population of individuals who had recently participated in psychophysiological experiments in our laboratory. After being informed that they would undergo a videotaped physical examination and psychological tests, subjects provided written informed consent.

On the basis of a Clinician-Administered PTSD Scale,²⁴ administered by a doctoral-level psychologist (N.B.L.), 12 female subjects exposed to CSA were classified as currently having PTSD and 9 as not having PTSD; 23 male Vietnam War combat veterans were classified as currently having PTSD and 15 as not having PTSD. Subject candidates were excluded if they had (1) previous but not current PTSD; (2) a history of major head injury involving loss of consciousness for a prolonged period (>10 minutes), tumor, epilepsy, cerebrovascular accident, or other neurologic disorder; (3) a history of dementia, amnesic disorder, mental disorder due to a general medical condition, schizophrenia, or other psychotic disorder; (4) alcohol or other substance dependence or abuse within the past year; (5) current inpatient status; (6) inability to abstain from psychotropics or other medications with potentially confounding neurologic or cognitive effects for at least 2 weeks prior to examination for any reason (including medical or therapeutic advice); or (7) participation in our previous preliminary study.²³

The Structured Clinical Interview for DSM-III-R²⁵ (administered by N.B.L.) revealed the following comorbid Axis I diagnoses. In women with PTSD exposed to CSA (n = 12), non-PTSD anxiety disorder was found in 6 (50%); major depression, 4 (33%); dysthymia, 3 (25%); eating disorder, 2 (17%); somatoform disorder, 1 (8%); past alcohol dependence or abuse, 4 (33%); and past other substance dependence or abuse, 3 (25%). In women without PTSD exposed to CSA (n = 9), non-PTSD anxiety disorder was found in 2 (22%); dysthymia, 1 (11%); past alcohol dependence or abuse, 1 (11%); and past other substance dependence or abuse, 1 (11%). In male veterans with PTSD (n = 23), non-PTSD anxiety disorder was found in 8 (35%); major depression, 15 (65%); dysthymia, 1 (4%); somatoform disorder, 1 (4%); past alcohol dependence or abuse, 15 (65%); and past other substance dependence or abuse, 11 (48%). In male veterans without PTSD (n = 15), non-PTSD anxiety disorder was found in 1 (7%); major depression, 1 (7%); past alcohol dependence or abuse, 6 (40%); and past other substance dependence or abuse, 3 (20%).

PROCEDURES

Neurologic Examination and History

The protocol for evaluating NSSs used in the present study incorporated techniques from several published

studies^{1,3,12,26-31} and represented a modification and refinement of the 37-item protocol used in our preliminary study.²³ Ten NSSs from that study were eliminated because they failed to differentiate the PTSD and non-PTSD groups. Twenty-seven NSSs were retained, and 14 new NSSs were added, resulting in 41 NSSs that were scored in the present study. The new protocol (available on request) assigned a score to each NSS on an ordinal scale (0-3) with specific anchors for each item. Neurologic examinations were performed by a neurologist/psychiatrist (T.V.G.) who was not informed of the subject's diagnosis. Each examination was videotaped and, along with the subject's figure drawings, sent for independent scoring by a trained second neurologist (A.S.T.) who was fully blind to diagnosis.

Following the examination, information regarding neurologic and medical conditions, past head injury, and neurodevelopmental problems was elicited via a structured interview (designed and administered by T.V.G.; available on request). Handedness was determined by means of a published inventory.³²

Psychometrics

All subjects completed the Michigan Alcoholism Screening Test (MAST),³³ a self-reported measure of lifetime alcoholism-related symptoms, and the Wender Utah Rating Scale,³⁴ a self-reported measure of childhood attention-deficit/hyperactivity disorder (ADHD) symptoms. An abbreviated version of the Wechsler Adult Intelligence Scale-Revised³⁵ was administered to the veterans. Estimated IQ was derived from the prorated scores of 5 subtests: information, arithmetic, picture completion, picture arrangement, and block design. Veterans also completed the Combat Exposure Scale.³⁶

Data Analysis

The overall statistical approach was analysis of variance (ANOVA) with 2 between-subjects factors: sample (CSA vs combat) and diagnosis (PTSD vs non-PTSD). Where appropriate, the within-subjects factor of rater (examiner [T.V.G.] vs videotape rater [A.S.T.]) was included. For categorical variables, Zelen exact tests³⁷ were substituted for ANOVA; in all instances, exact *P* values of constancy of association between strata (sample and diagnosis) were high ($P \geq .45$), so that the exact tests of unity of association were valid. Bonferroni corrections were used to adjust significance levels for analysis of the 41 individual NSSs ($P < .05/41 = .001$) and the 6 individual neuropsychiatric history items ($P < .05/6 = .008$). Pearson product moment correlations were calculated among variables of interest across all subjects and separately for the veterans for whom combat exposure and IQ data were also available.

RESULTS

DEMOGRAPHICS AND PSYCHOMETRICS

The subjects exposed to CSA were younger than the Vietnam War veterans (**Table 1**). As expected, subjects with PTSD scored higher on the Clinician-Administered PTSD Scale than subjects without PTSD. Subjects with PTSD

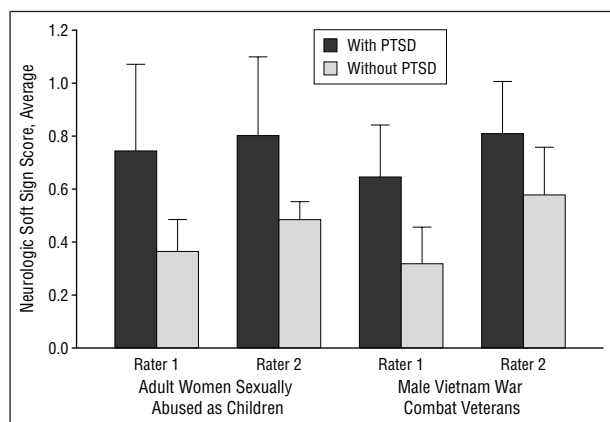
reported more lifetime alcohol-related symptoms on the MAST than subjects without PTSD. On the Wender Utah Rating Scale, subjects exposed to CSA reported more childhood ADHD symptoms than veterans, and subjects with PTSD reported more childhood ADHD symptoms than subjects without PTSD. Veterans with PTSD reported more severe combat exposure than veterans without PTSD. Veterans without PTSD had higher estimated IQs

Table 1. Demographic and Psychometric Characteristics*

Characteristic	Adult Women Sexually Abused as Children		Male Vietnam War Combat Veterans		Results of 2-Way ANOVAs					
	With PTSD (n = 12)	Without PTSD (n = 9)	With PTSD (n = 23)	Without PTSD (n = 15)	Sample		Diagnosis		Interaction	
					F _{1,55}	P	F _{1,55}	P	F _{1,55}	P
Age, y	42.8 (8.4)	43.4 (8.1)	46.0 (2.7)	49.2 (3.2)	8.8	.004	1.7	.20	<1.0	NS
Education, y	14.9 (1.4)	14.9 (2.3)	13.9 (3.0)	15.8 (2.2)	<1.0	NS	1.9	.17	2.0	.16
Wender Utah Rating Scale	50.8 (25.9)	21.0 (17.7)	27.5 (24.0)	11.1 (9.6)	8.4	.005	16.4	<.001	1.4	.25
Michigan Alcoholism Screening Test	6.9 (7.4)	3.9 (4.6)	15.9 (16.0)	3.0 (4.2)	1.8	.19	7.0	.01	2.7	.11
Clinician-Administered PTSD Scale	58.2 (21.9)	5.4 (5.7)	71.3 (19.4)	6.3 (9.7)	2.4	.13	165.7	<.001	1.8	.19
Combat Exposure Scale	31.4 (7.6)	16.1 (9.4)	5.5†	<.001
IQ, Wechsler Adult Intelligence Scale-Revised	105.7 (13.8)	120.5 (10.6)	3.3†	.002

*Values are given as mean (SD) except where indicated. ANOVA indicates analysis of variance; PTSD, posttraumatic stress disorder; NS, not significant; and ellipses, not applicable.

†t₅₆.



Group mean average neurologic soft sign scores in adult women sexually abused as children with (n = 12) vs without (n = 9) posttraumatic stress disorder (PTSD), and in Vietnam War combat veterans with (n = 23) vs without (n = 15) PTSD. Error bars indicate SDs. Rater 1 was the examiner; rater 2 was the videotape rater. For the comparison of subjects with vs without PTSD, $F_{1,110} = 58.4$ and $P < .001$. (See the "Neurologic Soft Signs" subsection of the "Results" section for details.)

than veterans with PTSD, but the mean of the latter was in the normal range.

NEUROLOGIC SOFT SIGNS

Because there were no significant sample or diagnosis interactions with the raters, means for the 41 individual NSSs (data available on request) were collapsed across raters. These ANOVAs revealed no sample main effect nor sample \times diagnosis interaction, significant at $P < .05$, for any NSS. Two NSS measures—"copy figures" ($F_{1,55} = 15.2$, $P < .001$) and "fist-palm-side" (left hand) ($F_{1,55} = 13.1$, $P < .001$)—distinguished subjects with and without PTSD at the Bonferroni-corrected significance level of $P < .001$.

An average NSS score was calculated for each subject by summing the scores on the individual NSS measure and dividing by the 41 NSSs examined. Interrater reliability was 0.74 (intraclass correlation coefficient). A 3-way ANOVA for average NSS scores (**Figure**) revealed significant main effects for diagnosis ($F_{1,110} = 58.4$, $P < .001$) and rater ($F_{1,110} = 27.6$, $P < .001$) but not for sample ($F_{1,110} = 1.2$, $P = .28$). None of the interactions was

significant ($F_{1,110} < 1$ for each). Average NSS scores collapsed across raters was significantly correlated with estimated IQ in the veteran sample ($r = -.55$, $n = 33$, $P < .001$) (IQ data unavailable in the CSA sample).

Five (42%) of 12 subjects with PTSD exposed to CSA and 0 (0%) of 9 subjects without PTSD exposed to CSA as well as 11 (48%) of 23 veterans with PTSD and 3 (23%; data unavailable for 2 subjects) of 13 veterans without PTSD reported a history of minor head injury involving only a brief loss of consciousness (<10 minutes) at some time in their lives (for sample, $P = .36$; for diagnosis, $P = .02$). To remove the potentially confounding contributions of a history of minor head injury and of past alcoholism, a hierarchical linear regression analysis was performed against average NSS scores collapsed across raters, entering data for history of minor head injury, MAST score, sample, and diagnosis, in that order. Sample remained nonsignificant ($F_{54,3} < 1$), whereas diagnosis was significant ($F_{53,4} = 22.6$, $P < .001$).

NEURODEVELOPMENTAL HISTORY

No sample or diagnosis main effect for any individual item reached the Bonferroni-corrected statistical significance level of $P < .008$ (**Table 2**). However, there was a significant effect of diagnosis for the composite history of one or more neurodevelopmental problems.

CORRELATIONS

The Clinician-Administered PTSD Scale score was significantly correlated with the average NSS score, history of a neurodevelopmental problem, childhood ADHD (Wender Utah Rating Scale) and alcoholism (MAST) symptoms (**Table 3**). In the veteran sample, the Clinician-Administered PTSD Scale score was negatively correlated with estimated IQ and positively correlated with severity of combat exposure (Table 3).

PREDICTIVE POWER

For working purposes, subjects were classified as neurologically compromised if they had a history of a neurodevelopmental problem or were in the upper half of a

Table 2. Numbers of Subjects With Neurodevelopmental History Items*

Neurodevelopmental Item	Adult Women Sexually Abused as Children		Male Vietnam War Combat Veterans		P†	
	With PTSD (n = 12)	Without PTSD (n = 9)	With PTSD (n = 23)	Without PTSD (n = 15)	Sample	Diagnosis
	Attention deficit	3/10 (30)	1/9 (11)	7/23 (30)	2/13 (15)	.99
Motor hyperactivity	2/11 (18)	0/9 (0)	5/23 (22)	0/13 (0)04
Learning problems	4/12 (33)	0/9 (0)	7/23 (30)	1/13 (8)	.99	.02
Repeated grades in school	1/12 (8)	0/9 (0)	9/23 (39)	1/13 (8)	.06	.03
Enuresis	2/11 (18)	1/9 (11)	4/23 (17)	3/13 (23)	.99	.99
Left-handed or ambidextrous	3/12 (25)	0/9 (0)	4/23 (17)	2/15 (13)	.99	.29
One or more of the above	8/12 (67)	2/9 (22)	16/23 (70)	3/13 (23)	.99	.001

*Data are presented as number of subjects/total number (percentage). Unavailable data not given. PTSD indicates posttraumatic stress disorder; ellipses, not applicable.

†Zelen exact test, Bonferroni correction of significance level to $P < .008$ for the top 6 items.

Table 3. Pearson Product Moment Correlation Matrices*

Subjects	r (P)					
	Average NSS Score	Neurodevelopmental Problem (NP)†	Wender Utah Rating Scale (WURS)	Wechsler Adult Intelligence Scale (IQ)	Combat Exposure Scale (CES)	Michigan Alcoholism Screening Test (MAST)
All subjects (N = 59)						
NSS
NP†	0.26 (.048)
WURS	0.27 (.045)	0.41 (.002)
MAST	0.46 (<.001)	0.17 (.20)	0.10 (.45)
Clinician-Administered PTSD Scale	0.52 (<.001)	0.44 (<.001)	0.42 (.001)	0.50 (<.001)
Male Vietnam War combat veterans (n = 38)						
NSS
NP†	0.30 (.08)
WURS	0.44 (.008)	.30 (.03)
IQ	-0.55 (<.001)	-.31 (.09)	-0.22 (.22)
CES	0.15 (.38)	.34 (.04)	0.20 (.23)	-0.46 (.007)
MAST	0.51 (.001)	0.15 (.40)	0.23 (.17)	-0.59 (<.001)	0.27 (.10)	...
Clinician-Administered PTSD Scale	0.57 (.001)	0.39 (.02)	0.43 (.01)	-0.59 (<.001)	0.71 (<.001)	0.54 (.001)

*NSS indicates neurologic soft sign; PTSD, posttraumatic stress disorder; and ellipses, not applicable.

†Point-biserial correlations for presence or absence, missing data in 2 subjects.

median split of all subjects according to average NSS scores. Of 35 subjects with PTSD, only 3 (9%; 1 from the CSA group and 2 veterans) were neurologically uncompromised. Of 22 subjects without PTSD (data unavailable for 2), only 7 (32%; 2 from the CSA group and 5 veterans) were neurologically compromised. The predictive power of neurologic compromise for PTSD diagnostic status was 82% (32/39). The predictive power of absence of neurologic compromise for non-PTSD status was 83% (15/18).

COMMENT

The results of this study replicate and extend our previous finding²³ of neurologic compromise in persons with chronic PTSD, as revealed by a more frequent history of neurodevelopmental problems and a greater number of objective NSSs in subjects with PTSD compared with trauma-exposed controls. The individual NSS items that

best discriminated subjects with PTSD from those without were copying 2- and 3-dimensional figures²⁹ and rhythmically and sequentially touching the thigh with the fist, then the palm, then the side of the left hand for 15 repetitions.²⁶ These were also the signs that best distinguished veterans with PTSD from those without in our previous preliminary study.²³

The NSSs were scored both by the examiner, who was not informed of subjects' diagnoses, and subsequently by a rater in another country (A.S.T.), who reviewed videotapes of the examinations without any knowledge of subject identity or diagnosis. The observed interrater reliability for average NSS score of 0.74 was good. Although the videotape rater overall assigned higher NSS scores than the examining rater, this did not interact with sample or diagnosis, and the videotape rater detected the same pattern of PTSD vs non-PTSD group differences across samples as did the examining rater.

A weakness of the historical data obtained from patients with a mental disorder is that the disorder, combined with the lapse of time, may influence retrospective self-reporting. However, in the present study, the significant association of history of a neurodevelopmental problem with objectively measured NSSs supports the validity of the historical data.

Neurologic compromise was evident both in a replication sample of Vietnam War combat veterans and in a sample of adult women exposed to CSA. The comparability of average NSS scores and of the PTSD vs non-PTSD differences in average NSS scores in the 2 samples is striking, given their differences not only regarding gender, but also regarding the type of trauma experienced.

Although none of our subjects were diagnosed with current alcohol dependence or abuse, the subjects with PTSD, especially the veterans, reported more severe symptoms of past alcoholism than the subjects without PTSD. However, the mean MAST score of the subjects with PTSD who were exposed to CSA, though higher than the subjects without PTSD who were exposed to CSA, was closer to the mean MAST score of the veterans without PTSD than it was to that of the veterans with PTSD; despite this, the mean average NSS score for the subjects with PTSD who were exposed to CSA was comparable to that of the veterans with PTSD. The association between PTSD diagnosis and (higher) average NSS scores remained significant after adjusting for the MAST score. These considerations suggest that the increased NSSs in the subjects with PTSD studied here cannot simply be regarded as the product of past alcoholism. We recognize that the statistical controls we employed to rule out the confounding effects of alcoholism and minor head injury do not provide the protection that would be afforded by excluding all such subjects if this were practical.

Several possible origins of a biological abnormality have been posited in PTSD.^{38,39} Neurologic compromise may reflect a preexisting risk for exposure to a traumatic event or a premorbid vulnerability for developing PTSD following such exposure. It may be the product of the traumatic exposure itself and/or the PTSD resulting from it. It may result from some consequence of PTSD, such as alcoholism. A limitation of this study is that the largely correlative data do not permit conclusions regarding causation. Only data collected prior to the traumatic exposure can definitively resolve these possibilities.

Research has suggested that NSSs reflect an underlying genetic predisposition for developing other psychiatric conditions. An increase in NSSs has been found in first-degree relatives of patients with schizophrenia.⁴⁰⁻⁴⁴ Relatives of probands with OCD with more NSSs have a significantly greater rate of having OCD than relatives of probands with OCD with fewer NSSs.⁴⁵ In a previous study,⁴⁶ we found that a lower estimated IQ at the time of induction into military service, ie, before deployment to Vietnam, significantly predicted the development of combat-related PTSD even after adjusting for combat exposure. In contrast, PTSD did not further lower IQ. These considerations led us to conclude that lower IQ represents a precombat vulnerability factor for PTSD. In the present study, average NSS score was negatively correlated with estimated IQ and positively correlated with a history of 1 or more (pretrauma) neurodevelopmental

problems, suggesting that the NSSs studied here in part reflect pretrauma neurologic compromise.

Theoretical considerations also support neurologic compromise as a vulnerability for developing PTSD. Elsewhere we have suggested that a diminished ability to cope with a traumatic event and its consequences owing to lower intelligence may increase the likelihood of the PTSD outcome.⁴⁶ Poorer coping by those with PTSD may also have a dysfunctional neurologic facet. Failure of cortical inhibitory control over conditioned emotional responses has been theorized to play a role in the pathogenesis of PTSD⁴⁷; such failure is more likely to occur in neurologically compromised individuals.

These considerations do not negate the importance of traumatic exposure in the genesis of PTSD. In the veterans, the correlation of combat exposure with PTSD symptoms was high ($r = 0.71$).

Although neither necessary nor sufficient for PTSD, the presence or absence of neurologic compromise had a high predictive value for the PTSD diagnosis outcome in this study. However, a limitation was that all the subjects with PTSD had experienced their traumatic events many years earlier and had long been suffering from the disorder. Therefore, the relationship with neurologic compromise should only be regarded as pertaining to chronic PTSD. It may be that the presence of antecedent neurologic abnormalities makes it less likely that patients with PTSD will recover, ie, predisposes them to a chronic course. Neurologic vulnerabilities may play a lesser role in acute PTSD; this question deserves investigation.

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