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Journal of Psychosomatic Research 48 (2000) 51–57

Journal of Psychosomatic Research

Psychiatric symptoms and distress differ between patients with postherpetic neuralgia and peripheral vestibular disease

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Received 9 April 1999; accepted 13 August 1999

Abstract

Objective: No previous studies have investigated the psychiatric characteristics of patients with postherpetic neuralgia (PHN). Similarly, no studies have been performed on patients with different chronic somatic symptoms due to a defined medical disease to compare the characteristics of psychiatric morbidity associated with each etiology. **Methods:** After completing the subscales of the Symptom Checklist 90-R, a psychiatrist administered the Diagnostic Interview Schedule to all subjects. The psychiatric comorbidity in 35 patients with pain due to PHN was compared with a control group of 34 patients with the nonpainful aversive symptom of vertigo due to a peripheral vestibular disorder that caused unilateral hypofunction. **Results:** PHN patients had significantly *more* symptoms of major depression and somatization disorder. No significant differences were found between groups for psychiatric diagnoses. Patients with PHN reported significantly *less* acutely distressing somatic symptoms. **Conclusion:** These results suggest that the psychiatric symptoms of patients with PHN are distinct from nonspecific acute distress and may be related to the experience of suffering from chronic neuropathic pain. Patients with PHN may not meet criteria for a psychiatric diagnosis, but their psychiatric comorbidity places them at substantial risk for increased pain, suicidal ideation, sustained disability, and the numerous complications of excessive medical evaluation and treatment. Patients with PHN should be evaluated specifically for psychiatric symptoms to reduce potential negative consequences through appropriate treatment.

Keywords: Postherpetic neuralgia; Neuropathic pain; Depression; Anxiety; Vestibular disorders; Vertigo

Introduction

The relationship between chronic pain syndromes and psychiatric disorders remains controversial. Several hypotheses have been considered. Although the two conditions could be present as a chance co-occurrence, they are probably either a manifestation of the same underlying pathophysiology or directly linked by cause and effect. Chronic pain could be the cause or consequence of psychiatric symptoms or disorders. Many medical conditions such as Parkinson's disease, thyroid dysfunction, and collagen vascular diseases are associated with increased rates of psychiatric diagnoses such as major depression, symptoms such as nervousness, or negative outcome such as suicide [1]. Fields proposed a neurobiology of pain and depression that could explain the high rates of comorbidity and interaction effects [2]. Although the explanations remain unclear, psychiatric morbidity is disproportionately common among the medically ill, especially in those patients complaining of pain [3–7].

Chronic pain is commonly associated with psychiatric disorders [8]. Katon and others have demonstrated a linear relationship between affective disorders and the number of chronic somatic symptoms, including pain complaints experienced by patients [9–11]. Approximately 60% of patients with depression report pain symptoms at the time of diagnosis [12–14]. Persons with

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0022-3999/00/$ – see front matter
PII: S0022-3999(99)00076-8

depression are at least twice as likely to develop a chronic pain condition such as headache, chest pain, and musculoskeletal pain compared to nondepressed individuals [15–17]. Depression was the most important variable associated with persistent chronic pain in these patients. In patients with chronic pain from diseases such as rheumatoid arthritis, several studies have demonstrated increased pain when depression is present even when controlling for disease activity [18–20].

Postherpetic neuralgia (PHN), a debilitating chronic neuropathic pain disease, is a common sequel to an episode of herpes zoster (shingles) in elderly patients [21]. Epidemiological studies have revealed that the duration of PHN is less than 1 year in 78% of patients with PHN, but that it can persist for years or indefinitely in others [22]. The reactivation of the varicella virus causes varying degrees of degeneration in primary afferent sensory fibers as well as in central sensory neurons. Morphological changes affecting the dorsal root ganglia cells, spinal cord, and peripheral nerves have been demonstrated in PHN patients [23–26]. PHN is characterized by ongoing pain and varying degrees of sensory deficits, allodynia, and hyperalgesia [27]. It is a prototypical neuropathic pain state that has been used as a model to study the pathophysiology of neuropathic pain and to develop new treatment strategies [28–30]. To date, no studies have described the psychiatric comorbidity of patients with PHN.

Eight to 50% of patients with a wide variety of chronic pain conditions referred to comprehensive pain programs for evaluation were found to have a *current* major depression [31]. The prevalence of major depression is increased three to four times in patients with chronic low back pain as compared with the general population [32]. Usually, patients with chronic medically *unexplained* somatic (somatoform) symptoms are the most likely to be suspected of having a psychiatric illness. Therefore, previous research has compared patients with medically unexplained somatic symptoms to control groups with the same somatic symptom caused by a medical disease to investigate differences in psychiatric morbidity attributable to *somatization* (i.e., the lack of a specific disease etiology for the chief complaint) [33–40]. To date, no formal research studies have compared patients with chronic somatic symptoms due to different diseases with defined etiologies in order to investigate the characteristics of psychiatric morbidity associated with a specific *medical etiology*.

The aim of this study was to explore the psychiatric characteristics of PHN. Because, by definition, patients with PHN have pain, this aim was achieved by comparing the psychiatric phenomenology of two different medical diseases characterized by aversive symptoms. This study describes the psychiatric characteristics of a group of patients (cases) with chronic pain from PHN and compares them to a group of patients (controls) with chronic vertigo from a peripheral vestibular disorder (PVD). The etiology of this neurological disease is unilateral vestibular hypofunction and is characterized by the aversive but nonpainful symptom of vertigo.

The hypotheses of this study were:

1. Patients with a *painful* aversive symptom due to a specific neuropathic disease (PHN) will report an *increased* number of *symptoms* of psychiatric diagnoses compared to patients with a *nonpainful* aversive symptom (vertigo) due to a specific vestibular disease (PVD).
2. Patients with PHN will meet criteria for *increased* rates of psychiatric *diagnoses* compared to patients with PVD.
3. Patients with PHN will *not* differ in the *distress* they report compared to patients with PVD, because both diseases are characterized by aversive somatic symptoms.

Methods

Subjects

Cases included 35 elderly patients (mean age = 71 years) with a confirmed diagnosis of PHN evaluated at an initial visit as part of a controlled clinical treatment trial. Controls included 34 patients (mean age = 67 years) with complaints of vertigo due to a confirmed diagnosis of a PVD with objective unilateral vestibular hypofunction. Controls were evaluated as part of enrollment in a larger psychiatric epidemiological study and were currently receiving treatment from an otolaryngologist specializing in the treatment of vestibular disorders. All subjects had experienced their primary symptom during the month prior to evaluation and reported a duration of symptoms of >6 months (mean duration of pain = 40 months; mean duration of vertigo = 51 months). No patient was receiving effective treatment for their respective condition. Subjects with vertigo or dizziness *without* known objective etiology were *not* included in the present study in order to compare only individuals with known medical diagnoses. All patients with PHN were screened for PVD and vice versa. None of the subjects had both diseases. Subjects were matched on demographic variables including age, education, gender, and analyses demonstrated no significant differences for ethnicity or duration of symptoms. Demographic information on the two groups is presented in Table 1.

Measures

Hopkins Symptom Checklist 90-R (SCL-90-R) Anxiety and Somatization Subscales. This measure was utilized to assess self-reported acute distress among the participants [41]. The SCL-90-R instructs subjects to rate the extent to which each of 90 physical or psychiatric

Table 1
Demographic variables for patients complaining of pain and dizziness

Variable	Pain (N = 35)	Dizziness (N = 34)	p
Age (mean ± SD years)	70.86 ± 12.49	67.32 ± 13.21	0.26
Education (mean ± SD years)	13.43 ± 2.94	13.58 ± 3.81	0.86
Female (%)	57	53	0.62
White (%)	89	94	0.12
Duration (mean ± SD months)	39.54 ± 47.28	51.17 ± 96.82	0.54

symptoms has bothered them significantly *during the past 7 days* on a scale from 0 (absent) to 4 (very severe). The reliability and validity of the SCL-90-R with psychiatric patients have been previously reported. In addition, this measure has been utilized in the assessment of patients with chronic pain [42]. The SCL-90-R assesses nine different types of psychological distress and three global measures of distress. To reduce the response burden for the PHN patients, who were being assessed for more specific psychiatric conditions such as depression with other instruments, only the anxiety and somatization clinical subscales were administered to assess their acute distress.

National Institute of Mental Health Diagnostic Interview Schedule (DIS), Version 3R. The DIS is a structured interview used as a diagnostic tool for psychiatric disorders with documented validity and reliability [43, 44]. Sections assessing demographics, somatization disorder, major depression, panic disorder, and generalized anxiety disorder were administered. Current (1-month prevalence) psychiatric diagnoses were made according to the *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition* (DSM-III-R) [45]. The cause of all psychological and somatic symptoms was assessed through a set of structured probe questions about medical evaluations as specified by the DIS. A computer version of the DIS was used for administration and scoring [46–48]. The DIS is a structured interview, which reduces bias inherent in not being blinded to other information about the subjects (Table 2).

Procedure

Participants with PHN completed the SCL-90-R subscales as part of a larger assessment packet mailed to them prior to an initial visit for a clinical treatment trial of PHN. An anesthesiologist (S.R.) or a neurologist (M.P.) specializing in neuropathic pain syndromes then confirmed their diagnosis of PHN. Participants with PVD also completed the SCL-90-R subscales as part of a larger assessment packet that was mailed to them after enrollment in a study of the psychiatric epidemiology of patients with chronic dizziness. An otolaryngologist or neurologist specializing in vestibular and balance disorders then confirmed their diagnosis of peripheral vestibular disorder (PVD). After confirming the disease diagnosis, the DIS interviews were administered by the same board-certified psychiatrist (M.C.) instead of a lay interviewer to ensure accurate coding of patient responses and to increase both validity and reliability of psychiatric symptoms and diagnoses.

Table 2
Group comparisons on DIS diagnoses

Diagnosis[a]	Pain	Dizziness	p
Major depression (%)	20	10	0.28
Generalized anxiety disorder (%)	17	10	0.68
Panic disorder (%)	3	0	0.65
Somatization disorder (%)	3	3	0.98
No diagnoses (%)	63	77	0.53

[a] Total percentage >100% because of two patients meeting criteria for two or more diagnoses.

Table 3
Group comparisons on DIS diagnosis symptom totals (mean ± SD)

Diagnosis symptom total	Pain	Dizziness	p
Major depression	1.69 ±1.92	0.34 ± 0.72	0.000
Generalized anxiety disorder	2.00 ± 3.57	0.72 ± 1.39	0.06
Panic disorder	0.91 ± 2.34	0.79 ± 1.47	0.81
Somatization disorder	2.94 ± 2.96	0.76 ± 0.99	0.000

Results

A series of chi-square analyses was conducted to compare the percentage of patients meeting diagnostic criteria for the DIS psychiatric diagnoses. No significant differences were found between psychiatric diagnoses in patients with PHN when compared to those with PVD. Table 2 shows the percentage of patients in each group meeting diagnostic criteria and the results of the chi-square analyses.

A series of *t*-tests was conducted to compare the number of psychiatric symptoms in the two groups. Because of multiple comparisons, a modified Bonferroni correction was used with the resultant α-significance level set at 0.033. Patients with pain (PHN) compared to patients with vertigo (PVD) endorsed significantly more symptoms of the DIS psychiatric diagnoses. Patients with PHN endorsed a mean of 1.69 vegetative depressive symptoms on the DIS compared to patients with PVD who had a mean of 0.34 symptoms [$t(62) = 3.55$, $p < 0.001$]. The PHN patients also endorsed significantly more somatization symptoms compared to patients with PVD [2.94 vs. 0.76, $t(62) = 3.80$, $p < 0.001$]. A trend toward patients with PHN endorsing more generalized anxiety disorder symptoms than patients with PVD was found [2.00 vs. 0.72, $t(62) = 1.82$, $p < 0.06$]. No differences were found for the number of panic disorder symptoms between the two groups. Table 3 shows the means, standard deviations, and significance levels for each analysis.

Table 4
Group comparisons on SCL-90 subscales (mean ± SD)

Subscale	Pain	Dizziness	*p*
Somatization	0.52 ± 0.49	1.04 ± 0.57	0.000
Anxiety	0.41 ± 0.42	1.28 ± 3.61	0.16

The two patient groups were compared on the subscales of the SCL-90-R to assess the severity of acute distress. Patients with the complaint of vertigo (PVD) endorsed significantly greater numbers of *distressing* somatic symptoms in the past week than patients with the complaint of pain (PHN; $t(63) = 3.95$, $p < 0.001$). The groups did not differ significantly on self-reported distressing anxiety symptoms ($p > 0.10$). Table 4 shows the means, standard deviations, and significance levels for each analysis.

Discussion

Previous research has demonstrated that patients with a medically *unexplained* aversive chief complaint (back pain, chest pain, dizziness, pelvic pain, syncope, tinnitus, fatigue, irritable bowel) have a significantly higher prevalence of both current and lifetime depressive, anxiety, and somatization disorders when compared to a medical control group with a well-defined medical disease due to a known etiology [33–40]. Many studies have also found increased rates of psychiatric diagnoses associated with individual medical diseases [1]. This is the first study to examine the psychiatric morbidity experienced by patients suffering from PHN. In addition, this is the first study to explore the psychiatric characteristics associated specifically with chronic neuropathic pain by comparing patients with PHN to patients with another aversive symptom (vertigo) from a different medical disease.

The results of this study demonstrate that patients suffering from PHN, a disease with chronic pain, compared to patients suffering from a disease with a chronic aversive but nonpainful vertigo have significantly more symptoms of major depression and somatization disorder and a strong trend toward more symptoms of generalized anxiety disorder. At the same time, patients with pain were found to experience less acute distress as evidenced by the report of fewer bothersome somatic symptoms than the control group of patients with vertigo. These findings describe the psychiatric characteristics of PHN, a neuropathic pain condition, as having increased numbers of symptoms of psychiatric diagnoses but not having increased symptoms of acute distress.

No significant differences were found in rates of psychiatric diagnoses between the two groups. However, it should be noted that, despite having subthreshold numbers of depressive and anxiety symptoms and not meeting diagnostic criteria for a psychiatric diagnosis, patients still suffer similar levels of morbidity and disability [49,50]. In fact, subsyndromal anxiety and depression are *more* common in medical patients than their respective Axis I disorders. These patients also incur higher health care costs when compared with patients meeting full criteria for a specific diagnosis, because the subsyndromal condition is less likely to be recognized as a psychiatric disorder. The result is more medical tests, follow-up visits, specialist referrals, and medication prescriptions.

When patients with a medical disease suffer from a psychiatric disorder, their use of *non*psychiatric medical care is double that of patients without a psychiatric disorder [51]. These high utilizers consume disproportionately more medical services than low utilizers. Several studies of high utilizers of primary care have described the psychiatric characteristics of these patients [52–54]. They suffer more psychological distress, greater numbers of chronic medical illnesses, and higher rates of psychiatric diagnoses (major depression, anxiety disorders, somatization disorder, and alcohol abuse).

When patients have a medical disease (tinnitus, vertigo, syncope, migraine) and comorbid psychiatric symptoms, they suffer equal and additive disability from these medical and psychiatric disorders [35,37,55–57]. They also experience significantly more deterioration in both social and vocational function and have a poorer self-appraisal of their physical health. The depressive symptoms of patients with rheumatoid arthritis were found to be significantly associated with negative health and functional outcomes as well as increased use of health services [58].

Patients with chronic pain report greater pain intensity, less life control, and more use of passive-avoidant coping strategies when depressed [18,59,60]. They also describe greater interference from pain and exhibit more pain behaviors than chronic pain patients without depression. Depression is the most significant predictor of pain persistence and the best predictor of application for early retirement in patients with acute low back pain [61]. Patients with depressive *symptoms* or a diagnosis of major depression have as much or more functional disability when compared to patients with chronic medical illnesses (diabetes, hypertension, arthritis, coronary artery disease) [62].

A survey of individuals with a variety of chronic nonmalignant pain conditions found that 50% had seriously considered suicide at some point in their illness [63]. In a study of patients who attempted suicide, 52% suffered from a somatic disease and 21% were taking analgesics daily for pain [64]. Patients with chronic pain successfully committed suicide at two to three times the rate found in the general population [65]. Additional studies have found that depression is a more powerful risk factor for suicidal ideation than chronic pain [66–68]. The

consequences of psychiatric morbidity in chronic pain syndromes are numerous and devastating.

As suspected, this study found that patients with PHN do not have an uncomplicated "pure" neuropathic disease. They experience significantly increased rates of depression, anxiety, and medically unexplained somatic symptoms in addition to chronic neuropathic pain. However, when compared to patients with chronic vertigo from a peripheral vestibular disorder, patients with PHN have lower levels of acute distress. Therefore, in PHN, the psychiatric symptoms are distinct experiences from acute distress that could be attributed to suffering from a disease that causes an aversive symptom like vertigo. These psychiatric symptoms associated with PHN may represent a specific relationship with chronic neuropathic pain.

The assessment of acute distress used in this study was the SCL-90, which is a self-report questionnaire that measures how much patients were bothered by a checklist of nonspecific somatic and psychological symptoms. In contrast, the psychiatric symptoms and diagnoses were ascertained by direct interview by a psychiatrist. The DIS evaluates specific symptom clusters of psychiatric diagnoses such as major depression. For symptoms of somatization disorder to be considered present, the symptoms have to be medically unexplained and the patient has to have sought medical evaluation, taken medication, or experienced interference with daily activities. Our results suggest that the pain from PHN is provoking less nonspecific distress than the vertigo of PVD but is associated with subthreshold psychiatric disorders.

Patients with PHN may experience less distress because they accept their pain more than patients suffering PVD accept their vertigo. Patients generally find it easier to understand the diagnosis of PHN because of the identifiable lesions and scarring caused by a "viral infection." Patients with a vestibular disease often have difficulty understanding the cause of vertigo and how peripheral vestibular hypofunction affects balance. Also, the pain of PHN is usually constant and therefore more predictable for patients. The vertigo of PVD is usually episodic with periods of remission complicated by unpredictable relapses depending on head position and environmental cues. Pain from PHN may interfere with daily activities because of fatigue or the inability to tolerate clothing or other forms of light touch. Vertigo affects a person's balance, mobility, and independence. This may cause more severe interference with daily activities, resulting in higher levels of generalized distress.

The limitations of this study include the small sample size, limited measures to assess acute distress and psychiatric phenomenology, reliability and validity of the DIS for making psychiatric diagnoses, comparing two separate diseases rather than one disease with/without pain, different research settings for each group, the psychiatrist not being blind to the disease diagnosis, and not having prospective data to examine the onset of the diseases in relation to psychiatric symptoms. The sample size may have limited power to detect additional differences between the two groups as evidenced by the strong trend toward significance in analyses of the generalized anxiety disorder symptoms and the much weaker trend in the SCL-90-R anxiety subscale. The psychometric data were limited by the degree of overlap between the two parent studies from which the patients were selected. Although more specific measures of acute distress could have been used, the SCL-90-R is a recognized instrument for this purpose.

The reliability and validity of the DIS have been criticized. However, Spitznagel and Helzer have argued that psychiatric clinical examination alone is not a diagnostic gold standard, the kappa statistic is not adequate to assess reliability because of its fluctuation due to diagnosis prevalence, and the DIS has good predictive validity for a number of outcome variables [69–71]. The main focus of this study was to investigate the psychiatric comorbidity of PHN. Because PHN is defined by pain, individuals who recovered from acute herpes zoster without developing pain would not be considered as having the same disease. This is supported by evidence of the differing morphological pathology in these patients [25]. Because the two study groups came from different research settings, and the patients likely differed in many ways that could not be controlled for by matching on demographic variables, all of the patients had a long duration of their primary symptom, had failed treatment for their condition, and were in a setting that was offering specialized or experimental treatment.

Even though patients with PHN may not meet criteria for a psychiatric diagnosis, their psychiatric comorbidity places them at substantial risk for increased pain, suicidal ideation, sustained disability, and the numerous complications associated with excessive medical evaluation and treatment. Patients with a neuropathic disease like PHN should be evaluated for psychiatric morbidity. When found, psychiatric symptoms should be considered a significant comorbidity that is likely to complicate the course and treatment of PHN. Future research should explore this relationship between chronic pain and psychiatric comorbidity in PHN to assess pathophysiological mechanisms, prospective changes in both pain and psychiatric symptoms after treatment, the interactive processes involved in the complicated psychological experience of chronic pain, the different aspects of medical diseases that influence the development of disability, and the strategies patients use to cope with chronic symptoms.

Acknowledgments

This work was supported by a grant from the National Institutes of Health (NINCDS P5O-NS32386) and a

National Research Service Award (5T32PE10001-04). We thank all of the patients who participated in this study. This research would not have been possible without their commitment to science.

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