

Sex differences in predictors of response to multidisciplinary treatment of chronic pain

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BACKGROUND: Multidisciplinary programs for treatment of chronic pain are generally effective, yet many patients fail to show significant improvement. The search for predictors of outcome has not explicitly considered sex.

OBJECTIVE: To examine mediation and moderation pathways through which sex may predict outcome.

DESIGN: Correlational outcome, exploratory, archival study.

PARTICIPANTS: A total of 156 chronic pain patients.

SETTING: Four-week multidisciplinary pain program.

PREDICTOR AND OUTCOME MEASURES: Predictor variables of pain level, activity interference and perceived pain helplessness were culled from patient charts. Outcome was assessed with staff ratings of patient progress.

RESULTS: While men responded to treatment more poorly than women, regressions suggested that the greater number of surgeries for men mediated this link. Further analyses revealed that sex acted as a moderator. Among women, perceived pain helplessness was negatively related to outcome, while married women with dissatisfying marriages responded more poorly than unmarried women and women with satisfying marriages. These variables were not significant predictors of outcome among men.

CONCLUSIONS: Men and women may be differentially characterized by various risk factors for treatment failure. Moreover, relationships between pretreatment psychosocial factors and outcome may depend on sex.

Key Words: *Chronic pain treatment, Outcome predictors, Sex differences*

Différences sexuelles dans les prédicteurs de la réponse à un traitement multidisciplinaire de la douleur chronique

PROBLÉMATIQUE : Les programmes multidisciplinaires pour le traitement de la douleur chronique sont généralement efficaces; cependant, nombreux sont les patients qui n'accusent aucune amélioration significative de leur état. La recherche sur les prédicteurs des résultats n'a jamais vraiment tenu compte du sexe.

OBJECTIF : Examiner les voies de médiation et de modulation à travers lesquelles le sexe peut être un prédicteur des résultats.

MODÈLE : Étude d'archives, exploratoire, et des résultats corrélationnels.

PARTICIPANTS : Un total de 156 patients souffrant d'une douleur chronique.

CONTEXTE : Programme multidisciplinaire de 4 semaines pour la douleur.

PRÉDICTEURS ET MESURES DES RÉSULTATS : Les variables des prédicteurs du niveau de douleur, de l'interférence des activités et de l'incapacité perçue liée à la douleur ont été recueillies dans les dossiers des patients. Les résultats ont été mesurés d'après l'évaluation du progrès des patients faite par le personnel.

RÉSULTATS : Les hommes tendaient à répondre moins bien au traitement, cependant, l'analyse de régression laissait croire que le nombre plus élevé de chirurgies pratiquées sur les hommes influençait ce lien. D'autres analyses ont révélé que le sexe agissait comme modérateur. Parmi les femmes, la perception de l'incapacité liée à la douleur n'était pas liée aux résultats, tandis que les femmes non satisfaites de leur vie de couple répondaient moins bien que les femmes célibataires ou satisfaites de leur vie de couple. Ces variables n'étaient pas des prédicteurs significatifs des résultats parmi les hommes.

CONCLUSIONS : Les hommes et les femmes pourraient être différemment caractérisés par une variété de facteurs de risque associés à l'échec du traitement. De plus, les rapports entre les facteurs psychosociaux existants avant le traitement et les résultats pourraient dépendre du sexe.

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Multidisciplinary approaches to chronic pain treatment have become widespread, and research attests to the efficacy of such approaches compared with no treatment or with treatment associated with single disciplines, such as medical management (1). Patients with chronic pain, however, do not all respond well to multidisciplinary pain treatment programs, and substantial failure and/or drop out rates are common (2,3). To understand better what contributes to treatment failure, investigators have attempted to uncover factors that may predispose certain chronic pain patients to respond poorly to treatment (4). Overall findings regarding predictors of treatment outcome have been mixed, and the magnitude of associations among these variables generally has been no more than moderate. Nevertheless, a few predictors of treatment failure have emerged, such as high levels of pain (5), depression (6), notable activity limitations (7) and low social support (8).

Sex is a potential predictor of treatment outcome that has received inadequate attention in the literature – a neglect that may be due, in part, to a lack of theoretically compelling reasons to expect men and women to respond differently to multidisciplinary pain programs. While recent research is beginning to provide physiological bases for predicting such sex distinctions (9,10), mediation relationships, which involve sex differences in certain functional and/or psychosocial factors, also may be proposed. It is plausible to anticipate sex differences in responses to multidisciplinary pain programs because men and women differ in functional and/or psychosocial variables that are linked to poor treatment outcome (eg, pretreatment activity levels, depression). That is, sex differences in response to multidisciplinary pain programs may be explained by sex differences in ‘third variables’ (ie, mediators) that have been shown to influence outcome adversely. Evidence supports that male and female chronic pain patients have different risk factors for treatment failure. For instance, Keefe et al (11) showed that men complained of higher pain levels than women. Such findings, however, have not been reported extensively.

It may also prove fruitful to consider whether sex moderates relationships among functional and/or psychosocial factors and outcome criteria such that associations between such factors and outcome may depend on the patient’s sex. In a cross-sectional study, for example, Haley and co-workers (12) found that depression was related positively to self-reported pain among women but not men. These findings hint that the relatively weak associations between predictors and outcome prevalent in research reports may be attributed, in part, to the moderating effects of sex. Thus, factors that predict responses to a multidisciplinary pain program may differ depending on whether the chronic pain patient is male or female.

The present study was exploratory. We used archival data to test whether sex predicted treatment outcome, and whether these differences were mediated by sex dissimilarities in factors such as pretreatment pain levels, activity interference, perceived helplessness and marital support. Where mediation relationships were not supported, the potential moderating effects of sex were evaluated. Given the dearth of literature on this topic, we offer no hypotheses regarding the direction or strength of associations.

PATIENTS AND METHODS

Potential subjects were 214 chronic pain patients who participated in the multidisciplinary pain treatment program at the Center for Rehabilitation of Lake Forest Hospital, Lake Forest, Illinois between January 1990 and December 1992. However, complete information on the study variables were unavailable for all patients, and some patients were excluded according to the criteria described below. Thus, the final sample comprised 156 patients.

Patients were not admitted to the Center for Rehabilitation with current alcohol or substance abuse disorders, or with a history of psychotic or bipolar disorders. All patients suffered from benign musculoskeletal pain and were not admitted if their pain was due to malignant conditions such as cancer. Only patients who had experienced pain for at least six months were included in this study. Sixty-five per cent of the patients indicated that the primary site of pain was in the lower back.

Women comprised 42% of the sample. Demographic data and statistical comparisons of men and women appear in Table 1. The distribution of the number of pain-related surgeries was skewed, with 44.5% of the overall sample reporting at least one surgery. Thus, a variable was computed that dichotomized ‘no surgery’ versus ‘at least one surgery’. As shown in Table 1, fewer women than men reported at least one pain-related surgery.

Pretreatment measures

This study relied on archival records of the Center for Rehabilitation. Demographic and pretreatment variables were gathered from a booklet routinely administered to all potential patients during initial evaluation. Scales or items that tapped self-reported physical and psychological adjustment, and marital support were chosen. Moreover, psychometric data on the scales or items in the booklet did not exist before this study, so the selection of scales and items for which such data could be derived based on the present sample was limited.

To assess ‘interference with functioning’ 17 items that tapped patients’ difficulties in performing various activities of daily living (ADL) (eg, getting in and out of bed) were used. Items appeared in a four-point Likert format, with high scores indicating high interference. The alpha coefficient of internal consistency for the 17 items was 0.91. A score for ADL was computed by summing the 17 items.

Four items that appeared in 10-point Likert formats were used to assess pain level, with 1 corresponding to ‘none’ and 10 corresponding to ‘extreme’. These items tapped pain level ‘at present’, and measured ‘usual’, ‘worst’ and ‘least’ pain levels during the past two weeks. The alpha coefficient of internal consistency for these items was 0.76; the items were z scored and summed to form a composite variable (PAIN), with high scores representing high pain.

Three items with five-point Likert formats were used to measure perceived helplessness toward pain (eg, to what degree do you feel helpless to change your present condition? to what degree do you feel able to cope with your pain?). The alpha coefficient of internal consistency for these items was 0.68, and so the items were z scored and summed to form a composite variable (HELPLESS), with high scores revealing high perceived helplessness.

TABLE 1
Demographic data and statistical comparisons of study participants

	Age (years)	Duration of pain (months)	Education (years)	Surgery	ADL	PAIN	HELPLESS	Marital satisfaction	OUTCOME
Women (n=66) *	40.38±9.2	21.88±15.0	12.45±2.8	32.2% (at least one)	39.88±11.5	-0.06±0.9	0.04±0.8	1.43±0.5	2.21±1.0
Men (n=90) *	38.71±8.2	21.19±13.3	11.68±3.2	57.2% (at least one)	41.89±8.2	0.07±0.9	-0.01±0.8	1.41±0.5	1.81±1.2
ANOVA or χ^2	F(1,154)=1.18, P>0.10	F(1,154)<1	F(1,154)=2.21, P>0.10	$\chi^2=5.41$, P<0.02	F(1,154)=1.50, P>0.10	F(1,154)<1	F(1,154)<1	F(1,101)<1	F(1,154)=4.92, P<0.03

*Data are represented as mean \pm SD. ADL Activities of daily living; HELPLESS Composite perceived helplessness; OUTCOME Ratings of discharge summaries; PAIN Composite pain level

Only one item in the patient booklet measured marital support, and it specifically tapped relationship satisfaction (ie, how would you describe your marital relationship?). The item was presented in a four-point Likert format. Twenty-five of the 121 married subjects did not complete the item so analyses with this item are based on only 96 married patients. Results of analyses of variance indicated that the 25 subjects who did not complete this item did not differ significantly from the remaining 96 married subjects on any demographic or pain-related variables. In addition, the distribution of responses to the marital satisfaction item was skewed; 58.7% of subjects used the descriptor 'very satisfactory', while responses of the remainder of subjects were divided among the other three descriptors. Thus, a variable was computed that dichotomized 'very satisfactory' versus 'less than satisfactory'.

Mean \pm SD for responses on the ADL, PAIN, HELPLESS and marital satisfaction variables for men and women, as well as statistical comparisons, appear in Table 1.

Treatment outcome

Within each patient's chart were narrative summaries of the course, progress and result of treatment written at discharge by the physician, physical therapist, psychologist and nurse assigned to each patient. These summaries represent general clinical impressions of patient response to treatment. Practitioners gave an account of how well a patient achieved the treatment goals with which that practitioner had been concerned. During the three-year period this archive data accumulated, post-treatment measures of interference with functioning, pain level and perceived helplessness were not collected habitually at the Center for Rehabilitation. Thus, the discharge summaries represent the sole measure of outcome.

Two raters, blind to all patient data, rated each set of discharge summaries written by the medical personnel. Patient outcome according to these summaries was rated on a five-point scale (0 – none, 1 – poor, 2 – some, 3 – good, 4 – excellent). Drop-outs (n=26) were included in the sample, and were given 0 as ratings to ensure that overall response to treatment shown by the sample was defined conservatively (13). For each rater, ratings for physicians, physical therapists, psychologists and nurses

conducted by each rater showed high internal consistency (alpha coefficients 0.95 and 0.96). These results showed that ratings for the four disciplines by each rater were highly inter-related; thus ratings were z scored and summed across disciplines to form composite scores for each rater.

Inter-rater reliability for these composite outcome ratings was then assessed. Correlation between the composite scores for rater 1 and rater 2 was $r=0.92$ ($P<0.0001$). In addition, a t test of the sample means of composite scores for rater 1 ($M=2.05$, $SD=1.17$) and rater 2 ($M=2.02$, $SD=1.14$) showed that the magnitude of the rater means for the sample did not differ ($t=0.48$). Thus, the discharge summary ratings of raters 1 and 2 were sufficiently similar for an average to be computed from these composites to derive a single treatment outcome variable (OUTCOME) for each patient.

Procedure

All patients seen at the Center for Rehabilitation were informed before assessment that any information collected might be used in statistical descriptions of patient characteristics, results of treatment and program quality assurance, but that patient names would not appear. All patients included in this study began an intensive multidisciplinary program (five days per week for four weeks) which was geared toward improving psychological coping and physical functioning. The program included treatment by a physician (if needed), physical therapy, occupational therapy, and individual and group sessions with psychologists.

RESULTS

Tests of mediators between sex and outcome

It was hypothesized that the extent to which men and women differed in response to treatment is a function of third variables, ie, mediators. To support such mediational models, specific significant associations were required (14). First, as shown in Table 1, women had significantly higher ratings on OUTCOME than men. Second, and consistent with previous research (4), zero-order correlations (Table 2) showed that scores on pretreatment ADL and PAIN, and whether pain-related surgery ('no surgery'/'surgery') had been conducted were associated significantly and negatively with response to treatment. Results of

TABLE 2
Zero-order correlations

	1	2	3	4	5	6	7	8	9
Age (years)	–								
Duration of pain (months)	0.29	–							
Education (years)	–0.23 [‡]	–0.06	–						
No surgery/surgery	0.09	0.30 [§]	0.00	–					
ADL	0.22 [‡]	0.23 [‡]	–0.03	0.19 [‡]	–				
PAIN	–0.08	0.00	–0.09	0.07	0.34 [¶]	–			
HELPLESS	0.03	0.04	–0.18 [‡]	–0.01	0.17 [‡]	0.25 [‡]	–		
Marital satisfaction*	0.01	–0.21*	0.21*	–0.13	–0.18*	–0.02	–0.21*	–	
OUTCOME	–0.06	0.09	0.06	–0.19 [‡]	–0.30 [§]	–0.23 [‡]	–0.14	0.03	–

*n=103, r=0.20, P<0.05; [‡]r=0.15, P<0.05; [‡]r=0.20, P<0.01; [§]r=0.26, P<0.001; [¶]r=0.33, P<0.0001. ADL Activities of daily living; HELPLESS Composite perceived helplessness; OUTCOME Ratings of discharge summaries; PAIN Composite pain level

TABLE 3
Summary of hierarchical regression analysis for variables predicting OUTCOME: Sex and HELPLESS

Predictor	B coefficient	SE	R ²	R ² change significance
OUTCOME = sex × HELPLESS				
No surgery/surgery	–0.33	0.18	0.036	0.02
Sex	–0.34	0.18	0.054	0.09
HELPLESS	–0.49	0.17	0.076	0.08
HELPLESS x sex	0.54	0.23	0.106	0.03
Constant	2.33			
OUTCOME = HELPLESS for Men				
No surgery/surgery	–0.22	0.25	0.01	ns
HELPLESS	0.01	0.17	0.01	ns
Constant	1.93			
OUTCOME = HELPLESS for Women				
No surgery/surgery	–0.48	0.25	0.057	0.05
HELPLESS	–0.49	0.15	0.198	0.001
Constant	2.38			

HELPLESS Composite perceived helplessness; ns Not significant; OUTCOME Ratings of discharge summaries; SE Standard error

ANOVAs in Table 1 indicate, however, that men and women did not differ on ADL or PAIN. Thus, sex was found to be not related significantly to these potential third variables, and so ADL and PAIN could not mediate the association between sex and OUTCOME (14).

However, the pattern of significant associations among sex, OUTCOME and the no surgery/surgery variable suggests that sex difference in OUTCOME may be partly attributable to sex differences in the number of surgeries. With sex dummy-coded,

results of hierarchical regressions indicated that, individually, sex accounted for 3.2% of the variance in OUTCOME (P<0.03), while the no surgery/surgery variable accounted for 3.6% of the variance (P<0.02). When the variance of the no surgery/surgery variable was controlled, the unique variance accounted for by sex was reduced to 1.9% (not significant). These results provide statistical support for a mediating role of the no surgery/surgery variable. Thus, findings suggest that men tended to have a poorer response to treatment than women partly because men were more likely to have had surgery for their pain, a factor independently linked to poor outcome.

Tests of sex as a moderator

Since ADL, PAIN and HELPLESS did not mediate the association between sex and OUTCOME, further models were evaluated to determine whether the relationships between these pretreatment variables and OUTCOME were moderated by sex. That is, analyses were performed to ascertain whether ADL, PAIN and HELPLESS were related to OUTCOME differently in men versus in women. Interaction terms were computed by multiplying ADL, PAIN and HELPLESS scores by sex. Hierarchical regressions were used to evaluate whether interaction terms accounted for additional variance in OUTCOME beyond that accounted for by the main effects. In addition, the effect on OUTCOME of the no surgery/surgery variable was controlled given the sex differences reported above.

The ADL × sex, and PAIN × sex terms were not significant predictors of OUTCOME. These null findings indicated that the negative associations between these pretreatment variables and OUTCOME were similar for men and women. However, the HELPLESS × sex term was a significant predictor of OUTCOME (Table 3), and so separate regression equations were computed for men and women (15). Results indicated that perceived helplessness about pain was significantly and negatively related to response to treatment only among women, accounting uniquely for 14.1% of the variance.

Regarding marital support, men and women did not differ on marital satisfaction (Tables 1,2), and such satisfaction was not

significantly related to OUTCOME. To test whether sex moderated the association between marital support and OUTCOME, three groups were formed based on marital status and reported satisfaction: unmarried; married/low satisfaction; and married/high satisfaction. When crossed with sex, the resulting cell sizes were unbalanced (eg, unmarried women: $n=16$; married/high satisfaction men: $n=35$), so hierarchical regressions were employed rather than ANOVAs because the former strategy is less vulnerable to unequal cell sizes (15). The three marital support groups were represented as three vectors (15). Vector 1 was coded to compare married/low satisfaction subjects (-1) with married/high satisfaction subjects (1), with unmarried subjects negated (0). Vector 2 was coded to compare unmarried subjects (-1) with married/low satisfaction subjects (1), with married/high satisfaction subjects negated (0). Vector 3 was coded to compare unmarried subjects (-1) with married/high satisfaction subjects (1), with married/low satisfaction subjects negated (0). Because three groups were used, only two vectors were required to represent the variance of the marital support groups through main effect or interaction terms in any given regression (16).

Two vector \times sex terms, which represented the marital support group \times sex interaction, accounted for significant variance in OUTCOME (R^2 increment = 0.058, $P < 0.02$) after the no surgery/surgery variable was controlled, and after the vector and sex main effects had been entered. The significant vector \times sex interaction suggested that the association between marital support and response to treatment depended on sex, so simple effects were analyzed by computing separate regression equations for men and women. As shown in Table 4, the main effect for vectors was not significantly related to OUTCOME among men, a result that suggests that marital support did not influence the treatment responses of men. Among women, the vectors' effect was significant, accounting for 12.8% of the variance, so further post hoc tests were conducted. Results indicated that vector 1 was related marginally and positively to OUTCOME (R^2 increment=0.053, $P < 0.08$), which means that married/high satisfaction women responded marginally better to treatment than married/low satisfaction women. Vector 2 predicted OUTCOME significantly and negatively (R^2 increment=0.122, $P < 0.008$), which signifies that unmarried women showed a better treatment outcome than married/low satisfaction women. Finally, vector 3 was not associated significantly with OUTCOME, which indicates that unmarried women and married/high satisfaction women responded to treatment comparably.

DISCUSSION

The primary purpose of this study was to explore sex differences in determinants of outcome following a multidisciplinary pain treatment program. Limited evidence was found for the notion that sex differences in pretreatment factors linked to poor outcome may mediate a relationship between sex and response to treatment. We found that the poorer outcomes shown by men were partly accounted for by their increased frequency of pain-related surgery. Analyses that conceptualized sex as a moderator showed that perceived helplessness regarding pain and marital support were related to treatment outcome differently in men

TABLE 4
Summary of hierarchical regression analysis for variables predicting OUTCOME: Marital support and sex

Predictor	B coefficient	SE	R ²	R ² change significance
OUTCOME = Marital support				
No surgery/surgery	-0.36	0.20	0.039	0.02
Sex	-0.37	0.18	0.067	0.06
Vector 1	0.11	0.20	0.068	ns
Vector 2	-0.40	0.22		
Vector 1 \times sex	-0.20	0.16	0.126	0.02
Vector 2 \times sex	0.61	0.29		
Constant	2.40			
OUTCOME = Marital support for men				
No surgery/surgery	-0.26	0.29	0.01	ns
Vector 1	-0.07	0.19	0.036	ns
Vector 2	0.22	0.21		
Constant	1.96			
OUTCOME = Marital support for Women				
No surgery/surgery	-0.53	0.27	0.060	0.07
Vector 1	0.11	0.17	0.188	0.02
Vector 2	-0.40	0.21		
Constant	2.45			

ns Not significant; OUTCOME Ratings of discharge summaries; SE Standard error

than in women. Results showed that high perceived helplessness and low marital support were associated negatively with responses to treatment only in women.

Although men were judged by the Center for Rehabilitation staff to have responded more poorly to treatment than women, sex accounted for only 3.3% of the variance in outcome ratings. The mediation model, which linked sex to outcome via differential rates of surgery, nevertheless offers some intriguing possibilities regarding sex-specific influences on treatment response. For example, future research may focus on the reasons why men may have more surgery than women (eg, more intractable beliefs about the somatic underpinnings of pain) and how these factors may, in turn, influence outcome.

Other results suggest that sex may moderate associations between psychosocial factors and treatment outcome. Although men and women did not differ significantly on pretreatment levels of perceived helplessness or marital satisfaction, the associations between these variables and response to treatment was significant only among women. These findings imply that many of the inconsistent or small relationships between predictors and outcome reported in past studies may have been attenuated by sex moderation. Thus, perceived helplessness about pain may constitute a robust predictor of outcome, but only among women.

The results for marital support also point to the potential importance of sex differences. Research indicates that the presence of marital support, broadly defined, has a positive impact on the psychological and physical adjustment of individuals with chronic illnesses (16). Among women in this sample, however, those who were dissatisfied with their marriages responded more poorly than unmarried women. Thus, marriage alone may not provide sufficient social support to women to facilitate rehabilitation from chronic pain, and a more satisfying relationship may be required for optimal adjustment (17).

Our findings must be interpreted with caution due to limitations inherent in this archival data set. Not only were measures used for which little psychometric data were obtainable, but also the quite subjective clinical impressions of the Center for Rehabilitation staff were our sole measure of outcome. On one level, staff ratings of outcome may have been unduly influenced by extraneous factors, such as the patient being liked by the staff. On another level, our predictors of poor outcome may have covaried with patient characteristics against which the staff have developed subtle biases, thereby affecting their judgements. For instance, patients with previous pain-related surgeries may embrace unyielding beliefs about the somatic origins of their pain, beliefs that may lead them to discount – vocally and readily – the cognitive/behavioral explanations promoted by the staff of this pain program, thus leading to poor opinions of patient response to treatment regardless of actual ‘objective’ progress. Without different measures of outcome, we are uncertain to what degree we assessed ‘outcome’. Despite these limitations, the composite variables and items that predicted outcome in the present study, such as initial pain levels and interference with functioning, were consistent with predictors of outcome found in previous research (4).

CONCLUSIONS

Sex differences in treatment outcome apparently have not been studied widely. This paper provides preliminary evidence that men and women may be differentially characterized by risk factors for treatment failure, and that sex may interact with psychosocial factors to predict outcome. Thus, men and women may not only react differently to the experience of chronic pain (12), but also their responses to multidisciplinary efforts to alleviate pain may be influenced by somewhat different phenomena. While this study was certainly exploratory, the results suggest that fur-

ther pursuit of the reasons underlying the sex discrepancies found may prove fruitful.

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