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EMOTIONAL REACTIONS TO PAIN PREDICT PSYCHOLOGICAL DISTRESS IN ADULT PATIENTS WITH SICKLE CELL DISEASE (SCD)

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ABSTRACT

Differentiating somatic from emotional influences on the experience of chronic pain has been of interest to clinicians and researchers for many years. Although prior research has not well specified these pathways at the anatomical level, some evidence, both theoretical and empirical, suggest that emotional reactions influence the experience of disease and non-disease-related pains. Other studies suggest that treatments directed at negative emotional responses reduce suffering associated with pain. The current study was conducted to explore the influence of emotional reactions to pain as a predictor of psychological distress in a sample of adult Blacks with Sickle Cell Disease (SCD). Using cross-sectional survey data, we evaluated whether negative emotional reactions to the experience of pain were predictive of psychological distress after controlling for the somatic dimension of pain and age in $n = 67$ Black patients with Sickle Cell Disease (SCD). Results showed that greater negative emotion associated with pain predicted Somatization ($p < .01$), Anxiety ($p < .05$), Phobic Anxiety ($p < .05$), and Psychoticism ($p < .05$). Increased negative emotion associated with pain was also predictive of the General Symptoms Index ($p < .05$) and the Positive Symptoms Total from the SCL-90-R ($p < .01$). We believe the current study demonstrates that negative emotional reactions to the experience of pain in adults with SCD are predictive of psychological distress above and beyond the influences of age and the direct nociceptive experience. We also believe these data to be valuable in conceptualizing the allocation of treatment resources toward a proactive approach with early identification of patients who are responding poorly for the purpose of potentially reducing later psychopathology. A deeper understanding of the ways that subpopulations cope with chronic disease-related pain may produce models that can be ultimately generalized to the consumers of the majority of healthcare resources.

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Key Words: depression, pain, negative emotional reactions, sickle cell disease

INTRODUCTION

Chronic pain remains one of the more poorly understood phenomena in medical and social science research. Although pain is the single most common reason to visit a physician [1, 2] and one of the most common reasons patients seek medical care [3], there remains controversy over the biological, psychological, and social basis of chronic pain. Many clinicians and scientists continue to debate the existence, for example, of fibromyalgia, chronic fatigue syndrome, and myofascial pains as manifestations of mental illnesses rather than physical disorders or biological syndromes [4]. Patients with these conditions often present with debilitating primary effects under conditions of unclear etiology and powerful secondary effects that can alter emotional states and facilitate misdiagnosis [5].

When present in patients with chronic pain, psychological symptoms such as depressed mood or elevated anxiety can be even more perplexing and difficult to identify due to their comorbidity and shared symptomatology [6-9]. Commonly shared symptoms of pain and depression, for example, include but are not limited to sleep and appetite disturbances, fatigue, reduced behavioral activity with anhedonia, social withdrawal, changes in weight, and decreased libido [10-12]. These depressive symptoms are less likely to be recognized by clinical providers when primary complaints are pain-related [13]. Many patients with chronic pain experience an increased prevalence of psychosocial crises that include job loss, the loss of roles in the family system, decreases in social functioning, and increased healthcare costs [14]. This shift in functioning and resource utilization can also be associated with depressive symptomatology [15]. Conversely, patients with depression may present with emotional symptoms [15] and painful somatic symptoms including, headaches [16], muscle aches, and backaches [17].

Negative mood states and stress predict physical symptoms of pain-related illnesses and vice versa (e.g., arthritis, irritable bowel syndrome, and recurrent abdominal pain in children) [17]. Studies have shown that fluctuations in negative mood and stress predict not only pain, but also psychosocial and functional outcomes [2, 5]. Clinicians and researchers alike have speculated that psychological disorders, such as depression or anxiety, can be associated with the onset of painful episodes in diseases like sickle cell disease (SCD), a class of inherited blood disorders (e.g., sickle cell anemia, sickle hemoglobin C, sickle beta thalassemia) characterized by a decreased quantity of red-blood cells capable of effectively carrying oxygen as a result of their shortened lifespan and sickled shape. Previously, this speculation was supported by predominately anecdotal evidence and retrospective studies [2]. However, in recent years, several investigations have provided evidence for a relationship between mood, stress, and pain in patients with SCD [6-8, 18]. To our knowledge, none of these previous studies have examined the impact of negative emotional responses to the experiences of chronic pain as the basis of the prediction of clinically relevant psychiatric dispositions in adult patients with SCD.

There is evidence of substantial variability in the presentation of negative mood symptoms, among ethnic groups and across cultures, but few if any of these models have been used as the basis of a study in a sample of Blacks [19-21]. The majority of patients with SCD in the United States are Black, have chronic pains, generally present with a high incidence and prevalence of psychopathology [7, 22-30], and are an ideal sample for such a study.

In the context of a general literature that documents the impact of pain on mood (2, 5, 17), and in the absence of findings in samples of Blacks with SCD, we asked: Can emotional reactions to pain in patients with SCD be used to predict differences in the magnitude of psychological distress? The primary aim of this study was to investigate the predictive value of the negative emotional dimension of pain on the magnitude of psychological distress in patients with SCD. We hypothesized that negative emotional reactions to pain would be significantly predictive of psychological distress in this population.

METHODS

Study Design

The current study represents a cross-sectional evaluation of data collected as part of a longitudinal investigation of the relationship of medical and psychosocial factors to pain in patients with SCD.

Participants

Participants were 67 adult patients diagnosed with SCD from the Duke University Comprehensive Sickle Cell Center. Inclusion criteria included a diagnosis of SCD provided by the study hematologist. Participants were excluded from the study if they were actively in an acute episode of pain or other urgent medical crisis at the time of clinic visit or if they were unable to read and comprehend the written instructions for testing. Patients were also excluded from analysis if they had a significant diagnosis other than SCD (e.g., history of psychotic episode in the past 6 months). The consent form and all study procedures were approved by the institutional review board at Duke University Medical Center.

Materials

Pain

The Short Form McGill Pain Questionnaire (SF-MPQ) [31] and a visual analogue scale were used to measure pain severity. The SF-MPQ is structured to assess qualitative and quantitative aspects of pain including location, intensity, quality, and temporal dimensions. Participants were asked to rate the current intensity of each pain-related adjective by circling “none, mild, moderate, or severe.” The measure has demonstrated validity and reliability with multiple pain

populations. Intra-class correlations, as estimates of reliability, for the sensory, affective, and average pain scores, are 0.96, 0.95, 0.88, and 0.89, respectively [32]. There is a very high correlation between scales of the long and short-forms of the McGill Pain Questionnaire.

Psychopathology

The Symptoms Checklist 90-items, Revised (SCL-90-R) [33] was used to evaluate the magnitude of common psychopathologies including Somatization (SOM; distress arising from perceptions of bodily dysfunctions), Obsessive-compulsion (O-C; irresistible thoughts, behaviors, or impulses), Interpersonal Sensitivity (I-S; feelings of personal inadequacy or uneasiness), Depression (DEP; dysphoric mood and other symptoms associated with depression), Anxiety (ANX; a tendency toward anxiety as manifest by nervousness, tension, and trembling), Phobic Anxiety (PHOB; a persistent fear response to a specific person, place, object, or situation), Hostility (HOS; thoughts, feelings, or actions that are associated with a state of anger), Paranoia (PAR; suspiciousness or the fear of loss of autonomy), and Psychosis (PSY; the perception of unusual experiences or interpersonal isolation). The SCL-90-R also has 3 global indices including General Severity Index (GSI; the current level and depth of negative emotional distress), Positive Symptom Distress Index (PSDI; intensity of symptoms as a function of the number of endorsed symptoms), and the Positive Symptom Total (PST; number of symptoms that patients endorse). Response options range from 0 (not at all) to 4 (extremely). Internal consistency for the subscales ranged from .77 to .90. Cronbach alphas for the global severity index (GSI) are high, ranging between .96 and .97 [33].

Social Desirability

The Marlow-Crowne Social Desirability Scale (MCSD) is often incorporated in studies to account for a study subject's tendency to respond to questions in a culturally desirable manner within the context of a current ethnic-cultural population under study. The original instrument was developed by Marlow and Crowne in 1960 [34]. The scale presents culturally approved behaviors with a low probability of occurrence. Higher scores represent an increased tendency to answer questions according to what the participant believes would likely please the proctor. Kuder-Richardson coefficient of internal consistency is .88 with a one-month test-retest correlation of .89.

Procedures

Study procedures have been described previously [6, 7, 22, 35]. Briefly, all patients were consented and enrolled individually in the current study during routine visits to the Duke University Comprehensive Sickle Cell Center. Patients

were identified by the study hematologist as suitable for participation based upon the patient's ability to read, and their characteristics matched against inclusion and exclusion criteria. They were then approached by study personnel about participation. All patients were given a brief verbal overview of the study, which included conducting a review of their historical patterns of healthcare utilization from their medical records, and then allowed to read the consent forms.

Participants were then provided a copy of the survey, moved to a relatively quiet or isolated portion of the waiting room when possible, and given instructions for completion of the survey by a member of the study team. Once complete, the survey was collected and an informal debriefing was provided.

Statistical Analyses

Statistical analyses were conducted using SAS [36]. Data were examined for normality, homoscedasticity, skewedness, kurtosis, and multicollinearity prior to analysis. The primary data analysis strategy was to conduct separate regression analysis models on the nine symptom scales and three global indices of the SCL-90-R. Following adjustment for age, the Sensory and Affective scales of the McGill Pain Questionnaire–Short Form were entered into the models to predict outcomes on the SCL-R-90.

RESULTS

Participants

Sixty-seven participants (n = 30 male and n = 37 female), mean age 36.82 ± 11.47 (range 18-70), mean years of education 13.28 ± 1.84 completed the assessment during the first year of evaluation. Thirty-two percent of patients were married, 48% were single, 17% were divorced/separated, and 3% were living with a significant other. Sixty-four percent of patients were employed at the time of assessment. Twenty-nine percent of patients reported that they had experienced "Anxiety," and 36% indicated that they had experienced "Depression" in the 30 days prior to assessment. Patients who endorsed these psychological symptoms did not differ in their age, education, tendency to report in a socially desirable manner, or reports of pain from patients who did not endorse the presence of these symptoms.

Zero-Order Correlations between Predictor and Outcome Variables

Generally, there were high intercorrelations among scales of the SCL-90-R ($p < .001$; Table 1). Further, the negative emotional dimension of pain was significantly positively correlated ($p < .05$) with all scales of the SCL-90-R except for Hostility ($p > .05$). The SCL-90-R scales were less strongly correlated with

Table 1. Zero-Order Correlations between Predictor and Outcome Variables

	MCSDS	SOM	O-C	I-S	DEP	ANX	HOS	PHOB	PAR	PSY	GSI	PSDI	PST	Age	Sensory	Emotional
MCSDS	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
SOM	−.060	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—
O-C	−.010	.456**	1	—	—	—	—	—	—	—	—	—	—	—	—	—
I-S	−.200	.471**	.833**	1	—	—	—	—	—	—	—	—	—	—	—	—
DEP	−.091	.582**	.807**	.762**	1	—	—	—	—	—	—	—	—	—	—	—
ANX	−.107	.593**	.767**	.753**	.821**	1	—	—	—	—	—	—	—	—	—	—
HOS	−.144	.394**	.518**	.547**	.512**	.618**	1	—	—	—	—	—	—	—	—	—
PHOB	−.036	.351*	.731**	.617**	.652**	.735**	.588**	1	—	—	—	—	—	—	—	—
PAR	−.059	.405*	.750**	.746**	.689**	.684**	.395**	.589**	1	—	—	—	—	—	—	—
PSY	−.190	.501**	.736**	.748**	.791**	.767**	.564**	.693**	.713**	1	—	—	—	—	—	—
GSI	−.089	.680**	.890**	.851**	.926**	.899**	.614**	.740**	.791**	.849**	1	—	—	—	—	—
PSDI	−.024	.592**	.712**	.576**	.740**	.637**	.408*	.535**	.554**	.612**	.786**	1	—	—	—	—
PST	−.130	.662**	.840**	.842**	.883**	.883**	.634**	.744**	.791**	.854**	.962**	.620**	1	—	—	—
Age	.152	−.236	−.102	−.275*	−.188	−.120	−.242*	−.118	−.084	−.207	−.228	−.194	−.229	1	—	—
Sensory	.088	.353*	.303*	.275*	.289*	.317*	.167	.200	.159	.287*	.346*	.296*	.314*	.033	1	—
Emotional	−.034	.459**	.352*	.318*	.320*	.402*	.213	.107*	.282*	.378*	.431*	.345*	.437*	.025	.723**	1

Note: MCSDS = Marlowe-Crown Social Desirability Scale; SOM = Somatization; O-C = Obsessive-Compulsive; I-S = Interpersonal Sensitivity; DEP = Depression; ANX = Anxiety; HOS = Hostility; PHOB = Phobic Anxiety; PAR = Paranoid Ideation; PSY = Psychoticism; GSI = Global Severity Index; PSDI = Positive Symptom Distress Index; PST = Positive Symptom Total; Sensory = Sensory Subscale of the SF-MPQ; Emotional = Affective Subscale of the SF-MPQ.

*$p < .05$; **$p < .001$.

age and the sensory dimension of pain. Age was significantly positively correlated with Interpersonal Sensitivity ($p < .05$) and Hostility ($p < .05$), while the Sensory experience of pain was significantly positively correlated with SOM, O-C, I-S, DEP, ANX, and PSY symptom scales, well as the GSI, PSDI, and PST ($p < .05$). Social desirability was unrelated to any of the study variables.

Association between Negative Emotional Responses and Psychopathology

After covarying for age and the sensory dimension of pain, the negative emotional dimension of pain was found to be significantly associated with SOM ($F[3, 62] = 7.75$, $p < .01$, $R^2 = 0.27$) and ANX ($F[3, 62] = 5.39$, $p < .01$, $R^2 = 0.21$). In addition, the negative emotional dimension of pain was also found to be significantly associated with PHOB ($F[3, 62] = 2.86$, $p < .05$, $R^2 = 0.12$), and PSY ($F[3, 62] = 4.88$, $p < .01$, $R^2 = 0.19$). Lastly, the negative emotional dimension of pain was predictive of the GSI ($F[3, 62] = 6.72$, $p < .001$, $R^2 = 0.25$) and the PST ($F[3, 62] = 6.81$, $p < .001$, $R^2 = 0.25$). Regression coefficients are presented in Table 2. The negative emotional dimension of pain was not predictive of the O-C, I-S, DEP, HOS, or PAR symptom scales as well as the PSDI.

DISCUSSION

To our knowledge, this is one of only two studies to evaluate the relationship between negative emotional reactions to pain and subsequent psychological outcomes in adult patients with SCD. Previous studies have identified the somatic experience of pain as significant in predicting negative emotional states, healthcare utilization, and quality of life [37]. We extended these previous findings to include that the negative emotional reaction to the somatic experience of pain, controlling for the magnitude of nociceptive experience, was predictive of psychological distress which included anxiety about health and other issues, elevated levels of distrust, and the increased belief that one is isolated by experiences that are disparate from the general population. Negative emotional reactions to pain were also predictive of the number of symptoms endorsed by patients who have SCD, and the level and depth of negative emotional distress.

These results are consistent with past studies in other populations that have found a relationship between psychological symptoms and the experience of chronic pain in patients with SCD [7, 22, 32, 35, 38]. Pain perception and psychological disposition are intricately intertwined, with one affecting the other. More broadly, the experience of pain influences and is influenced by biological, cognitive, and emotional processes all experienced in a social

Table 2. Association between Negative Emotional Responses to Pain and Psychiatric Outcomes

SCL-90-R Outcomes	Predictors	B	S.E.
Somatization (SOM)	Age	–7.06*	3.08
	Sensory	.073	0.22
	Affective	1.29**	0.47
Anxiety (ANX)	Age	–7.79	4.19
	Sensory	.11	0.29
	Affective	1.43*	0.65
Phobic Anxiety (PHOB)	Age	–3.63	3.37
	Sensory	–.09	0.24
	Affective	1.11*	0.52
Paranoid Ideation (PAR)	Age	–2.69	3.49
	Sensory	–.13	0.24
	Affective	1.08†	0.54
Psychoticism (PSY)	Age	–7.70	4.03
	Sensory	.06	0.28
	Affective	1.34	0.62
Depression (DEP)	Age	–6.95	4.11
	Sensory	.21	0.29
	Affective	.87	0.63
Hostility (HOS)	Age	–8.14*	3.83
	Sensory	.06	0.27
	Affective	.66	0.59
Obsessive-Compulsive (O-C)	Age	–3.48	3.64
	Sensory	.15	0.25
	Affective	.92	0.56
Interpersonal Sensitivity (I-S)	Age	–9.53	3.87
	Sensory	.17	0.27
	Affective	.90	0.60
General Severity Index (GSI)	Age	–8.25*	3.80
	Sensory	.13	0.27
	Affective	1.40*	0.59
Positive Symptom Distress Index (PSDI)	Age	–6.13	3.44
	Sensory	.15	0.24
	Affective	.86	0.53
Positive Symptom Total (PST)	Age	–8.14*	3.76
	Sensory	.01	0.26
	Affective	1.60**	0.58

*$p < .05$; **$p < .01$; †$p = .05$.

context [25, 35, 39, 40]. Our study suggests that beyond previous findings, negative affective reactions to pain, independent of the magnitude of the somatic experience, are predictive of a range of anxieties and fears, and even the magnitude of symptoms reported by patients.

Beyond previous studies, however, the current results highlight the need to better resource patients with SCD to manage and control their responses to pain as a way of possibly reducing later psychological distress. For example, it is possible that patients who have access to care providers and well-defined plans for responses when painful crises arise may respond differently and with greater anxiety and fear than patients without such resources. In the current model, such reaction may be associated with later and more complicated negative psychological consequences. In essence, the nature, unpredictability, and intensity of pains in adult patients with SCD may produce a more intense and debilitating overall experience, and potentially more affective morbidities among patients who view and then respond to their disease state as negative. Previous studies, in non-SCD samples, have demonstrated that individuals who experience intense physical pain are more likely to endorse and experience high levels of psychological distress and vice versa [41, 42]. These models should increasingly be applied to understanding reactions to SCD pain and related psychopathology.

We also found that the tendency to ruminate and obsess, to be overly sensitive to the opinions of others, and the tendency to be sad or hostile were not predicted by negative reactions to experience of pain. Unfortunately, the current state of the pain literature does not provide substantial guidance to interpret these findings. For example, some studies indicate that emotionally disturbed individuals report higher pain intensities then their healthier counterparts; whereas other studies have shown that individuals with negative emotional disturbance have high thresholds and tolerances for pain [43, 44]. We do, however, believe that further research will begin to elucidate the complicated relationship between negative emotional reactions to pain and subsequent psychopathology in patients with SCD.

We recognize that many scientists conceptualize behavioral manifestations of negative emotional states like hostility as the product of cognitive processes like rumination among patients with pain [45, 46]. These manifestations are subsequently the products of multidimensional social, interpersonal, psychological, and biological factors (e.g., anger, negative perception, cynicism, appraisals concerning others, etc.) that are differentially experienced and coped with [2, 6, 22, 47-54] across racial, ethnic, age, gender, and other demographic characterizations [21, 35, 39] as well as genetic predispositions [9]. Better understanding the interaction of such factors with reports of acute and chronic pain is a growing mission for many clinical and academic researchers. Additional prospective investigations are needed, if the desire is to better understand what is unique about these relationships among patients with SCD and why they are not predicted by emotional reactions as are other related variables.

Limitations

The primary limitation to the current study is the modest sample size within a limited sample of adult patients with SCD. This limitation precluded a substantial increase in N for potentially more power, and limited extensive exploration of the influence of additional demographic factors on outcome variables of interests. We did not present power analyses in the current article, particularly because we were adequately powered to see significance in a majority of analyses that we conducted and presented in the Results section.

Secondarily, the authors acknowledge that reactions to acute episodes of pain may substantially differ from reactions to a more non-crisis chronic pain. For example, the degree to which patients are likely to catastrophize in response to a sudden and acute episode of acute pain may differ substantially as compared to their reactions to a more chronic familiar pain. The primary role of factors that have historically been associated with explaining such differences in reactions to acute and chronic pain in the general population are largely unexplored in patients with SCD. We also note that there may be little difference between multiple and repeated acute episodes of pain across a lifespan and a single chronic enduring (chronic) pain. Hence, we view the study of chronic pain in patients with SCD as a stable and reliable indicator of nociceptive experience, and likely the best estimate of disability. We note that future studies must begin to better understand the difference between a repeat acute pain over time and a chronic pain, and the impact of the difference, if it exists, on disability and functionality.

We view better understanding these factors as legitimate and necessary for future studies. Although negative emotion and other cognitive behavioral factors have been shown to independently predict increased reports of pain and psychosocial dysfunction among patients with SCD [55-58], a substantial amount of the variance is still left unexplained suggesting that further exploration is warranted.

We view our study as the impetus for additional rigorous prospective exploration. No previous studies have explored the impact of negative reactions to pain in the manifestation of clinically relevant psychiatric dispositions in adult patients with SCD. We view this study as a very important first step toward characterizing reactions to SCD-related pain on risk for psychopathology in adults.

Lastly, the current study demonstrates that, in a sample of Black adults with SCD, the initial emotional reactions to pain predict longer-term psychological distress independent of age. We believe that the model established by this study should be replicated and has the potential to elucidate the important role that psychological distress has on opiate utilization patterns, dyspnea, sleep dysfunction, and other clinical outcomes among patients with SCD in the United States and around the world [59-67].

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