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BRIEF COMMUNICATION

Post-traumatic stress disorder among patients with chronic pain and chronic fatigue

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ABSTRACT

Background. Fibromyalgia (FM), a chronic pain condition of unknown aetiology often develops following a traumatic event. FM has been associated with post-traumatic stress disorder (PTSD) and major depression disorder (MDD).

Method. Patients seen in a referral clinic (N = 571) were evaluated for FM and chronic fatigue syndrome (CFS) criteria. Patients completed questionnaires, and underwent a physical examination and a structured psychiatric evaluation. Critical components of the diagnostic criteria of FM (tender points and diffuse pain) and CFS (persistent debilitating fatigue and four of eight associated symptoms) were examined for their relationship with PTSD.

Results. The prevalence of lifetime PTSD was 20% and lifetime MDD was 42%. Patients who had both tender points and diffuse pain had a higher prevalence of PTSD (OR=3.4, 95% CI 2.0-5.8) compared with those who had neither of these FM criteria. Stratification by MDD and adjustment for sociodemographic factors and chronic fatigue revealed that the association of PTSD with FM criteria was confined to those with MDD. Patients with MDD who met both components of the FM criteria had a three-fold increase in the prevalence of PTSD (95 % CI 1.5-7.1); conversely, FM patients without MDD showed no increase in PTSD (OR= 1.3,95 % CI 0.5-3.2). The components of the CFS criteria were not significantly associated with PTSD.

Conclusion. Optimal clinical care for patients with FM should include an assessment of trauma in general, and PTSD in particular. This study highlights the importance of considering co-morbid MDD as an effect modifier in analyses that explore PTSD in patients with FM.

INTRODUCTION

Fibromyalgia (FM) and chronic fatigue syndrome (CFS) are two well described clinical conditions of uncertain aetiology with closely related symptoms of pain and fatigue (White *et at.* 2000) and similar demographic and clinical features (Buchwald & Garrity, 1994; Aaron & Buchwald, 2001). More specifically, they are both characterized by an onset often related *to* physical (e.g. infectious or post-traumatic) or psychosocial stressors (Aaron & Buchwald, 2001), a high rate of depressive symptoms and co-morbid major depressive disorder (MDD) (Morriss *et at.* 1999; Okifuji *et at.* 2000), and reduced 24 h urinary or morning plasma cortisol (Parker *et al.* 2001). Despite these similarities, these two conditions differ in other neuroendocrine profiles related *to* the hypothalamic-pituitary-adrenal axis (Parker *et al.* 2001).

Although studies have demonstrated an association of FM and CFS with MDD, more recent research suggests that post-traumatic stress disorder (PTSD) may be more closely linked to

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FM. Two separate investigations of FM patients revealed a surprisingly similar prevalence (56 % and 57 %) of 'PTSD-like symptoms' (Sherman *et at.* 2000; Cohen *et at.* 2002); another study of PTSD patients demonstrated a 21 % prevalence of co-morbid FM (Amir *et at.* 1997). Likewise, CFS has been associated with a high rate of early life victimization (Van Houdenhove *et at.* 2001), and some Gulf War veterans have developed a CFS-like illness after their return to the US (Lange *et at.* 1999), yet an association of CFS and PTSD has not reported. One methodological concern in comparing the degree of association of FM and CFS with a specific psychiatric illness is that FM can be diagnosed irrespective of the presence of any physical or psychiatric illness (Wolfe *et at.* 1990), but many medical and certain psychiatric diagnoses are exclusionary for a diagnosis of CFS (Fukuda *et at.* 1994).

In this study, we examined PTSD in a large sample of patients with pain or fatigue who were seeking a medical evaluation. Because of the asymmetry in physical and psychiatric exclusions for FM and CFS, we focused on the critical components of the criteria of these two conditions without regard to exclusions. This allowed us to have a much larger sample size, and is also consistent with clinical practice, where clinicians rarely have access to systematic psychiatric diagnoses that might be used to exclude the diagnosis in CFS patients. With this sample, we examined the following questions: (1) What critical components of the FM and CFS criteria are correlated with a lifetime diagnosis of PTSD?; and (2) Does MDD modify the association of these FM and CFS components with PTSD? This latter question was addressed because the majority of PTSD cases, even in community samples, have a lifetime or current diagnosis of MDD.

METHOD

Patients

The patients were a consecutive series of adults presenting for the evaluation of symptoms of fatigue at the University of Washington Chronic Fatigue Clinic. The clinic accepts both self- and physician-referred patients; individuals were not required to meet case definitions for either FM or CFS in order to be seen. All patients completed a questionnaire, battery of self-report measures, and a structured psychiatric diagnostic interview. A laboratory assessment consisted of a complete blood count with differential, erythrocyte sedimentation rate, 12-factor automated chemical analysis, liver and thyroid function tests, and antinuclear antibodies. The medical examination included the palpation of the 18 tender points specified by the American College of Rheumatology criteria for FM (Wolfe *et al.* 1990).

FM and CFS criteria components

All patients were evaluated for the two major criteria components of FM, tender points and diffuse pain (Wolfe *et al.* 1990). We used 19 questions relating to the occurrence, duration, location, and severity of pain to define diffuse pain. According to the literature, it was defined as pain above and below the waist, on both sides of the body and along some part of the axial skeleton lasting at least 3 months (Wolfe *et al.* 1990). Tender points were defined by sufficient pain on palpation (4 kg/cm^2) at a minimum of 11 of 18 specific locations during a standardized physical examination performed by an experienced clinician. Using these data, we defined four mutually exclusive and exhaustive categories: neither tender point nor diffuse pain, tender point only, diffuse pain only, both tender point and diffuse pain. Similarly, patients were also evaluated for the two major criteria components of CFS, chronic fatigue and four of eight specific symptoms (Fukuda *et al.* 1994). Of note, there are no physical examination criteria for CFS analogous to tender points for FM. The fatigue component was assessed by six questions about its duration, severity, and functional impact and 24 items on the occurrence, severity, and overlap with fatigue were used to determine if four of the eight symptoms specified by the case definition were present. Again, four mutually exclusive and exhaustive categories were defined: neither chronic fatigue nor four symptoms, chronic fatigue only, four symptoms only, both chronic fatigue and four symptoms). Since our objective was to compare the association of the characteristic signs and symptoms of FM (tender points, chronic pain) and CFS (chronic fatigue) with PTSD, we did not use the medical and psychiatric exclusions that are necessary to make a formal diagnosis of CFS. This choice is also consistent with the fact that the CFS definition was arrived at by

consensus and not empirically (as the FM definition was) and with clinical practice, where practitioners seldom apply psychiatric exclusions because they do not routinely do the structured diagnostic interviews required for this.

Psychiatric diagnoses

The National Institutes of Mental Health Diagnostic Interview Schedule (DIS) Version III-A is a highly structured interview that uses a computer algorithm to assign current (within the past month) and lifetime diagnoses based on the Diagnostic and Statistical Manual-III-R criteria. This instrument was administered by trained interviewers before patients had been clinically evaluated and was used to diagnose. PTSD and MDD, along with other disorders not the subject of this analysis (i.e. dysthymia, bipolar disorder, schizophrenia, generalized anxiety and panic disorder, eating disorders, alcohol and substance abuse, and somatization disorder) (Robins & Helzer, 1985). The analysis focused on the lifetime assessment of PTSD and MDD.

Statistical analysis

Logistic regression analyses were used to examine the association of the FM and CFS criteria components with the lifetime "diagnosis of PTSD. Initial analysis estimated unadjusted odds ratios and 95 % confidence intervals (CI) for each FM and CFS criteria component with PTSD; subsequent analyses obtained estimates simultaneously adjusting for age, sex, years of education, and FM and CFS components. Formal statistical testing was based on likelihood ratio chi-squares comparing models with and without the FM and CFS criteria components. To assess the effects of MDD, this analysis was repeated after stratification by a lifetime history of MDD.

RESULTS

A total of 571 patients (464 female, 108 male), ranging from 16 to 79 years of age (mean years = 42.0, S.D. = 10.6), were included in the analysis. Overall, 93 % were Caucasian, 49 % were married and 46 % were employed. The average years of education was 14.7 (S.D.=2.5, range = 8-20 years). The prevalence of lifetime PTSD and MDD were high in this sample (PTSD=20%, MDD=42%). Of these 571 patients, 34 had both FM components alone, 325 both CF components alone, 134 had both components of FM and CF, and 78 failed to meet the above criteria (i.e. did not have both components for either FM or CFS). The proportion of patients in these two groups (FM and CF) with exclusionary medical of psychiatric diagnoses, as well as the number of these two kinds of diagnoses, were not significantly different in patients with FM and CF *(X^2=0.17, P=0.68; X^2=0.55, P=0.46)* for proportions with at least one diagnosis; and *F(1* ,357) = 0'03, *P=0.86* and *F(1,357)* =2.06, *P=0.15* for numbers of diagnoses. Table 1 shows the association between the FM and CF criteria components and lifetime PTSD. In both the unadjusted and adjusted analysis the FM components were significantly associated with lifetime PTSD. Compared to the referent group of patients without tender points or diffuse pain, those with tender points only or diffuse pain only did not have an increased prevalence of lifetime PTSD. However, in both unadjusted and adjusted analyses, patients who met both tender point and diffuse pain criteria were at a significantly increased likelihood to have a diagnosis of PTSD compared to patients who met neither criteria. Conversely, the CF criteria components were not associated with a lifetime diagnosis of PTSD in either the adjusted *(P=0.99)* or unadjusted *(P=0.99)* analysis.

Table 2 examines the adjusted association of the FM criteria components with lifetime PTSD after stratification by lifetime MDD. Among patients without lifetime MDD, the two components of FM and lifetime PTSD were not associated *(P=0.97).* However, among patients with lifetime MDD, the FM components and lifetime PTSD were strongly associated *(P</=* 0.001). In particular, compared to patients without either tender points or diffuse pain, those with only tender points or only diffuse pain had virtually identical odds of PTSD. In contrast, patients with both tender points and diffuse pain were 3.2 times more likely (95 % CI=1.4-7.1) to be diagnosed with lifetime PTSD. An MDD stratified analysis of the CF criteria components could riot be conducted because the overlap between MDD and PTSD with CF symptoms was so great that insufficient numbers were available to perform the analyses.

Table 1. *The unadjusted and adjusted association of FM and CFS criteria components with lifetime PTSD*

Criteria components	Unadjusted model ($N=571$) OR	95% CI	Adjusted model† ($N=571$) OR	95% CI
Fibromyalgia				
Neither tender points nor diffuse pain‡ ($N=176$)	1·0		1·0	
Tender points only ($N=54$)	1·1	0·5–2·6	0·9	0·4–2·2
Diffuse pain only ($N=173$)	1·0	0·6–1·9	1·0	0·5–1·9
Tender points and diffuse pain ($N=168$)	3·4	2·0–5·8	2·8	1·6–4·8
	$\chi^2=31·06$, df=3, ***		$\chi^2=21·04$, df=3, **	
Chronic fatigue syndrome				
Neither chronic fatigue nor CFS symptoms‡ ($N=5$)	1·0		1·0	
Chronic fatigue only ($N=17$)	0·9	0·1–10·7	1·0	0·1–14·4
CFS symptoms only ($N=90$)	1·0	0·1–9·5	0·9	0·1–9·2
Chronic fatigue and CFS symptoms ($N=459$)	1·0	0·1–9·2	0·9	0·1–9·0
	$\chi^2=0·07$, df=3, NS		$\chi^2=0·06$, df=3, NS	

† Adjusted for gender, age, years of education and FM and CFS criteria components.
‡ Referent group.
** $P<0·01$; *** $P<0·001$; NS, not significant.

Table 2. *The adjusted association of FM criteria components with lifetime PTSD (odds ratios and 95% confidence intervals),† stratified by lifetime major depressive disorder (MDD)*

FM criteria components	No lifetime MDD ($N=332$) OR	95% CI	Lifetime MDD ($N=239$) OR	95% CI
Neither tender points nor diffuse pain‡	1·0		1·0	
Tender points only	1·0	0·3–3·6	0·7	0·2–2·4
Diffuse pain only	1·1	0·4–3·0	0·7	0·3–1·7
Tender points and diffuse pain	1·3	0·5–3·2	3·2	1·5–7·1
	$\chi^2=0·28$, df=3, NS		$\chi^2=21·25$, df=3, ***	

† Adjusted for gender, age, years of education and CFS components.
‡ Referent group.
*** $P<0·001$; NS, not significant.

Finally, FM patients with PTSD ($N=59$) were not more symptomatic than FM patients without PTSD ($N=109$) with respect to both pain ($F(1,162)=2·62$, $P=0·11$) and fatigue ($F(1,163)=0·06$, $P=0·80$), measured on the bodily pain and vitality scales of the SF-36.

DISCUSSION

These findings document a significant association between the presence of the criteria components of the FM diagnosis and a lifetime diagnosis of PTSD. In contrast, neither the chronic fatigue nor the associated symptoms that are required to diagnose CFS were associated with PTSD. However, the relationship of the two FM components with PTSD appeared to be confined to patients with a lifetime history of MDD. The tender points and diffuse pain components represent different aspects of the FM diagnostic criteria; because tender points and pain *per se* are not part of the PTSD or MDD diagnostic criteria, criterion overlap cannot account for the relationship observed here. Furthermore, FM patients with PTSD did not have more severe symptoms of pain than FM patients without PTSD. Similarly, anxiety symptoms are not part of the FM criteria, although fatigue is a core diagnostic symptom in MDD, suggesting that criterion overlap can account in part for the strong relationship between CF components and MDD.

Although pain is not a diagnostic criterion for PTSD, several studies have shown that persistent pain is frequently associated with symptoms of PTSD among patients with chronic headache (Chibnall & Duckro, 1994), chronic pain (Benedikt & Kolb, 1986), and among those with PTSD following painful traumatic injuries (Geisser *et al.* 1996). In addition, in the National Comorbidity Study PTSD was strongly related to unexplained somatic symptoms (Kessler *et al.* 1995). Because our study, like the others cited above, is cross-sectional, we cannot determine

which condition preceded or contributed to the other. However, recent neuroimaging investigations have demonstrated that similar brain areas, such as the anterior cingulate cortex, are involved in both the regulation of pain (Coghill *et al.* 1999) and the emotional dysregulation of PTSD (Shin *et al.* 1997). Given the potentially shared biological substrate, it seems plausible that the relationship between pain and PTSD is bi-directional; pain can serve as a provocative traumatic stimulus for the development of PTSD, and the hyperarousal, stress intolerance, and selective attention typical of PTSD may exacerbate pain. Not surprisingly, patients with both conditions have more severe symptoms and disability, whether the focus is FM (Sherman *et al.* 2000), or PTSD (Amir *et al.* 1997).

This study has several limitations. First, since our sample was seen in a tertiary referral center, our findings are not generalizable to other settings. For example, the frequency of PTSD and MDD in our patients was likely higher, and the severity of illness greater, than among primary care patients. This makes an association between
disorders more likely, although we know of no systematic recruiting bias that would result in the specific FM-PTSD association observed here. Secondly, we did not examine the traumatic event(s) on which the PTSD diagnosis was based. In this regard, since FM may follow a musculoskeletal injury (Buskila & Neumann, 2000), frequently a motor vehicle accident, the association we observed may be explained by a response to the traumatic event present at the illness onset. Thirdly, all of our measures, including the psychiatric diagnoses and subjective pain on palpation of tender points, are self-reported, hence our findings could be the result of an over-reporting bias. However, it seems unlikely that PTSD symptoms would be selectively over-reported among patients with both components of FM but not among those experiencing the two CFS components, where we found no association.

The findings noted here suggest that, at the very least, optimal clinical care for patients with FM must include a careful assessment of trauma in general, and PTSD in particular. This study also highlights the importance of considering co-morbid MDD as an effect modifier in any analyses that explore determinants of PTSD in FM patients. Future research should assess whether treatment targeted toward PTSD could improve symptoms of FM. Other areas of interest include the examination of the natural history of FM and PTSD to ascertain the temporal relationship of these disorders and the identification of specific environmental or traumatic events that trigger FM. Studies of FM patients without PTSD might also reveal whether traumatic events that do not result in musculoskeletal injury lead to the development of FM. Finally, neuroimaging and neuroendocrinological investigations of the basis for association of FM and PTSD are in order.

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