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Differences in Pain, Psychological Symptoms, and Gender Distribution Among Patients with Left vs. Right-Sided Chronic Spinal Pain

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Abstract

Objective—To determine pain levels, function, and psychological symptoms in relation to predominant sidedness of pain (right or left) and gender in patients being treated for chronic spinal pain.

Design—Prospective cohort study

Patients—Patients with chronic neck or low back pain undergoing a nerve block procedure in a speciality pain medicine clinic

Interventions/Outcomes—Patients completed the Hospital Anxiety and Depression Scale and the Brief Pain Inventory just prior to the procedure. Pain history and demographic variables were collected from a chart review. Chi-square, Pearson correlations, and multivariate statistics were used to characterize the relationships between side of pain, gender, pain levels, pain interference, and psychological symptoms.

Results—Among 519 subjects, men with left-sided pain (n=98) were found to have significantly greater depression and anxiety symptoms and worse pain-related quality of life (p<.01), despite having similar pain levels as men with right-sided pain (n=91) or women with left or right-sided pain (n=289). In men, psychological symptoms had a significantly greater correlation with pain levels than in women (p<.01).

Conclusion—In this sample, men with left-sided spinal pain report worse quality of life and more psychological symptoms than women. These data provide clinical evidence corroborating basic neuroscience findings indicating that the right cerebral hemisphere is preferentially involved in the processing of pain and negative affect. These data suggest that men appear more right hemisphere dominant in pain and affect processing. These findings have implications for multidisciplinary assessment and treatment planning in men.

Keywords

chronic pain; gender; laterality; psychopathology

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Introduction

The right cerebral hemisphere is more involved than the left hemisphere in the processing of pain[1] and negative emotions.[2,3] The cerebral hemispheres exhibit central neuro-anatomical asymmetry in autonomic nervous system function, with the sympathetic nervous system being controlled primarily in the right hemisphere for contralateral peripheral nervous system activity. In other words, the embryology of the sympathetic nervous system is such that it is preferentially activated by stimulation on the left side of the body. Conversely, the parasympathetic nervous system is left-lateralized centrally and right lateralized peripherally.[4,5]

Thus, an emerging body of literature supports these linked hypotheses: 1) that right-sided cortical regions are preferentially involved in perceptions of chronic pain, and 2) that left sided-pain is associated with greater disturbances in affect. Enhanced pain sensitivity in healthy volunteers has been associated with increased right frontal compared with left frontal brain activity, as measured by EEG.[6] In studies of transient induction of depressed mood, similar right-sided enhanced activity has been seen on EEG.[7] Consistent with the right hemisphere dominance in emotional response, **s**ymptoms which present unilaterally, as in conversion disorders, occur more frequently on the left than right side.[8-10] Moreover, pain, numbness, or paresthesia diagnosed as having a somatoform etiology present more frequently on the left side[9,11] and psychopathology, as indicated by MMPI scores for hysteria and hypochondriasis, are greater for patients with left- than right-lateralized chronic pain.[12] Pain complaints have also been found by Merskey and Watson [13] and others [6,14] to occur more frequently on the left than on the right side of the body, especially in depressed patients. Gagliese and colleagues[12] found that right-hand dominant patients with left-sided pain are more disturbed psychologically and report greater disruptions in their lives than do patients with right-sided pain.

In sum, there is basic neuroscience and clinical evidence for lateralization of pain and psychopathology towards the left side of the body, consistent with the theory that the right cerebral hemisphere dominates the processing of pain and affect. Most of the clinical evidence comes from psychiatric populations who have a large somatoform component to their illness, and most of the basic neuroscience evidence comes from studies of small samples of healthy volunteers. It is unknown whether this lateralization phenomena also manifests in larger populations of those with chronic pain due to a somatic etiology primarily, such as those with chronic neck or back pain and radicular complaints. Presumably, these patients have no physiological reason outside of the brain to exhibit lateralization, such as possible differences in the functioning of the left vs. right spinal cord, peripheral nervous system, or musculoskeletal system. An important question in populations with a medical etiology for pain then becomes, are there differences in pain and affective symptoms between those with left vs. right-sided pain? If so, such data would suggest that one mechanism by which the brain is involved in the “chronification” of pain is through differences in how pain and negative emotions are processed in the two hemispheres. Such evidence would deepen our understandings of the neurobiology of pain and emotional processing.

Based on these and other observations about lateralization of pain and affect processing preferentially by the right hemisphere, the objective of this study was to determine differences in psychosocial characteristics and pain behaviors between patients with left-sided versus right-sided chronic spinal pain being treated by neural blockade. It was hypothesized that there would be more psychological and behavioral dysfunction in left-than right-sided chronic pain patients.

Methods

Design and setting

This was a prospective, cross-sectional cohort study performed in a single, large, urban, university-based pain management center. After IRB approval from Brigham and Women's Hospital, patients undergoing spinal injections for neck or low back pain were invited to participate. Data collection consisted of questionnaire surveys and de-identified medical records review. The surveys were collected as part of a clinical initiative to track procedural outcomes.

Inclusion criteria

After giving verbal consent, subjects were included if, based on the decision by the treating physician, they were to receive facet joint injections, radiofrequency lesioning of the facet joints, or transforaminal epidural steroid injections. Subjects had axial low back or neck pain, and may or may not have had a radicular pain component. All subjects had an initial evaluation by the treating physician which concluded that there was an anatomical or structural basis explaining at least a portion of their pain complaints, such as facet arthropathy, degenerative disc disease or a herniated disc, spinal stenosis, or neuroforaminal narrowing. This evaluation included a review of either a spine MRI or CT scan. In deciding to perform a neuroaxial blockade procedure, the treating physician determined whether the MRI or CT findings are concordant with a patient's pain complaints, and only if the findings are concordant does the physician proceed with a nerve block. While a significant percentage of people have lumbar spine MRI abnormalities and no pain,[15] the standard practice in pain medicine for deciding to perform a nerve block is to ascertain whether there are positive correlations among pain complaints, exam findings, and spinal imaging results.[16]

Data collection

All measures were administered the day of and prior to the procedure. In addition to these surveys (the Brief Pain Inventory and the Hospital Anxiety and Depression Scale—see below), demographic information and pain history were gathered from medical records review, although complete psychiatric history information was not available. While brief, these two surveys measure the areas of pain, function, and psychological symptoms. These are the primary areas of importance in the assessment of patients with chronic pain.[17,18] Classifying the predominant side of pain was determined through triangulating the patient-completed pain diagram on the Brief Pain Inventory, records review, and considering which side the procedure was performed. Even predominantly axial low back pain can favor one side in many patients.

Brief Pain Inventory (BPI)—The BPI is a 15 item questionnaire assessing pain location, and 0-10 ratings of pain intensity, relief, quality, pain-related quality of life, and function. It has been validated in cancer and non-cancer pain conditions.[19] The activity interference items measure separate domains of function, such as pain interference with activity, sleep, or work. The activity interference items have shown a high correlation with other functional and quality of life measures, such as the SF-36.[20] These items ask on a 0-10 scale (0=does not interfere, 10=completely interferes), "Circle the one number that describes how, during the past 24 hours, pain has interfered with your:"

Hospital Anxiety and Depression Scale (HADS)—The HADS is a 14-item self-report survey designed for populations with medical illness.[21] It does not include somatic symptoms, such as fatigue and sleeplessness, which may otherwise be attributable to pain. It asks patients to rate depression and anxiety symptom over the past week on a four-point

Likert scale. It has been validated in several medical illness populations and has been used extensively in chronic pain patients. The HADS has a sensitivity and specificity of .66-.97 for a DSM-IV major depression or generalized anxiety disorder diagnosis.[22] Those with anxiety or depression subscale symptom scores of ≥9 are considered to have high anxiety or depression symptoms, and this cutoff score has a high correlation to the presence of a comorbid anxiety or depression disorder.[22] Of note, the cut-off scores on the HADS for significant psychiatric comorbidity in noncancer pain patients have shown to be lower than in those with cancer pain. Given the inherent interrelationships between anxiety and depression symptoms, the combined anxiety and depression subscale scores can serve as a measure of total negative affective symptoms (negative affect symptom score).[23] This approach has been used by the authors in previous studies, and it has proven to be a meaningful method for understanding relationships between chronic pain and psychological symptoms.[24,25]

Data Analysis

Chi-square, Pearson Correlations Coefficients, the Wilcoxon signed-rank test, and multivariate analysis of variance (MANOVA) were used to characterize the relationships between sidedness of pain, pain ratings, function ratings, and psychological symptoms. MANOVA is useful in analyzing relationships between predictors and multiple dependent variables that may be related. MANOVA tests initially whether groups differ along a combination of outcome variables (e.g., the test statistic Roy's Largest Root), and thus provides protection against inflating the false positive rate in testing multiple dependent variables.[26] MANOVA is most suited to situations in which the dependent variables are related conceptually and correlated statistically (such as 24 hour average pain levels and current pain rating).

Results

Data was collected from 519 patients, 298 females and 221 males. Patients were classified as having left-sided, right-sided or bilateral pain (Table 1). In comparing the left vs. right-sided patients, no significant differences were found between the frequency of patients with left-sided (n=223) and right-sided (n=216) pain (Chi^2= .14, p = 0.7) or frequency of pain location in the left vs. right groups (neck or low back, p=.36). MANOVA revealed no significant left- vs. right-sided differences in pain history variables (Roy's Largest Root, p=.92). Individual significance values were; duration of pain (p=.97), worst pain (p=.67), least pain (p=.16), average pain (p=.70), and pain right now (p=.60).

Despite the ratings of pain being similar between groups, the left-sided pain patients had significantly greater depression symptoms, and reported significantly greater interference of pain with their mood (Roy's Largest Root, p=.035): anxiety p=.251, depression p=.008, total negative affective symptoms p=.04, interference with mood p=.029, and interference with enjoyment of life p=.258. Men accounted for the majority of differences in psychological symptoms between the left and right-sided groups. None of these comparisons among females were significant (Roy's Largest Root, p=.56). Compared with men, women did report higher pain levels, overall (Roy's Largest Root, p=.006). Individual items were; pain at worst p=.003, pain at least p=.009, pain on average p=.006, pain now p=.23.

Table 2 displays differences between left and right-sided pain patients in men (n=178) and women (n=251) for the pain interference psychological items of the BPI (mood and enjoyment of life) and the mood symptom ratings on the HADS. Compared with men with right-sided pain (n=91), men with left-sided pain (n=98) had significantly greater interference with mood, higher depression scores, and higher total negative affective symptoms scores (Roy's Largest Root, p=.049). In women these comparisons were not significant (Roy's Largest Root, p=.56).

To further test whether the relationships between mood and pain are more pronounced in men than women in this sample, we examined the Pearson correlation coefficients among pain, function items, and mood against gender, separately in men and women (Table 3). We then compared whether the correlations were greater in men than women. These results show that in 16/18 male-female dyad comparisons of the magnitude of the correlation coefficients between the mood and pain or function items were significantly greater among men (Wilcoxon signed-rank test, p<.01). In other words, the greater strength, or values, of the correlations in men indicate that mood symptoms had a more significant relationship to pain and function in men than women.

Discussion

Our results indicate that men with left-sided pain suffer greater affective distress, depression symptoms, and pain interference with psychological health than those with right-sided spinal pain. In this sample, the correlations between pain and psychiatric symptoms were more pronounced in men than in women, despite women reporting greater pain on average. These results are consistent with findings from neuroimaging studies indicating that the right cerebral cortex is preferentially involved in the processing of pain and negative emotions.[27] More specifically, Symonds and colleagues reported that in male and female healthy volunteers given experimental pain stimuli during fMRI scanning, that the right cerebral hemisphere was more activated in men and that the right hemisphere in men and women was more involved with the attentional aspects of pain perception, compared with the left hemisphere.[28] Other neuroimaging studies indicate that negative emotions are preferentially processed in men in the right hemisphere, compared with women.[29,30] Our findings support a greater right than left hemispheric involvement centrally in left-sided male, chronic pain patients, thus suggesting that men with left-sided chronic pain are more vulnerable to the development of psychiatric comorbidities. Such findings may be clinically significant for male patients with left-sided chronic pain who may benefit from psychotherapeutic or psychopharmacologic intervention at a greater rate, in addition to neural blockade and other pain treatments.

Evidence in right-handed, healthy volunteers indicates that pain thresholds are lower for pain applied to the left hand than the right hand, such as with pressure, electrical, or cold-pressor stimuli.[6,31-33] Handedness was not collected in our study. The size of our sample leads us to think that most likely the incidence of left-handedness in our sample was the same as in the general population, ~15%, and was unlikely to differ between men and women. In terms of other clinical populations, the studies cited in the introduction indicating the left-sided predominance of pain were performed primarily in populations with somatoform pain disorders. Our results contrast with these findings in that pain ratings of spinal etiology did not differ in those with right vs. left-sided pain. To our knowledge, our results represent one of the first studies to document that spinal pain of a somatic (i.e., degenerative) etiology on the left side of the body is associated with greater psychiatric symptoms in men, but not increased pain. While one can argue that our results are somewhat subtle, the sample size speaks against these being spurious findings.

Further evidence comports with our findings. Geschwind and colleagues noted that prenatal testosterone slows the growth of the left hemisphere in males.[34] This may lead to a greater tendency for right hemisphere dominance in men, a classic theory with significant supporting evidence that men are more right-brained and women more left-brained.[35] Yet, it has been observed that women tend to experience more pain than men, and that pain in

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females is associated with greater negative affect.[36] Rhudy and colleagues have critiqued this notion and argue that most of those studies in humans suffer from small sample sizes and poor control for intra- and inter-individual differences in pain and mood experience and reporting.[37] While females did report greater pain levels in our study, pain was less correlated to psychological symptoms in women than in men (particularly among men with left-sided pain). In a large clinical sample, Verenich reported that among 1406 patients hospitalized for low back pain, men reported significantly greater pain on the left compared with women ($P<.001$).[38]

In sum, there is empiric evidence that men and women tend to report different levels of pain, sidedness of pain, and psychological symptoms in relation to pain.[39] The relationships between gender and these three variables, as well the relationships among these variables themselves are not clear. Our findings add to this body of work by providing data from a clinical sample of spinal pain patients and by providing evidence for links between gender, sidedness of pain, and the relationships between pain and psychological symptoms.

Indeed, a neurobiological basis for our findings is emerging from neuroimaging studies of pain and emotional processing. The insula is one of the key cortical areas of the brain's "pain matrix" which is involved in processing pain and affect.[40] Stimulation of the right insula produces sympathetic effects (tachycardia and pressor response), while stimulation of the left insula produces parasympathetic effects (bradycardia and lower blood pressure).[41] The right anterior insula is also more selectively activated in neuroimaging studies of thermal pain, muscle pain, visceral pain, anger, fear, and anxiety.[27] Similarly, in studies of vagus nerve stimulation for depression, stimulation is performed on the left vagus nerve because it is more effective[42] and has been shown to activate the left anterior insula and deactivate the right anterior insula.[27] Thus, in our clinical sample, those with left-sided spinal pain are preferentially activating the right insula and other right-sided cortical areas of the medial pain system, which process pain and affect.[43] Preferential stimulation of the right hemisphere in men may then induce greater negative affect.

There are limitations of our work that deserve discussion. First, lateralization of pain may instead be a function of behavior related to occupation and right/left dominance. Since the majority of the population is right handed and right footed, the muscles and joints on the left side may be less strong and flexible. However, in previous work by the authors, patient data including craniomandibular functioning, health status, coping strategies, SCL-90R and Beck Depression Inventory was obtained from the National Institute of Dental and Craniofacial Research TMJ Implant Registry and Repository (NIDCR TIRR) Etiology Study. Although there was no significant difference in severity of pain between the left- and right-sided pain groups, the left-sided pain patients reported significantly more psychological symptoms in more than half of the SCL-90R scales and more parafunctional habits (such as nail biting, bruxism, and grinding) than right-sided patients.[44] Since there is no dominant side for facial muscles and joints and yet left-sided TMJ patients reported greater psychological distress, these findings speak against the notion that right sided dominance and left-sided neglect explain why those with left-sided spinal pain have more negative affective symptoms. Secondly, there is no data on whether the psychological symptoms preceeded or followed spinal pain. But, the majority of evidence indicates that affective disorders, such as major depression, most commonly follow the onset of pain and appear to be induced by the chronic pain syndrome.[45]

Conclusions

There is a burgeoning literature on individual differences in pain perception and treatment response.[46] The present study expands this body of work on inter-individual differences by illustrating significant relationships among sidedness of pain, gender, and psychological symptoms. Our findings from a large sample of patients provide greater clinical confirmation of many of the results suggested by neuroimaging research, which have only been performed in small samples of healthy subjects. Our results also suggest that the clinician should be aware that men with left-sided spinal pain may be more likely to suffer affective disturbances. This patient group may benefit to a greater degree to psychiatric or psychological treatment, as an adjunct to pharmacological, rehabilitative, or interventional treatments.

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Table 1

Demographics and Pain History

Variable	**(N=519)**
Age (mean, ±sd, range)	54.9 ± 19.0; range 17-91
Gender (% female)	57.4
Race (% Caucasian)	69.4
Pain Duration (% > 5 y)	42.6
Pain Location (% low back)	77
Laterality of Pain (%)	43.0 left
	41.6 right
	15.4 bilateral
BPI Scores (all subjects, mean ±sd)	
Pain at Worst	7.6 ± 1.7
Pain at Least	4.7 ± 2.4
Average Pain	6.2 ± 1.8
Pain Right Now	6.1 ± 2.4
Interference with…	
General Activity	6.5 ± 2.4
Mood	5.8 ± 2.8
Walking Ability	6.3 ± 2.8
Normal Work	6.9 ± 2.5
Relations With Others	4.7 ± 3.0
Sleep	6.0 ± 3.0
Enjoyment of Life	6.6 ± 2.7
HADS Scores (all subjects, mean ±sd)	
Anxiety Score	8.3 ± 4.4
Depression Score	7.9 ± 4.0
Total Negative Affective Symptoms	16.2 ± 7.6

Table 2

Left vs. Right Pain and Psychological Symptoms by Gender

MEN			
Variable	**Left (n=98)**	**Right (n=91)**	***Sig***.
BPI Items (mean ±sd)			
Interference with Mood	6.1 ± 2.9	5.0 ± 2.9	p=.015
Interference with Enjoyment of Life	7.0 ± 2.5	6.3 ± 3.0	p=.12
HADS Scores (mean ±sd)			
Anxiety Score	8.5 ± 4.6	7.6 ± 4.5	p=.21
Depression Score	8.6 ± 4.2	6.9 ± 4.1	p=.007
Total Negative Affective Symptoms	17.1 ± 8.1	14.5 ± 7.9	p=.034
WOMEN			
Variable	**Left (n=126)**	**Right (n=125)**	***Sig***.
BPI Items (mean ±sd)			
Interference with Mood	6.2 ± 2.8	5.9 ± 2.7	p=.43
Interference with Enjoyment of Life	6.8 ± 2.5	6.9 ± 2.7	p=.87
HADS Scores (mean ±sd)			
Anxiety Score	8.8 ± 4.1	8.5 ± 4.5	p=.65
Depression Score	8.3 ± 3.8	7.8 ± 3.9	p=.26
Total Negative Affective Symptoms	17.1 ± 6.9	16.3 ± 7.7	p=.39

Table 3

Correlations between Pain, Function, and Mood in Men vs. Women

(Female n=298, Male n=221)			
Variable	***Sex***	***Anxiety***	***Depression***
Pain at Worst	Female	.17*	.23*
	Male	.31*	.20*
Average Pain	Female	0.12	.17*
	Male	.35*	.28*
Interference with…			
General Activity	Female	.15*	.31*
	Male	.51*	.46*
Mood	Female	.44*	.49*
	Male	.55*	.59*
Walking Ability	Female	.15*	.26*
	Male	.39*	.37*
Normal Work	Female	.22*	.42*
	Male	.51*	.51*
Relations With Others	Female	.44*	.54*
	Male	.51*	.57*
Sleep	Female	.25*	.26*
	Male	.51*	.41*
Enjoyment of Life	Female	.36*	.56*
	Male	.49*	.56*

* = p<.01, Pearson Correlation Coefficient