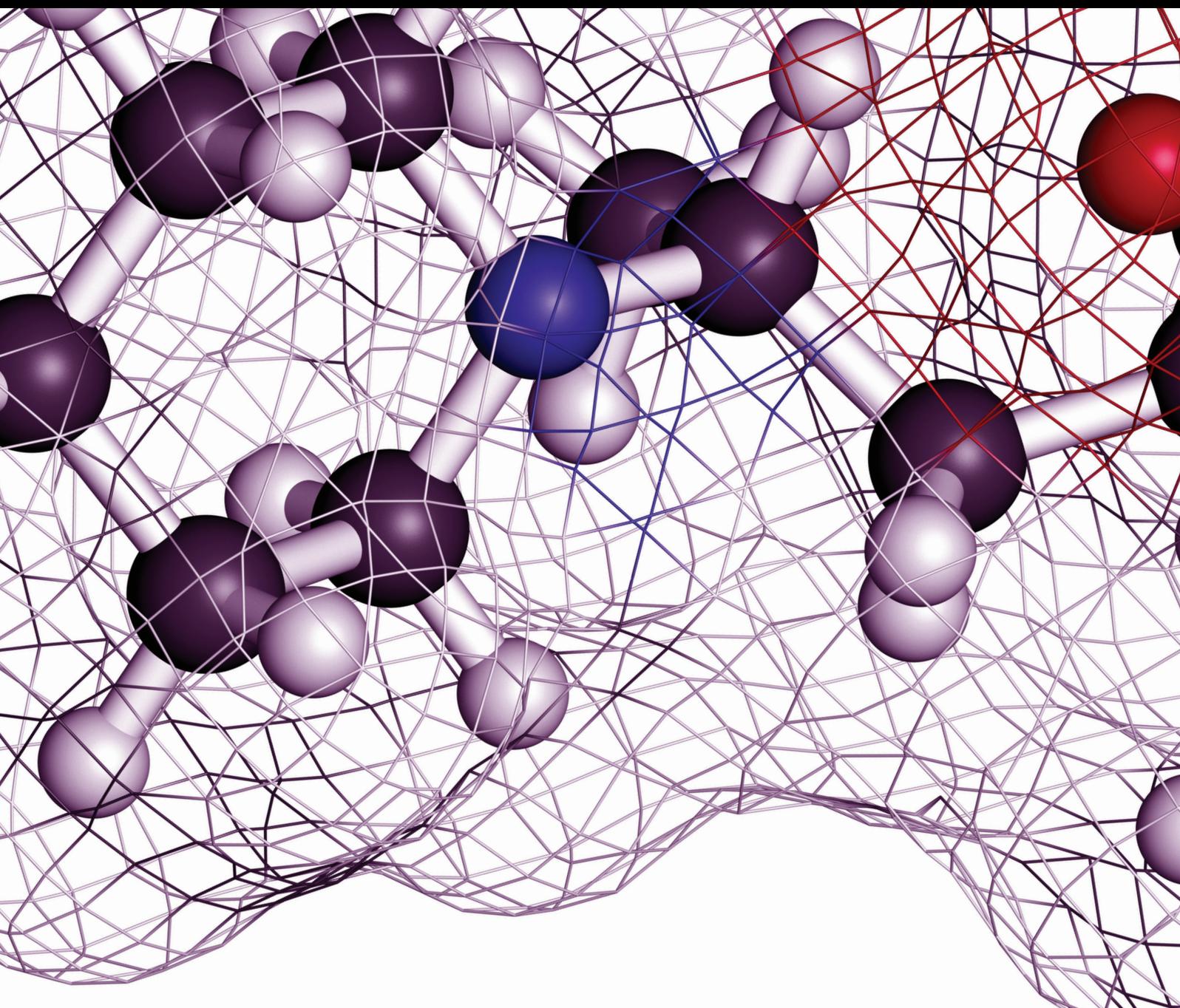


Pain Research and Management

Psychological Aspects and Quality of Life in Chronic Pain

Lead Guest Editor: Panagiotis Zis

Guest Editors: Athina Vadalouka, Giustino Varrassi, and Antonella Paladini





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Editorial

Psychological Aspects and Quality of Life in Chronic Pain

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Pain, if not the worst, is one of the worst symptoms that a patient experiences and has a detrimental effect on the patients' quality of life [1]. Chronic pain, usually defined as lasting for a period of more than 3 months, is prevalent in a variety of diseases including peripheral neuropathy [2–8], neurodegenerative diseases [9, 10], and cancer [11]. Presence of chronic pain has an independent additional burden to patients' mental health, increasing significantly the risk of depression [12]. Successful management of pain, with both pharmacological and nonpharmacological approaches, can improve the quality of life and ameliorate patients' mental health status [13–18].

In this special issue, the readers will find ten articles, covering a wide spectrum of types of pain and types of interventions and comprising “Association of depression/anxiety symptoms with neck pain: a systematic review and meta-analysis of literature in China” by F. Liu et al.; “Pain intensity is not always associated with poorer health status: exploring the moderating role of spouse personality” by C. Suso-Ribera et al.; “Topical review: basic psychological needs in adolescents with chronic pain—a self-determination perspective” by A. Riggenbach et al.; “The mediating effect of central sensitization on the relation between pain intensity and psychological factors: a cross-sectional study with mediation analysis” by H. Shigetoh et al.; “Negative affect, type D personality, quality of life, and dysfunctional outcomes of total knee arthroplasty” by M. Vogel et al.; “Pain acceptance and its associated factors among cancer patients in mainland China: a cross-sectional study” by X. Xu et al.; “Reward processing under chronic pain from the perspective of “liking” and “wanting”: a narrative review” by X. Liu et al.;

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Conflicts of Interest

The editors declare that there are no conflicts of interest.

Panagiotis Zis
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Athina Vadalouka
Antonella Paladini

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Research Article

Personality and Personality Disorders in Medication-Overuse Headache: A Controlled Study by SWAP-200

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Background. Medication-overuse headache (MOH) is a type of chronic headache, whose mechanisms are still unknown. The impact of psychological factors has been matter of debate from different perspectives. The role of personality and personality pathology in processes involved in MOH development has been advanced but was poorly studied. The hypothesis of addiction-like behaviors sustaining the drug misuse has been examined and reached contrasting findings. **Objectives.** This study is aimed at detecting personality and its disorders (PDs) in MOH, with a specific attention to the addiction aspect. **Methods.** Eighty-eight MOH patients have been compared with two clinical populations including 99 patients with substance use disorder (SUD) and 91 with PDs using the Shedler-Westen Assessment Procedure-200 (SWAP-200), a clinician-report tool that assesses both normal and pathological personality. MANCOVAs were performed to evaluate personality differences among MOH, SUD, and PD groups, controlling for age and gender. **Results.** MOH patients were predominantly women and older. They showed lower traits of the SWAP-200's cluster A and B disorders than SUD and PD patients, who presented more severe levels of personality impairment. No differences in the SWAP-200's cluster C have been found, indicating common personality features in these populations. At levels of specific PDs, MOH patients showed higher obsessive and dysphoric traits and better overall psychological functioning than SUD and PD patients. **Conclusion.** Although MOH, SUD, and PD populations have been evaluated in multiple sites with different levels of expertise, the study supported the presence of a specific constellation of personality in MOH patients including obsessive (perfectionist) and dysphoric characteristics, as well as good enough psychological resources. No similarities to drug-addicted and personality-disordered patients were found. Practitioners' careful understanding of the personality characteristics of MOH patients may be useful to provide a road map for the implementation of more effective treatment strategies and intervention programs.

1. Introduction

Medication-overuse headache (MOH) is a type of chronic headache associated with the overuse of one or several forms of acute painkilling treatments and a consequent worsening of a preexisting headache. First described in the 1980s [1], this disease is included in Third Edition of the International

Classification of Headache Disorders (ICHD-3), [2], even if the scientific debate on the nosology, definitions of overuse, and pathophysiological mechanisms is still ongoing [3]. MOH is a worldwide problem, with prevalence rates ranging between 1 and 2%, most commonly among women between 40 and 50 years of age [4]. MOH represents 55–70% of the population that consults headache centers [5].

Although the progressively increasing use of acute medications is widely considered the most important factor for transforming episodic headaches into MOH [6, 7], the role of psychological factors has also been underscored in many empirical investigations, mainly in terms of psychopathology (especially anxiety and mood disorders [8]), with psychiatric comorbidity representing a well-known negative prognostic factor [9–11].

Antecedent anxiety and depression have been suggested to have a crucial role in the development of MOH [12]. However, after almost 30 years since the first studies on psychiatric disorders in conjunction with headaches [13], it is not possible to go beyond the simple description of a comorbid association with (mostly) anxiety and/or mood disorders [14]. Thus, it is important to scrutinize the generic concept of “psychiatric comorbidity” by studying personality and individual psychological factors other than psychiatric ones. Although Wolf’s description of a “migraine personality” (i.e., ambitiousness, extreme tidiness, perfectionism, inflexibility, and resentment) dates back to 1937 [15], research on personality and headache is scarce and inconclusive. From this perspective, studying personality and its disorders (PDs) may be fruitful as it takes into account that a growing body of literature supports a robust association of personality pathology and health problems [16, 17]. The attempt to depict a pain-prone personality is ongoing [17], with higher avoidance harm and lower self-directedness (assessed by the Temperament and Character Inventory [18]), as the most distinguishing candidate personality features of chronic pain patients. Harm avoidance and self-directedness have been examined in headache but contrasting research findings have been obtained [19–22]. The presence of personality pathology has been linked more frequently to chronic, rather than episodic headache [23]. Bigal et al. [24] have used the clinical scales of the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) [25] and found no difference between MOH and chronic migraine, compared to migraine and new daily persistent headache. Conversely, some research has been conducted using the Structured Clinical Interview for DSM-IV Personality Disorders (SCID-II) [26] and considered the DSM [27, 28] classification of three PD clusters (cluster A includes schizoid, paranoid, and schizotypal disorders, characterized by odd or eccentric features; cluster B includes antisocial, borderline, narcissistic, and histrionic disorders, characterized by dramatic and impulsive patterns of behavior; and cluster C includes avoidant, dependent, and obsessive-compulsive disorders, characterized by anxious or fearful patterns of behavior). These studies have found that chronic migraine was associated with an overall prevalence of about 80% for any personality disorder [29, 30], with obsessive-compulsive personality disorder as the most prevalent. Interestingly, a study on physical comorbidity in patients with PDs evidenced the prevalence of cluster C (avoidant, dependent, and obsessive disorders in conjunction with recurrent headache [31].

From the MOH aspect, some studies focused on dependence from drugs as the psychological mechanism supporting medication overuse. Some authors suggested a link between MOH patients and those with addiction spectrum disorders [32, 33]. Genetic research to appraise gene polymorphism association in MOH and detect genes related to drug dependence pathways in the MOH population did not produce any definitive conclusion [34]. Neuroimaging studies on MOH found abnormalities in cerebral regions linked to dependence and addiction [35, 36]. Studies that assessed personality using the MMPI-2 highlighted a completely different personality configuration compared to patients with drug addiction [37]. It must be noted that the use of the MMPI-2 has been criticized because many items use somatic symptoms to assess underlying traits [17, 38], which may confound the assessment among chronic pain sufferers. Hence, there is a need to identify new assessment tools, rather than base evaluations on self-report measures that may suffer from a lack of sufficient criterion validity (e.g., [39]).

The main aim of the present study was to examine personality and its disorders in patients with MOH using a clinician-report personality measure, the Shedler-Westen Assessment Procedure-200 (SWAP-200), [40, 41]. We performed an exploratory analysis of personality characteristics within a group of MOH patients that have been compared to a group of patients with addiction and a group of patients with PDs.

2. Materials and Methods

2.1. Participant Sampling. The population samples analyzed in the present study were recruited in diverse centers within the Italian National Health System that specialize in the treatment of clinical populations with 3 three forms of diseases. A team of expert practitioners were directed to select (a) a group of chronic headache patients (MOH) enrolled at the IRCCS “C. Mondino National Institute of Neurology Foundation” in Pavia; (b) a group of patients with the DSM-5 [28] substance use disorder (SUD) enrolled at the therapeutic community “Villa Renata” in Venice; and (c) a group of patients with PDs enrolled at Italian psychological associations for the treatment of personality pathology in Rome, Genoa, Milan, and Turin. According to the inclusion criteria of the study, these patients were at least 18 years old, had no psychotic disorder or syndromes with psychotic symptoms, and had no mental retardation or clinically relevant cognitive impairment.

Practitioners’ assessment is the source of data used in this empirical investigation. A neurologist, clinical psychologists, and psychiatrists were asked to conduct three or four clinical interviews and yield accurate information regarding the patients who met the study’s criteria. They also completed a comprehensive diagnostic assessment procedure to assess patients’ personality disorders and psychological functioning. All participants provided written informed consent. The study protocol received ethics approval from the local research ethics review board.

2.2. Practitioners. The sample consisted of 1 neurologist, 15 clinical psychologists, and 5 psychiatrists ($N = 21$). Thirteen were women and 8 were men. The mean age of all practitioners who rated patients by SWAP-200 was 43 years ($SD = 5.37$, range = 33–52). The average length of their clinical experience was 14 years ($SD = 5.20$, range = 4–20). The main clinical-theoretical orientation of psychologists/psychiatrists was psychodynamic ($N = 19$); only one clinical psychologist had a systemic family approach. All assessors had received the same formal training in the use of SWAP-200.

2.3. Patients. Our population consisted of 278 Caucasian patients who were subdivided in the following samples.

2.3.1. Medication-Overuse Headache Group. This group consisted of 88 consecutive in-patient MOH, diagnosed according to the ICHD-III beta criteria [2]. Sixty-seven were women and 21 were men. Their mean age was 46.88 ($SD = 9.97$, range 19–64). The patients were diagnosed by a neurologist (GS) who collected clinical information on headache and sociodemographic data, along with the history of present and previous use of medications and/or other substances. The same neurologist verified the eligibility criteria. The mean duration of chronic headache was 6.1 years (range: 5 months–29 years), and the mean duration of symptomatic drug overuse was 4.7 years (range: 6 months–28 years). On the basis of the data contained in the headache diaries, we recorded an average of 23 headache days (range: 15–30), 22 days of symptomatic drug intake (range: 10–30), and 39 doses taken monthly (range: 10–220).

2.3.2. Substance Use Disorder Group. This group consisted of 99 patients, diagnosed according to the DSM-5 criteria (present/absent) for substance-related and addictive disorders. Fifty-seven were women and 42 were men. Their mean age was 22.89 ($SD = 4.62$, range 18–45). The majority of them indicated heroin as the primary substance of abuse. The assessment took place, on average, 1.6 months after the patients' admission. At the time of recruitment, the patients had abstained from drugs for an average of 3 months.

2.3.3. Personality Disorder Group. This group consisted of 91 patients, diagnosed according to the PD criteria (present/absent) of the DSM-5 classification system. Forty-five were women, and 46 were men. Their mean age was 36.88 ($SD = 11.20$, range 20–65). Sixteen had cluster A diagnoses (including paranoid, schizoid, and schizotypal disorders), 29 had cluster B diagnoses (including antisocial, borderline, histrionic, and narcissistic disorders), and 46 had cluster C diagnoses (including avoidant, dependent, and obsessive-compulsive disorders). They had no comorbid SUD. Seventy-five percent of the patients were from private practice, and the remaining 25% were from public mental health institutions.

2.4. Measures

2.4.1. Clinical Questionnaire. We used a questionnaire for the neurologist, clinical psychologists, and psychiatrists to collect comparable general information from the different patient populations. The patients' sociodemographic data, age at onset of the disorder, and drug consumption were collected. Moreover, this questionnaire gathered general information on all practitioners (such as gender, age, years of experience, training, and clinical orientation).

2.4.2. Shedler-Westen Assessment Procedure-200. The Shedler-Westen Assessment Procedure-200 (SWAP-200) [40–44] is a validated and reliable instrument designed to provide a comprehensive assessment of patient personality and psychological functioning based on the quantification of observations from therapists or clinical observers. This Q-sort instrument consists of a set of 200 personality-descriptive statements, written in jargon-free language near to clinical experience, to be used by practitioners with varying theoretical orientations and levels of experience. The assessor arranges these 200 statements into eight different categories ranging from 0 (*irrelevant or not descriptive of the person*) to 7 (*most descriptive*). Based on the Q-sort method [45], the SWAP-200 requires the assessor to assign a specified number of items to each score category (8 items in pile 7; 10 items in pile 6; 12 items in pile 5, etc.) in order to comply with the fixed distribution. The SWAP-200 assessment provides (a) a personality diagnosis expressed as the matching of the patient assessment with 10 personality disorder scales, which are clinical prototypes of the DSM-IV and DSM-5 [27, 28] personality disorders (PD scales) and (b) a personality diagnosis based on the correlation/matching of the patient's SWAP description with 11 styles/syndromes of personality derived empirically via Q-factor analysis (Q-factors). It also includes a dimensional measure of psychological strengths and adaptive functioning. All SWAP-200 PD scales and Q-factors make it possible to obtain both categorical and dimensional diagnoses. In further detail, the presence of one or more personality disorders is established when one or more PD scale and/or Q-factor score (in standardized T points) is ≥ 60 and the score on the high-functioning scale is ≤ 60 ; if the score ranges from 55 to 60, then the subclinical traits of that personality disorder or style are present. The SWAP-200 has been extensively shown to have very good validity and reliability in several studies conducted on different clinical populations (e.g., [46–49]).

2.5. Statistical Analysis. Statistical analyses were performed using SPSS 20 for Windows (IBM, Armonk, NY). The chi-square test and analysis of variance (ANOVA) were carried out to explore differences among MOH, SUD, and PD patient groups on gender and age, respectively. Then, a series of multiple analyses of covariance (MANCOVAs) with Bonferroni post hoc analyses ($p < 0.05$) were performed to assess MOH, SUD, and PD group differences on patients' personality disorders and psychological functioning

(assessed using the SWAP-200) while controlling for gender and age as covariates. In the first MANCOVA, the data on patients' personality pathology were analyzed at the PD cluster level (by aggregating the SWAP-200 paranoid, schizoid, and schizotypal PD scales for cluster A; the SWAP-200 antisocial, borderline, histrionic, and narcissistic PD scales for cluster B; and the SWAP-200 avoidant, dependent, and obsessive-compulsive PD scales for cluster C). Further, for each patient, the average scores of the SWAP-200 PD scales that comprised each cluster were calculated. Conversely, in the second and third MANCOVAs, the data were analyzed at the single-disorder level by using the SWAP-200 PD scales and Q-factors, respectively.

3. Results

3.1. Differences among MOH, SUD, and PD Patient Groups on Demographic Characteristics. First, MOH, SUD, and PD patient groups were compared on gender and age. As expected, there were significant differences on these two demographic variables. The three patient groups differed on gender ($\chi^2(2) = 13.16, p = 0.001$). Men were more likely to be classified as SUD (38.9% of men versus 33.5% of women) and PD patients (41.7% of men versus 27.1% of women), while women were more likely to be classified as MOH patients (19.4% of men versus 39.4% of women). Moreover, the patient groups significantly differed on age, $F(2,275) = 170.72, p < 0.001, \eta^2 = 0.55$. The ANOVA's results revealed that SUD patients ($M = 22.89$) were younger than PD patients ($M = 37.01$) and PD patients were younger than MOH patients ($M = 46.88$).

3.2. Differences among MOH, SUD, and PD Patient Groups on Personality Pathology and Psychological Functioning. The main aim of the study was to compare the MOH, SUD, and PD patient groups on personality pathology (at the level of PD clusters) and psychological functioning (evaluated using the SWAP-200) while controlling for the effects of gender and age. A first MANCOVA was performed using patient groups as the independent variable, the three clusters of the SWAP-200 PD scales as dependent variables, and gender and age as covariates. The results revealed significant main effects for the groups (Wilks's $\lambda = 0.70, F(6,542) = 17.47, p < 0.001, \eta^2 = 0.16$), while no significant effect was found for gender (Wilks's $\lambda = 0.99, F(3,271) = 0.83, p = 0.48, \eta^2 = 0.01$) and age (Wilks's $\lambda = 0.98, F(3,271) = 1.62, p = 0.19, \eta^2 = 0.02$). Follow-up univariate analyses with Bonferroni post hoc tests ($p < 0.05$) indicated that all three patient groups significantly differed on the SWAP-200's clusters A and B, while no difference was revealed on cluster C (Table 1). In particular, SUD patients showed higher mean scores of clusters A and B as compared to those obtained by the PD and MOH patients.

The second MANCOVA was conducted to investigate the differences among the MOH, SUD, and PD patient groups on personality disorders and global psychological functioning (assessed using the SWAP-200 PD and high-

TABLE 1: Differences among patient groups on the three clusters of SWAP-200 PD scales while controlling for gender and age.

SWAP-200	MOH group (n = 88)		SUD group (n = 99)		PD group (n = 91)		F(2, 273)	η^2
	M	SD	M	SD	M	SD		
Cluster A	43.98 ^a	0.77	49.86 ^b	0.75	46.30 ^c	0.61	11.06***	0.08
Cluster B	41.76 ^a	0.83	54.89 ^b	0.80	48.42 ^c	0.66	47.58***	0.26
Cluster C	49.61	0.81	47.70	0.79	48.32	0.65	1.14	0.01

Note. MOH group = medication-overuse headache group; SUD group = substance use disorder group; PD group = personality disorder group; SWAP-200 = Shedler-Westen Assessment Procedure-200; η^2 = measure of effect size in analysis of covariance. Alphabetical superscripts indicate significant differences in post hoc analyses. Means with different alphabetic superscripts (a, b, and c) were statistically significant, while means with identical alphabetic superscripts were found not to be significantly different; *** $p < 0.001$.

functioning scales) while controlling for the effects of gender and age (as covariates). The results showed that the gender had a significant effect on personality variables (Wilks's $\lambda = 0.90, F(11, 263) = 2.62, p < 0.01, \eta^2 = 0.09$), while no effect of age was found (Wilks's $\lambda = 0.94, F(11, 263) = 1.43, p = 0.16, \eta^2 = 0.06$). The MANCOVA's findings revealed that even after adjusting for covariates, there were significant effects for the groups on the SWAP-200 PD and high-functioning scales (Wilks's $\lambda = 0.49, F(22, 526) = 10.28, p < 0.001, \eta^2 = 0.30$). Further, the post hoc analyses by Bonferroni's correction showed significant differences among the MOH, SUD, and PD patient groups on all SWAP-200 PD scales, with the exception of the schizoid and avoidant personality disorders (Table 2). MOH patients had significantly lower scores in the SWAP-200 paranoid, schizotypal, antisocial, borderline, histrionic, narcissistic, and dependent PD scales and higher scores in the SWAP-200 obsessive PD and high-functioning scales than those obtained by SUD and PD patients.

Finally, the last MANCOVA was conducted to examine the differences among the MOH, SUD, and PD patient groups on personality styles/syndromes derived empirically from the SWAP-200 (Q-factors), while controlling for the effects of gender and age (as covariates). The findings revealed that gender had a significant effect on personality variables (Wilks's $\lambda = 0.88, F(11, 263) = 3.22, p < 0.001, \eta^2 = 0.12$), while age did not show any effect (Wilks's $\lambda = 0.95, F(11, 263) = 1.38, p = 0.18, \eta^2 = 0.05$). The MANCOVA's results demonstrated that even after adjusting for covariates, there were significant effects for the groups on the SWAP-200 Q-factors (Wilks's $\lambda = 0.40, F(22, 526) = 13.87, p < 0.001, \eta^2 = 0.37$). Moreover, the post hoc analyses by Bonferroni's correction showed significant differences among MOH, SUD, and PD patient groups on all SWAP-200 Q-factors, with the exception of the paranoid, schizoid, and dysphoric: avoidant personality styles/syndromes (Table 3). MOH patients had significantly lower scores in the SWAP-200 antisocial, histrionic, narcissistic, dysphoric: emotionally dysregulated, dysphoric: dependent-

TABLE 2: Differences among patient groups on the SWAP-200 personality dimensions and psychological functioning while controlling for gender and age.

SWAP-200 PD scales	MOH group (n = 88)		SUD group (n = 99)		PD group (n = 91)		F(2, 273)	η^2
	M	SD	M	SD	M	SD		
Paranoid	41.57 ^a	1.05	50.72 ^b	1.01	45.92 ^c	0.83	14.29 ^{***}	0.10
Schizoid	46.79	0.96	47.88	0.93	46.96	0.77	0.31	0.00
Schizotypal	43.59 ^a	0.95	50.97 ^b	0.92	46.03 ^c	0.75	12.10 ^{***}	0.08
Antisocial	43.20 ^a	0.86	53.56 ^b	0.83	47.69 ^c	0.68	27.67 ^{***}	0.17
Borderline	38.71 ^a	1.10	56.60 ^b	1.07	47.52 ^c	0.88	49.44 ^{***}	0.27
Histrionic	42.11 ^a	1.07	56.40 ^b	1.03	50.03 ^c	0.85	34.34 ^{***}	0.20
Narcissistic	43.00 ^a	0.95	53.01 ^b	0.92	48.45 ^c	0.76	20.99 ^{***}	0.13
Avoidant	47.69	0.95	46.82	0.92	46.62	0.76	0.41	0.00
Dependent	47.43 ^a	1.06	52.08 ^b	1.02	49.10 ^{a,b}	0.84	4.04 [*]	0.03
Obsessive	54.03 ^a	1.00	44.15 ^b	0.96	48.96 ^c	0.80	17.62 ^{***}	0.11
High-functioning	63.05 ^a	1.09	45.38 ^b	1.05	54.89 ^c	0.87	49.29 ^{***}	0.27

Note. MOH group = medication-overuse headache group; SUD group = substance use disorder group; PD group = personality disorder group; SWAP-200 = Shedler-Westen Assessment Procedure-200; η^2 = measure of effect size in analysis of covariance. Alphabetical superscripts indicate significant differences in post hoc analyses. Means with different alphabetic superscripts (a, b, and c) were statistically significant, while means with identical alphabetic superscripts were found not to be significantly different; * $p < 0.05$; *** $p < 0.001$.

TABLE 3: Differences among patient groups on the SWAP-200 personality styles/syndromes while controlling for gender and age.

SWAP-200 Q-factors	MOH group (n = 88)		SUD group (n = 99)		PD group (n = 91)		F(2, 273)	η^2
	M	SD	M	SD	M	SD		
Antisocial	43.36 ^a	0.85	53.94 ^b	0.82	47.86 ^c	0.67	29.64 ^{***}	0.18
Schizoid	46.42	0.96	48.18	0.93	46.69	0.77	0.80	0.01
Paranoid	48.40	3.38	49.15	3.27	47.02	2.69	0.15	0.00
Obsessive	60.21 ^a	1.14	44.90 ^b	1.10	53.96 ^c	0.91	34.40 ^{***}	0.20
Histrionic	48.70 ^a	1.05	54.09 ^b	1.01	52.48 ^b	0.83	5.70 ^{**}	0.04
Narcissistic	41.10 ^a	1.03	48.65 ^b	0.99	45.47 ^c	0.82	17.27 ^{***}	0.11
DS: avoidant	49.86	0.95	46.69	0.92	47.54	0.76	2.47	0.02
DS: high-functioning neurotic	58.38 ^a	0.98	47.13 ^b	0.95	53.90 ^c	0.78	25.20 ^{***}	0.16
DS: emotionally dysregulated	41.92 ^a	1.05	51.89 ^b	1.02	46.16 ^c	0.84	16.96 ^{***}	0.11
DS: dependent-masochistic	41.42 ^a	1.06	57.45 ^b	1.03	49.62 ^c	0.84	43.00 ^{***}	0.24
DS: hostile-externalizing	43.95 ^a	1.06	50.68 ^b	1.02	47.52 ^a	0.84	7.65 ^{**}	0.05

Note. MOH group = medication-overuse headache group; SUD group = substance use disorder group; PD group = personality disorder group; SWAP-200 = Shedler-Westen Assessment Procedure-200; DS = dysphoric subfactor; η^2 = measure of effect size in analysis of covariance. Alphabetical superscripts indicate significant differences in post hoc analyses. Means with different alphabetic superscripts (a, b, and c) were statistically significant, while means with identical alphabetic superscripts were found not to be significantly different; ** $p < 0.01$; *** $p < 0.001$.

masochistic, and dysphoric: hostile-externalizing Q-factors and higher scores in the SWAP-200 obsessive PD and DS: high-functioning neurotic Q-factors than those obtained by SUD and PD patients.

4. Discussion

The present study sought to investigate personality characteristics and psychological functioning in a clinical population with MOH using the SWAP-200, a valid and reliable clinician-report instrument. A group of patients with this kind of chronic headache was compared on specific individual variables (gender and age) and personality dimensions to two different clinical groups including patients with SUD and PDs, respectively.

Overall, the results showed that MOH is most prevalent in women and older patients, thus confirming previous research (e.g., [4, 50]). Moreover, the study indicated that

distinct personality traits distinguish MOH from SUD and PD patients, regardless of demographic characteristics, in a clinically meaningful manner. The findings demonstrated significant differences at the level of SWAP-200 PD clusters A and B among these clinical populations. MOH patients presented low traits of personality syndromes characterized by affective flattening, interpersonal deficits in close relationships, odd behaviors and eccentric and idiosyncratic reasoning processes or beliefs, or by impulsivity and emotional dysregulation, severe impairments in interactions with others, and identity and behavior disturbances. Conversely, there were no differences among MOH, SUD, and PD patients at the cluster C level. These results elucidate a consistent overlapping of anxious traits in these populations and, especially, support the data of empirical studies, showing a strong association among patients with recurrent headache and avoidant, dependent, and obsessive-compulsive PDs [31].

Looking at the specific and nuanced results in Tables 2 and 3, MOH patients seem to show a specific personality configuration including obsessive (perfectionist) and dysphoric features that is completely different from the configuration of the SUD group. Notably, these results support previous research using the MMPI-2 [37, 51]. In detail, at the level of the SWAP-200 PD scales (Table 2), MOH patients presented a personality and psychological functioning that is different from that of SUD and PD patients and is characterized by the highest obsessive traits and the lowest paranoid, schizotypal, antisocial, borderline, histrionic, narcissistic, and dependent characteristics. These results were partially confirmed in terms of personality styles or SWAP-200 Q-factors (Table 3). Obsessive and dysphoric/high functioning neurotic traits were the most representative features of MOH patients as compared to SUD and PD groups, which were mostly characterized by histrionic, antisocial, dysphoric/dependent-masochist, dysphoric/emotionally dysregulated, and dysphoric/hostile-externalizing features.

Interestingly, in our study, borderline personality characteristics (in terms of SWAP-200 PD scales) are poorly represented in MOH patients, despite a study that showed an increased risk of developing MOH when migraine is comorbid with a borderline personality disorder (BPD) [52]. These findings were confirmed in terms of Q-factors of the SWAP-200, given that chronic headache patients did not present any personality style (histrionic, dysphoric: emotionally dysregulated, or dysphoric: dependent-masochistic Q-factors) that is typically linked to BPD [41]. This aspect deserves further attention because epidemiological research shows that individuals who screened positive for BPD had a high prevalence rate of chronic pain (19%) and a 12-month headache rated in 42% of patients with BPD [53].

From the side of the SUD group, the role of borderline (and antisocial) personality disorder (cluster B) is a clear-cut finding that is already recognized in the literature [54]. Obviously, this aspect further supports the psychological differences of MOH and drug addiction in the likely behavioral mechanisms supporting drug misuse. The psychological dimensions featuring MOH patients seem to be more related to the side of obsessiveness, bearing in mind that it is distinct from the obsessive-compulsive disorder [40, 41]. The study of personality features may be a key to explaining the route to medication overuse that, we hypothesized, is very different from a simple addiction to analgesic drugs [55] or “obsessive-compulsive disturbances for abused drugs” [56]. The prototypic description of obsessive personality [40, 41] refers to “patients excessively devoted to work and productivity, to the detriment of leisure and relationships. . . with difficulty acknowledging or expressing anger. . . self-critical, tending to set unrealistically high standards for themselves, showing little tolerance for their own human defects, and expecting themselves to be “perfect.” These individuals may adhere rigidly to daily routine and become anxious and uncomfortable when they are altered.” In this psychological framework, analgesics might become a necessary crutch with which to cope with life demands in spite of recurrent pain and not a way to seek

pleasure or to escape from reality as may occur in addiction. Finding a genetic explanation for such specific behavior (drug misuse in chronic headache patients) is intriguing [34], but many aspects need to be taken into consideration. Addiction, as in many behaviors affecting health with negative outcomes, is the result of genetic and environmental variables. Twin studies have established that the heritability, or the proportion of the variation in the population trait of addiction, ranges between 40% and 70% [57]. These data leave a considerable margin to environmental influences. Recently, it has been outlined that the beginning of drug taking behavior is more under environmental influences, while the progression to addiction seems to be associated with genetic influences [58]. Coping with a recurrent painful condition, often from infancy or adolescence (MOH patients had a long-lasting history of chronic pain), may be very challenging and the “dependence” from pain relief may pass through excessive drug intake. In our opinion, this psychological (or behavioral) mechanism is far removed from that substance addiction. SUDs have been theoretically, for example, by the self-medication theory [59], and empirically (e.g., [60]) linked to emotional suffering, rather than physical pain; drugs are used as a coping mechanisms in the attempt to relieve or change a range of under-regulated and overwhelming painful affect states, often related to premorbid and co-existing mental health disorders, such as mood, anxiety, and posttraumatic stress disorders [61–63].

A final note on the psychological health index defined by the SWAP-200 high-functioning scale is clinically relevant. This index assesses the resemblance or match between the patient and an ideal prototype representing optimal psychological health [40, 41] and serves as a global measure of personality functioning. Interestingly, MOH patients scored very high on this scale compared to both SUD and PD patients. The results suggested that patients with MOH show significant psychological resources and strengths in the milieu of an obsessive and dysphoric personality, while patients with SUD and PDs present globally more severe levels of psychological impairment. This aspect strongly supports the potential positive role of psychological interventions, both as a psychoeducational (for preventing drug misuse) and psychotherapeutic one. When working with specific clinical populations, such as the MOH patient group, practitioners should consider personality characteristics able to moderate treatment outcomes [64, 65].

Our study is not free of limitations. First, all patients were enrolled from clinical settings and we are not sure that they are representative of patient population with MOH, SUD, and PDs (Berkson’s bias [66]). Future studies might enroll a patient group from the general community to compare personality characteristics in the MOH population and extend the generalizability of the study’s findings. Moreover, the stability of some results over time should be verified by longitudinal research. Secondly, MOH patients were interviewed as inpatients, while SUD and PD samples were evaluated in the outpatient setting. Further empirical investigations in this area should seek to address these issues by involving diverse and wide patient samples, taking into

account the distribution of the severity of pathology and various clinical conditions. Furthermore, the different populations were evaluated in multiple sites with different expertise. We attempted to control for the possible confounding effects (e.g., a common questionnaire for data recording and training for SWAP administration and interpretation) to the best of our abilities. Finally, demographic differences among the groups might have partially influenced the results that we observed, although we have adjusted for these specific variables in all of the analyses and the effect size (η^2) estimations were mostly of a moderate or large magnitude [67].

In summary, this study supports the presence of a specific constellation of personality in MOH patients that included obsessive (perfectionist) and dysphoric traits, as well as good enough psychological resources. No similarities with drug-addicted and personality-disordered patients were found. In particular, substantial differences between MOH and SUD patients seem to confirm the results of previous research [37, 51]. Overall, these findings may be useful in providing a road map for the implementation of effective treatment strategies and intervention programs among this clinical population with chronic headache.

Data Availability

The data of this study are not available due to ethical concerns. We must protect patient privacy and security and follow the ethical rules of our institutions and their restrictions on data sharing.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Review Article

Quality of Life in Painful Peripheral Neuropathies: A Systematic Review

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Objective. Neuropathic pain is a common presenting complaint of patients with peripheral neuropathy (PN) and is considered one of the most disabling neuropathic symptoms, with detrimental effects on patients' quality of life (QoL). The aim of this review was to overview the current literature that focuses on QoL in painful PN of various aetiologies. We sought to clarify the direct effect of pain and its treatment on patients' QoL. **Methodology.** A systematic computer-based literature search was conducted using the PubMed database to search for papers on QoL in painful PN. Information was extracted regarding prevalence, demographics, and response to treatment where relevant. **Results.** We identified 66 articles eligible for inclusion. The vast majority of studies ($n = 47$) focused on patients with diabetic PN. Other aetiologies of painful PN where QoL has been studied to date include gluten, immune-mediated, HIV, chemotherapy-induced, and chronic idiopathic axonal polyneuropathy. Pharmacological treatment is the mainstay in managing pain and has a direct positive and independent effect on the overall QoL. Other nonpharmacological approaches can also be of benefit, either alone or as adjuvant treatments, and are discussed. **Conclusion.** The findings demonstrate that QoL is impaired in painful PN and should not be neglected in clinical practice. Patients' pain management and subsequent impact on QoL should routinely be assessed and monitored.

1. Introduction

The term "peripheral neuropathy" (PN) refers to disorder of the peripheral nervous system. Robust epidemiological data on polyneuropathies of any cause are lacking. Very few studies have accurately assessed the prevalence of polyneuropathy. When confirmed with nerve conduction studies, the prevalence of polyneuropathy is estimated to be about 5% in people aged 55 years or more [1]. Thus, polyneuropathy is considered to be a common neurological disease.

Classification of PN depends upon a mixture of phenomenological, neurophysiological, pathological, and

aetiological parameters [2]. The commonest form of PN is the chronic axonal length-dependent sensorimotor polyneuropathy. Neuropathic symptoms can be divided into sensory and motor. Sensory symptoms include tingling; pins and needles; numbness; tightness; burning; pain; and sensory ataxia. Motor symptoms include muscle cramps, stiffness, weakness, and wasting [3].

Neuropathic pain is prevalent, presenting in approximately two-thirds of patients with PN [4–10] with minimal variability across its aetiological classifications, and is considered to be one of the most disabling neuropathic symptoms having a detrimental effect on patients' mental health [11] and leading to poor quality of life (QoL).

The aim of this study was to systematically review the current literature regarding QoL in patients with painful PN. We aimed to evaluate any variations in QoL between the different PN subtypes and more specifically clarify what is the direct effect of pain in patients' QoL. The effect of the various treatments on the overall QoL is also discussed. To our knowledge, this is the first systematic review on the topic.

2. Methodology

2.1. Search Strategy. A systematic computer-based literature search was conducted on 11 December, 2018, using the PubMed database. We evaluated all articles published between the dates of 1 January 1998 and 11 December 2018. For the search, we used three Medical Subject Headings (MeSH) terms that had to be present in the title or the abstract. Term A was "quality of life" or "qol." Term B was "pain" or "painful." Term C was "neuropathy" or "polyneuropathy" or "ganglionopathy" or "neuronopathy." "Human species," "English language," and "full-text available" filters were applied in our search.

2.2. Inclusion and Exclusion Criteria. In order to be included in this review, articles were required to meet the following criteria: [1] original articles; [2] study human subjects; [3] written in English language; [4] refer to painful peripheral neuropathy; [5] refer to the QoL of subjects. The exclusion criteria for the articles were as follows: [1] book chapters, reviews, meta-analyses, letters to the editor, and editorials not providing new data and study protocols; [2] articles not referring to patients with painful peripheral neuropathies; [3] articles with a lack of individual results for the painful peripheral neuropathies, even if these subjects were included in the study; [4] articles which did not explore QoL as an outcome measure in sufficient depth.

2.3. Synthesis of Results. This study is reported in accordance with the "Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines" [12]. A database was developed using the Statistical Package for Social Science, version 24 for Mackintosh. Pooled frequencies and descriptive characteristics of demographic parameters were extracted.

2.4. Compliance with Ethical Guidelines. This article is based upon previously published studies. The article is in compliance with the journal's ethical guidelines.

3. Results

3.1. Selected Studies. The PubMed search identified 477 articles, and a total of 412 articles were excluded during the eligibility assessment. A further article was added after scanning the references of the included studies. The PRISMA chart displays the process of article selection (Figure 1). In total, 66 articles met the inclusion criteria. Case series

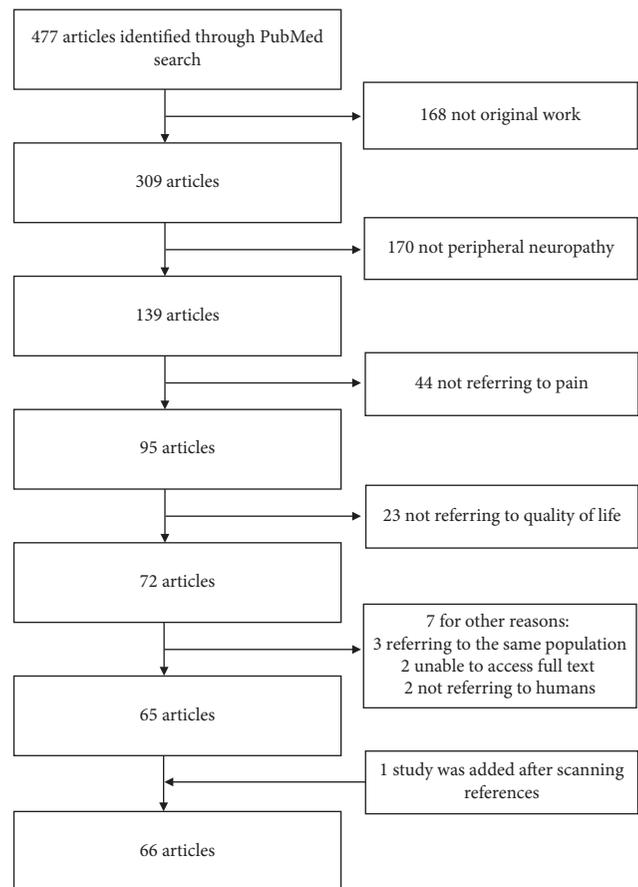


FIGURE 1: PRISMA chart.

constituted the commonest type of paper (45.5%), closely followed by randomised controlled trials (43.9%). The number of articles per decade since 1998 has rapidly increased, with the biggest increment between the years 2010 and 2018. The vast majority of articles were on diabetic PN (71.2%). A summary of article characteristics has been demonstrated in Table 1.

3.2. Assessment of QoL. In total, 19 different tools were used to assess QoL in PN patients. The most commonly utilised tools were the SF-36 (34.8%) and the EQ-5D (22.7%), both of which are generic health status measurements. A number of disease-specific questionnaires were employed, such as the NeuroQol (6.1%), a specifically validated neuropathy and foot ulcer instrument [13]. A tabulated breakdown of the named questionnaires used in articles included in this review is provided in Table 2.

3.3. Quality of Life across Painful Neuropathies of Different Aetiologies. A selection of studies examined aetiologically heterogeneous populations of patients with PN. The disability caused by PN has been shown to correlate with a decrease in QoL, and it has been demonstrated that painful PN is associated with a poorer QoL compared to painless PN, regardless of the cause [14–19]. The majority of the

TABLE 1: Characteristics of the papers included in the review.

Total number of papers included in this review	66
Type of paper (%)	
Case series	30 (45.5)
Case-controlled study	7 (10.6)
Randomised controlled trial	29 (43.9)
Mean number of patients with painful neuropathy, per paper (SD)	125.1 (122.5)
Male to female ratio	1:1
Aetiology of polyneuropathy, number of papers (%)	
Chronic idiopathic axonal	2 (3.0)
Chemotherapy-induced	4 (6.1)
Diabetic	47 (71.2)
Genetic	1 (1.5)
Gluten	1 (1.5)
HIV	3 (4.5)
Immune-mediated	1 (1.5)
Multiple aetiologies	6 (9.1)
Sarcoidosis	1 (1.5)
Number of publications per decade	
Until 2000	3 (4.5)
2000–2009	16 (24.2)
2010–2018	47 (71.2)

TABLE 2: Questionnaires used to assess quality of life.

Questionnaire	N (%)*
Brief Pain Inventory	7 (10.6)
Child Health Questionnaire	1 (1.5)
Diabetic peripheral neuropathic pain impact measure	1 (1.5)
EQ-5D	15 (22.7)
Functional Assessment of Cancer Therapy/ Gynecologic Oncology Group-Neurotoxicity (fact/ GOG-ntx) Questionnaire	1 (1.5)
Medical Outcomes Study HIV Health Survey	1 (1.5)
Neuropathic Pain Impact on Quality of Life (NePIQoL) Questionnaire	1 (1.5)
NeuroQoL	4 (6.1)
Norfolk Quality of Life Questionnaire-DN	4 (6.1)
Nottingham Health Profile	1 (1.5)
PART-Q30	1 (1.5)
QLQ-C30	2 (3.0)
QLQ-CIPN20	1 (1.5)
Quality of life index	1 (1.5)
Questionnaire not specified/unvalidated	6 (9.1)
SF-12	2 (3.0)
SF-36	23 (34.8)
Sheehan disability score	2 (3.0)
World Health Organization Biomedical Research and Education Foundation quality of life score	1 (1.5)

*A number of papers used more than one questionnaire.

available literature, however, focuses on neuropathies of specific aetiologies, and therefore, we present the available knowledge per neuropathy type in the following.

3.3.1. Diabetic Peripheral Neuropathy. QoL is one of the most important aspects of patients' lives affected by diabetes, both due to its effect on the long-term prognosis and on the economic burden of the disease.

(1) *Direct Effect of Pain.* Throughout the literature, numerous studies have evaluated the effect of pain on QoL and consistently found that those with painful diabetic peripheral neuropathy (DPN) have an impaired QoL, particularly in relation to their reduced physical activity [20–29]. In a large study conducted by Won et al., it was shown that patients with higher pain intensity experienced the worse QoL [28].

(2) *Socioeconomic Status.* In a study that was conducted by daCosta DiBonaventura et al., it was shown that patients with painful DPN not only have a significantly worse QoL compared to patients with painless DPN and healthy controls but also patients with painful DPN have more comorbidities and are from lower socioeconomic backgrounds [26]. Sufferers of painful DPN have often suffered from diabetes for a longer duration of time and lack compliance in management of their condition [26]. The financial implications of this, both due to direct and indirect costs, can lead further to a reduced QoL [26]. Direct costs include hospitalisations and healthcare provider visits, whilst indirect costs include time off work due to illness and additional care from family and friends to help manage their condition.

(3) *Sleep.* Sleeping disorders are common in painful DPN. A vicious cycle is established, as a lack of sleep can worsen the perception of pain, which as a result leads to an increased burden of disease [15, 22, 27, 29].

(4) *Mental Health.* Stress can exacerbate the pain perceived by patients with DPN, as it does for most patients with all types of chronic pain [27]. Pain will lead to higher stress levels, creating another vicious cycle, which leads to poorer QoL.

Depression and anxiety also have an impact on perceived QoL. Depressed patients may report lower QoL at baseline in clinical trials and subsequently negative treatment effects [11, 19, 29, 30]. Research has shown that painful DPN is associated with catastrophic and anxiety provoked thinking, which as a result leads to a perceived decline in physical activity and subsequent reduction in QoL [30, 31]. Geelen et al. illustrated that patients with DPN suffer from various fears including those of hypoglycaemia, negative evaluation, falling, and fatigue and some of these fears are associated with a reduced QoL and increased disability [32]. These observations are relevant to clinical practice, as they provide a theoretical framework on the psychosocial consequences of painful DPN, which can enable designing treatment strategies to address these specific fears. The same study group looked into pain catastrophizing, defined as a negative cognitive set brought about during actual or anticipated pain experience, and showed that it is associated with a decline in physical activity and an increased perception of disability and decreased QoL in patients with painful DPN [31].

(5) *Effect of Treatments on QoL.* A lack of curative treatment for DPN means that treatment approaches are aimed both at decelerating the disease's progression through better glycaemic control and at pain management [22, 33]. Evidence

of earlier diagnosis of DPN and addressing foot care issues promptly can reduce the effect of the disease on QoL [20]. Schumacher et al. identified that other members of the multidisciplinary team can play an important role in the earlier identification of painful DPN and assist them in receiving the appropriate care [24].

(6) *Improving Glucose Control.* Rokicka et al. compared the effects of intravenous (the study group) versus subcutaneous (control group) delivery of insulin [34]. Both were comparable in terms of their reduction of pain in patients. A more intensified insulin regime resulted in an overall improved condition of general health although an improvement in QoL was only observed in control subjects.

(7) *Anticonvulsants.* Three randomised controlled trials looking at the effect of pregabalin compared to placebo found significant improvements in many aspects of QoL, including mental health and sleep, in patients who were refractory to previous treatments [35, 36].

Lacosamide has a long-term safety profile and sustained efficacy in PDN. Apart from treating pain, use of lacosamide leads to improvements in the “physical functioning” and “vitality” subdomains of the SF-36 [37, 38].

Gabapentin has proven to be an effective pain relief and has demonstrated additional benefits in improving patients sleep quality and mood [39].

(8) *Cannabinoids.* Conflicting evidence exists regarding the use of cannabinoids in painful conditions [17]. The first trial assessing the efficacy of a cannabis-based medicinal product (nabiximols) has shown it to be no more efficacious than placebo [40]. However, the results of this trial are contradictory to later findings, where the cannabinoid nabilone has been found to have similar benefits upon pain relief, sleep, and anxiety compared to gabapentin when used as a monotherapy as well as an adjuvant therapy [17]. Whilst the specific reason for this conflict is unclear, it should be noted that these are very different medications in that nabilone is a synthetic, oral capsule delivery cannabinoid, whilst nabiximols is a cannabis extract with oro-mucosal delivery and they do not have the same active compositions.

(9) *Antidepressants.* A Japanese-based study comparing 40 mg to 60 mg of duloxetine found that both doses are tolerable and effective and can be considered long-term treatment options for improving pain severity and QoL [41]. Furthermore, when in a study comparing duloxetine with pregabalin, despite both having a significant effect in reducing DPN pain, duloxetine was found to have better efficacy [42]. The cost-effective analysis determined that duloxetine was dominant to pregabalin as calculated using incremental cost-effectiveness ratio with QoL as the unit of outcome.

Amitriptyline and nortriptyline were found to have equal tolerability and efficacy in painful DPN both as monotherapy and as adjuvant therapies; however, no statistically significant changes were noted in overall QoL [43].

(10) *Opioids.* Tramadol is well established as being safe and effective in the treatment of painful DPN [44] and when given together with acetaminophen have shown improvements in pain intensity, QoL, mood, and function compared to placebo [45]. Similarly, controlled-release oxycodone is effective, safe, and has demonstrated significant improvements in QoL [46].

(11) *Topical Agents.* Capsaicin is the most studied topical agent for painful DPN and has proven beneficial in pain control as well as improving patient QoL [47, 48]. In a large, phase 3-randomised, 52-week study, capsaicin (8% patches) in addition to standard care of treatment was well tolerated and effective. The observed safety evaluations may have been biased by the open-label design of this study [47].

One, small, randomised controlled trial evaluated the application of topical *Citrullus colocynthis* fruit extract showing that it can decrease pain and may have some effect on the physical domain of QoL [48].

A double-blind randomised controlled trial found that topical nutmeg extracts reduce pain in painful DPN and improve overall QoL after 4 weeks of treatment; however, these effects were not superior to placebo [49].

(12) *Nutritional Supplementation.* Vitamin E supplementation has been found to have a significant role in controlling pain in DPN, leading to an overall improvement of QoL after prolonged treatment [50]. Alam et al. reported that the administration of a single high dose of Vitamin D showed significant improvements in the emotional distress subscale of the NeuroQoL, in addition to improvements in pain-related symptom scores [13].

The effects of alpha-lipoic acid were found to have a clinically significant impact on controlling neuropathic pain and improving overall QoL in a cohort of patients taking this agent orally [51]. Similarly, LMF-MC-PP (L-methylfolate-methylcobalamin-pyridoxal-5-phosphate) is a nutritional treatment for DPN that was shown to be effective in reduction of pain intensity and improvement in QoL [52].

(13) *Surgical Interventions.* Patients with PN are prone to superimposed entrapment neuropathies, and in these cases, surgical decompression has been proven to significantly relieve pain [53], with patients' QoL also subsequently improving [54].

Spinal cord stimulation (SCS) is an invasive treatment for chronic pain, based on electrical stimulation of the dorsal columns [55]. It has proven to be an acceptable treatment modality in patients who do not respond to conventional medical treatment [55–58]. In an open-label study conducted by De Vos et al., as well as a reduction in intake of pain medication, SCS showed improvement on sleep that persisted for 6 months [58].

(14) *Other Nonpharmacological Treatments.* Despite the practice of mindfulness meditation showing to have a positive effect on physical and psychological outcome in varied patient populations, no significant improvements

were noted in a pilot study looking at PDN, including QoL [33].

Low-frequency pulsed magnetic field magneto-stimulation showed no advantage over sham exposure in reducing pain intensity, decreasing sleep disturbance, or improving QoL [59].

Findings from a randomised, double-blind, placebo controlled trial suggest that the administration of photon stimulation resulted in significant improvements in sensation, social functioning, and mental health; however, further studies are needed to investigate different doses and durations of treatment [60].

Although rarely addressed in the literature, wearing static, permanent magnetic insoles produces a significant reduction in pain, either as an adjunctive or monotherapy [61].

Aromatherapy massage has been found to be a safe, effective, low-risk treatment option with high compliance rates, with both pain and QoL scores significantly improving after 4 weeks of treatment [62]. However, this was a small ($n = 46$), unblinded, noncontrolled study.

3.3.2. Gluten Neuropathy. Peripheral neuropathy is a common extraintestinal manifestation of serologically confirmed gluten sensitivity (positive gliadin antibodies and/or tissue transglutaminase or endomysium antibodies) [7, 11, 63]. Up to 55% of patients with gluten neuropathy experience pain [64]. The resultant neuropathic pain is associated with poorer mental health status, and amelioration of overall pain and health status can be achieved with a gluten-free diet [7, 63, 64]. Zis et al. demonstrated that a strict gluten-free diet (as evidenced by the elimination of gluten sensitivity-related antibodies) results not only in better scores on the pain domain of the SF-36 but also in better scores on the overall health change domain (how patients perceive their overall health across time).

3.3.3. Immune-Mediated Neuropathy. Anti-myelin associated glycoprotein antibody (anti-MAG) neuropathy is a type of immune-mediated neuropathy. Rajabally et al. showed that presence of pain has a significant impact on QoL. This study brings new insights on the practical management of patients with anti-MAG neuropathy, in indicating that neuropathic pain and pain related to cramps play a significant role in the impairment of function and the overall QoL in affected patients [53].

3.3.4. Chemotherapy-Induced Peripheral Neuropathy. Many chemotherapy treatments induce peripheral neuropathy (CIPN), and it is a persistent problem beyond treatment [5, 65]. Results from a recent study have shown that painful CIPN independently affects the overall patient QoL although general health was rated as high.

Duloxetine has been tried as a treatment of painful CIPN in 2 studies [66, 67] and was found to have statistically and clinically significant improvements in pain and QoL when compared to placebo. In addition to exploring the analgesic

effects of duloxetine, it has been shown that patients with better baseline emotional health, such as feeling less worried or anxious, are four times more likely to respond to duloxetine [66].

Opioids such as tapentadol have also been used in the treatment of CIPN. Galie et al. found QoL scores were significantly improved after treatment, thus proving a correlation between treating pain and subsequently QoL [68].

3.3.5. HIV-Related Polyneuropathy. HIV-related polyneuropathy is prevalent in HIV patients; however, the exact cause is unknown. Hypothesized mechanisms include altered immunity, nutritional factors, infectious processes and as a result of the adverse effects of highly active antiretroviral therapy causing damage to the peripheral nervous system [69–71].

Regarding pharmacological therapies, although capsaicin is effective in treating pain associated with HIV-associated PN, it has not shown a significant improvement of the overall QoL [70, 72].

Nonpharmacological therapies include hypnosis, which has not only shown reduction in pain intensity but an improvement in QoL and a reduction in depression-related symptoms [71]. This benefit was found in patients for 7 weeks, irrespective of whether or not they were taking pain reduction medication.

Moreover, Knezevic et al. presented the first reports of spinal cord stimulation in two patients refractory to conservative treatments [69]. Both patients reported significant improvements in their ability to carry out daily activities, an overall increase in QoL, and a reduction in the use of opioid analgesics, demonstrating this to be a safe and viable treatment option. An important limitation to this would be ensuring the CD4 counts of potential recipients are within safe limits, as those who are severely immunosuppressed could increase their susceptibility to infection when undergoing spinal cord stimulation [69].

3.3.6. Genetic Neuropathies. Only one study in our review evaluated the effect of painful Charcot–Marie–Tooth (CMT) disease (mainly CMT1 and CMT2) on QoL in a paediatric population and found pain negatively affects QoL [73].

3.3.7. Haemodialysis-Related Neuropathy. PN is a common occurrence in haemodialysis patients and has been related to an impaired QoL. Reduced QoL is independently related to worse clinical outcomes and increased mortality in haemodialysis patients [16]. Atalay et al. found significant improvements in QoL in patients with PPN treated with gabapentin and pregabalin, through a reduction of pain intensity [16].

3.3.8. Sarcoidosis-Related Neuropathy. Sarcoidosis is an inflammatory disease affecting many tissues, including dysfunction of small nerve fibres, the prevalence of which is

grossly underestimated [74]. High-dose glucocorticoids have been the mainstay of treatment but however are associated with unacceptable side effects. In a randomised, double-blind, pilot study, Heij et al. demonstrated that ARA 290, a peptide designed to activate the innate repair receptor that initiates cytoprotection, anti-inflammation, and healing, is a safe and effective treatment option, including improvement in QoL [74].

3.3.9. Chronic Idiopathic Axonal Polyneuropathy. Chronic Idiopathic axonal polyneuropathy (CIAP) is a term describing neuropathies with sensory and motor involvement, in a length-dependant distribution. It is slowly progressive, insidious, with no identifiable aetiology despite extensive diagnostic work-up [3, 75]. CIAP is correlated with a worse QoL in the energy/fatigue domain, the emotional well-being domain, and the general health perception domain [8]. In a small, open-label trial, lidocaine (5% patches) was found to significantly improve pain and QoL in CIAP [76].

4. Conclusions and Future Directions

This systematic review has identified the following key points:

- (i) Pain has an additional negative impact on QoL in patients with PN, regardless of the aetiology of their neuropathy.
- (ii) The treatment of neuropathic pain is universally the same, and current guidelines for the treatment exist [77]. Treatment of pain can further ameliorate QoL.
- (iii) It has been highlighted that specific diets (based on the aetiology of the neuropathy) can play an additional role in improving QoL, for example, diet control in diabetes and a gluten-free diet in gluten neuropathy.
- (iv) This systematic review has highlighted that only one paper focuses on a paediatric population, where the cause of the neuropathy was CMT. In order to better understand the QoL in adult populations, further assessment of genetic neuropathies should be studied using a variety of population ages.
- (v) It is likely that patients with PN suffer from comorbidities that are affecting the QoL independently to the burden caused by the painful peripheral neuropathy. Comparing the QoL of groups of patients with PN of different aetiologies using multivariate statistics can eliminate this risk of bias.
- (vi) The majority of the tools for evaluating QoL that were used in the papers included in this review were generic (i.e., SF-36). Designing and validating tools for evaluating QoL in patients with PN are important. Such tools should capture and weigh accordingly specific to PN domains that might be affected.

Additional Points

Limitations. (i) A more comprehensive search using other databases other than PubMed would have produced a greater number of articles eligible for final analysis. (ii) Many of the studies based a diagnosis of peripheral neuropathy on clinical interpretation or self-reported questionnaires. Consequently, selection bias may be present. A more robust and reliable diagnostic tool would be using neurophysiological studies throughout the studies.

Disclosure

The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Review Article

Reward Processing under Chronic Pain from the Perspective of “Liking” and “Wanting”: A Narrative Review

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The therapeutic goals of patients with chronic pain are not only to relieve pain but also to improve the quality of life. Chronic pain negatively affects various aspects of daily life, such as by decreasing the motivation to work and reward sensitivity, which may lead to difficulties in daily life or even unemployment. Human and animal studies have shown that chronic pain damages reward processing; the exploration of associated internal mechanisms may aid the development of treatments to repair this damage. Incentive salience theory, used widely to describe reward processing, divides this processing into “liking” (reward-induced hedonic sensory impact) and “wanting” (reward-induced motivation) components. It has been employed to explain pathological changes in reward processing induced by psychiatric disorders. In this review, we summarize the findings of studies of reward processing under chronic pain and examine the effects of chronic pain on “liking” and “wanting.” Evidence indicates that chronic pain compromises the “wanting” component of reward processing; we also discuss the neural mechanisms that may mediate this effect. We hope that this review aids the development of therapies to improve the quality of life of patients with chronic pain.

1. Introduction

Chronic pain is a worldwide problem for which effective treatment is lacking [1]. It is associated with physical disability, cognitive impairment, and negative psychological states, including anxiety, depression, and an increased risk of suicide [2–4]. Thus, chronic pain is composed of long-term physical and psychological pain, and an important goal of its treatment is to improve patients’ quality of life [5]. Chronic pain-induced psychological changes may interfere with the processing of rewards, defined as “objects or events that generate approach and consummatory behavior, produce learning of such behavior, represent positive outcomes of economic decisions and engage positive emotions and hedonic feelings” (page 1, second paragraph) [6]. Given this definition, reward processing has several components, including the noticing

of reward-related cues, bursts of motivation, hedonic perception, and reinforcement learning [7, 8]. Patients with chronic pain may lose pleasure in life and/or motivation to work [9, 10], decreasing their sensitivity to rewards [11], but the mechanism by which chronic pain affects reward processing remains unclear. Exploring changes in reward processing under chronic pain may facilitate the improvement of treatment.

Researchers have used the incentive salience theory to explain reward processing during depression. This approach divides reward processing into “liking” and “wanting,” both of which are decreased under major depression [12–14]. “Liking” is the pleasurable experience derived from sensory input, usually dependent on reward stimulus’ properties, and “wanting” is the internal motivational component related to the acquisition of reward stimuli [15]. In this review, we summarize studies of reward processing during chronic

pain and discuss related neural mechanisms from the perspective of incentive salience theory.

2. Reward-Related Behaviors in Patients with Chronic Pain

2.1. Natural Reward-Related Behaviors during Chronic Pain. Studies conducted with healthy volunteers have shown that acute physical pain can increase the motivation to attain rewards under laboratory conditions [16, 17]. However, natural reward-related behaviors in patients with chronic pain may be more complicated. In a cross-sectional study, Geha and colleagues [11] found reduced hedonic perception of palatable food in patients with CLBP; “liking” ratings for palatable puddings were significantly lower among patients with CLBP than among controls, whereas sensory ratings of intensity, sweetness, creaminess, fattiness, and oiliness, as well as “liking” ratings for sugar-containing drinks, were similar in the two groups. These results indicate that patients with CLBP had normal senses of taste, but decreased food-related pleasure. In another study, patients with chronic back pain had lower detection thresholds for gustatory stimuli (i.e., bitter, salty, sweet, and sour) than did controls, with no significant difference in “pleasant” and “unpleasant” ratings for these stimuli between groups [18]. Thus, whether chronic pain affects the derivation of pleasure from gustatory stimuli remains a matter of debate.

2.2. Reward Sensitivity in Patients with Chronic Pain. The term “reward sensitivity” is used to describe positive beliefs about the probability of future rewards [19]. High reward sensitivity helps to identify and motivate repetition of pleasurable activities, whereas low reward sensitivity reduces the motivation to engage in such activities and facilitates the development or aggravation of depressive symptoms [20]. Anhedonia, a typical symptom of depression, is defined as loss of sensitivity to pleasure and motivation to acquire reward [13, 19]. In early studies, the 66-item Physical Anhedonia Scale (PAS) was used to assess physical anhedonia symptoms in patients with chronic facial and low back pain [21, 22]. PAS items encompass loss of the ability to feel pleasure from eating, drinking, touching, sex, temperature, smells, and sounds. Thus, the PAS inventory assesses mainly the capacity to hedonically perceive events and stimuli during daily activity. Patients with chronic pain reported high levels of physical anhedonia in these studies, suggesting that chronic pain reduces the emotional pleasure response.

The Behavioral Activation Scale/Behavioral Inhibition Scale (BAS/BIS), based on these behavioral approach system/behavioral inhibition system characteristics [23], has been used to assess reward sensitivity in human subjects. The behavioral approach system is sensitive to reward signals, and the behavioral inhibition system could be activated by aversive stimuli [19, 24]. Using the BAS/BIS scales, Elvemo et al. [25] found reduced reward responsiveness, defined as tendency to respond positive in the context of desired events or cues of potential future reward, in female patients with chronic idiopathic, visceral, and musculoskeletal pain, but

no difference in reward drive, defined as the tendency to pursue reward, between these patients and a control group. They also observed significant higher physical anhedonia in chronic pain patients measured with the Beck Depression Inventory II. Becerra-García and Robles Jurado [24] used questionnaire, based on the behavioral approach system, to assess reward sensitivity in female patients with fibromyalgia, finding significantly reduced behavioral approach system activity, which could be interpreted as poor response to environmental incentives and reduced reward approach behavior. These studies have revealed the correlation between chronic pain and low reward sensitivity.

2.3. Goal Pursuit Behaviors in Patients with Chronic Pain. Researchers have examined motivation through assessment of the pursuit of goals [26–29], conceptualized as “internal representations of desired states, where states are broadly construed as outcomes, events, or processes” (Page 338, paragraph 1) [26]. Goal pursuit may be related to reward processing [30, 31], and its relationship to chronic pain has been explored using the daily diary method. Hardy et al. asked women with fibromyalgia to record feelings of pain, emotional distress, and fatigue and to rate goal conflicts in daily activity, including household and job tasks and interpersonal relationships, using daily diaries [32]. They found that goal pursuit behaviors resulted in greater subjective feelings of pain and that emotional distress mediated the perception of goal conflicts. Mun et al. used the daily diary method to assess daily goal conflicts in patients with chronic pain [10], finding that pain intensity was related positively to interference with work goals and that this effect was moderated by pain acceptance. Semistructured interviews have also been used to investigate daily goal conflicts in patients with fibromyalgia, revealing more self-reported pain-induced goal conflicts (most commonly affecting household, social, and interpersonal goals) in these patients than in healthy individuals [28]. These studies show that chronic pain inhibits daily goal pursuit activities. Under chronic pain, some short- and long-term goals may become unattainable [27], which may lead to the loss of positive feedback and attenuate the reward processing of goal pursuit behaviors. However, the direct relationship between reward processing and goal pursuit behaviors during the chronic pain remains to be discussed.

The aforementioned studies are summarized in Table 1. These researchers adopted different experimental paradigms, and the results consistently indicated that chronic pain disrupted various aspects of reward processing. Under some conditions, the effects of chronic pain on the emotional and sensory aspects of reward processing may be separate [11, 18]. Moreover, chronic pain and its management were found to affect daily activities by inducing more goal conflict, which may lead to the adaptive reduction of reward-seeking motivation. In the following sections, we introduce incentive salience theory and use this perspective to present research on reward processing under chronic pain. As only few human studies have directly explored the relationship between chronic pain and reward processing using incentive

TABLE 1: Reward-related behaviors in patients with chronic pain.

Study	Disorders	Test	Measurement	Results
Geha et al. [11]	Back pain	Rating sugary drinks	Liking	No change
			Wanting	No change
			Sweetness	No change
		Rating fat puddings	Intensity	No change
			Liking	Decrease
			Wanting	No change
Small and Apkarian [18]	Low back pain	Rating sucrose solution	Sweetness	No change
			Intensity	Increase
Marbach and Lund [21]	Facial pain and TMJ pain	PAS	Anhedonia	Increase
Marbach et al. [22]	Back pain or facial pain	PAS	Anhedonia	Uncorrelated to pain intensity
Elvemo et al. [25]	Various	BIS/BAS	Reward drive	No change
		BDI	Anhedonia	Increase
		BIS/BAS	RER	Decrease
Becerra-Garcia and Robles Jurado [24]	Fibromyalgia	SPSRQ	RER	Decrease
Claes et al. [28]	Fibromyalgia	Semistructured interview	Goal conflicts	Increase
Hardy et al. [32]	Fibromyalgia	Daily diary	Goal conflicts	Increase
Mun et al. [10]	Not mentioned	Daily diary	Goal conflicts	Increase

Abbreviations: TMJ, temporomandibular joint; PAS, Physical Anhedonia Scale; BIS, Behavioral Inhibition Scale; BAS, Behavioral Activation Scale; BDI, Beck Depression Inventory; SPSRQ, Sensitivity to Punishment and Sensitivity to Reward Questionnaire; RER, reward-induced emotional responsiveness.

saliency theory, we describe here mainly evidence derived from animal research in the following chapters. Although animal studies are not entirely a representative of human studies, they may provide important reference for future human studies and facilitate the understanding of how chronic pain affects reward processing.

3. Reward Processing during Chronic Pain in Animal Studies

3.1. Incentive Saliency Theory. Incentive saliency theory has been applied widely to explain reward processing in individuals with psychiatric disorders, such as drug addiction, gambling disorders, overeating [15, 33, 34], major depression [12–14], and schizophrenia [35]. Within the framework of this theory, “wanting” can be motivated by reward-conditioned cues, and thus may involve associative learning, attention, and memory retrieval. As “wanting” can be translated into motivation and bursts of reward-seeking behavior (i.e., approach behaviors and attempts to obtain stimuli), some researchers refer to it as “incentive saliency” [15, 36, 37]. In the context of the consumption of delicious food, “liking” is the pleasurable emotional experience induced via the activation of peripheral sensory (gustatory, tactile, and/or olfactory) receptors, which triggers nerve impulses and activates the reward circuit [38]; “wanting” is the internal desire and wish to repeat the experience triggered by the smell or sight of the food [15, 39].

“Liking” and “wanting” have been measured using specific experimental paradigms. As the hedonic experience dominates during the consumption of reward stimuli [40], the pleasurable sensory stimulus of sweetness has often been used to measure “liking.” The sucrose preference test (SPT) measures the consumption of sucrose-containing water,

which could reflect the pleasurable sensory input of this activity in animal studies [13]. Taste reactivity is another classical paradigm used to measure “liking,” through the scoring of animals’ orofacial expressions and behavior during the consumption of sucrose-containing water; tongue protrusion and paw licking, for example, are regarded as behavioral indices of pleasure [36, 41, 42]. A more diverse set of paradigms is used to measure “wanting,” as the degree of motivation to acquire reward stimuli. Experiments have involved reward-seeking or goal pursuit tasks [15, 43], such as T-maze navigation for rats [41]. The self-administration (SA) model with natural rewards or addictive drugs has also been used widely to measure “wanting” through quantification of the amount of reward earned in rats (e.g., by lever presses or nose pokes) [44–46]. “Wanting” has also been measured by quantifying rats’ daily consumption of food or water [43, 47, 48].

3.2. Effects of Chronic Pain on “Liking”-Related Behaviors. Animal studies of the effect of chronic pain on reward-related behaviors are summarized in Table 2. As the decreased preference for sucrose in the SPT is often explained as anhedonia, this test has been used widely to examine the comorbidity of chronic pain and depressive emotion in animal research. Several studies have shown that chronic pain decreases rodents’ preference for sucrose-containing water. For example, Dellarole et al. reported that chronic constriction injury (CCI) in mice induced neuropathic pain that decreased the 1% sucrose-containing water preference, reduced body weight, and degraded the physical state of the rats’ coats; this process was combined with neuroplastic remodeling in the hippocampus, a key emotional area [49]. Thus, the authors concluded that CCI induced depressive emotion. Wang et al. reported that spared nerve injury (SNI)

TABLE 2: Reward-related behaviors in animals with chronic pain.

Study	Species	Reward stimuli	Pain model	Test (results)
Dellarole et al. [49]	Mouse	SW	CCI	SPT (decrease)
Wang et al. [50]	Rat	SW	SNI	SPT (decrease)
Wu et al. [51]	Mouse	SW	SNI	SPT (decrease)
Bura et al., 2013	Mouse	SW	PSNL	SPT (decrease)
Amorim et al. [52]	Rat	SW	Arthritis	SPT (decrease)
Liu et al. [53]	Rat	SW	Fibromyalgia	SPT (decrease)
Shi et al. [54]	Rat	SW	SNL	SPT (no change)
Shi et al. [55]	Rat	SW	CFA	SPT (no change)
Su et al. [56]	Rat	SW	SNI; CFA	SPT (decrease)
Urban et al. [57]	Mouse	SW; food; water	SNI; CCI; CFA	SPT (no change); food intake (no change); water intake (no change)
Bravo et al. [58]	Rat	Cereals	CCI	Food intake (no change)
Goffier et al. [59]	Rat	SW; water	SNI	SPT (decrease); water intake (no change)
Okun et al. [60]	Rat	Food	CFA, SNL	SA with PR (CFA decrease, SNL no change); SA with FR (no change); tasty reactivity (no change)
Schwartz et al. [61]	Mouse	SW; food	CFA; SNI	SPT (no change); SA with PR (decrease); SA with FR (no change); food intake (no change)
Hipólito et al. [62]	Rat	SW	CFA	SA with PR (decrease); SA with FR (no change)
Schwartz et al. [63]	Rat	SW	SNI	AAT (decrease)

Abbreviations: SW, sucrose-containing water; SNI, spinal nerve injury; SPT, sucrose preference test; CCI, chronic constriction injury; CFA, complete Freund's adjuvant injection; SNL, spinal nerve ligation; SA, self-administration; PR, progressive ratio protocol; FR, fixed ratio protocol; PSNL, partial ligation of the sciatic nerve; AAT, avoidance-reward approach task.

induced neuropathic pain that decreased rats' preference for sucrose-containing water [50]. Neuropathic pain has also been found to attenuate the hedonic perception of sweetness in mice [51, 52]. Reduced sucrose preference has also been observed in other chronic pain models, such as those of monoarthritis [64] and fibromyalgia [53].

Other animal studies employing the SPT have revealed no reduction of sucrose preference during chronic pain [60, 61]. Urban and colleagues investigated the daily behaviors of mice, including their hedonic perception during the SPT [57]. After SNI or complete Freund's adjuvant (CFA) injection, the animals' preference for water containing 2% sucrose, daily food and water consumption, and weight remained unchanged for weeks. Shi et al. used the SPT to explore the interaction between chronic pain and depression [54], but they observed that spinal nerve ligation (SNL) alone was not sufficient to decrease rats' preference for water containing 1% sucrose. In other researches, Shi et al. also reported CFA-induced chronic pain inflammatory is not enough to decrease the sucrose preference [55]. Bravo et al. examined depressive symptoms in rats with CCI and similarly found that neuropathic pain did not affect the preference for sweet cereals, food consumption, or body weight [58].

Thus, results regarding the effects of chronic pain on "liking" are inconsistent. One possible reason is that the SPT is not a stable index and can be influenced by many factors, such as experimental conditions, animal types, and chronic pain models. For example, some researchers performed the SPT within 2 weeks after the induction of chronic pain models [56, 59], which may be an insufficient time period to allow for alteration of the "liking" component.

3.3. Effects of Chronic Pain on "Wanting"-Related Behaviors. Chronic pain has shown divergent effects on "wanting" behavior, according to the experimental protocol used (Table 2). Some researchers have adopted SA models to explore the effects of chronic pain on reward-seeking behaviors using fixed ratio (FR) and progressive ratio (PR) protocols. Under the FR protocol, animals must press a lever or perform a nose poke a fixed number of times to earn a reward. Under the PR protocol, the number of actions required to obtain the reward increases, making reward acquisition progressively more difficult. Hipólito and colleagues reported that CFA injection-induced inflammatory pain did not affect rats' sucrose pellet SA behavior under an FR protocol, but that this behavior was attenuated under a PR protocol with sucrose pellets or 50 $\mu\text{g}/\text{kg}$ heroin, but not the seeking behaviors to high dose of heroin (200 $\mu\text{g}/\text{kg}$) [62]. Schwartz et al. trained mice to nose poke to obtain reward pellets and built chronic pain models with CFA injection and SNI, respectively [61]. They observed that these treatments decreased the nose poke behavior to food pellets under a PR protocol, but did not affect nose poke behavior or daily food consumption under an FR protocol. Similarly, Okun et al. observed that CFA injection-induced inflammatory pain transiently decreased SA lever pressing in rats under a PR protocol, whereas SNL did not affect SA behavior or daily water or food consumption under an FR protocol [60].

Decreased reward-seeking motivation under chronic pain has also been demonstrated using the pain avoidance-reward approach task. Schwartz et al. [63] trained rats to seek small and large rewards (water containing 3% and 10% sucrose, respectively) with the probability of experiencing laser-induced heat pain. The rats maintained SA behavior for

both sucrose concentrations while ignoring the heat pain attacks. After SNI, neuropathic pain reduced SA behavior for the small reward, but did not affect large reward seeking. These results might be interpreted as reflecting the motivational value of reward decrease under chronic pain.

Differences in the difficulty of animals' reward acquisition among experimental paradigms (i.e., between FR and PR protocols) may have led to the divergent results regarding the effect of chronic pain on "wanting" behavior. Most SA studies performed with PR protocols have shown that chronic pain decreases "wanting," whereas those performed with FR protocols have shown no effect on SA behavior or daily food or water intake [57, 58, 59], which may reflect the subjective perception of the effort required to complete the task. Researchers believe that, at a certain breakpoint (BP), animals stop nose poking or lever pressing because they perceive that earning the reward is no longer worth the effort. Thus, the BP has been considered to reflect the internal motivation to obtain the reward, which is measured more suitably with a PR protocol than with an FR protocol or the measurement of spontaneous food and water intake [65]. Therefore, we consider that SA models with PR protocols reflect more advanced "wanting" components, which are much more sensitive to chronic pain.

4. Modulatory Mechanisms of Chronic Pain on Reward Processing

Pharmacological activation of the dopamine (DA) system, which is one kind of the neurotransmitter closely related to reward, by amphetamine has been found to enhance food intake ("wanting"), but to have no effect on taste reactivity ("liking") in rats [41, 48, 66, 67]. The role of the opioidergic system in reward processing has also been examined; pharmacological stimulation of mu, delta, and kappa receptors in the anterior-posterior nucleus accumbens (NAc, a hedonic "hotspot") increased tasty reactivity scores and food intake [43, 66, 68].

Many studies have shown that chronic pain can alter the DA and opioidergic systems. In rats, chronic inflammatory and neuropathic pain reduced morphine-induced conditioned place preference (CPP), increased the expression of kappa receptors in the NAc, and downregulated mu receptors in the ventral tegmental area (VTA). These processes were combined with suppression of morphine-induced DA release in the NAc [69–71]. Hipólito et al. reported that CFA-induced inflammatory pain downregulated the expression of mu receptors in the VTA and reduced the baseline DA level in the NAc, which had the combined effect of reducing food SA behavior [62]. Human research also showed the mu receptors in patients with chronic pain were downregulated [72, 73].

Otherwise, findings from a recent animal study suggest that D2-like receptors are involved in reward-seeking behavior. Specific ablation of medium spiny neurons that express D2-like receptors (D2-MSNs) in the ventrolateral striatum reduced goal-directed behavior in mice, executing a three-choice serial reaction-time task [74]. Optogenetic inhibition of D2-MSNs before lever presentation in an SA

model also decreased the BP under a PR protocol in rats [74]. Another recent study showed that the downregulation of D2-MSNs under chronic pain correlated with decreased reward-seeking motivation in mice; SNI and CFA injection inhibited the excitatory postsynaptic potential of D2-MSNs, but not that of D1-MSNs, in the NAc [61]. The authors also found that the food-seeking behavior of these animals was inhibited under a PR protocol, but not under an FR protocol; sucrose-containing water preference and daily food consumption were unchanged. Neuroimage results from human research also support that D2-like receptor was downregulated by chronic pain. A PET study showed decreased availability (dysfunction) of D2-like (D2 and D3) receptors in the ventral striatum in patients with chronic non-neuropathic back pain [75]. Similar observations were made in female patients with fibromyalgia [76].

"Wanting"- and "liking"-related brain structures have been reviewed by Robinson et al. [15]. They proposed that the "liking" and "wanting" brain systems overlapped in mesolimbic structures. Pharmacological disruption of NAc could decrease the "wanting" behaviors such as spontaneous food and water intake [41, 48, 66, 67]. Besides, Schwartz et al. have reported that the neuropathic pain could decrease the neural activities in the mPFC-NAc pathway and suppress the reward-seeking behaviors in the pain avoidance-reward approach task in rats [63]. The above studies indicate the potential neural mechanism that mediate the inhibition of reward processing in chronic pain, including DA system, mu receptor, D2-like receptor, and mPFC-NAc pathway; however, further experiments are still needed to explore these mechanisms.

5. Limitations

The main limitation of this study is related to the differences between animal and human studies of changes in reward-related behaviors and neural mechanisms. For example, Pool et al. argue that differences in the definitions of "wanting" and "liking," which are more conflicted in humans than in animal research, lead to the use of animal-based experimental designs that do not distinguish "wanting" and "liking" in humans [40]. Experimental results from animal research can provide reference, but could not equal with results from human research and could not apply the conclusion to human research. Systematic human research needs to be performed to acquire more evidence on reward processing in the context of chronic pain.

6. Conclusion and Future Directions

In this review, we employed incentive salience theory to describe evidence on reward processing under chronic pain. The distinction of "liking" and "wanting" components of reward processing may aid discrimination of the effects of chronic pain on pleasurable sensory input and reward-seeking motivation. Based on evidence accumulated to date, we conclude that chronic pain reduces "wanting" behaviors. Bursts of reward-seeking behavior involve cognitive processes such as attention, working memory,

and associative memory retrieval. Patients with chronic pain are sensitized to pain-related information, and pain management occupies their attentional resources [77, 78]. As a result, long-term chronic pain-induced attentional impairment might conflict with reward-seeking behavior, leading to the adaptive reduction of “wanting.” In addition, some studies have shown that chronic pain can decrease “liking” behaviors.

The effect of chronic pain on reward processing seems to differ between the sexes. Chronic pain has been found to decrease reward-related behaviors (i.e., sexual behavior and sucrose preference) in female, but not in male, animals [79, 80]. Sexual hormones may mediate reward processing, given the higher prevalence of food addiction and drug abuse in female than in male rats [81]. In human research, females are also more vulnerable to chronic pain than males [82, 83]. Future studies should thus explore sex differences in the vulnerability of reward processing to chronic pain.

The “liking” and “wanting” perspective may provide a new way of thinking about reward processing under chronic pain. First, according to this perspective, reward sensitivity and reward-seeking motivation can change without affecting each other. Therefore, this framework could explain fundamental research findings that chronic pain does not decrease the ability to discriminate pleasurable sensory input, but does reduce reward-seeking behavior [60, 61]. Second, this perspective can be used to examine the comorbidity of chronic pain and drug addiction. Incentive salience theory has been used widely to explain drug addiction in humans and animals; for example, some addictive drugs sensitize the “wanting” system, resulting in compulsive drug-seeking behavior [15, 81]. Patients with chronic pain are more likely to have contact with analgesics such as morphine and heroin, increasing the risk of drug addiction. Third, this perspective may enhance targeted drug treatment to improve reward processing in patients with chronic pain, as beyond psychological dissociation, “wanting” and “liking” are distinct in terms of brain structure and neurochemistry. Finally, as chronic pain is a worldwide problem that severely compromises the quality of daily life, further research should be conducted to explore whether this perspective can be applied to improve the well-being of patients with chronic pain.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Research Article

The Mediating Effect of Central Sensitization on the Relation between Pain Intensity and Psychological Factors: A Cross-Sectional Study with Mediation Analysis

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Background. Central sensitization (CS) and psychological factors are associated with pain intensity; however, the mediating role of CS on the relation between psychological factors and pain intensity remains unclear. **Objectives.** We performed mediation analysis to investigate how CS mediates relation between psychological factors and pain intensity. **Methods.** Twenty patients with musculoskeletal pain were included in this cross-sectional study. Central sensitization inventory (CSI), one pain intensity-related outcome measure (Short-Form McGill Pain Questionnaire 2 (SFMPQ2)), and three psychological outcome measures (Hospital Anxiety and Depression Scale (HADS), Pain Catastrophizing Scale-4 (PCS), and Tampa Scale for Kinesiophobia-11 (TSK)) of all participants were assessed. The mediation analysis with a bootstrap sampling procedure was used to assess the indirect effects. The level of significance was set at 5%. **Results.** Mediation analysis showed that the HADS-anxiety, HADS-depression, and PCS had significant indirect effects on the pain ratings of CSI. Additionally, the direct effect was significant only for PCS. **Conclusions.** The relationship among anxiety symptoms, depression symptoms, and pain intensity was completely mediated by CS. Furthermore, the relationship between catastrophic thinking and pain intensity was partially mediated by CS. Our findings suggest that CS mediates relation between psychological factors and pain intensity, and CS-focused intervention may be important.

1. Introduction

Many musculoskeletal pain conditions, such as osteoarthritis [1, 2], low back pain [2, 3], and persistent neck pain [4, 5], are associated with hypersensitivity, which is induced by central sensitization (CS). The International Association for the Study of Pain defines CS as the “increased responsiveness of nociceptive neurons in the central nervous system to their normal or sub-threshold afferent input” [6]. This definition is used as the physiological concept of CS. Recently, the International Association for the Study of Pain released a new term, nociplastic, designed to be a third descriptor to be used instead of “central” or “central sensitization” [7]. Nociplastic pain is defined as “pain that arises

from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain.” Nociplastic pain relates to hypersensitivity, including hyperalgesia. Nociplastic pain is used as the clinical concept of CS.

The central sensitization inventory (CSI) was recently developed as a comprehensive screening instrument for CS [8]. The use of CSI has also been recommended as one component of an algorithm to detect CS in patients with chronic pain [9], particularly in patients with musculoskeletal pain [10]. Several studies revealed that pain intensity was associated not only with psychological factors [10–12] but also with CSI score [3, 10, 11, 13, 14]. The CSI cutoff

score has been recommended as a CSI score of >40 , and it is based on the presence or absence of central sensitivity syndromes (CSSs) [15]. However, this is only a cutoff score, and even those with a CSI score of less than 40 may also have effects of CS. In fact, the previous study reported that the average score of CSI score was low in the Japanese version of CSI, and patients diagnosed with 1 or more CSSs scored lower on the CSI than 40 [13]. The CSI score in the previous study may be affected by the disease and the region of the subject. Patients who were referred to a multidisciplinary pain center, which specializes in the assessment and treatment of complex pain and psychophysiological disorders, including CSSs reported high CSI scores (>40) [15]. However, patients who were recruited from the community-based physiotherapy program reported low CSI scores (mean = 24.6; SD = 12.0) [16]. Focusing on the cultural differences, the Japanese mean score of the CSI (mean = 21.91; SD = 13.31) [13] was lower than the American (mean = 52.4; SD = 14.3) [15] and Spanish (mean = 24.6; SD = 12.0) [16] samples. Thus, although there is a cutoff score of CSI, it may be better to pay attention to the amount of numerical values not cutoff score, as the CSI score may also be affected by the cultural differences and disease.

Studies, such as those cited above, did not determine how CS and psychological factors influence pain intensity in any relationship [3, 10–14]. Psychological factors are reportedly associated with pain intensity, but pain intensity is not always increased by negative emotions [17, 18]. For instance, anxiety reportedly has direct correlation with pain intensity [10–12], but not always has correlation with pain [17]. Also in depression, catastrophic thinking, and kinesiophobia, several reports suggested that pain intensity was related to these psychological factors [10–12], but several reports also suggest that pain intensity was not always correlated with these psychological factors [18]. We thought that the existence of CS will affect these inconsistent reports, and we hypothesized that CS mediates relationships between psychological factors and pain intensity. However, the mediating role of CS on the relationship between psychological factors and pain intensity has never been investigated. Mediation analysis could help determine how CS and psychological factors modify pain intensity in any relationship, and we believe that this knowledge will contribute to the selection of optimal treatments based on the pathology of pain-related CS in clinical settings.

The primary aim of this study was to reveal how CS mediates relation between psychological factors and pain intensity. We hypothesized that CS mediates relation between psychological factors and pain intensity.

2. Methods

2.1. Participants. In total, 20 patients were recruited from an orthopedic clinic. Patients aged between 16 and 86 years and having musculoskeletal pain, such as pain involving the neck, shoulder, low back, or knee, were included (Table 1). Previous studies have reported that CS occurs in multiple sites such as the knee [1, 2], lumbar region [2, 3], and neck [4, 5], so we did not limit the pain site. Therefore, we would

TABLE 1: Characteristics of the participants.

	Mean (SD) or N (%)
Age (years)	67.5 (15.6)
Gender (female)	12 (60)
Pain area	
Neck	3 (15)
Low back	11 (55)
Shoulder	4 (20)
Knee	2 (10)
Pain duration (months)	24.3 (41.4)
Central Sensitization Inventory (CSI)	24.0 (12.7)
Short-Form McGill Pain Questionnaire 2 (SFMPQ2)-total	41.6 (35.5)
Hospital Anxiety and Depression Scale (HADS)-anxiety	5.9 (4.3)
Hospital Anxiety and Depression Scale (HADS)-depression	6.3 (3.7)
Pain Catastrophizing Scale (PCS)-4	6.9 (2.0)
Tampa Scale for Kinesiophobia (TSK)-11	13.1 (6.2)

like to investigate the effect of CS on musculoskeletal pain without identifying sites and diseases susceptible to CS. Also, we did not limit the pain duration to investigate various pain conditions. Exclusion criteria were patients diagnosed with brain or spinal cord injury, neurological disease, or dementia. The study protocol conformed to the Declaration of Helsinki. The participants provided written informed consent before the study began. This study was approved by the ethics committee of Kio University Health Sciences Graduate School (approval no. H30-06).

2.2. Procedure. Demographic data (age, sex, pain area, and duration), CSI, one measure of pain intensity-related outcomes (Short-Form McGill Pain Questionnaire 2 (SFMPQ2) [19], and three measures of psychological outcomes (Hospital Anxiety and Depression Scale (HADS) [20], Pain Catastrophizing Scale-4 (PCS) [21], and Tampa Scale for Kinesiophobia-11 (TSK) [22]) of all participants were assessed.

The Japanese version of CSI was used to assess CS [13]. CSI consists of 2 parts. Part A is a questionnaire comprising 25 self-report items and is used to assess health-related symptoms that are common to CSSs. Part B was not used in this study. Higher scores indicate more severe CS. CSI had good internal consistency (Cronbach's $\alpha = 0.89$). A factor analysis yielded 5 major factors [13].

SFMPQ2 was used to assess pain intensity [19] and includes items that assess 22 qualities of pain and the intensity of each quality on an 11-point numerical rating scale. The total score is calculated from the sum of the 22 items. Higher scores indicate more severe pain. SFMPQ2 had good internal consistency (SFMPQ2-total: Cronbach's $\alpha = 0.86$) [19]. There were significant correlations between SFMPQ2-total and other functional assessments (VAS: $\rho = 0.54$, SFMPQ-total: $\rho = 0.79$) [19].

HADS was used to assess anxiety and depression as one of psychological factors [20]. HADS contains 14 items

and 2 subscales. The two subscales independently assess depression and anxiety. Higher scores indicate more severe anxiety and depression. HADS-anxiety had good internal consistency (HADS-anxiety: Cronbach's $\alpha=0.80$), and HADS-depression had not good internal consistency (HADS-depression: Cronbach's $\alpha=0.50-0.61$) [20]. The correlations of the HADS-anxiety scores and the state-trait anxiety inventory (STAI) were 0.63–0.65. The correlations of the HADS-depression scores and Zung's self-rating depression scale (SDS) were 0.46–0.50 [20].

PCS-4 was used to assess catastrophic thinking as one of psychological factors [21]. PCS-4 is a shorter version of a 13-item PCS and contains 4 items. Higher scores indicate more severe catastrophic thinking. PCS-4 had good internal consistency (Cronbach's $\alpha=0.86$) [21]. There were significant correlations between PCS-4 and PCS-13 ($r=0.96$) [21].

TSK-11 was used to assess kinesiophobia as one of psychological factors [22]. TSK-11 is a shorter version of a 17-item TSK and contains 11 items. Higher scores indicate more severe kinesiophobia. TSK-11 had good internal consistency (Cronbach's $\alpha=0.74-0.87$) [22]. A factor analysis yielded 2 major factors [22].

2.3. Statistical Analysis. Mediation analysis was performed to assess the indirect effects of CSI on the relationship between psychological factors and pain intensity. The CSI was used as a continuous variable not as a dichotomous (presence or absence of CS by a cutoff score), because it was difficult to distinguish CS clearly into dichotomous, and the CSI was used as a continuous variable in this study for mediation analysis. To assess mediation, the following conditions had to be met [23]. (a) The effect of the independent variable on the dependent variable without the mediated variable is evaluated. (b) The effect of the independent variable on the mediated variable is assessed. (c) The role of both the independent and mediated variables on the dependent variable is evaluated. A bootstrap sampling procedure, as recommended for small sample sizes, was used to determine the significance of indirect effects [24]. This process involved using the sample as a population reservoir from which a large number of random samples were drawn and continuously replaced so that they had an equal likelihood of being randomly selected on all subsequent drawings. In the present study, we specified 1000 bootstrap iterations, as previously described [24]. In the mediation model used, the bootstrapped values of the 95% confidence interval that do not contain 0 between their lower and upper limits were considered to be significant mediators [25]. The statistical analyses were performed with HAD [26]. The level of significance was set at 5%.

3. Results

3.1. Sample Characteristics. A summary of the demographic characteristics and clinical profile of all participants is provided in Table 1. In total, the mean score of CSI-J was 24.0 ± 12.7 (mean \pm SD).

3.2. Mediation Analysis. We investigated whether CSI mediated the relationship between psychological factors and pain intensity. The tested model is illustrated in Figure 1. Table 2 shows that the direct effects of the hypothesized model were statistically significant only for PCS. In addition, it shows that the 95% BC bootstrapped CI for the indirect effects of HADS-anxiety (95% BC bootstrapped CI, 0.208–7.176 with 1000 resamples), HADS-depression (95% BC bootstrapped CI, 0.714–6.780 with 1000 resamples), and PCS (95% BC bootstrapped CI, 0.437–9.589 with 1000 resamples) on pain ratings of CSI was significantly different from zero. However, the 95% BC bootstrapped CI for the indirect effect of TSK (95% BC bootstrapped CI, -0.367 to 5.155 with 1000 resamples) was not significantly different from zero. These results revealed that the relationships between PCS and SFMPQ2-total were partially mediated by CSI. In addition, the relationship among HADS-anxiety, HADS-depression, and SFMPQ2-total was completely mediated by CSI.

4. Discussion

We used mediation analysis to investigate the relationship between pain intensity of CS and psychological factors. The results showed that the relationship among anxiety symptoms, depression symptoms, and pain intensity was completely mediated by CS. Moreover, the relationship between catastrophic thinking and pain intensity was partially mediated by CS.

Several cross-sectional studies showed that both psychological factors and CS affected pain intensity [3, 10–14]. Similarly, the present study showed that all psychological factors had significant total effects on pain intensity. Based on the results of the mediation analysis, although only catastrophic thinking had a direct effect on pain intensity, psychological factors were mediated in pain through CS. Thus, psychological factors apparently affected pain intensity, but CS directly affected the pain intensity in practice.

This is the first study to demonstrate that the effects of psychological factors (i.e., anxiety, depression, and catastrophic thinking) on pain intensity were mediated by CS. This may be biologically plausible because high CS scores indicate the dysfunction of supraspinal processing [27]. Previous studies have reported that negative emotion impairs the descending inhibitory pathways [28, 29]. For example, one previous study reported that the diffuse noxious inhibitory control was impaired in patients with chronic pain who have depression [29]. Thus, pain modulation may be induced not only by negative emotion but also by central nervous system distortion. In clinical settings, consideration should be given to CS, which is modified by psychological factors and may be effective for pain treatment. A previous study reported that rehabilitation exercises were effective on CS, pain, disability, and fear avoidance belief in patients with chronic nonspecific low back pain [3], suggesting that rehabilitation exercises improve CS. Progress in the study regarding rehabilitation is expected in the future.

This study showed that catastrophic thinking directly affected pain without mediation through CS. This may be

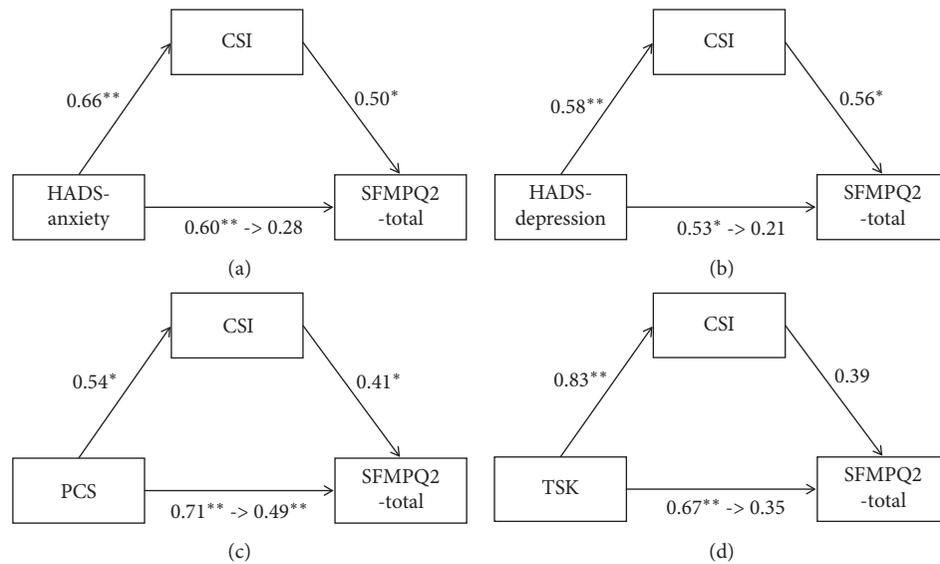


FIGURE 1: Central sensitization inventory (CSI) mediates the relationship between psychological factors and Short-Form McGill Pain Questionnaire 2 (SFMPQ2). Standardized betas are shown. (a) Hospital Anxiety and Depression Scale (HADS)-anxiety is the independent variable. (b) HADS-depression is the independent variable. (c) Pain Catastrophizing Scale-4 (PCS-4) is the independent variable. (d) Tampa Scale for Kinesiophobia-11 (TSK-11) is the independent variable. * $p < 0.05$; ** $p < 0.01$.

TABLE 2: Mediation analysis: the role of CSI as a mediator.

Path/effect	β	SE	p value/95% BCCI
<i>a</i> HADS-anxiety → CSI	0.659	0.522	0.002
<i>b</i> CSI → SFMPQ2-total	0.496	0.632	0.043
<i>c</i> (direct effect) HADS-anxiety → SFMPQ2-total	0.277	1.861	0.239
<i>c'</i> (total effect) HADS-anxiety → SFMPQ2-total	0.604	1.540	0.005
<i>a</i> × <i>b</i> (indirect effect) HADS-anxiety → SFMPQ2-total	0.327	1.729	(LL = 0.208, UL = 7.176)
<i>a</i> HADS-depression → CSI	0.578	0.655	0.008
<i>b</i> CSI → SFMPQ2-total	0.559	0.592	0.018
<i>c</i> (direct effect) HADS-depression → SFMPQ2-total	0.206	2.015	0.345
<i>c'</i> (total effect) HADS-depression → SFMPQ2-total	0.530	1.896	0.016
<i>a</i> × <i>b</i> (indirect effect) HADS-depression → SFMPQ2-total	0.323	1.501	(LL = 0.714, UL = 6.780)
<i>a</i> PCS → CSI	0.537	1.252	0.015
<i>b</i> CSI → SFMPQ2-total	0.414	0.485	0.029
<i>c</i> (direct effect) PCS → SFMPQ2-total	0.492	3.053	0.012
<i>c'</i> (total effect) PCS → SFMPQ2-total	0.715	2.889	0.0004
<i>a</i> × <i>b</i> (indirect effect) PCS → SFMPQ2-total	0.222	2.362	(LL = 0.437, UL = 9.589)
<i>a</i> TSK → CSI	0.830	0.269	0.00001
<i>b</i> CSI → SFMPQ2-total	0.390	0.859	0.223
<i>c</i> (direct effect) TSK → SFMPQ2-total	0.347	1.759	0.277
<i>c'</i> (total effect) TSK → SFMPQ2-total	0.671	0.996	0.001
<i>a</i> × <i>b</i> (indirect effect) TSK → SFMPQ2-total	0.324	1.395	(LL = -0.367, UL = 5.155)

SE, standard error; BC, bias corrected; CI, confidence interval; LL, lower limit; UL, upper limit.

biologically plausible because catastrophic thinking has cognitive factors such as attention to pain. A previous study reported that even with lower anxiety and depression scores, higher catastrophic thinking affected the pain intensity [30], thereby possibly indicating that catastrophic thinking affects pain intensity as a cognitive factor and not as an affective factor. Moreover, affect and attention changed pain intensity by different descending inhibitory pathways [28]. The attention to pain activated the pain pathway that is associated with pain intensity. Thus, attention to pain, such as the

careful catastrophic thinking, may increase pain intensity by activating the pain pathway. Although we did not directly evaluate these biochemical data, such mechanisms can be assumed to be involved. In clinical settings, considering the attention to pain may be effective for the pain is modified by the catastrophic thinking.

This study had several limitations. First, the outcomes of CS were merely those measured by CSI. Second, the sample size was relatively small. However, we adopted a bootstrap sampling procedure to determine the significance of the

indirect effects. Third, we could not determine the mechanisms underlying the relationship between pain intensity of CS and psychological factors because this study did not measure neurotransmitter levels.

5. Conclusion

To our knowledge, this is the first study to investigate mediation by CS for the effects of psychological factors on pain intensity. The relationship among anxiety symptoms, depression symptoms, and pain intensity was completely mediated by CS. Additionally, the relationship between catastrophic thinking and pain intensity was partially mediated by CS. Our results suggest that CS mediates relation between psychological factors and pain intensity and CS-focused intervention may be important.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Research Article

Living with Chronic Pain: A Qualitative Study of the Daily Life of Older People with Chronic Pain in Chile

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One of the main causes of chronic pain in older people is spine deformity, an abnormal curvature of the spine. The purpose of this study is to improve understanding of the experience of chronic pain produced by spinal deformity in older people and understand how cultural factors may affect this experience. A qualitative study was performed with 10 older people. Participants were encouraged to describe a typical day in their life, including the factors that affect their pain and how their quality of life had been affected since experiencing chronic pain. The semistructured interviews were transcribed and analyzed using open coding. Pain caused by spine deformity produces disability, affecting how older people perform their daily activities, causing them to adapt their households and physical positions to perform these tasks, albeit slowly or incompletely. Chronic pain also affects emotional states and social relationships because older people become unable to undertake physical activities that they performed in the past. The close relationship with adult children and friends, typical in Latin cultures, is a source of comfort and support. At a community level, adaptation of public services (such as public transportation) must be improved.

1. Introduction

Chronic pain is pain that lasts more than 3–6 months that adversely impacts the well-being of the affected individuals [1], limiting and reducing their physical activity, social relations, and energy levels [2]. When pain is widespread, it is common for people to regard their body as a crippling obstacle [3], resulting in them having to change their normal lives while simultaneously harbouring feelings of helplessness and vulnerability [4]. They experience shame and fear of rejection and feel as if they are a burden to others [5]. In turn, this leads to feelings of isolation and a fear of the future [6]. Among the four main causes of pain are spinal issues [7], e.g., those caused by the curvature of the spine in older adults [8]. Spine deformity includes asymptomatic curves and progressive or disabling deformities [9]. Spine imbalance requires a high amount of energy to try to maintain balance,

causing people to become fatigued and feel pain [10, 11]. The deformity also produces feelings of insecurity, lack of attractiveness, depression, and social isolation [12].

Pain interferes with the daily activities of people and disrupts every facet of their lives, causing a range of frustrations that stem from the invisibility of the pain and associated limitations in the diagnosis and treatment thereof [13]. Chronic pain also has serious detrimental effects on the social and familial environment of people. As a consequence, a multidisciplinary approach to treatment that includes the family and social context is required [14]. Furthermore, understanding the subtleties of the experience of pain may help health professionals to devise diagnoses and treatments that are more suited to the characteristics of each particular population. Thus, additional research is required into populations with different ethnic backgrounds to assess how ethnicity and culture can influence the experience of chronic

pain [15]. Likewise, studies have suggested the existence of ethnic-based differences based on the threshold and intensity of pain and their impact on patients [16, 17]. Additional research that makes reliable comparisons between Latin American countries and other regions is needed [18]. This work provides insight into the experience of Chilean older adults with chronic pain, describing through a qualitative study how pain affects their daily lives and their wellbeing and explaining our findings through the Chilean cultural and societal context.

1.1. The Chilean Context: Older People. In Chile, approximately 30.6% of its population will be over 60 years old by 2050 [19]. Pain caused by the back, knees, hips, and other joints is the most commonly cited health problem among older people in Chile [20]. In this section, we briefly describe how older people live in Chile. Chilean society is based on social links built around primary relationships [21], in which goals and interests of the group take precedence over those of the individual [21]. The burden of managing Chilean families is primarily borne by women, especially in terms of household chores and care-related tasks, whereas men are traditionally viewed as the financial providers [22]. It is common for two or three generations to live under one roof; for example, 59% of older people live with one of their children and contact with offspring who do not live in the same house as their parents is regular [20], usually taking the form of a monthly family meeting [23]. These intergenerational relationships work in both directions in terms of emotional support, advice, and practical help, such as caring for a grandchild [20], which 35.7% of older people in Chile do at least once a week [20]. Within the Chilean family, older people occupy a position of respect [21].

In relationships between older people and their adult children, there is a filial obligation that consists of the provision of economic and emotional support to the former during their old age. From the point of view of the child, this relationship is seen as a way of repaying the past debt of moral education and dedication bestowed upon them by their parent(s), whether or not they live in the same home in the present [23]. Nevertheless, older people in Chile have shown limited support for this type of obligation [20]. In general, older people continue to actively perform their own personal and household chores as part of their desire not to become overly dependent on others [23], which is one of the most common concerns of people within this age group in Chile [20]. However, older people often turn to their family, especially their children, for needs relating to, for example, transportation to the hospital or assistance in terms of their essential daily activities [20, 23].

1.2. Chronic Pain in Chile. Non-oncological chronic pain is estimated to occur in 32% of the adult population in Chile, and approximately 70% receives some drug treatment for chronic pain [24]. The level of chronic pain is divided into the following: mild (11.8%), moderate (65.7%), and severe (20.8%) [24]. Chronic pain is more frequent in women and in older people [25]. It has been mentioned that chronic pain

is an important cause of disability and is responsible for a high social and financial burden in Chile, since the consequences associated with chronic pain are expensive for health systems and for society in general [26].

In Chile, there is a National Program of Pain Relief and Palliative Care of the Ministry of Health, which is intended for cancer patients. Through this program, units focusing on pain have opened up both in private and public healthcare centers, which now also deal with other types of pain. Regarding pain management in Chile, several issues have been described, e.g., the long duration of symptoms, insufficient response to medical treatment, high use of anti-inflammatory drugs, and low use of specialized services in pain management [24].

Therefore, the objective of this work is to generate a more comprehensive understanding of the experience of pain in the daily lives of older people with spine deformity in Chile. Semistructured interviews were conducted with ten older people who endure chronic pain, with the objective of understanding their experiences of living with this condition in the Chilean context.

2. Materials and Methods

The study was exploratory, descriptive, and comprehensive, using a qualitative methodology, thereby enabling the reader to comprehend real-life experiences from the perspective of the participants [27]. We conducted semistructured interviews. The interview is the most common format for data collection in qualitative research [28]. Semistructured interviews are those where participants have to answer open questions [28]. These types of interviews are carried out only once, with an individual or with a group [29]. These interviews are based on a guide, which is a schema with questions or topics that serve the purpose of exploring many participants in a systematic and exhaustive way, as well as to keep the interview focused on the objective [29].

We used a 32-item checklist for qualitative studies to report this work [30]. This approach was used to understand the perception of people with spine deformity in regard to how they live with chronic pain, from a Chilean cultural perspective.

2.1. Data Collection. For this study, older people with chronic pain and spine deformity were recruited from a university hospital in Santiago, Chile, to participate in a semistructured interview. The interviews were conducted in Spanish by one (native Spanish-speaking) researcher during a period of 4 months in a location selected by the participant: either the hospital, a coffee shop or their own home. There was no pilot testing. Interviews were semistructured; participants were encouraged to describe a typical day in their life, including the factors that affect their pain and how their life had changed since experiencing chronic pain and spine deformity. Each interview lasted 30–60 minutes and was audiotaped and transcribed verbatim. Following the interview, participants were asked to complete three questionnaires with the objective of obtaining demographic data:

- (i) Oswestry Disability Index (ODI) is a self-administered questionnaire used to evaluate limitation of activities regarding daily life [31].
- (ii) Scoliosis Research Society-22r patient questionnaire evaluates the effect of idiopathic scoliosis and its treatment from the perspective of the patient in five domains [32]. There are 22 questions, and the questionnaire is scored so that 1 is the worst response and 5 the best [33].
- (iii) World Health Organization Quality of Life (WHOQOL-BREF) survey assesses the perception of individuals in relation to their culture, value systems, and personal goals and concerns [34].

These questionnaires were selected because they are validated in their respective field and can give us information of the participants about their quality of life, their disability, and their deformity, which allow us to have a better profile of the group of participants.

2.2. Participants and Data. Orthopaedic surgeons from the university hospital in which participants were recruited passed the relevant study information to the individuals involved. If they decided to subsequently take part, the first author contacted them to arrange the details of their participation. The inclusion criteria for participation were as follows: aged over 65, Spanish-speaking, resident in Chile, and experiencing spine deformity, and pain for at least six months. People with hearing or speech problems, as well as illiterate individuals (because the participant must fill out questionnaires), were excluded from participating due to the nature of the study.

The participants were eight women and two men, ranging in age from 67 to 79 ($md = 73$, $SD = 4.13$). Five of them were housewives, three were employed, and two retired. The participants had experienced chronic pain for an average of 5.1 years ($min. = 1$ year, $max. = 18$ years); six of them smoked ($md = 21.5$ years), one was a passive smoker, one did not smoke, and two chose not to answer the question about whether they were a smoker. The quality of life of the participants, according to the WHOQOL-BREF questionnaire, indicates that physical health and social relationships were the lowest scoring dimensions in this group.

Table 1 displays age, gender, spinal issue, and ODI and SRS-22r scores for all study participants. According to the ODI questionnaire, there are 5 levels of disability [35]:

- (1) 0%–20% (minimum disability): the patient can perform most of life's activities
- (2) 21%–40% (moderate disability): the patient experiences more pain and difficulty when sitting, lifting objects, and standing
- (3) 41%–60% (severe disability): pain remains the main problem in this group and daily activities are affected
- (4) 61%–80% (crippled): back pain affects all aspects of the patient's life
- (5) 81%–100%: these patients are bedridden or exaggerating their symptoms

The level of disability was minimal for two participants, moderate for four, severe for three, and exaggerated for one person.

2.3. Data Analysis. Data analysis was conducted in Spanish (language of the participants and researchers). Open codification (based on the grounded theory methodology) was used for data analysis, since the aim of the study was to describe and, therefore, understand the perspective of participants [36]. We used an inductive process and analytical operations geared towards answering our question. Subsequently, each single interview extract was compared with additional extracts in order to identify any similarities and differences. This analysis generated codes that were grouped into subcategories until the main ones were obtained [36]. The Atlas.ti program was used to facilitate this process (<https://atlasti.com>).

To ensure the methodological accuracy of the results, a triangulation strategy was used [37], which involved the participation of two researchers from different areas of study: nursing and computing; for which there were different points of view when analyzing the data. This helped to give rise to an intersubjective agreement on the generated categories. Both researchers jointly codified two randomly selected interviews, creating a list of initial codes. Thereafter, the remaining eight interviews were shared between the two authors, who codified them individually using the initial codes. Regular meetings were held to assess agreement on the coding and analysis and improve or modify the generated codes iteratively. Data saturation was reached at the sixth interview. Transcripts were subsequently re-read several times, and themes were identified by means of a process of repetitive interpretation, synthesizing, and theorizing. Finally, a consensus was reached on the generated categories.

2.4. Ethical Considerations. The study protocol was approved by the university ethics committee (15-339). Prior to the interviews being conducted, participants received oral and written information about the aim of the research, while written consent to the overall study was subsequently provided by each individual. Participants were informed that their involvement was voluntary, that anonymity would be guaranteed, and that they could withdraw from the study at any time.

3. Results

Following the descriptive analysis of the 10 semistructured interviews with older people with chronic pain and spine deformity, five main categories emerged: impact of pain on the patient, pain control strategies, treatment by the doctors, daily routine, and social support. The model (Figure 1) is patient-centered, since only older people with chronic pain were interviewed; therefore, all categories are related to the patient. The doctor-patient relationship is the patient's perception regarding his/her treatment. Pain is related to the

TABLE 1: Participant characteristics.

No.	Age	Gender	Type of spinal issue	ODI score (%)	SRS-22r score
1	68	F	Spinal fracture and deformity	100	1.36
2	79	F	Spinal fracture	56	2.57
3	76	M	Spinal deviation and fracture	4	4.68
4	76	F	Spinal deformity	38	3.50
5	76	F	Multiple spine fractures	40	2.50
6	74	F	Spinal deformity	44	2.82
7	67	F	Spinal deformity, osteoporosis	49	1.90
8	76	F	Lumbar osteoarthritis	40	3.00
9	67	F	Vertebra fracture	18	4.29
10	72	M	Spinal deformity	30	3.23

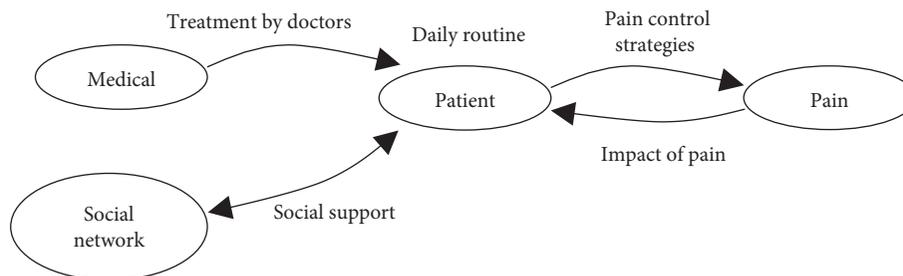


FIGURE 1: Descriptive analysis: a diagram of the main categories.

patient in two ways: (1) how the pain impacts the person (arrow from pain to patient); (2) how the person controls the pain he/she feels (arrow from patient to pain). Finally, the person's social network is affected by the disease, and their support (or lack thereof) also affects the older people. This section explains these categories. Quotes taken directly from the interviews and translated from Spanish to English are provided below.

3.1. Daily Routine. Participants were asked about a typical day in their lives, including the main obstacles that they have to overcome and the factors (environmental or psychological) that affect the intensity of their pain.

In the morning, participants get up and out of their beds unaided before taking their medicine and having breakfast. They then wash. They explained how they had refurbished the bathroom in order to be able to wash and bathe more securely and without help. To provide brief context, it should be noted that it is common for the shower to be set within the bathtub in Chile.

I now realize that I could fall over at any time, that this or that could happen to me. I made some changes to my bathroom, took the bath out, installed a shower space, which is about this high, so I don't have to lift my legs much to get in, meaning that I won't stumble. I've got handrails, in the bathroom, to hold on to, but I don't wash standing up in the shower because it's a nightmare for me, which is why I've got a special seat, like a special stool, and I use the showerhead to splash myself with water. I use the soap to wash myself, but it takes me a long time.

After washing, participants get dressed. Some do this slowly albeit on their own, while others require help, for example, from their children:

It takes me a long time, but I can do it. With the bra, I can't do it up from the back. I put it on from the front and pull it up. To undo it, I turn it around because I can't do that normally either.

The majority of participants do not work and therefore undertake domestic chores after the completion of their personal hygiene routines. A common theme that arose in the accounts of the participants is whether or not they receive assistance in performing these domestic chores. In particular, this included whether or not they employ a nana (housekeeper) to assist them in certain domestic tasks.

I find it difficult to make the bed, I... I simply tidy it up. Later, when my daughter or the nana come, they make it properly. I just tidy it up, I don't make it properly. I mean, I do it lazily. Afterwards, when I have to run an errand, pay the bills, or go to the doctors, I go out, and a young girl comes (to help out in the house) once a fortnight. I keep some areas clean, where I can, and when the young girl comes, she does a more thorough clean.

In the evenings, the participants rest or carry out light activities, such as watching television, sharing time with grandchildren, knitting or, in some cases, attending physiotherapy sessions or medical appointments. Furthermore, none of the interviewees are responsible for caring for their grandchildren. Rather, they mentioned that they simply visit

them on a regular basis and frequently accompany them on daily activities.

After lunch, I walk to my son's house, which is nearby, about one block in fact. There I take care of my grandson, with the help of the nana too. I just accompany them really. I rest a bit with him, and we go for a walk at about half past four. We walk for an hour, or an hour and ten minutes. Slowly, but we walk for an hour and ten minutes. That's what we do every day.

Finally, participants go to sleep, but in some cases, they wake up at night, because they feel pain.

No, I can't sleep very well. I used to sleep soundly [...] I think all of this is the result of all the traumas I've been having, health wise...

3.2. Impact of Pain on Older People. Pain produces disability and affects the way in which the participants are able to perform their daily activities. The majority can sit without problems, but they find other activities (walking, standing, and lifting items) more difficult.

Sometimes, to go to the bathroom, I can't even get there... especially when I have to hold myself up, I wake up wanting to cry because I think I'm going to fall [...] it's because I find it a real effort to stand up.

Chronic pain affects the emotional state of the participants involved in this study. Each female interviewee claimed to have (or have had) symptoms of depression (e.g., anhedonia). They suffer so severely from depression that they feel like another person entirely.

I feel really downcast, with no desire to do anything, because to top it all I have depression [...] I used to be really active, and now I'm not the same person.

Despite a number of participants using medicine for their depression, the majority of those who experience bouts of depression receive no medical attention for their symptoms. For example, they mentioned that rather than seeking out medical assistance, have sought support in spirituality via prayer:

No, none. What greatly helps me are the (Catholic) saints. I pray to our Lady of Guadalupe, to the Virgin Mary... I pray to all my saints, always.

The majority of participants feel that their social life has been limited and reduced by their pain. Two of the reasons for this are that they are unable to undertake the physical activities that they performed in the past and that they feel that other people are unable to empathize with them.

For two reasons: because I feel diminished and because people diminish you. They don't pay attention to you. It's as

if you are just left out of certain things. I have a friend here in Santiago, and she likes walking even more than I do. She likes going out. And so, I do... but I can't keep up with her. She makes me walk fast. Only once did she do this, and now I don't go out with her anymore.

The primary means of public transportation in Santiago is via the subway system or bus service. During their interviews, the participants indicated that these forms of transport were problematic. For example, the movement of the buses increases their levels of pain; the drivers close the doors too quickly when passengers are trying to disembark the bus; and most subway journeys have to be undertaken standing up, causing additional pain. In addition, accessibility is poor, for example, a number of subway stations lack facilities for people with physical disabilities:

When I [...] return home, there is no elevator in the closest station to where I live. There is no escalator either, so I go up the stairs slowly and I get to the top feeling exhausted, as though I have no more energy left.

However, this category presented dichotomous elements, since other participants mentioned that pain does not affect them as much, for example, regarding sleep or mood.

Not at all. It's part of life.

3.3. Social Support. The participants were satisfied with the social support they receive from their friends. These findings suggest that, although people have decreased their social activity, they still feel that their friends offer them support. This could be because friends maintain contact and provide support to them. For example, they mentioned that despite not being able to leave the house, their friends visited them at home:

*I have a group of friends and we all got together on Friday mornings to have coffee in J** coffee house, and the best part is, well... now, they come and see me. But like I said, it's not the same anymore.*

Most of the participants live with their adult children. The additional household members provide help with transportation and chores and take care of them.

My daughter calls me regularly. My son too, and they look after me well. I'm not alone because I'm with them.

However, some of the participants feel that their family members do not fully understand their disease. Specifically, this problem stems from the limited communication that exists between members of the family, stating that these kinds of issues are not discussed in the household.

I feel like I have no family support, and that communication with the family—especially with the people who I live

with on a daily basis—is a bit complicated because they work. So, in terms of communication, they often get home from work and do this, that or the other, and then simply go to bed... so communication is really lacking. If there were more communication, maybe the family environment would be more enjoyable.

They felt they were bothersome to their family and that their family no longer took them seriously. This causes them to downplay things and withhold their true feelings.

... because I get the feeling that they think that I'm doing it to myself, that it's a way of trying to draw attention to myself because I feel bad, in pain. I express it in the way I want to, and sometimes I have to hold back...

3.4. Treatment by Doctors. Regarding medical support, the participants are satisfied with the treatment received to date and they would return to receive the same treatment again. The majority of the participants have sufficient information and understanding about their illness and treatment, to the extent that some of them were able to describe their medical conditions in detail.

It's one of the things that caught my attention: the doctor was always very attentive. I mean, the doctor didn't just ask questions in passing; he gave me his diagnosis and information about what to do at home. He was always very attentive and that is why I trusted him. I felt comfortable, and I still feel comfortable with him.

3.5. Pain Control Strategies. It was difficult for participants to describe their pain. Rather, they recalled factors that contribute to its increase or decrease, or the feelings that it induces.

It's so difficult [...] it's hard to explain... How do I explain it? On one hand, it's tough to explain, and on the other, understanding the pain is difficult, because someone else would have to feel it. Even my daughter told me it can't hurt like that... well, but it can't be like that, but it hurts, what do you want me to do? You don't have a broken back. It's broken, what can I say... I didn't make it up... look at my X-ray...

In order to carry out their daily activities, participants frequently adopt certain actions or physical positions that help to mitigate their pain. These actions and positions have been borne out of the personal experience of each participant and were not taught by a health professional. As such, this behaviour should be understood of as a reaction and/or way to simply get through the day. For example, they described the position that they adopt in order to do the washing up: *"I stand up and go to the sink, walking with my legs apart, and straight, in line with my shoulders... that way I don't feel any pain"*. Another form of mitigating pain is to take short breaks, such as sitting or lying down: *"even when I'm cooking, sometimes I have to lean on something because*

I'm in so much pain, and I have to go and lie down in bed for a while, rest for about ten minutes and then I get back up and carry on with my chores."

The treatment received by participants in Chile with symptoms such as those experienced by the participants of this study includes medicine and/or physiotherapy sessions. Some participants use painkillers and the majority require this type of drug in order to be able to go about their daily lives.

Some participants additionally use alternative therapies to reduce their pain:

The most effective thing for me has been acupuncture. It has helped me quite a lot. It doesn't make the pain go away completely but it does lessen it. But this approach involves commitment and I'm going to keep it up. I asked the doctor about it and he said yes, absolutely. [...] Among things that are not medical-based, acupuncture is what I like the most, and it's paying off.

Participants mentioned that they have trouble sleeping at night and that in order to mitigate their pain, they have to find a physical position that allows them to go to sleep, or they take sleeping pills.

Well, I've always slept badly. It's difficult for me. I have suffered from insomnia in the past, but now it's more because if I roll over in bed I have to hold on to the headboard in order to move, and by then I have woken up. I find nights hard... they're difficult for me.

In spite of the difficulties of living with this disease, the participants interviewed in this study attempt to be positive and remain active. For example, *"I try not to spend too long lying down. I try to walk, to anywhere I can. I walk to the kitchen, I try to do other things too... things that I can manage"*. Likewise, they employ a range of strategies to control their emotional state:

I'm not saying that I don't get down sometimes, because I'm not perfect. [...] If I'm feeling a bit down, like I don't want to get up, I get up anyway. I don't let it overcome me. Sometimes I can't even be bothered to cook for myself, but I still make something all the same. I took a little course on controlling my mental state and I'm using what I learned now. I never used to use it, it always seemed pointless to me... but now I find it really useful.

4. Discussion

Chronic pain is a complex phenomenon, composed of dichotomous categories and characterized by multiple components that modify and/or alter its manifestation and increase or decrease its intensity. These results are comparable to previous related research [6, 15, 38]. Older people in this study described their pain experience as incapacitating and, therefore, life changing, impeding the execution of daily activities and requiring rest after their completion. In previous studies, older adults with vertebral deformities had functional

limitations and difficulty with activities of daily living [39]. Older people in Chile, however, do not want to depend on other people, so they try to do their personal grooming and housekeeping activities, although they do slowly or incompletely, sometimes requiring assistance anyway.

A further area of difficulty faced by the participants in their daily lives is public transportation; this restricts their ability to leave their homes to undertake personal tasks and attend doctor's appointments or social activities. Chilean seniors like to communicate face to face or meet with members of their peer group in person, but problems in public transportation minimize the possibility that they can carry out this type of social interaction. This finding is particular to the location of our research, as many subway stations do not have elevators, some do not have escalators, and buses generally have a few high steps. Evidence of similar issues have been found in other developing countries, e.g., older women with vertebral fractures chose to use private, rather than public, transportation [12].

Chronic pain has further repercussions on personal experiences related to emotional well-being and social relationships. With respect to social relations, participants are prevented from attending social events or are limited to making plans in advance due to the unpredictable nature of the disease [14]. Therefore, the social life of participants living with chronic pain is limited or reduced. However, our study shows general satisfaction in regard to the support received from friends, despite indications that their social relations have changed since they began to experience chronic pain. Older people in Chile usually prefer to meet members of their peer group in person, for recreational activities, mutual support, and general company, as well as to share common experiences [40]. The aforementioned is due to the close relationships that they culturally have with friends and families. In our study, participants felt that friends and family are in contact with them, either through home visits or phone calls, which generates a feeling of support. The cultural obligation for families to provide care for older people, combined by the participants' feelings that others are not empathetic towards their condition, causes some tension in family relationships. This suggests that treatment of these people should include their families, in order for them to understand the complexity of this disease.

Regarding emotional well-being, the two participants who said that they had experienced no bouts or symptoms of depression as a result of their back pain were men. In contrast, the remaining eight participants, all of whom were women, indicated that they had either had or still have certain symptoms of or, indeed, diagnosed, depression. These findings coincide with evidence provided by a Canadian investigation in which people with chronic pain and who experience major depression are primarily older women [41]. In Chilean culture, women traditionally have the responsibility to manage household chores and care-related tasks, so not being able to fulfil them causes frustration, stress, and depression.

Satisfaction with medical treatment and the trust of participants in their physicians is stated in interview

testimony. The way in which participants perceive health care professionals, in regard to their availability, explanation of treatment, and susceptibility to the feelings of the affected individual, can be an important factor in their trust of the treatment received. Practitioners who try to form warm and friendly relations with their patients show more positive results in terms of patient health than practitioners who conduct their consultations in an impersonal, formal, or uncertain manner [42]. There is evidence of patient satisfaction with doctors who are sensitive to their experience [43], and the inverse has also been reported [15, 44]. Participants in our study were treated by only one team of physicians with a similar demeanor and training, which explains the participant's satisfaction with their treatment.

Faced with their chronic pain and spine deformity, the study participants stated that they try to retain a positive mental attitude and have developed coping strategies to mitigate the pain in the daily lives. These strategies include adopting analgesic positions, utilizing a range of devices, avoiding the execution of certain actions, taking pain medicine, and requesting assistance from others. Therefore, they have adapted to their new reality of living with a spine condition, particularly in relation to the chores and activities that they are able to carry out. It should be noted that the coping strategies of our participants have arisen from the basis of their understanding of their condition and their personal experiences; according to their interviews, the coping strategies were not taught or provided by health care professionals.

5. Conclusions

This study found that pain caused by spine deformity is a unique, personal, and subjective experience with no clear or specific definition. As a consequence, it is difficult for the individuals who experience this pain to characterize and describe what they feel, and it is equally hard for people who do not experience it to understand what it is like. This article has described the experience of older people living with chronic pain brought about by spine deformity, specifically in relation to the Chilean context. This research provides an in-depth understanding of the day-to-day life experiences of the subjects and how the chronic pain affects their quality of life from a cultural and contextual perspective.

The results suggest that these participants have very close ties with their children, so the family must be part of the treatment, so that the family can understand the situation they are undergoing. In addition, governments must improve the conditions of public transport, which helps people with chronic pain to move to medical care and meet with families and friends, thus improving their quality of life.

Data Availability

The interview data used to support the findings of this study have not been made available because they are restricted by the Pontificia Universidad Católica Ethics Committee in order to protect patient privacy.

Conflicts of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Research Article

Pain Acceptance and Its Associated Factors among Cancer Patients in Mainland China: A Cross-Sectional Study

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Background. Pain acceptance is associated with disability, pain interference, depression, and anxiety. Few studies have been conducted on the acceptance of cancer pain and its correlates. **Objectives.** The aim of this study was to examine the level and correlates of pain acceptance in cancer patients from mainland China. **Setting and Participants.** The study comprised 156 cancer patients in a tertiary cancer hospital in Hunan Province of China. **Design.** The study is based on a cross-sectional survey design. **Subjects and Methods.** The 8-item Chronic Pain Acceptance Questionnaire (CPAQ-8) was completed by 156 cancer patients with chronic pain from a tertiary cancer hospital. Demographics, pain, and negative mood assessed by the Hospital Anxiety and Depression Scale (HADS) were explored in relation to the CPAQ-8 scores using descriptive univariate analysis. **Results.** For the 156 patients, the mean CPAQ-8 score was 25.99 (SD = 8.56; range: 9 to 44). The scores were associated with age, gender, marital status, pain duration, number of pain sites, and duration of taking analgesics. The total scores on the CPAQ-8 and its two subscales (activity engagement and pain willingness) were negatively correlated with the HADS scores. **Conclusions.** The findings suggest that the prevalence of pain acceptance is relatively low for Chinese cancer patients. The cancer pain acceptance is affected by age, gender, pain duration, number of pain sites, and duration of taking analgesics. The acceptance of cancer pain is negatively correlated with depression and anxiety. Therefore, patients with risk factors for low pain acceptance should receive more attention in Chinese medical settings.

1. Introduction

In 1995, the American Pain Society (APS) voiced the slogan “pain: the fifth vital sign” to elevate awareness of pain treatment among healthcare professionals [1]. As the third global public health problem, chronic pain (CP) refers to pain or discomfort that has persisted continually or intermittently for longer than three months [2]. The prevalence of moderate to severe general CP among Dutch adults was estimated to be 18% [3], whereas estimates for Canada ranged from 11% to 44% of the adult population [4]. In a systematic review of 52 studies, the prevalence of cancer-related pain ranged from 33% to 64% of cancer patients,

making it one of the most common and troublesome symptoms affecting patients with cancer [5]. Chronic pain is significantly associated with lower quality of life and higher psychological distress [6]. Moreover, pain could cause the onset of depressive or anxiety disorder in 15.5% of participants with no previous history of the disorder and no current depression or anxiety [7], and the coexistence of depression and anxiety with chronic pain is strongly related to more severe pain [8].

Cognitive behavioral therapy (CBT) is one of the best-known nonpharmacological interventions that have been studied extensively for chronic pain. An integrative review concluded that CBT reduced pain intensity in 43% of trials

[9]. However, a review that applied strict inclusion criteria in identifying studies for analysis showed that CBT produced small effects on pain, particularly at follow-up, which may be caused by the lack of a clear treatment process within CBT [10]. In recent years, there has been growing interest in acceptance and commitment therapy (ACT), the third wave of CBT, which focuses on helping people disengage from unsuccessful efforts to control or avoid an unpleasant experience and instead accept it and move forward, pursuing valuable goals [11]. It has roots in learning theory and basic processes of language and cognition guided by relational frame theory [12]. ACT is based on the psychological flexibility model. Psychological flexibility has been defined as the capacity to persist in or change behavior, guided by one's goals that incorporate conscious and open contact with thoughts, feelings, and sensory experiences [12, 13]. The ultimate goal of ACT is to increase psychological flexibility through six core processes: acceptance, defusion, self-as-context, present moment, values, and committed action [11]. An ACT-based treatment for chronic pain patients could reduce levels of depression, pain-related anxiety, physical and psychosocial disability, and pain intensity and significantly increase psychological flexibility [14, 15]. In ACT-oriented interventions, psychological flexibility has been found to play a mediating role in improving functioning and life satisfaction in people with chronic pain [16].

Acceptance is a key part of ACT core processes. It involves the active and aware embracing of those private events occasioned by one's history without unnecessary attempts to change their frequency or form, especially when doing so would cause psychological harm [11]. An ACT cross-sectional study on participants with chronic pain found that acceptance may have a mediating effect on change in physical functioning [17]. Psychological flexibility is not easy to measure, but acceptance, which is related to psychological flexibility [18], can be assessed by a questionnaire. The higher a person's pain acceptance level, the better his/her psychological flexibility.

Pain acceptance is individuals' willingness to continue to actively experience pain along with related thoughts, feelings, and actions to move forward with their goals or act on their values while experiencing pain [19]. It can be assessed by the Chronic Pain Acceptance Questionnaire (CPAQ) [20, 21], which has been found to have the best overall reliability and validity among a number of pain acceptance questionnaires [22], including two subscales, pain willingness, and activity engagement. Pain willingness reflects efforts directed at controlling pain, while activity engagement reflects the degree to which a person continues to engage in personally meaningful activities despite pain.

A number of intervention studies have indicated that ACT can increase pain acceptance, improve quality of life, and decrease pain intensity and anxiety symptoms [23, 24]. Pain acceptance predicts depressive symptoms, pain-related negative affect, pain interference, performance in everyday living activities, inpatient hospitalizations, and painkiller consumption [25, 26]. Additionally, pain acceptance mediates the relationships between perceived injustice and physical function, opioid use status, and pain intensity [27].

Higher pain willingness is associated with lower disability and pain interference; less depression, anxiety, stress, and isolation; and more mindfulness [28–30]. In addition, the acceptance of cancer pain is related to increased psychological well-being and decreased depressive symptoms and pain catastrophizing [31]. Therefore, paying close attention to patients' pain acceptance status and helping them to accept and acknowledge their pain could help them adapt to pain and ensure better functioning and quality of life despite chronic pain.

Although some research has been conducted on pain acceptance, few studies have examined pain acceptance and its correlates among cancer patients. The present study aimed at examining the level and correlates of pain acceptance in cancer patients from mainland China in order to understand the general pain level among cancer patients and identify patients with poor pain acceptance, which can facilitate the implementation of ACT interventions as early as possible.

2. Methods

2.1. Design. We used a cross-sectional survey design, where patients were nested in wards of Hunan Cancer Hospital, a tertiary cancer hospital in the middle south of mainland China.

2.2. Subjects and Procedure. Cancer patients with chronic pain consented to participate in the study in a tertiary cancer hospital in Hunan Province of China from November 2016 to May 2017. In China, hospitals are accredited as primary hospitals (community health centers), secondary hospitals (local hospitals or regional hospitals), or tertiary hospitals (comprehensive general hospitals and large specialized hospitals). Tertiary hospitals have the most highly skilled professionals and the best medical resources, which draw patients from all over China. Therefore, adequate samples were available in the hospital for our study. The inclusion criteria were that patients (1) were diagnosed with cancer; (2) were aged 18 and over; and (3) had a duration of pain >3 months, with pain everyday or almost everyday. The exclusion criteria were that patients had (1) a history of psychosis, cognitive impairment, or communication disorders or (2) participated/been involved in certain psychotherapy programs within the previous three months.

The sample size was estimated by the statistical calculation formula of a cross-sectional survey of related factors [32]. According to a previous report [21], the standard deviation of CPAQ-8 was 9.36, assuming the admissible error does not exceed 3 [33], on the basis of a two-tailed α at a significance level of <0.05, at least 150 subjects are required to detect for status survey and related factors analysis of CPAQ-8. The research was endorsed by the Ethics Review Committee of the Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University/Hunan Cancer Hospital (No. SBQLL-2016-002). Prior to the enrolment of the study, participants were clearly informed the objectives, confidentiality considerations, and the

anonymity in data collection, analysis, and report. All of the questionnaires were completed by individuals with no interference. The investigators assisted those who could not complete the questionnaires independently. The process was voluntary, and participants could choose to discontinue at any time. All participants signed an informed consent form. For the patients who scored very pathologically in both questionnaires, the psychological counselors who worked in the psychological care unit of the hospital will provide free psychological comfort and counseling.

2.3. Measures. All the primary data were collected by investigators of the research team. Demographic and clinical information were collected with a brief demographics survey including participants' age, gender, education, marital status, economic status, and self-perceived religiosity information. The pain information items assessed the number of pain sites, pain duration, and medication use of subjects.

The acceptance of chronic pain was measured with the 8-item Chronic Pain Acceptance Questionnaire (CPAQ-8), a validated short version of the original CPAQ 20-item scale [20]. Four items (1, 3, 5, 6) assess activity engagement (AE), and four of them (2, 4, 7, 8) evaluate pain willingness (PW). The items are rated using seven-point scale ranging from "never true" to "always true" (0 to 6). When obtaining the total score, pain willingness is reverse-scored. The maximal score of the questionnaire is 48, with higher scores indicating better acceptance of pain. The Chinese version of the CPAQ-8 has excellent reliability and validity, with an alpha coefficient 0.84, CMIN/DF = 1.832, NNFI = 0.962, CFI = 0.98, GFI = 0.967, and RMSEA = 0.061 [21].

Anxiety and depression levels were assessed with the Hospital Anxiety and Depression Scale (HADS), which is a 14-item inventory used to examine the degree of anxiety and depression disorders of patients in nonpsychiatric hospitals [34]. The HADS has two subscales—the anxiety subscale (HADS-A) and depression subscale (HADS-D)—each consisting of seven items. A four-point Likert scale (0–3) is used to rate the items. A higher score represents more severe psychological distress. This instrument is widely used in clinical settings, and the Chinese version used in the current study has sound reliability, with Cronbach's alpha coefficient 0.832. Cronbach's alpha coefficients of the HADS-A and HADS-D subscales are 0.753 and 0.764, respectively [35].

2.4. Data Management and Statistical Analyses. Data were entered by two persons, and the missing and outlier data were examined carefully later. Descriptive statistics were used to describe the baseline characteristics and outcome measures. We treated CPAQ-8 and HADS scores as continuous variables and baseline characteristics as nominal categorical variables. The independent sample's *t*-test and one-way analysis of variance (ANOVA) were conducted to identify patient demographic characteristics and pain information associated with pain acceptance.

To further explore the correlation between pain acceptance and HADS, we measured Pearson's product-moment correlation coefficients. All of the statistical tests were two-

tailed. A *P* value <0.05 was considered statistically significant. Data analyses were performed using IBM SPSS Statistics 22 for Windows (IBM Corp., Armonk, NY).

3. Results

3.1. Sample Characteristics. A flow diagram outlining the selection of the study participants is shown in Figure 1. To increase the power of test, a total of 186 cancer patients were registered in the present study. One ineligible subject was excluded primarily because of having a history of communication disorder, whereas 21 ineligible subjects had participated in psychotherapy programs in the past three months. Of the eligible patients, five refused to participate during the process, and three questionnaires had missing data. Finally, a total of 156 questionnaires (response rate, 83.9%) were included in the analysis. The amount of participants could meet the estimated sample size.

Table 1 shows data on patient demographics and pain characteristics. Participants averaged 52.3 years of age (range: 24 to 77). Eighty-three (53.2%) of the patients were male, and 73 (46.8%) were female. Most of them (148, 94.9%) were married, and 150 (96.2%) were not religious. As for pain information, 134 (85.9%) of the participants had pain that lasted for 3–6 months, 135 (86.5%) had no more than three pain sites, 148 (94.9%) were using painkillers, and 140 (89.7%) had taken the analgesic for 3–6 months.

3.2. Relationship between Sample Characteristics and Pain Acceptance. The *t*-test (gender, marital status, self-perceived religiosity, pain duration, condition of painkillers usage, and duration of taking analgesics) and ANOVA (age, education, economic status, and number of pain sites) were used to examine the relationships between participants' general information and pain acceptance. As seen in Table 1, the results showed that victims' pain acceptance was significantly correlated with their age ($P = 0.048$), gender ($P < 0.001$), marital status ($P = 0.001$), pain duration ($P = 0.022$), number of pain sites ($P = 0.010$), and duration of taking analgesics ($P < 0.001$) but had no significant correlation with the condition of painkiller usage.

3.3. Correlation Analysis of Pain Acceptance and Negative Emotions. Pearson correlation coefficients were calculated to explore the relationship between pain acceptance and psychological distress. As expected, the results showed that high acceptance was associated with low anxiety and depression. The strongest relationships were found for the HADS total score and the CPAQ-8 ($r = -0.625$, $P < 0.01$), pain willingness ($r = -0.585$, $P < 0.01$), and activity engagement ($r = -0.554$, $P < 0.01$) (Table 2).

4. Discussion

This study aimed at exploring the level of pain acceptance among cancer patients in China, as well as its correlations with general information and HADS. We found that the average prevalence pain acceptance of Chinese cancer

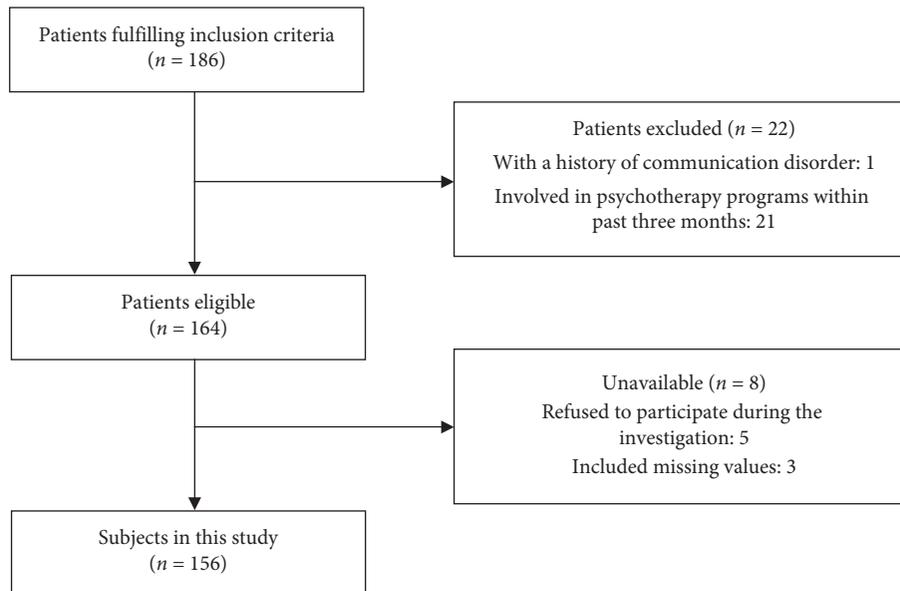


FIGURE 1: Flow chart outlining derivation of the sample.

patients was 25.99 (8.56), which was lower than the result of 27.90 (6.55) for chronic pain participants in Australia [36] and the result of 32.78 (9.36) for noncancer chronic pain patients in China [21]. Different from other nonmalignant chronic pain, cancer pain is a complex physiological, pathological, and emotional experience. It can be related to the tumor itself, diagnostic/therapeutic procedures, or treatment-associated adverse events [37]. According to a systematic review, the overall prevalence of cancer-related pain could range from 50 to 70% [5]. In another study, 31–45% of patients rated their pain intensity as moderate or severe [38]. Cancer pain is closely linked to insomnia, fatigue, and increased perceived disability. The patients are often preoccupied by their suffering and fear of death, which would greatly impair their acceptance of pain. They find it hard to be involved in normal life, participate in value-direct activities, and pursue their own goals in the presence of pain.

Our univariate analysis showed that different socio-demographic data, including age, gender, pain duration, number of pain sites, and duration of taking analgesics, were associated with distinct levels of pain acceptance. We found that the pain acceptance of participants aged over 70 ranked the highest, followed by those aged between 51–70 and 18–30, whereas those aged 31–50 had the lowest acceptance. This finding partially differs from that of a previous study, which verified that age is positively associated with pain acceptance [39]—in other words, older patients will have better pain acceptance. One possible reason for the discrepancy is the economic and social diversity of the subjects. Some of the participants in the middle age range of 31–50 years of age were born after the one-child family planning policy of the early 1980s in China. They need to support the elderly and raise the young in their family and have undertaken tremendous burdens. Once they have been admitted to hospital as cancer patients, they will suffer from great pressure, which could influence their pain acceptance.

Compared with women, we found that men had better pain acceptance. Personal characteristics may lead to the low level of pain acceptance in female cancer patients. However, another study argued that because of close family and friends in their social life, women with CP would have greater social support, which helps to promote pain acceptance [40]. A possible explanation for the contrast is that, in the context of Chinese traditional culture, women are more likely to suffer from stigma, value vanity, and conceal their real feelings.

Furthermore, our results showed that the degree of pain acceptance decreases as the number of pain sites increases. Cancer patients who suffer from multisite pain have to make pain control their top priority and may have trouble getting on with their normal routine. The fear of pain hinders them in leading a full life. Our results also showed that participants with longer durations of pain and analgesic usage had higher acceptance scores, which is consistent with a previous study [39]. The likely reason for this is that the cancer patients gradually adapt to the change brought by pain. Patients with longer pain and analgesic usage durations have more pain control knowledge and experience; they can take active initiative to reduce the physical and psychological impact of pain in daily life and choose to spend their time in a meaningful way in their daily lives according to their own values.

Our findings suggested that the pain acceptance level of married patients is significantly lower than that of those who are single, divorced, or widowed. The reason may be that married patients have to shoulder more family responsibilities and pressures. However, most of the participants in our study (94.9%) were married. The sample size of unmarried, divorced, or widowed patients was too small to reflect the real differences in patients' levels of acceptance.

Consistent with past research [21, 41–43] and hypotheses, bivariate correlation coefficients demonstrated that AE, PW, and total pain acceptance were negatively correlated

TABLE 1: Relationships between sample characteristics and pain acceptance.

Characteristics	Total (<i>n</i> = 156)		Pain acceptance (mean ± SD)	<i>t</i> / <i>F</i>	<i>P</i> value
	<i>n</i>	%			
Age (years)				2.699	0.048
18–30	9	5.8	26.4 ± 11.3		
31–50	61	39.1	23.7 ± 9.0		
51–70	75	48.1	27.4 ± 7.8		
>70	11	7.0	28.7 ± 6.6		
Gender				11.796	<0.001
Male	83	53.2	31.5 ± 5.7		
Female	73	46.8	19.7 ± 6.8		
Education				0.477	0.699
Illiteracy/primary school	28	17.9	27.5 ± 7.0		
Middle school	63	40.4	25.4 ± 8.3		
High school	52	33.3	26.2 ± 9.1		
College or above	13	8.3	25.0 ± 11.0		
Marital status				−3.517	0.001
Married	148	94.9	25.5 ± 8.3		
Unmarried	8	5.1	36.0 ± 7.3		
Religious faith				−0.002	0.999
No	150	96.2	26.0 ± 8.6		
Yes	6	3.8	26.0 ± 7.1		
Income (RMB)				0.439	0.646
<3,000	74	47.4	26.6 ± 8.7		
3,000–5,000	60	38.5	25.7 ± 8.2		
>5,000	22	14.1	24.8 ± 9.5		
Pain duration (months)				−2.320	0.022
3–6	134	85.9	25.4 ± 8.4		
>6	22	14.1	29.9 ± 8.7		
Number of pain sites				3.881	0.010
1	53	34.1	28.6 ± 7.5		
2	37	23.7	26.1 ± 8.9		
3	35	22.4	25.3 ± 8.8		
>3	31	19.8	22.3 ± 8.5		
Analgesic application				0.256	0.798
No	8	5.1	26.8 ± 10.4		
Yes	148	94.9	26.0 ± 8.5		
Duration of analgesic use (months)				6.303	<0.001
<3	9	5.8	15.3 ± 2.9		
3–6	125	80.1	26.3 ± 7.9		
>6	14	9.0	29.9 ± 10.2		

TABLE 2: Correlations between CPAQ-8 and HADS.

Anxiety and depression	Pain acceptance		CPAQ-8
	Activity engagement	Pain willingness	
HADS-A	−0.461**	−0.479**	−0.515**
HADS-D	−0.534**	−0.573**	−0.608**
HADS total score	−0.554**	−0.585**	−0.625**

***P* < 0.01 (two-tailed). CPAQ-8: 8-item Chronic Pain Acceptance Questionnaire; HADS: Hospital Anxiety and Depression Scale.

with anxiety and depression levels; that is, higher acceptance of chronic pain is closely linked with lower depression and anxiety. A survey conducted in 686 patients with chronic pain also showed that high pain acceptance can reduce anxiety and depression [44]. This might be due to pain acceptance representing the ability to engage in activities in

the presence of pain without struggle [45]. In contrast, one study found that there was no significant effect of pain acceptance on depression [46]. This inconsistency may result from the heterogeneity of participants and may also be related to the small sample size of participants in that study.

Our study has several strengths. First, although many researchers have conducted surveys on chronic pain acceptance, most of the subjects had noncancer pain; furthermore, because of the differences in culture, economy, and healthcare systems, there was a need to carry out a study among secular Chinese cancer patients. To the best of our knowledge, this was the first study to explore pain acceptance among cancer patients in mainland China using CPAQ-8. Second, little has been known regarding the influencing factors of cancer-related pain acceptance, and our study helped clarify these. Third, with the proper application of our findings, early recognition and intervention

for low-acceptance individuals could be developed, which would serve as an important and innovative non-pharmacological intervention for pain.

This study also has certain limitations. First, this was a cross-sectional survey conducted in a single tertiary cancer hospital. Because of the limited sample sources, whether and to what extent our subjects could represent other cancer patients in China remains to be determined. Samples from cancer and pain departments in comprehensive hospitals and community clinics should be examined in future studies. Second, the disease information, such as the tumor stage, antineoplastic treatments effect, and life prognosis, is not reported in the sample characteristics. These factors might influence the level of pain acceptance. The next steps will commit to address the potential sources of bias. Third, the recruited participants did not receive any interventions in the hospital before the survey; hence, further empirical studies should measure the pain acceptance of patients before and after interventions. Finally, cancer pain is a comprehensive experience consisting of multiple dimensions that cannot be evaluated merely by questionnaire. A qualitative design is needed to gain insight into patients' feelings, ideas, and perceptions of pain in future research.

5. Conclusions

The present study contributes to the understanding of Chinese cancer patients' pain acceptance. The pain acceptance of Chinese cancer patients is relatively low compared with the findings for those with nonmalignant pain. Age, gender, pain duration, number of pain sites, and duration of taking analgesics are all factors that influence pain acceptance. Depression and anxiety are negatively correlated with the acceptance of chronic pain. Based on our findings, cancer patients who are aged between 31 and 50, female, affected by multiple-site pain and a short period of pain, taking painkillers for less than three months, and in a state of anxiety or depression should receive more attention in Chinese medical settings. Based on the awareness of pain acceptance, healthcare professionals should implement effective individualized acceptance-oriented interventions such as ACT to enhance pain acceptance and alleviate negative emotions, such as depression and anxiety.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Review Article

Topical Review: Basic Psychological Needs in Adolescents with Chronic Pain—A Self-Determination Perspective

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This topical review outlines the resilience pathway to adaptive functioning in pediatric pain within a developmental perspective. Self-Determination Theory proposes that the satisfaction of one's basic psychological needs (for autonomy, relatedness, and competence) is crucial for understanding human flourishing and healthy development. However, the role of the basic psychological needs received little attention in a pediatric-pain population. Yet, we propose that need satisfaction may be a resilience factor and need frustration a risk factor, for living with chronic pain. In this topical review, we first discuss two major models that have been developed to understand pain-related disability: the fear-avoidance model of pain and the ecological resilience-risk model in pediatric chronic pain. Both models have been used with children and adolescents but do not include a developmental perspective. Therefore, we introduce Self-Determination Theory and highlight the potentially moderating and mediating role of the basic needs on pain-related disability in children and adolescents. Taken together, we believe that Self-Determination Theory is compatible with the fear-avoidance model of pain and the ecological resilience-risk model in pediatric chronic pain and may deepen our understanding of why some adolescents are able to live adaptively in spite of chronic pain.

1. Introduction

Children and adolescents frequently experience pain [1]. About 25% of young people report persistent pain (>3 months) [2] and 8% of them describe their pain as severe and disabling [3, 4]. Thus, chronic pain can significantly disrupt the development of children and adolescents and hamper the pursuit of personal goals [5–7]. Paradoxically, at the same time, many youngsters with chronic pain are able to live adaptively and pursue personal goals, in spite of experiencing chronic pain [3, 6, 8, 9]. An important question to consider, then, is *why* some children and adolescents are able to live adaptively and to continue pursuing their personal goals in spite of their chronic condition, while others are not. The aim of this topical review is to outline the resilience pathway to adaptive functioning in pediatric pain within a developmental perspective. Specifically, we draw upon Self-Determination Theory (SDT [10]) to argue that the satisfaction of one's basic psychological needs and their contextual support are important resources for adolescents to

live adaptively with chronic pain (Figure 1). Thereby, we consider various types of chronic pain, as evidence has shown that the emotional, behavioral, and psychosocial factors influencing functional disability are generally similar across different types of pain [11].

For many years, the Fear-Avoidance Model of pain (FAM) [12] partially explains the dynamics involved in chronic pain and has been one of the principal guiding frameworks for research on chronic pain in both adults [13] and children [14, 15]. This model describes risk mechanisms for disability at emotional (e.g., fear), cognitive (e.g., catastrophizing), and behavioral (e.g., avoidance) levels and has been extended to the interpersonal context [16]. First created in the context of chronic low back pain [17], the relevance of FAM has been generalized to other types of pain, such as headache [18], abdominal pain [19], neuropathic pain, and complex regional pain syndrome [20]. Recently, resilience mechanisms leading to recovery and adaptive living (as opposed to fear and avoidance) have

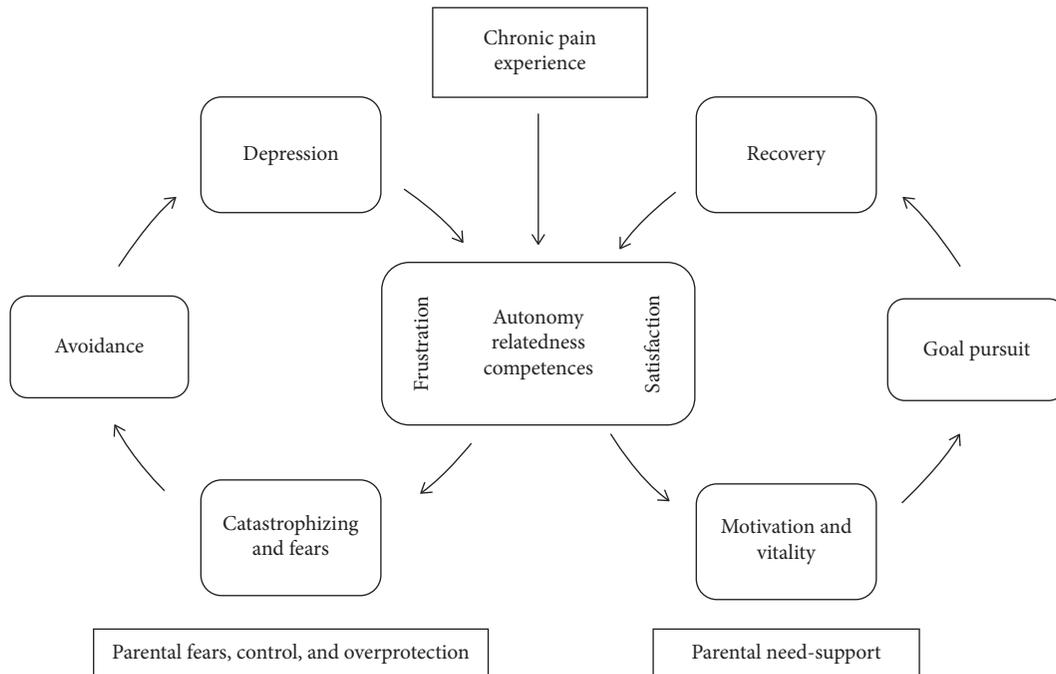


FIGURE 1: A Developmental Goal Pursuit Model of Chronic Pain. Need satisfaction facilitates goal pursuit while need frustration leads to avoidant behaviors. A need-supportive context improves needs satisfaction.

received increasing attention. In this context, restoring and pursuing personal goals (i.e., personally valued goals, such as school, professional, sporting, or social goals) has been shown to be an “antidote” to the fear-avoidant downward spiral among both adults and children [6, 21–23]. The ecological resilience-risk model of pediatric chronic pain [24] aimed at deepening the understanding of resilience mechanisms in chronic pain, identifying resilience factors (such as optimism, positive emotions, and positive social interactions) that may foster adaptive living with chronic pain. In this context, personal goal pursuit would be considered as resilient mechanisms for adaptive living while fears, catastrophizing, and depression would be considered as risk factors.

However, although some research highlighted the importance of the development in pain-related outcomes [25, 26], none of those models explicitly considered developmental variables in their perspective of risks and resilience. In that respect, SDT [10, 27] may shed light on developmental processes related to risk and resilience in the context of chronic pain. SDT posits that personal goal pursuit, and optimal development in general, is facilitated through the satisfaction of one’s basic psychological needs (for autonomy, competence, and relatedness) and through the contextual support of these needs [28, 29]. In addition, SDT provides insight into the conditions under which parental involvement brings about positive or negative outcomes on need satisfaction.

This topical review aims to connect concepts coming from different theoretical fields. Specifically, by discussing the potential relation between the basic psychological needs, resilience resources (and more specifically the pursuit of personal goals), and risk factors (described in

terms of fear-avoidant mechanisms), we hope to foster our understanding of what makes adaptive living possible among youngsters with chronic pain. We will argue that children’s and adolescents’ psychological needs may often be frustrated by pain, but also that the contextual support of these needs may function as a resilience resource. Further, we will discuss the influence of parental need support on adolescents’ need satisfaction and goal pursuit. After introducing the fear-avoidance model of pain (with its extension on interpersonal mechanisms and goals pursuit) and the ecological resilience-risk model, we will present Self-Determination Theory and the basic psychological needs. Then, we will review the existing literature in pediatric chronic pain through the lens of SDT. Finally, we will provide an outline for future research and discuss clinical implications.

2. Fear-Avoidance and Resilience in the Context of Pediatric Chronic Pain

The *Fear-Avoidance Model of pain* [12] describes why and how people with pain may develop a chronic pain syndrome. This model asserts that when perceiving pain as threatening, an individual might have catastrophic thoughts and respond with pain-related fear and avoidance behavior which, in turn, would result in declines in functioning [12]. This, in turn, may lead to a vicious circle where fear leads to more avoidance, more pain, and impairment, as well as an increased risk for persisting pain. This theoretical model has been a major framework for guiding pain research and management in children, adolescents, and adults [13–15, 23]. In other words, fear and avoidance can be considered as risk factors for increasing

pain-related disability. The FAM also shows that engaging in important personal goals (e.g., professional, familial, or leisure goals) helps to get out of the downward spiral of fear and avoidance and may lead to recovery and adaptive living [30].

Initially, the FAM only considered individual variables—and not so much interpersonal ones—for defining risks and resources towards living with chronic pain. The *Interpersonal Fear Avoidance Model of pain* (IFAM; [16]) aimed to take into account interpersonal and contextual dynamics as well: indeed, one's response to pain is not only an individual process, as people are embedded in an interpersonal context, which may influence their experiences and reactions to pain. For example, in the context of pediatric pain, parental distress may considerably influence negatively the child's pain-related outcomes [31–35] and the perpetuation of pain-related disability [36, 37]. To illustrate, parents who interpret a child's pain expression through their own catastrophic thoughts and pain-related fears are more likely to engage in maladaptive parenting behaviors and to provide “miscarried” help, such as overprotecting their child, giving special attention, or keeping the child home from school [38–40]. Unfortunately, such miscarried help would further prevent the child from engaging in daily activities [16, 31, 41–43], as well as from pursuing his/her personal goals [44, 45]. In other words, by doing so, overly involved parents would involuntarily perpetuate their child's pain-related disability. It is also important to note that parental responses may also be influenced by the child's own personality and relation to his/her pain [46–48]. For example, children and adolescents who catastrophize about their pain and who engage in maladaptive behaviors (e.g., avoidance) might make it difficult for the parent to encourage engaging in adaptive behaviors.

A third model related to FAM, the *Goal Pursuit Model of Pediatric Chronic Pain* [6, 49] has recently been proposed. This model encompasses the interpersonal context of the IFAM [16] and goal pursuit as proposed in the FAM [23]. This goal pursuit model specifically focuses on child factors (e.g., the motivation to pursue a specific goal, pain-related anxiety, or fears) and parent factors (e.g., overprotective behaviors, anxiety, or fear about their child's pain), as both could hinder or encourage goal pursuit behaviors in youths with chronic pain [6].

Finally, the *ecological risk-resilience model of pediatric chronic pain* [24] describes resources and mechanisms that may lead to recovery and sustainability while living with chronic pain, identifying both individual and interpersonal resilience factors. Resilience is defined as a person's ability to respond effectively to adversity and people's resilience resources are influenced by developmental, social, cultural, and environmental factors [50]. For example, optimism, mindfulness, or positive emotions are considered as individual resilience resources, while positive peer relationships, social connectedness, or parents' and teachers' support are interpersonal resilience resources. In addition, specific resilience mechanisms might be activated when being confronted with pain. Individual resilience mechanisms are,

for example, self-efficacy, and psychological flexibility (i.e., responding in an effective and flexible way to adverse events, such as chronic pain [51]). Examples of interpersonal resilience mechanisms are parent's active coping, promotion of behavioral activation, and parents' psychological flexibility (encompassing values-based action, pain acceptance, and emotional acceptance) [52, 53]. By contrast, fears and catastrophizing are individual risk mechanisms, while depression and anxiety are individual risk factors. Parent solicitous responses, parent catastrophizing, and fears are interpersonal risk mechanisms, while parent poor health status constitutes a risk factor [24].

Taken together, researchers increasingly agree that (1) it is important to consider the interpersonal context and (2) the pursuit of personal goals may predict positive outcomes among children and adolescents with chronic pain, potentially serving as a resilience factor. However, the discussed models do not so much incorporate a developmental approach. Yet, doing so may help explain why one would engage either in goal pursuit or avoidant behaviors. Herein, we propose that Self-Determination Theory [54] may help us gain further insight into the factors that facilitate personal goal pursuit among children and adolescents with chronic pain.

3. The Added Value of Self-Determination for Understanding Pediatric Chronic Pain

Self-Determination Theory (SDT; [10, 27]) is a macrotheory of human motivation, emotion, and personality and can be situated within the positive psychology movement, as it attempts to explain how to support and enhance personal growth and human flourishing [55]. A key assumption of this theory is the existence of three basic psychological needs—the need for autonomy, competence, and relatedness. These needs are considered to be innate psychological nutrients, as their satisfaction would be essential for psychological growth, subjective well-being, and optimal human functioning, whereas their frustration would lead to maladjustment and the development of psychopathology [29, 56]. When satisfied in their need for *autonomy*, one would experience a sense of volition, personal choice, and psychological freedom in one's actions [29]. Autonomy frustration, by contrast, involves feeling forced or coerced to act in a certain way. Competence satisfaction refers to feeling effective and capable to achieve desired outcomes [57], whereas competence frustration involves feelings of doubt and failure concerning one's efficacy. The need for *relatedness* refers to the experience of intimacy and genuine connection with others [57]. Relatedness frustration involves the experience of relational exclusion and loneliness. Table 1 provides a summary and brief examples of the three basic psychological needs in the context of chronic pain. A growing body of research shows that regardless of age or cultural background, the satisfaction of these needs contributes to individuals' well-being, social adjustment, and motivation [28, 29, 58]. In addition, research increasingly confirms that need frustration may result in ill-being, maladjustment, and even psychopathology

TABLE 1: Definitions and examples of how children's/adolescents' three basic psychological needs can be satisfied or frustrated.

	Needs satisfaction	Needs frustration
Autonomy	Experiencing a sense of volition, personal choice, and psychological freedom in one's actions	Feeling forced or coerced to act in a certain way
Competence	Feeling capable to achieve desired outcomes	Feelings of doubt and failure concerning one's efficacy
Relatedness	Feelings of intimacy and genuine connection with others	Feelings of relational exclusion and loneliness

[56, 59–62]. Furthermore, there are studies showing that need frustration is also predictive of a lowered motivation to engage in personally valued goals [63].

Further, SDT underscores the importance of the environment for the satisfaction (vs. frustration) of one's psychological needs, with the parents playing a particularly crucial role throughout childhood and adolescence [10, 64]. In that respect, previous research found that an autonomy-supportive parenting style, which is characterized by perspective-taking, choice provision, and the support of initiative, is predictive of adolescent need satisfaction, which in turn is associated with higher well-being [65, 66] and less problem behavior [67]. Conversely, controlling parenting, which is characterized by the use of coercive, critical, and authoritarian parenting practices and a tendency to enforce the child to act, feel, or think in parent-imposed ways [68], is predictive of the frustration of the child's basic psychological needs, which in turn would relate to more internalizing and externalizing problems [69]. In addition, research drawing upon SDT showed that autonomy-supportive contexts foster children's pursuit of personally valued goals, as such contexts that satisfy children's psychological needs [70].

A limited number of studies applied the SDT framework in the context of health behavior. For example, it was shown that psychological need satisfaction facilitates the successful attainment of health-related goals (e.g., sticking to a diet; Ryan et al. [71]). Only a few studies have been conducted in a pain context. In one study among adolescents from the general population, it was found that teachers' support of autonomy and competence was a protective factor against school absence in youngsters with severe pain problems [9]. In a recent study among partners of adults with chronic pain, Kindt et al. [72, 73] found that higher levels of autonomously motivated help by partners (i.e., feeling free to help versus feeling forced to help) were related to better well-being, need satisfaction, and relationship quality which, in turn, related to better pain-related outcomes [72, 73]. Moreover, a longitudinal study by [74] showed that spousal autonomy support had a positive effect on well-being and need satisfaction of people with chronic musculoskeletal pain, and this is independent of pain intensity [74]. These findings suggest that a Self-Determination perspective is relevant in the context of chronic pain and especially for understanding mechanisms of goal pursuit within an interpersonal context.

4. Basic Psychological Needs in the Context of Chronic Pain

For children and adolescents with chronic pain, the presence of pain may challenge need satisfaction and the pursuit of

personal goals considerably [75, 76]. Thus, the frustration of their basic needs may explain why chronic pain is predictive of diminished goal pursuit, disability, and functional difficulties, hence playing a mediating role. At the same time, the contextual support of their needs may play a moderating role. That is, it may constitute a resilience factor that explains why some adolescents do well (and continue doing well), even under conditions of high pain. In other words, parents' (and other adults') need support would buffer against the negative effects of chronic pain for adolescents' functioning, as it would positively affect adolescents' need satisfaction.

The mediating role of the psychological needs and the moderating role of a need supportive context are summarized in Figure 1 and are elaborated in the next sections.

4.1. Autonomy and Chronic Pain

4.1.1. *Autonomy as a Mediator: "My Freedom and My Choices Are Constraint by My Pain"*. The development of a sense of autonomy is claimed to be a crucial developmental task for adolescents [77], which can be impaired because of chronic pain [26, 31]. However, the topic of autonomy in adolescents with chronic pain has received little attention until now. First, it is important to clarify the definition and conceptualization of autonomy, as it is a highly debated issue in the developmental literature [78, 79]. In that respect, recent research increasingly underscores the importance of distinguishing between two conceptualizations of autonomy, which has important implications for the question whether autonomy is (always) adaptive for adolescents, or whether offering too much autonomy may imply certain risks. A first definition of autonomy, which is rooted in SDT, conceptualizes autonomy as self-endorsed or *volitional functioning*, which refers to the extent to which one acts upon personally endorsed interests, values, and goals and feels a sense of freedom in his/her choices and actions [29, 79]. The opposite involves controlled or *pressured functioning*, in which case one feels obliged or coerced to act or think in certain ways. For example, in a chronic pain context, an adolescent's autonomy may be observed when his/her choices are congruent with his/her values and interests, for example, when an adolescent wants to become a doctor because he/she likes helping people in difficulty. Importantly, this conceptualization of autonomy should be distinguished from a definition of autonomy as *independence*, which refers to the extent to which one thinks, behaves, and takes decisions without relying on others [80]. The opposite of independence, then, is *dependence* or reliance on others, especially on parents. For instance, when an adolescent with chronic pain needs help from his/her parents to get to school, he/she is (functionally)

dependent on the parents. Research among normally developing adolescents has shown that independence (e.g., in family decision-making) gradually increases throughout adolescence [81]. However, research equally found that too much independence, especially when granted too early in adolescence, may relate to maladaptive functioning, including lowered well-being and more problem behavior [82]. Volitional functioning, by contrast, is unequivocally linked to more adaptive functioning, including higher subjective well-being, less behavioral problems, and higher-quality relationship with friends, regardless of adolescents' age [79, 83].

It is important to note that, in adolescence, independence and volitional functioning are not completely orthogonal, that is, there is a modest but positive relation between volitional functioning and independence [79, 83, 84]. In other words, independence may, on average, set the stage and allow for volitional functioning in adolescence. As these two conceptualizations of autonomy are distinct, several combinations are possible. Specifically, an adolescent may choose to decide independently because he/she personally values making the decision by him/herself, which constitutes volitional independence. However, he/she could also act independently because he/she feels pressured to do so. To illustrate, an adolescent might decide by himself about what to study at school because he personally values such independent behavior (i.e., volitional independence). However, he could also decide independently because he feels obliged to figure out things by himself, because his parents believe that he is old enough to decide and take care of his own business (i.e., pressured independence). Similarly, dependency might be volitional or pressured. An adolescent might choose to follow the decision of his/her parents because he/she fully endorses and values their opinion (i.e., volitional dependence) or he/she might follow his/her parents' decision to avoid feelings of guilt or for reasons of loyalty (i.e., controlled dependence; [83]).

This differentiation between autonomy as independence vs. volitional functioning is of crucial importance in the context of chronic pain. That is, chronic pain may easily impair one's independence; nevertheless, one's feelings of volition could remain relatively unaffected, because one may still act upon personally valued choices, even with chronic pain. However, to our knowledge, research on pediatric pain never took into account the distinction between volitional functioning and independence and mostly focused on the implications of pain for one's (in)dependent functioning. As our paper draws upon the SDT framework, we refer to "independence" when discussing studies focusing on adolescents' independent functioning (e.g., independence in decision-making, or distancing from parents) and "autonomy" when we refer to the adolescents' volitional functioning (i.e., acting in congruence with one's personal interests and values).

Previous research among adolescents with chronic pain indicated that these adolescents perceive themselves, and are perceived to be, more dependent on their parents than their peers [5]. That is, they report higher levels of closeness to their parents, show higher levels of dependence on them,

and report lower levels of independent decision-making [44, 46, 85]. Thus, these findings suggest that pain may impair adolescents' independence and may prevent them to undertake developmentally appropriate activities, such as attending school and spending time with friends or taking on certain responsibilities (e.g., completing chores at home; [26, 31, 44, 85]). Nevertheless, given the cross-sectional design of past studies, it remains unclear whether the high level of dependence is due to pain, or whether high levels of dependence cause the emergence of pain symptoms [26]; longitudinal research would be needed to shed light on the directionality of effects. Although autonomy might be thwarted by chronic pain, when satisfied, it might have positive effects on pain-related outcomes. Hence, supporting autonomy seems of crucial importance, as is discussed below.

4.1.2. An Autonomy-Supportive Context as a Moderator: "Feeling Supported by My Parents Helps Me to Live with Pain". In the developmental psychological literature, it is well accepted that an autonomy-supportive context (e.g., from parents, teachers, or peers) yields benefits for adolescents' psychological well-being, growth, and development [66]. Research increasingly suggests that this may also be the case in the context of pediatric pain (Palermo, 2012); [86, 87]. For example, one study showed that teachers' autonomy support (i.e., support of volitional functioning) was a protective factor for adolescents' school functioning, as it related to a higher school frequentation, better school grades, and less bullying experiences in highly impaired children and adolescents with chronic pain [9]. Similarly, in adults with chronic pain [72, 88] and in adults with diabetes [89, 90], autonomy support from a health-care provider and autonomously motivated help from the partner were both protective factors, predicting better adjustment for the person with pain or diabetes. Moreover, both autonomy support and autonomously motivated help had positive effects on treatment adherence and lead to better short-term and long-term treatment outcomes [89–91].

Some research focused on parents' support of independence in children with diabetes. These studies found that health outcomes were more positive, and treatment adherence was better when parents supported independent behaviors in the adolescent [92–94]. However, these studies focused on parental support of the adolescent's independence and not on the adolescent's autonomy as volition. Nevertheless, those findings support the idea that an autonomy-supportive context may be a resource, explaining why some adolescents do well (and even thrive) despite their heightened levels of pain.

From a Self-Determination perspective, parental involvement may be experienced as either autonomy-satisfying or rather as autonomy-frustrating, depending on the way in which it is implemented. For instance, parental overprotection, which is a type of over-involvement, is more likely to be perceived as controlling and hence, autonomy-frustrating, yielding either opposition and resistance (so rather externalizing types of problems) or

unhealthy dependence (and rather internalizing problems) [69]. However, when parental involvement is conveyed in an autonomy-supportive way, where parents are sensitive for the adolescents' needs, as well as for their values and goals, parental involvement is less likely to lead to problematic outcomes. In sum, a context of parental, teacher, or health-care autonomy support may foster autonomy satisfaction among adolescents with chronic pain, thus buffering against the negative effects of pain and pain-related disability. Future research is needed to test this in the context of pain.

4.2. Competences and Chronic Pain

4.2.1. Competence as a Mediator: "Because of My Pain, I Can't Concentrate at School and My Grades Decline". Adolescents' feelings of competence are often compromised by chronic pain, because engaging in school and leisure activities and performing physically is often a challenge in the presence of pain [95–99]. Many studies showed that chronic pain is associated with higher school absenteeism and a decline in school grades [3, 97, 100–103]. Surprisingly, however, this decline in school grades is not directly correlated with pain intensity [9, 101]. Moreover, research has shown that adolescents with chronic pain experience higher levels of worrying and more fear of failing than their healthy peers, particularly regarding academic or athletic performances [104, 105]. That is, experiencing pain interference in academic performances brings frustration in the need for competence, which may contribute to avoidance behaviors and patterns of long-term disability [101, 106]. A review by Sinclair et al. [34] found that feelings of incompetence among adolescents with chronic pain were associated with increased activity avoidance and disability and limited the development of adequate strategies to manage pain [34]. Prolonged avoidance and absenteeism might in turn intensify the feeling of incompetence and decrease the motivation to attend school or any other activity, thus creating a downward spiral: chronic pain impairs the satisfaction of the need for competence, which, in turn, triggers avoidant mechanisms, further impacting the well-being of adolescents with chronic pain negatively.

Another aspect of competence is self-efficacy, which, in this context, involves an adolescent's self-perception of being capable of dealing successfully with pain [34]. Self-efficacy in adolescents with chronic pain was positively correlated with quality of life, fewer somatic, behavioral or emotional symptoms, and higher self-esteem [107]. Moreover, higher levels of self-efficacy related to lower levels of experienced pain and other pain-associated symptoms, such as depression and catastrophizing thoughts [107, 108]. In adults with chronic pain as well, feelings of self-efficacy were associated with several positive outcomes, such as better health and physical functioning, and more satisfaction at work and with lower levels of pain intensity, disability, and less depression and fatigue [109]. In sum, competence frustration and perceptions of self-efficacy may mediate the relation between pain and functional disability. In addition, a potential bidirectional relationship between competence

and pain-related outcomes might be observed. That is, pain might impair adolescents' feelings of competence satisfaction, yet at the same time, competence satisfaction (and its support) might foster adaptive living with chronic pain, as is argued below.

4.2.2. A Competence-Supportive Context Is a Moderator: "Feeling Supported in My Competences Helps Me to Pursue Important Goals". Although adolescents' feelings of competence can be challenged by the presence of pain, a competence-supportive context may be a moderating factor in the relation between pain and functional disability [98]. Youngsters are less inclined to use avoidant mechanisms and are likely to experience less pain-related disability when they feel supported by parents, teachers, or peers in their need for competence, through their engagement in an academic, social, or athletic context [34, 95]. To illustrate, a study by Bursch et al. [108] showed that children from parents who were the most confident about their child's ability to manage pain experienced less somatic symptoms and a better functioning in the child [108]. Thus, parental provision of competence support and their confidence in their child's ability to deal with pain might reduce avoidant behaviors (e.g., towards school or leisure activities) and limit the resulting decline in competences.

Not only parents' but also teacher support may be important. A study of Vervoort et al. [9] showed that teachers' competences support of children with pain improved school attendance despite pain and minimized bullying experiences. Therefore, parents' or teachers' support of the adolescents' competences and self-efficacy may have a moderating role and may constitute a resource to limit avoidant mechanisms, pain-related functional disability, and thus facilitate the pursuit of personal goals.

4.3. Relatedness and Chronic Pain

4.3.1. Relatedness as a Mediator: "Living with Pain Makes Me Feel Lonely and Misunderstood". The third need distinguished within SDT is the need for relatedness, which can also be frustrated by chronic pain. Indeed, adolescents with chronic pain frequently report difficulties in social functioning [110–113]. They often feel different and misunderstood by their peers, partly because living with pain makes them having to carry more responsibilities than other adolescents of their age [96, 111, 114]. For example, they have to know how to deal with medication or to make conscious choices about their activities in order to avoid potential negative consequences (e.g., more pain, more fatigue) [31]. Compared to healthy adolescents, those with chronic pain report less social peer acceptance have fewer friends [99, 104, 115], more often report frustration about their social acceptance [116], and are more likely to suffer from social isolation (Carter et al., 2002); [115, 117]. In addition, they experience more peer victimization and show more fear of rejection than other adolescents [111, 115, 118–120] (Greco et al., 2007; Hjern et al., 2007).

Adolescents with chronic pain are also said to be over-reliant upon their parents for taking care of their social needs because they do not engage in interactions outside the home-setting [46]. For example, children and adolescents often prefer not to spend time with friends when the level of pain is too intense or might become intense during the social event [111]. Moreover, there is an inverse relation between social isolation and the motivation to engage in activities; that is, their isolation caused by pain in turn decreases their motivation to participate in social, leisure, and school activities [5, 7, 99, 101, 106]. In other words, relatedness frustration may explain (i.e., mediate) the relation between chronic pain and social avoidance, which may instigate a downward cycle. That is, avoiding social situations may yield more social isolation and relatedness frustration, further decreasing their motivation to attend social activities.

4.3.2. A Relatedness-Supportive Context as a Moderator: "Good Time Spent with My Friends Distracts Me from My Pain". As stated above, positive social interactions might be challenged by chronic pain [96, 97, 111], yet, at the same time, they bring important short-term and long-term benefits. For example, Eccleston et al. [5] found that peer relationships and positive social interactions with peers are protective factors in the development of adolescents with chronic pain, minimizing the risk for adolescents to suffer from social isolation. Moreover, positive social interactions had positive consequences for their levels of pain and pain management and it decreased avoidance mechanisms [24, 49]. Further, adolescents described perceived peer support and talking about pain with close friends as a resource, because it was related to better functional ability and better quality of life [26, 107, 114]. Similarly, research on patients with fibromyalgia and rheumatic diseases showed that higher perceived social support predicted fewer adjustment problems and fewer symptoms of depression and anxiety [107, 121]. Not only peers, but also the family context may play an important role in pain-related social avoidance. Indeed, perceived social support from one's family was found to play a moderating role as it relates to more child-reported quality of life [107]. However, when parents restrain activity involvement and peer relationships because of their own pain-related fears and anxiety, it increases pain-related avoidance in the adolescent [16].

To sum up, experiencing social support and having satisfying and positive relationships with friends and family seems to be a protective factor that may decrease the risk of avoidance behaviors. Thus, even though if it is often threatened by pain, experiencing a sense of relatedness may be considered as an important resource for adolescents with chronic pain.

5. Research and Clinical Implications

5.1. Implications for Future Research. Our topical review discussed how basic need satisfaction is a resilience pathway

to adaptive functioning in pediatric pain. A growing amount of literature exists on resilient mechanisms that help people to live adaptively with pain. Optimism, positive emotions, and social and family support are considered as resilience factors [24]. Inspired by previous work [9, 122], we propose that the satisfaction of the needs for autonomy, relatedness, and competence are resilience factors, as well as the parents' and teachers' support of these needs. That is, need satisfaction and experiencing a need-supportive context would facilitate living adaptively with pain and facilitate recovery. On the contrary, when children are frustrated in their needs and when they grow up in a need-thwarting environment, which could be the case when living with chronic pain, they might feel discouraged to attend valued activities and pursue personal goals. Thus, need frustration is considered as a risk factor that might increase functional disability.

In this paper, we joined the forces of two different research fields, that is, the psychological development and the pediatric pain literature, to deepen our comprehension of resources and risk mechanisms when living with chronic pain. SDT may yield interesting insights into dynamics involved in chronic pain, as it highlights the potential protective role of need satisfaction and need-supportive interactional context. This approach is substantially different from other approaches, such as the FAM [12], which primarily has a psychopathological approach to study pain-related functional disability and mainly focuses on risks and maladaptive behaviors. These models have been questioned [21, 123, 124], and new approaches increasingly consider chronic pain as an abnormal situation to which patients respond normally, rather than a normal situation to which people respond maladaptively [21]. Considering people with chronic pain as "normal" involves developing theories that are not (only) based on a psychopathological model but also on models representing normal development. Moreover, SDT also may help to better understand under which conditions parental involvement is helpful and adaptive and when it is problematic (e.g., in the case of overprotection, which is likely to be experienced as need-frustrating).

The above theoretical suggestions concerning the moderating and mediating role of the basic psychological needs should be empirically tested, with quantitative and qualitative methods. According to our knowledge, no studies to date have assessed associations between chronic pain, need satisfaction, and parental need-support, among children or adolescents suffering from chronic pain. In the same vein, the relation between pain and personality traits related to the needs (i.e., controlled, autonomous, and impersonal orientation) [54] should also be explored, as personality traits might influence the way people live their life with chronic pain, as this was shown for various clinical groups (e.g., [125]). The use of existing validated questionnaires assessing basic psychological need satisfaction and frustration, and its contextual support [28] would be welcome in a pediatric pain population. In addition, qualitative research is also desirable in order to gain a more in-depth understanding of the nature of basic need satisfaction and frustration in the context of chronic pain. The way parents deal specifically with their child's chronic pain should be

explored, and the consequences of parental practices for child's experiences of need satisfaction and frustration should also be tested. Moreover, some child's factors, as for instance his/her response to pain or his/her personality, might also be controlled, as they could influence parental responses to the child's pain. Finally, observational research (i.e., through the use of videos and interactions coding schemes) also would be relevant in order to avoid self-report bias when assessing the effects of social interactions on the basic psychological needs, pain management and goal pursuit.

5.2. Clinical Implications. If empirical research is able to provide support for our hypothesized model, the present framework might have implications for clinical practice. Focusing on adolescents' psychological needs and the pursuit of personal goals might help fostering resilience through the exploration of potential resources for living with pain. Several clinical interventions based on an SDT approach have shown their relevance for various health issues. For example, supporting the patient's autonomy [73, 90], encouraging autonomous motivation to change health behaviors [126, 127], and internalizing a feeling of competence [128] have been found to be helpful for improving treatments outcomes and physical health in diverse clinical groups (e.g., obese children, patients with chronic pain, and tobacco-dependent people) (Ryan et al., 2008). Those resilience factors then could be important levers for pain management, both at the individual and interactional level. Indeed, when parents observe their child in pain, they might start worrying and might be inclined to increase their involvement to help them cope with their pain, paradoxically worsening the adolescents' pain experiences [16, 129, 130]. By contrast, when parents are supportive of their child's psychological needs, they are more likely to alleviate the negative consequence of their pain experiences. Parents can do so by, for instance, being sensitive for their child's valued goals and by helping them to find his/her way to achieve it despite chronic pain. For example relatedness need-supportive parenting may involve supporting the adolescent's wish to spend time with friends despite knowing the risk for the child to hurt and the possible negative consequences (e.g., more fatigue, more pain). On the opposite, overprotective parents might prefer keeping the adolescent home to rest instead of allowing him/her to do sport with friends (or any other personally valued activities) as they may worry that the engagement in such activities would worsen the child's pain symptoms. However, these practices ironically would bring frustration in the need for relatedness and, over the longer term, decrease the adolescent's motivation to attend social activities because he/she might feel rejected from the group of peers.

Those examples show the relevance of integrating therapeutic programs that originate from the developmental literature to improve (1) need satisfaction in youths with chronic pain and (2) parental support of their child's/adolescent's needs. Both might improve pain therapies and treatment outcomes. For example, programs fostering need-

supportive parenting (e.g., the "how-to parenting program"; [131–133]) could be adapted and implemented in the context of families with children with chronic pain.

6. Conclusion

The developmental context is often neglected in the pediatric pain literature [26], but it could provide important information to understand resilience mechanisms to live adaptively with chronic pain. As discussed in the present paper, Self-Determination Theory may provide a developmental framework that can foster our understanding of why adolescents with chronic pain are likely to adopt avoidant behaviors or, by contrast, to pursue personal goals and live adaptively. Further research into developmental pediatric pain models might improve our theoretical understanding of chronic pain and inform future clinical interventions.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

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Research Article

Negative Affect, Type D Personality, Quality of Life, and Dysfunctional Outcomes of Total Knee Arthroplasty

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Background. Type D personality (TDP) is a sign of tapered stress and compromises treatment outcomes including those of hip arthroplasty. The common dissatisfaction with total knee arthroplasty (TKA) is predicted by fear avoidance, pain catastrophizing and emotional lability, with poor quality of life (QoL) reflecting these strains. This study is the first to investigate the influence of TDP on TKA assuming (1) negative affect (NA) to be linked to fear avoidance and to increased dissatisfaction with TKA and (2) the expression of NA and social inhibition (SI) to not be stable over time. **Method.** We studied 79 participants using the brief symptom inventory-18, the pain-catastrophizing scale, the Tampa scale of kinesiophobia, the SF-36, and the WOMAC pre-operatively and 12 months postoperatively. *T*-test and regression were used to compare the variables of interest between groups built based upon outcome severity. **Result.** NA at follow-up predicted knee pain ($p = 0.02$) and knee function ($p < 0.01$) at follow-up. Contrarily, increased expressions of NA/SI at follow-up were predicted by NA ($p = 0.04$) and rumination ($p = 0.05$) at the baseline. **Conclusion.** The present results suggest the postoperative increase of NA to be linked to dysfunctional outcomes of TKA due to an interaction with pain catastrophizing. Baseline self-rated physical health did not connect to the dissatisfaction with TKA 1-year postoperatively.

1. Introduction

Chronic pain is a widespread medical problem of an equifinal character usually involving psychological, psychosomatic, and psychosocial factors [1–3]. The fear avoidance model of chronic pain is a widely accepted and influential psychological model for the explanation of chronic pain [4]. It posits that pain catastrophizing and kinesiophobia (i.e., the fear of movement and re-injury) constitute a magnifying focus of attention directed at somatosensory perceptions, thus inflating this perception in terms of a pain-related exaggeration of fearful anticipation of the pain getting worse and worse. In addition, the fear

avoidance model also views psychosomatic and psychiatric disorders, such as depression or panic disorder, as conditions usually enhancing this zoom on pain signals [5]. Osteoarthritis (OA), a degenerative joint disease, serves well as an example of the progressive, complex, and multifaceted nature of chronic pain [6]. Regarding TKA, which is an ultima-ratio therapeutic option for the chronic painful condition created by OA of the knee, its results are compromised by pain catastrophizing, depression, and other psychopathology [7, 8]. This effect is obviously based on the underlying association between chronic pain and emotional vulnerability determined at a personality level, which is being reflected by the reported associations between

neuroticism and borderline criteria on one hand and worse outcomes of TKA on the other [9, 10]. Type D personality (TDP), introduced by Denollet et al. [11], refers to a general inclination to psychological distress, with the main source of that distress being the components of TDP, negative affect (NA), and social inhibition (SI). Denollet [12] depicts TDP as a personality configuration predisposing to reticence, distress, and conscious suppression of emotions. NA is described as depression, dysphoria, anxiety, hostility, anger, or irritability [13, 14]. SI, on the contrary, is understood as a tendency to not express these negative emotions to others [14]. The synergism between these two personality characteristics is deemed to maximize the experience of chronic stress in those affected [14, 15]. Therefore, TDP does not necessarily surprise by its link to chronic stress-mediated medical conditions such as cardiovascular disease [14, 16]. Lambertus et al. [17] have recently shown that there is a marked comorbidity of TDP with psychiatric disorders, mainly social phobia, dysthymia, and personality disorders (e.g., avoidant or compulsive). TDP is also a risk factor regarding total hip arthroplasty (THA) [18], while it has not yet been investigated with regard to arthroplasty of the knee. However, certain findings regarding TDP, other psychopathology, or its underlying cognitive and emotional processes suggest a meaning of TDP also in knee OA and related arthroplasty. Wong et al. [9] have reported NA to foster catastrophic thinking, including the catastrophic attributions to pain. Likewise, Leeuw et al. [19] opine the pain threshold to be lowered by NA, and Vlaeyen and Crombez [20] argue alike with regard to disability in the context of chronic pain. Pain catastrophizing, in turn, is an important predictor of the postoperative algofunction [7] which raises interest in exploring its interplay with NA and SI in the context of TKA. Along these lines, negative affectivity is linked to chronic pain [21] with this relationship being reflected by a link between TDP and (worse) outcomes of hip arthroplasty [18]. Not least, the frequent coincidence of anxiety, depression, and osteoarthritis led [22] to refer to this constellation as a “triple whammy” suggesting it to represent one entity altogether rather than one entity plus comorbidities. Hence, negative affectivity is apparently linked not only to outcomes of total hip arthroplasty but also to OA itself. Yet, no study so far has addressed TDP in the context of TKA.

Given the reported association between TDP and catastrophizing, we speculate that it extends to pain catastrophizing lending an explanation for the association between chronic pain and TDP. Moreover, we speculate, based on prior research, this effect to be mainly accounted for by NA [9]. On the contrary, social inhibition, by its very nature, predisposes to finding oneself alone with one’s problems, making less use of social support and establishing less quality of life [23, 24]. Hence, we are expecting a more detrimental effect of SI on QoL. Regarding the course of TDP, we expect varying expressions of it, based upon several studies reporting a subgroup, in whom TDP is not stable. Suchlike was found in patients with myocardial infarction [25], cardiac disease [26], and dialysis [27]. Regarding the expected instability of TDP over time, we also wonder

whether it may be an expression of maladaptive coping strategies rather than their cause. At any rate, TDP is linked to lowered quality of life in a variety of diseases, e.g., multiple sclerosis [28], coronary artery disease [29], diabetes mellitus [30], and rheumatoid arthritis [31]. NA is held responsible for effectuating the loss in QoL [31]. Therefore, an increase in the features of TDP, and especially in NA, is likely linked to a decline of quality of life (QoL), based on the literature in the field.

2. Method

Seventy-nine patients scheduled for elective primary TKA for osteoarthritis were included in the present study. 72% of the patients lived with a partner, 48% had attended junior high school or have had higher education, 8% of the patients had no training qualification, 13.33% had attended university, and 65.3% had made an apprenticeship, while 4% were unemployed, 56% received a pension, and 32% worked on a regular base. Written informed consent was obtained from all the patients. The study was approved by the local institutional review board. Participants were asked to fill in questionnaires assessing the variables of interest of psychopathological distress, type D features, kinesiophobia, and pain catastrophizing, as well as QoL. This study compares the data collected before the operation and after 1 yr of follow-up. The mean age of the participants was 66.28 (11.26) years. The groups with persistent pain (68.12 ± 11.37 vs. 65.07 ± 11.25 yr; $t = 1.12$, $p = 0.3$), persistent dysfunction (68.41 ± 11.85 vs. 64.98 ± 10.91 yr; $t = 1.51$, $p = 0.1$), and reactive TDP (68.22 ± 12.17 vs. 65.07 ± 11.07 yr; $t = 1.16$, $p = 0.3$) did not differ from those without regarding age.

2.1. Questionnaire Measures. Knee pain and knee function were assessed using the WOMAC pain and function subscales (WOMAC A and WOMAC C). Cronbach’s α of the WOMAC range from 0.8 to 0.96, and their psychometric properties are judged good [32]. The WOMAC used in this study was the Likert version in the format of a numerical rating scale ranging from 0 to 10.

The brief symptom inventory (BSI-18) [33], a short version of the symptom check list 90, assesses symptoms of depression, anxiety, and somatization in three subscales. Internal consistency for the subscales ranges between 0.79 and 0.91, discriminant and convergent validity are deemed good, and the scale is useful as a screening for psychological distress in physically ill populations.

The pain-catastrophizing scale (PCS) is a 13-item rating scale comprising the subscales rumination (PCS-Rumi), magnification (PCS-Magni), and helplessness (PCS-Help). It assesses thoughts and feelings about pain experience on a 5-point Likert scale. The PCS has proven adequate to excellent internal consistency (Cronbach’s α : total score: 0.87, PCS-Rumi: 0.87, PCS-Magni: 0.66, and PCS-Help: 0.78) [34].

The Tampa scale of kinesiophobia (TSK) is a thirteen-item rating scale rated on a 4-point Likert scale. Assessing fear of movement and re-injury, it is a valid and reliable

instrument with Cronbach's α being 0.73 for its German version [35]. The TSK is divided into two subscales termed "activity avoidance (AA)" and "somatic focus (SF)."

The short form 36 (SF-36) assesses eight dimensions of subjective health and two summary scores (the physical and the mental component score, PCSc—this naming shall avoid confusion with the pain-catastrophizing scale, PCS, and the MCS. Reliability, validity, and sensitivity of the SF-36 are deemed excellent also regarding the German version [36]. The SF-36 comprises the dimensions physical functioning, role physical, bodily pain, general health, vitality, social function, role emotional, and mental health and can be summed up using the mental as well as the physical component score.

The outcome variables knee pain (WOMAC A) and knee function (WOMAC C) were dichotomized using the lowest tertile as the cut-off point, allowing for the comparison of the worst third with the remaining group reporting better results. Using severity tertiles is a proven procedure [37] for studying the outcomes of TKA. These groups will be referred to as the persisting pain taxon and the persisting dysfunction taxon. In addition, we used a group variable derived from the follow-up measures of NA and SI. By subtracting the total score of the DS14 after 1 year from the preoperative measure, we arrived at a subset of participants in whom the result had a negative sign. This group is referred to as "reactive TDP," as the corresponding participants had obviously had experienced an increase of their load of NA/SI during the follow-up. We used *t*-testing to compare continuous variables between groups and χ^2 testing to compare categories. Reported results are understood as two-tailed. Linear as well as binary regressions were then used for the prediction of the outcome variable, at which we used the continuous outcomes knee pain and knee function in linear and the categorical outcome reactive TDP in binary regression, as dependent variables. We selected the independent variables for these procedures according to their significance in the preceding *t*-tests. In addition, we entered the highly interrelated worst function or pain taxon, respectively, as predictors of each other and as a control for mutually shared variance. All regressions were controlled for gender, and no stepwise procedure was applied.

3. Results

The following primary outcomes (mean (SD)) need reporting: WOMAC A baseline/follow-up: 5.26 (2.21)/10.94 (10.63); WOMAC C baseline/follow-up: 5.02 (2.30)/44.84 (35.52); NA baseline/follow-up: 8.19 (6.06)/5.34 (4.61); SI baseline/follow-up: 6.87 (4.84)/8.58 (4.18); baseline BSI-total score 6.78 (7.66); baseline PCS total score 17.18 (12.24); and baseline TSK total score 21.05 (6.61). Sociodemographic aspects (partnership, education, and working situation) lacked associations with the persistent pain taxon and with reactive TDP, but there was an association between the persistent dysfunction taxon and not working full-time ($\chi^2 = 20.84$, $p < 0.01$) and between the dysfunctional taxon and not being married as well as living separate from one's partner ($\chi^2 = 10.34$, $p = 0.04$). The persisting pain and the

persisting dysfunction taxons were highly interrelated ($\chi^2 = 32.79$, $p < 0.01$). The category of type D personality as assessed at baseline was linked to the persisting pain taxon ($\chi^2 = 4.46$, $p = 0.04$) but lacked associations with the persistent dysfunction ($\chi^2 = 0.79$, $p = 0.04$) and the reactive TDP taxon ($\chi^2 = 2.28$, $p = 0.1$).

Those belonging to the persistent pain taxon had worse pain and function also at baseline. Moreover, they showed remarkable psychopathological distress but no elevated scores of pain catastrophizing and kinesiophobia. Members of the persistent dysfunction taxon did not differ from the remaining two-thirds with regard to baseline knee pain and knee function. They did, however, report more pain and negative affectivity at follow-up. Regarding the SF-36, we found a more detrimental effect of the persistent pain taxon on QoL than we observed regarding the persistent dysfunction taxon. On the contrary, those belonging to the reactive type D taxon were not associated with a deterioration of QoL. Tables 1 and 2 show the respective mean values, SDs, and statistics of the group comparisons.

Pain and function at follow-up were best predicted by NA at follow-up. Membership of the reactive type D taxon was best predicted by NA and rumination at baseline. The entire statistics are shown in Tables 3–5. Hence, the outcomes, knee pain and knee function, were interrelated in the present sample but also influenced by NA, which apparently is being reinforced through cognitive processes (e.g., rumination) in reflection of the respective participant's dysfunctional attempt to cope with TKA.

4. Discussion

Comparing the more satisfied patients with those unsatisfied 1 year after TKA revealed that the latter had endorsed more psychopathological distress and fear avoidance initially, especially if they belong to the persistent pain taxon. Regarding QoL, the members of the dysfunctional and the persistent pain taxon had reported a decrease mainly with respect to the physical dimensions of QoL. Membership in the persistent pain taxon was best predicted by the persisting dysfunction taxon but also by NA. A surprising finding was the discovery of a reactive TDP taxon in 29 of 75 participants (38.67%) during the 1 yr follow-up, i.e., a group with rising NA/SI levels during the follow-up.

The prevalence of primary TDP at the baseline was lower than that reported for other contexts, e.g., fibromyalgia coinciding with TDP in 57% [38], myocardial infarction coinciding with TDP in 14–25% [23], coronary artery disease coinciding with TDP in 18% [39, 40], heart disease coinciding with TDP in 20–25% [22], and joblessness coinciding with TDP in 53% [41]. In their critical evaluation of the construct of TDP, Coyne and Voogd [42] highlight the notion that scoring high on two correlated measures of stress, NA and SI, is a sign of massively tapered distress. Hence, the prevalence of TDP in any given population may be viewed as a marker of the distress which this population is exposed to. Obviously, an acute illness (e.g., a myocardial infarction) is more stressful than a chronic condition, such as osteoarthritis, and especially, being struck by a sudden

TABLE 1: *t*-Testing comparing the taxon-derived groups regarding knee pain and knee function (fu) as well as psychometric measures.

	Womac A (fu)	Womac C (fu)	Womac C (fu)	PCS total	PCS Rumi	PCS Magni	PCS- Help	TKS- tot	TKS- SF	TKS- AA	BSI GSI	BSI som	BSI dep	BSI anx	NA	SI	NA (fu)	SI (fu)	
Low pain relief	6.45	23.15	6.18	81.91	19.7	6.96	4.12	8.96	32.12	9.27	13.84	10.11	2.96	4.07	3.07	9.11	7.63	7.15	9.37
High pain relief	1.68	8.91	2.02	29.02	13.28	4.62	2.77	7.09	7.32	3.35	4.5	9.04	3.24	3.34	2.95	6.03	6.37	5.53	3.44
<i>t</i>	4.75	4.64	4.53	26.2	16.55	6.12	3.52	7.0	20.12	7.98	12.14	4.78	1.0	2.39	1.41	8.06	6.57	4.48	8.42
<i>p</i>	2.14	4.12	2.16	22.07	11.48	4.42	2.68	5.42	5.96	2.77	3.77	5.16	1.62	3.21	1.95	6.03	4.1	3.7	4.41
	3.44	10.22	3.1	8.83	1.08	0.77	0.9	1.23	1.91	1.78	1.74	2.82	2.95	2.36	2.96	0.73	0.78	2.22	0.97
	<0.01	<0.01	<0.01	0.3	0.4	0.4	0.2	0.06	0.08	0.09	<0.01	<0.01	<0.01	<0.01	0.04	0.5	0.4	0.03	0.3
Low fct	6.0	22.67	6.01	90.43	16.0	5.43	3.14	7.43	21.55	8.55	13.0	9.48	2.67	3.67	3.14	9.19	5.95	8.55	10.05
High fct	1.84	10.73	1.85	24.01	11.93	4.18	2.48	6.05	7.29	2.98	4.77	9.5	3.15	3.64	3.15	6.45	5.7	5.35	2.96
<i>t</i>	5.02	5.83	4.7	25.46	18.23	6.72	3.85	7.87	20.88	8.35	12.52	5.94	1.4	2.85	1.71	8.06	6.88	4.54	8.33
<i>p</i>	2.02	5.59	2.24	17.37	12.05	4.48	2.83	6.0	6.03	2.85	3.76	6.41	2.2	2.4	2.38	5.32	4.07	3.54	4.29
	1.74	6.79	2.25	12.68	0.71	-1.12	-0.99	-0.28	0.4	0.26	0.44	1.8	1.9	0.94	2.08	0.74	-0.76	3.64	1.66
	0.09	<0.01	0.09	<0.01	0.5	0.3	0.3	0.8	0.7	0.8	0.7	0.08	0.06	0.4	0.04	0.4	0.4	<0.01	0.1
TDPr	5.05	14.62	5.33	56.29	13.24	4.41	2.62	6.21	20.82	8.32	12.5	5.45	1.21	2.62	1.66	5.62	4.9	6.48	10.07
No TDPr	2.15	13.43	2.33	42.49	11.32	4.35	2.0	5.73	6.49	2.79	4.12	5.26	1.73	2.35	1.91	4.91	3.1	5.24	3.54
<i>t</i>	5.42	8.77	4.8	34.28	19.87	7.51	4.23	8.48	21.41	8.5	12.91	7.85	2.11	3.37	2.37	10.04	8.15	4.76	7.85
<i>p</i>	2.26	8.07	2.28	26.41	11.87	4.22	2.79	6.14	6.46	3.09	4.01	8.88	3.09	3.12	3.08	6.02	5.45	4.07	4.23
	-0.69	2.11	0.93	2.76	-2.4	-3.05	-2.67	-1.59	-0.38	-0.25	-0.43	-1.47	-1.59	-1.11	-1.24	-3.47	-2.93	1.59	2.35
	0.5	0.04	0.4	<0.01	0.02	<0.01	<0.01	0.1	0.7	0.8	0.7	0.2	0.1	0.2	0.2	<0.01	<0.01	0.1	0.02

Fu: at follow-up; WOMAC A: knee pain; WOMAC C: knee function; PCS: PCS-Rumi: subscale magnification of the PCS; PCS-Magni: subscale rumination of the PCS; PCS-Dep: subscale helplessness of the PCS; TSK-SF: subscale somatic focus of the TSK; TSK-AA: subscale activity avoidance of the TSK; BSI-som: subscale somatization of the BSI; BSI-dep: subscale depression of the BSI; BSI-anx: subscale anxiety of the BSI; NA: subscale negative affect of the DS-14; SI: subscale social inhibition of the DS-14.

TABLE 2: *t*-Testing comparing the taxon-derived groups regarding the subscales of the SF-36.

	Physical functioning	Role physical	Bodily pain	General health	Vitality	Social functioning	Role emotional	Mental health	Physical component score	Mental component score
Low pain relief	19.1	15.63	21.92	47.21	41.27	56.5	48.61	61.12	23.79	48.6
High pain relief	16.15	33.63	16.32	17.98	21.74	29.34	47.12	18.46	8.28	12.35
<i>t</i>	33.78	30.49	30.85	57.41	54.29	76.3	62.41	68.74	29.25	53.1
<i>p</i>	22.47	42.14	16.98	17.1	16.43	23.38	47.46	16.27	8.09	10.53
	-2.9	-1.6	-2.13	-2.34	-2.86	-3.14	-1.16	-1.81	-2.65	-1.59
	<0.01	0.1	0.04	0.02	<0.01	<0.01	0.2	0.08	0.01	0.1
Low fct	16.25	14.47	19.26	51.21	41.08	56.88	61.40	62.8	22.19	51.4
High fct	16.21	32.61	12.99	16.35	22.02	27.05	48.77	20.48	7.68	12.54
<i>t</i>	33.64	26.7	31.27	54.89	53.37	74.73	57.78	66.56	29.11	51.69
<i>p</i>	22.2	40.13	17.27	17.84	16.6	25.07	47.35	17.74	7.84	11.46
	-3.2	-1.17	-2.72	-0.77	-2.48	-3.0	0.28	-0.75	-3.23	-0.29
	<0.01	0.3	<0.01	0.4	0.02	0.01	0.8	0.5	<0.01	0.9
TDPPr	22.86	26.85	27.39	56.32	49.11	70.09	60.71	68.71	26.33	53.34
No TDPPr	21.41	44.36	19.65	18.01	21.69	31.61	48.05	17.15	9.12	11.54
<i>t</i>	32.91	27.38	28.71	51.25	50.79	69.19	54.76	63.4	28.71	49.38
<i>p</i>	22.3	39.0	16.54	18.0	18.32	23.99	47.61	17.71	8.55	11.65
	-1.89	-0.05	-0.3	1.15	-0.35	0.13	0.51	1.24	-1.1	1.38
	0.06	1	0.7	0.3	0.7	0.9	0.6	0.2	0.3	0.2

TDPPr: reactive TDP taxon.

TABLE 3: Linear regression, dependent variable: knee pain at follow-up.

Total model: <i>df</i> = 13; <i>F</i> = 2.76; <i>p</i> = 0.005; <i>R</i> ² = 0.42	<i>B</i>	Std. error	Beta	<i>T</i>	Sig.	CI lower	CI upper
Gender	4.33	2.87	0.19	1.51	0.14	-1.44	10.09
NA (fu)	0.77	0.32	0.32	2.41	0.02	0.13	1.41
BSI-som	0.90	1.09	0.20	0.82	0.41	-1.29	3.09
BSI-dep	-0.51	0.86	-0.13	-0.59	0.56	-2.24	1.23
BSI-anx	-0.94	1.13	-0.22	-0.83	0.41	-3.21	1.33
WOMAC A	0.97	1.21	0.19	0.80	0.43	-1.47	3.41
WOMAC C	0.89	1.34	0.18	0.67	0.51	-1.80	3.59
Physical functioning (SF-36)	0.01	0.12	0.02	0.08	0.94	-0.24	0.26
Bodily pain (SF-36)	0.17	0.14	0.27	1.17	0.25	-0.12	0.45
General health (SF-36)	-0.03	0.09	-0.05	-0.36	0.72	-0.21	0.15
Vitality (SF-36)	-0.02	0.10	-0.03	-0.19	0.85	-0.21	0.17

fu: at follow-up; NA: negative affect; WOMAC A: knee pain; BSI-som: subscale somatization of the BSI; BSI-anx: subscale anxiety of the BSI; BSI-dep: subscale depression of the BSI.

TABLE 4: Linear regression, dependent variable Womac-C (fu).

Total model: <i>df</i> = 9; <i>F</i> = 4.16; <i>p</i> < 0.01; <i>R</i> ² = 0.43	<i>B</i>	SE	β	<i>T</i>	<i>p</i>	CI lower	CI upper
Gender	4.60	9.40	0.06	0.49	0.63	-14.29	23.49
NA (fu)	3.45	0.99	0.43	3.50	<0.01	1.47	5.44
BSI-anx	-0.37	2.08	-0.03	-0.18	0.86	-4.55	3.81
Physical functioning (SF-36)	-0.32	0.36	-0.18	-0.88	0.38	-1.04	0.41
Bodily pain (SF-36)	-0.23	0.33	-0.11	-0.70	0.49	-0.90	0.44
Vitality (SF-36)	-0.05	0.29	-0.03	-0.18	0.86	-0.63	0.53
Physical component score (SF-36)	-0.60	0.94	-0.14	-0.64	0.53	-2.50	1.29
Employment status	0.84	0.81	0.13	1.04	0.30	-0.78	2.47
Family status	1.65	3.54	0.06	0.47	0.64	-5.46	8.76

BSI-anx: subscale anxiety of the BSI; NA: negative affect.

threat to life is conceivably linked to extreme levels of emotional and mental distress. Additionally, socioeconomic influences are predictors of TDP [41], underscoring the importance of the social dimensions of health and the necessity of a bio-psychosocial framing of health and illness,

especially with regard to chronic pain. Notably, the central processing of social exclusion is partly based on the same neurobiological substrates as the processing of physical pain [43], which may be mirrored by the persistent pain taxon's restriction in their social role function.

TABLE 5: Binary regression, dependent variable: reactive TDP taxon.

Cox and Snell R^2 : 0.44; Nagelkerke R^2 : 0.59	B	SE	Wald	df	p	Exp(B)	CI lower	CI upper
Gender	-0.46	0.65	0.50	1.00	0.48	0.63	0.18	2.25
PCS-SUM	-0.16	0.09	3.10	1.00	0.08	0.85	0.71	1.02
PCS-Magni	0.20	0.24	0.73	1.00	0.39	1.22	0.77	1.95
PCS-Rumi	0.37	0.19	3.72	1.00	0.05	1.45	0.99	2.10
NA	0.14	0.07	4.05	1.00	0.04	1.15	1.00	1.32
SI	0.09	0.08	1.10	1.00	0.29	1.09	0.93	1.29

PCS-sum: total score of the PCS; PCS-Magni: subscale magnification of the PCS; PCS-Rumi: subscale rumination of the PCS; NA: negative affect; SI: social inhibition.

Study hypotheses: contrary to our expectations, we did not find TDP related to worse outcomes of TKA, although it has been reported to coincide with worse outcomes after hip arthroplasty [18, 19]. Rather, the present results are suggestive of a dimensional increase in NA/SI to connect to worse outcomes, although Vissers et al. [18] report TDP to be associated with worse outcomes of THA and reduced QoL 3 months postoperatively [19], which may be a point in time too close to the operation for the acute distress to vanish. Pain at 3 months postoperatively would have to be classified as on the edge of becoming chronic, while still reflecting mechanisms of acute pain related to the recent operation [44]. Moreover, the respective research was not occupied with the knee, but the hip. Given the difference between these indications with regard to the joint function and statics involved, one might speculate that the habit of restrictive and relieving posture may lead to functional problems as a result of malposition due to fear of pain and re-injury [3]. Along these lines, White et al. [45] report a large proportion of patients with knee OA to need help with their personal care and routine needs. They also experience a faster decline in gait speed allowing for less participation to be reached as the disorder progresses, compared to OA of the hip [46].

However, kinesiophobia, as assessed by the TSK, was not linked to the algofunctional outcome 1 yr postoperatively, in the present study. In addition, kinesiophobia decreased during the follow-up, but 39% of the participants experienced the opposite regarding the dimensions of TDP. As our study hypothesis regarding the nonstability of TDP was confirmed, the question arose whether changes in TDP during a postoperative follow-up should be considered a sign of TDP being a mode of adaptation to the operation rather than a sign of being a prerequisite of dysfunctional adaptation. In fact, changing loads of TDP symptoms connected to a stressor are not in line with the view of TDP as a stable trait but suggest TDP to reflect a state altered through the stressor. Coyne and de Voogd [42] state that there may be “inflection points for NA and SI” as dimensions, increasing their influence on the outcome under study, and our results suggest a ruminating coping style in connection with the extensive experience of knee pain and knee dysfunction prior to TKA to participate in such a system of outcome modulators. Notably, this effect seems to be attributable to NA, not SI. Indeed, the prediction of the worst function taxon by NA and rumination points at a synergism between the sufferer’s cognitive appraisal of her or his painful physical restrictions and a corresponding

affective state is ever changing for the worse. This finding is suggestive of a subgroup of patients undergoing TKA whose ruminating habit of coping finally seems to lower the pain threshold via the induction of negative affectivity [21]. SI, on the contrary, lacked an association with pain and dysfunction of the knee in the present study. Though speculatively, we interpret this finding as related to the differential psychological nature of NA and SI. SI reflects an interpersonal function, whereas NA refers to intrapsychic perceptions. Even though interpersonal dimensions may be correlated to physical outcomes in medicine, this connection is presumably indirect and mediated through the affective, i.e., intrapsychic, evaluation of being interpersonally handicapped, which manifests as NA. The importance of NA for the prediction of postoperative maladaptation is additionally highlighted by findings linking it to psychophysical and neurophysiological predictors of pain, such as the reduction of the conditioned pain modulation and facilitated temporal summation (i.e., inhibitory and excitatory pain modulation processes [47]). After all, different avenues of research bear clues for the categorization of patients at risk of persistent pain after TKA, of which clinicians may wish to make use of in order to improve the results of TKA. On this note, the lack of psychological well-being and the corresponding self-concept as highly incapacitated by their osteoarthritis of the knee are also reflected in a decline of self-rated QoL. Of particular importance, at least with the present study in mind, is the remarkable difference with regard to baseline QoL between those with the poorest outcomes and those who fare better after TKA. An obvious question with regard to the dissatisfaction with TKA is whether the above-outlined attitude changes following a surgical procedure. If not so, the respective patients are likely to continue to characterize themselves as socially handicapped, i.e., making less use of social support as a means of coping [48]. At the same time, severe pain along with emotional lability and pain catastrophizing seem to effectuate postoperative maladaptation. Reasons for this are likely to be found within the scope of individual psychological predispositions, e.g., personality characteristics or a history of trauma [10, 49]. Although emotional lability is linked to QoL in the present study in terms of a trend, the latter was not dramatically worse in the reactive TDP taxon. It was, however, connected to higher baseline scores on the mental component score of the SF-36, underscoring the psychosomatic nature of the interaction between TDP features, TKA and QoL. Again, the self-perception as being isolated and lacking social support may be a reaction to TKA, but it

likely oftentimes exists prior to TKA. This, notwithstanding any diseased state, results in multidimensional changes affecting not only physical health but also the socioeconomic status and psychological well-being. Hence, one should bear in mind that QoL is a multifinal concept, projecting various changes in the perception of one's body and mind as well as one's social surrounding and capacities in the process of a medical treatment. That is why, Drewett et al. [50] insist that QoL indices do not reflect the specific result of an operation but rather the extent to which an individual is satisfied by the physical, emotional, and social circumstances of her or his life. Meanwhile, QoL is not restricted to being an outcome but it may at any given time reflect changes at psychological, perceptive, and social levels rather than being a correlate of the medical success of a specific medical treatment in the first place. Therefore, a participant failing to benefit from TKA without a medical cause may partly do so because no change in the above-outlined attitude has occurred. Schneider and Braungardt [51] refer to that clinical attributional style, which apparently structures the doctor-patient relationship on the part of clinicians, as medicalization, that is, labelling the causes of illness as medical and making the indication for a medical treatment based thereon, although the respective pathogenic agent would have rightly been classified as psychosomatic or psychosocial.

In conclusion, the present results are indicative of a complex interaction involving rumination, the experience of pain, negative affectivity, and, not least, disability and its subjective impression. While the data do not allow for any causal explanations, they do have clinical implications and a seminal potential. TDP may not be a trait but seems to function as a state which is induced by surgery-related stress. Both, TDP and QoL, are not outcomes of surgery but reflections of the psychosomatic mechanisms involved in coping with TKA. Future research will face the task of identifying psychological markers indicative of a maladaptive potential and of testing psychotherapeutic interventions aiming at improving the patient's emotional, interactional, and adaptive competencies. Rumination and NA may be reasonable candidates for the early detection of maladaptive copers and worthwhile targets for psychotherapeutic interventions. Moreover, the worse the pain before the operation, the greater the expectation of the patient's dissatisfaction with TKA will have to be. This argues clearly for not delaying the operation under the acceptance of the worsening of knee pain, and it calls for a sufficient pain relief especially in the perioperative phase. As to the caveats of the present study, which is the first to report on TDP in TKA and therefore needs replication, its cross-sectional character and the limited sample size need to be mentioned. The sample is not representative of all patients undergoing TKA, and its generalizability is restricted by the lack of a control group.

Data Availability

The SPSS data used to support the findings of this study are available from the corresponding author upon request.

Ethical Approval

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent

Informed consent was obtained from all individual participants included in the study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Research Article

Pain Intensity Is Not Always Associated with Poorer Health Status: Exploring the Moderating Role of Spouse Personality

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Background. Past decades have seen a surge of studies investigating the role of spouses in chronic illness. The present study explored an interpersonal model of health-related quality of life in chronic pain settings. Spouse personality was tested as a moderator of pain intensity-to-health associations in patients with chronic pain. **Methods.** This is a cross-sectional study. Participants were 185 noncancer chronic pain patients and their spouses. Patients were mostly females (58.4%). Mean age was approximately 56 years for patients and spouses. Patients completed a measure of pain intensity, health-related quality of life, and personality. Spouses also reported on their personality characteristics. Spouse personality was used as the moderator in the relationship between patients' pain intensity and health status. Patient personality was used as a covariate in the moderation analyses. **Results.** Spouse neuroticism moderated the relationship between pain intensity and physical health status, while spouse introversion moderated the pain-to-mental health association. **Conclusions.** Results support the idea that the relationship between a chronic stressor, namely, chronic pain, and health-related quality of life may be complex and contextually determined by spousal characteristics. Clinical implications are discussed in the context of couples.

1. Introduction

Chronic pain is a common and disabling disease [1–3]. Similar to other chronic illnesses [4, 5], spouses of pain patients have been argued to play an important role in the disease due to their caregiving role [6]. In chronic pain, spouse responses to patients' pain behavior have been the focus of most research [7], while the influence of spouse personality characteristics has been mostly overlooked. This is surprising because personality traits have been consistently associated with mental and physical health status across healthy and sick populations, including chronic pain [8, 9].

Personality can be defined as relatively stable ways in which people think, feel, and behave [10]. The five-factor model of personality (FFM), which describes personality in terms of five dimensions (neuroticism, extraversion,

agreeableness, openness to experience, and conscientiousness), is currently the dominant framework for personality. In the FFM, neuroticism is understood as a tendency to be emotionally unstable and to experience negative emotions (i.e., anxiety, depression, and anger). Neuroticism is considered a risk factor for health as it has been associated with poorer physical functioning, increased worry about symptoms, and greater mental distress. Conversely, extraversion and conscientiousness tend to be associated with better health outcomes, including physical functioning and mental well-being. Extraverts tend to be optimistic, physically active, and socially competent, while conscientiousness is associated with high self-discipline, dutifulness, and low risk taking. Agreeableness and openness, which are the socio-affective and intellect dimensions, respectively, have the less consistent and weakest associations with health outcomes [9, 11, 12].

Consistent with the literature on neuroticism, when spouse interaction styles are characterized by negative emotionality (i.e., preoccupied and fearful or angry and critical), patients tend to report increased mental distress. By contrast, the relationship between these negative responses and pain intensity and physical disability levels is weaker and inconsistent, and the role of arguably positive spouse behaviors, such as solicitous and validating responses, is still inconclusive [13–17]. One limitation of existent research is that spouse factors are argued to have a direct effect on patient outcomes. However, it is also possible that spouse characteristics influence patients' status by moderating (i.e., reducing or aggravating) the impact that pain has on health [7]. This is consistent with the Transactional Model Of Health, which emphasizes that challenges of the painful condition occur in a social (family) context and argues that spouse factors can improve or exacerbate stressors [18].

There is, indeed, some support for this contextual (i.e., moderating) role of spouse personality in the context of couples. For instance, a study showed that spouse neuroticism influenced the associations between everyday problems and affect and physical symptoms in older couples [19]. In another investigation, the relationship between patient personality and patient psychological health differed as a function of spouse personality [20]. What these studies suggest is that the relationship between stressors (i.e., everyday problems and certain personality styles) and patient health can be influenced by spouse characteristics. The extent to which spouse personality can also be an important contextual factor in the presence of a chronic stressor, such as pain, remains unexplored.

The present study aims at testing whether the negative influence of patient pain (stressor) on patient health-related quality of life (outcome) is moderated by psychological factors in the spouse (e.g., spouse personality; contextual factor). Research has consistently shown that health-related quality of life decreases with pain [21, 22]. Based on previous research showing that neuroticism, introversion, and low conscientiousness are also associated with poor health status [9], we expect that the aforementioned spouse psychological characteristics will impose low health-related quality of life in pain patients irrespective of pain levels (i.e., the burden of pain is increased).

2. Methods

2.1. Design, Participants, and Settings. This observational study was conducted at the Pain Clinic of the Vall d'Hebron Hospital in Barcelona, which is a tertiary care pain clinic. This clinic was selected because it was the home institution of the corresponding author, C. S. R., when the study was conducted. Also, past research by our team has revealed that patient characteristics at this clinic are comparable to those of other tertiary pain clinics [23], so the results obtained might be applicable to a considerable number of pain clinics.

Eligibility criteria included (i) having a diagnosis of chronic noncancer pain (>3 months of duration), (ii) having an appointment at the Pain Clinic of the Vall d'Hebron Hospital between January 2014 and December 2015, and (iii)

being married at the time of assessment. Consecutive sampling was used for recruitment, which started in January 2014 and finished in December 2015. One month prior to the patients' appointment at the Pain Clinic, the lead researcher, C. S. R., explored the eligibility criterion of having a diagnosis of chronic pain in the electronic medical records and ICD-9 code 338.2. Patients meeting this criterion were called to explore the eligibility criterion of marital status. If they were married and willing to participate in the study, two letters were sent to the patient's home, one for the patient and the other for the spouse. For both, each letter included a description of the goals, procedures, and possible risks of participating in the study, together with the contact information of the lead researcher, C. S. R., the informed consent form, and the questionnaires.

Couples were asked to complete the forms separately and were given an envelope that had to be sealed and returned to the physician the day of the patient's first visit to the Pain Clinic. All participants provided their written consent to participate in the study and did not receive any economic compensation for their participation.

The Ethics Committee of the Vall d'Hebron Hospital in Barcelona approved the current study.

2.2. Measures

2.2.1. Spouse Personality. The NEO five-factor Inventory (NEO-FFI) [10] evaluates five dimensions of adult personality, namely, neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. Of these, only neuroticism, extraversion, and conscientiousness appear to be consistently associated with health outcomes in chronic pain settings [8, 9, 12]. However, because this is a novel approach to the role of personality in chronic pain, the moderating role of openness and agreeableness will also be investigated.

In the NEO-FFI participants rate their degree of agreement on a 5-point Likert scale (0 = *totally disagree*; 4 = *completely agree*). Each of the five personality dimensions is composed of 12 items, so scores for each dimension range from 0 to 48. The internal reliability of the personality dimensions in our study ($0.64 < \alpha < 0.84$) was comparable to previous findings ($0.66 < \alpha < 0.81$) [10, 24].

2.2.2. Patient Pain Intensity. Current pain intensity was assessed with a Numerical Rating Scale, which has become a standard in the measurement of pain [25] and is widely recommended due to its compliance rate, responsiveness, and ease of use [26]. Participants in our study rated their pain from 0 = *no pain* to 10 = *worst possible pain*.

2.2.3. Patient Health-Related Quality of Life. Physical and mental components of quality of life were assessed with the Short Form-36 Health Survey [27], which has become one of the most widely used instruments for the assessment of health-related quality of life [28]. Physical aspects include the ability to perform daily activities (Physical Functioning)

and work-related activities (Role Physical), plus the average intensity of pain in the last four weeks (Bodily Pain). Some elements correlate to physical and mental health, such as the perception of present and future health (General Health), the evaluation of personal energy (Vitality), and the interference of health problems in their interpersonal life (Social Functioning). The remaining components, namely, the role of emotions on functioning (Role Emotional) and psychological well-being (Mental Health), mainly reflect psychological aspects of health [21]. A composite score can be obtained for physical and mental health using the aforementioned subscales. The use of these composite scores is often recommended for methodological reasons [29]. However, the use of the physical composite in the present study would be problematic because it contains a pain subscale, which would contaminate the relationship between the dependent variable (i.e., health) and the independent variable (i.e., pain intensity). Thus, physical health was measured by means of the Physical Functioning scale. The Mental Composite Score is not contaminated by the presence of pain intensity ratings, so it was used to assess overall mental health to reduce the number of statistical tests. Scales and composite scores in the Short Form-36 have a 0–100 range. High scores represent better functioning. The internal consistency in our study ($0.86 < \alpha < 0.95$), which is calculated for the 8 subscales, was consistent with previous findings ($0.78 < \alpha < 0.94$) [30].

2.2.4. Covariates. Patient age, sex, pain duration, educational level, and personality were used as covariates due to their relationship with patient health status [8, 31]. Patient education was coded as 0 = “less than 12 years of education” and 1 = “more than 12 years of education.” Patient personality was assessed with the NEO-FFI, the same measure that was used to evaluate spouse personality.

2.3. Statistical Analyses. The moderating effect of spouse personality on the relationship between pain and health-related quality of life in the patient was tested using multiple linear regressions. In the regressions, patient sex, age, and personality were included as covariates in the first block. Patient pain intensity was entered next. The third and the fourth blocks included spouse personality and the interaction term (patient pain intensity * spouse personality), respectively. Multiple regression diagnostics included an analysis of multicollinearity (i.e., two predictors are linear combinations of one another) and a test of unusual and influential data (i.e., whether certain observations are responsible for the results).

All analyses were computed using SPSS version 22 [32].

3. Results

3.1. Sample Characteristics. From January 2014 to December 2015, 515 phone calls were made. In total, 203 patients met the eligibility criteria, so a letter was sent to these patients and their spouses. Eighteen patients did not return the protocol (either them or the spouse lost interest in the

study). The final sample comprised 185 chronic pain patients and their spouses (91.1% response rate). All couples were heterosexual. Patients had an average age of 56.55 years ($SD = 13.59$) and were mostly females (58.4%). The mean age for spouses was 56.66 years ($SD = 13.85$) and 41.6% were females. Approximately 94% of participants were born in Spain. Academic degree was similar for both samples, with approximately half of the participants having achieved more than 12 years of education (47.3% of patients and 50.3% of spouses). Patients had been suffering pain for an average of 6.55 years ($SD = 8.57$). Pain was mostly located in the back (58.8%) and neck (11.1%).

Means and standard deviations of study variables are presented in Table 1. Mean pain intensity was 7.71 ($SD = 1.56$) with a range of 3 to 10. The sample would be characterized as experiencing moderate to severe pain [33]. Scores for patients' physical and mental health status were comparable (between +1 SD and -1 SD) to those of previous investigations assessing similar pain populations [34–36]. Compared with population norms, mean values on physical and mental composite scores were, respectively, 2 SD and 1 SD below the mean of the general population in Spain [37]. Pain patients in this sample were significantly more physically disabled and psychologically distressed than the general population. Mean scores for spouse and patient personality were comparable (within 1 SD) with previously reported scores in the general population in Spain [24, 38].

3.2. Moderation Analyses. Before performing the moderation analyses, all predictors were centered. Patient openness and agreeableness were not used as covariates due to their weak associations with patient health-related quality of life and to reduce multicollinearity problems.

Spouse neuroticism moderated the association between patients' pain intensity and patient Physical Functioning (Table 2), while spouse extraversion moderated the pain-to-mental health relationship (Table 3). In a moderation analysis, this should be interpreted as revealing that the contribution of the independent variable (i.e., patients' pain intensity) on the dependent variable (i.e., physical and mental health) varies among different levels of the moderator (i.e., spouse neuroticism and extraversion). For example, the positive interaction coefficient between spouse neuroticism and patient pain intensity in the prediction of physical functioning ($\beta = 0.19$, $p = 0.009$, 95% $CI = 0.08, 0.54$) means that patient pain intensity is less intensely associated with physical functioning at higher levels of spouse neuroticism. On the contrary, the negative coefficient in the interaction between extraversion and pain intensity in the prediction of mental health ($\beta = -0.17$, $p = 0.014$, 95% $CI = -0.30, -0.03$) reveals that patient pain intensity is less intensely associated with mental health at low levels of spouse extraversion. No moderation effect was found for spouse openness to experience, agreeableness, and conscientiousness.

Post hoc analyses were then performed to explore if the simple slopes were significant and in the expected direction. Simple slopes are often calculated at one standard deviation

TABLE 1: Means and standard deviations of patient and spouse characteristics.

	Patient	Spouse
Age	56.82 (13.60)	56.66 (13.85)
Pain duration (years)	6.56 (8.57)	
<i>Personality</i>		
Neuroticism	20.05 (8.45)	24.19 (7.05)
Extraversion	26.99 (7.54)	31.79 (5.53)
Conscientiousness	32.43 (6.87)	24.54 (8.96)
Openness	31.86 (6.84)	26.26 (8.08)
Agreeableness	30.88 (6.20)	22.74 (7.41)
<i>Pain and health status</i>		
Pain intensity	7.71 (1.56)	
Physical Functioning	34.80 (23.65)	
Mental Composite Score	39.04 (12.44)	

from the sample mean, but its use has been argued to be arbitrary and sample specific, which might limit the generalizability of the findings (i.e., what is high in one sample might be moderate or low in another sample) [39]. Thus, we plotted the moderation using the Spanish population norms for low (percentile 30) and high (percentile 65) neuroticism and extraversion, which are 16 and 23 for neuroticism and 28 and 35 for extraversion [40]. As reflected in Figure 1, the relationship between patient pain intensity and patient physical functioning at daily activities was strongest when spouse neuroticism was low ($\beta = -0.47$, $t = -4.22$, $p < 0.001$; 95% CI = -14.08 , -5.03) or moderate ($\beta = -0.55$, $t = -4.67$, $p < 0.001$; 95% CI = -12.31 , -4.90), as opposed to high ($\beta = -0.33$, $t = -2.82$, $p = 0.006$; 95% CI = -7.17 , -1.23).

The post hoc probing with extraversion as a moderator (Figure 2) showed similar results to those obtained for neuroticism. Specifically, pain intensity was not significantly associated with mental health for participants with an introverted (low in extraversion) spouse ($\beta = -0.15$, $t = -1.5$, $p = 0.115$; 95% CI = -2.38 , 0.26). On the contrary, pain intensity was significantly related to mental health when the spouse extraversion was either high ($\beta = -0.34$, $t = -2.43$, $p = 0.019$; 95% CI = -6.58 , -0.61) or moderate ($\beta = -0.53$, $t = -3.22$, $p = 0.003$; 95% CI = -8.46 , -1.87).

Multiple regression diagnostics revealed no problems of model fit to the data. Specifically, the variance inflation factor, which reveals to what extent the variance is inflated due to multicollinearity, was lower than 2 for all predictors. To test the existence of influential cases, we assessed how the regression coefficients changed by excluding an observation by means of the standardized DFBETA, with a particular interest in the interaction coefficient. All values were smaller than 1, suggesting that none of the observations substantially influenced the model [41].

4. Discussion

The present investigation aimed at exploring the moderating role of spouse personality in the relationship between pain intensity and health-related quality of life in patients with chronic pain. Based on previous research showing pain intensity and certain personality dispositions (i.e., neuroticism, introversion, and low conscientiousness) associated with poor

health outcomes [4, 9], we expected that spouse neuroticism, introversion, and low conscientiousness would add to the burden of pain by imposing poor health across pain levels. Our results partially support our hypothesis. On the one hand, the predicted moderation occurred for spouse neuroticism and extraversion. On the other hand, these findings were not replicated for conscientiousness, and the moderation of neuroticism and extraversion only occurred for physical and mental components of health-related quality of life, respectively.

Research has repeatedly shown that experiencing pain impacts negatively on the physical and mental health status of individuals [42–45]. In our study, this was replicated when spouse neuroticism and introversion were low or moderate (i.e., health-related quality of life decreased with pain). However, pain intensity was weakly or non-significantly associated with health outcomes when spouse neuroticism or spouse introversion were high, indicating similar levels of (low) functioning irrespective of the intensity of the stressor (pain) and suggesting that spouse personality adds to the burden of pain on health-related quality of life, especially at lower levels of pain intensity. A mechanism by which spouse personality might influence pain-health associations is proposed in accordance with the Transactional Model Of Health [18], although this remains speculative and further conclusions cannot be drawn from the present study results.

The Transactional Model Of Health and more recent discussions on interpersonal models of health in chronic pain [7, 18] propose that spouse appraisal might enhance similar cognitive patterns in patients, ultimately explaining patient behavior and health-related quality of life. Individuals scoring high in neuroticism tend to be fearful and preoccupied and report poor mental and physical health status [46–48]. Similarly, spouses' worry and negativity towards the patient's pain behavior has been associated with impaired physical and mental health of pain patients [17, 49]. According to the Transactional Model of Health, the moderating effect of spouse neuroticism revealed in the present investigation would be explained by means of modeling mechanism by which spouse preoccupation and worry would enhance similar affective and cognitive reactions in patient. These affective states are known to lead to maladaptive behaviors (i.e., avoidance of movement and disuse of painful body parts due to fear) and, ultimately, to impaired physical status [50], which would be consistent with our findings.

In our study, pain-to-health associations in the patient also varied as a function of spouse extraversion. Specifically, patients whose spouses presented low levels of extraversion (i.e., introversion) showed poor mental health irrespective of the intensity of their pain. Research in chronic pain has indicated that optimism, social interactions, and physical activities are key factors associated with the mental well-being of pain patients [23, 51–53]. However, evidence suggests that individuals low in extraversion are not very physically active, pessimistic, and have little interest for social interactions [9, 54]. Again, though this is only a hypothesis, a possible mechanism explaining these results is

TABLE 2: Moderation analysis of neuroticism in the relationship between pain intensity and Physical Functioning.

Block	Independent variables	β	95% CI	t	p	R^2	F	p
1	Patient age	-0.22	-0.62, -0.13	-3.01	0.003	0.104	4.05	<0.001
	Patient sex	<0.01	-6.24, 6.40	0.02	0.981			
	Pain duration	-0.08	-0.70, 0.17	-1.21	0.229			
	Educational level	0.03	-4.93, 8.14	0.49	0.628			
	Patient N	-0.01	-0.43, 0.37	-0.13	0.899			
	Patient E	0.15	0.03, 0.87	2.12	0.035			
	Patient C	0.06	-0.28, 0.66	0.80	0.424			
2	Patient pain intensity	-0.45	-8.94, -4.73	-6.41	<0.001	0.138	30.25	<0.001
3	Spouse N	-0.01	-0.35, 0.39	0.12	0.907	<0.001	<0.01	0.969
4	Spouse N * patient pain	0.19	0.08, 0.54	2.65	0.009	0.021	7.01	0.009

Note. R^2 is adjusted. R^2 and F refer to changes in each block. Reported beta values are standardized and correspond to the final model. N, neuroticism; E, extraversion; C, conscientiousness.

TABLE 3: Moderation analysis of extraversion in the pain-mental health relationship.

Block	Independent variables	β	95% CI	t	p	R^2	F	p
1	Patient age	0.08	-0.05, 0.20	1.17	0.244	0.265	10.50	<0.001
	Patient sex	-0.06	-4.67, 1.60	-0.97	0.334			
	Pain duration	-0.06	-0.33, 0.11	-0.95	0.341			
	Educational level	0.10	-0.89, 5.79	1.45	0.150			
	Patient N	-0.36	-0.70, -0.30	-4.86	<0.001			
	Patient E	0.11	-0.04, 0.38	1.58	0.116			
	Patient C	0.10	-0.07, 0.41	1.39	0.166			
2	Patient pain intensity	-0.25	-3.03, -0.90	-3.65	<0.001	0.030	8.37	0.004
3	Spouse E	0.02	-0.18, 0.24	0.29	0.770	<0.001	<0.01	0.995
4	Spouse E * patient pain	-0.17	-0.30, -0.03	-2.47	0.014	0.016	6.10	0.014

Note. R^2 is adjusted. R^2 and F refer to changes in each block. Reported beta values are standardized and correspond to the final model. N, neuroticism; E, extraversion; C, conscientiousness.

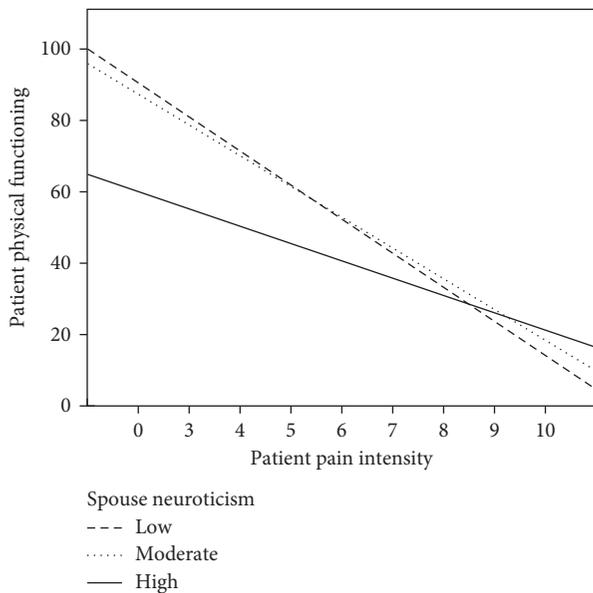


FIGURE 1: Neuroticism as a moderator of the relationship between pain intensity and Physical Functioning.

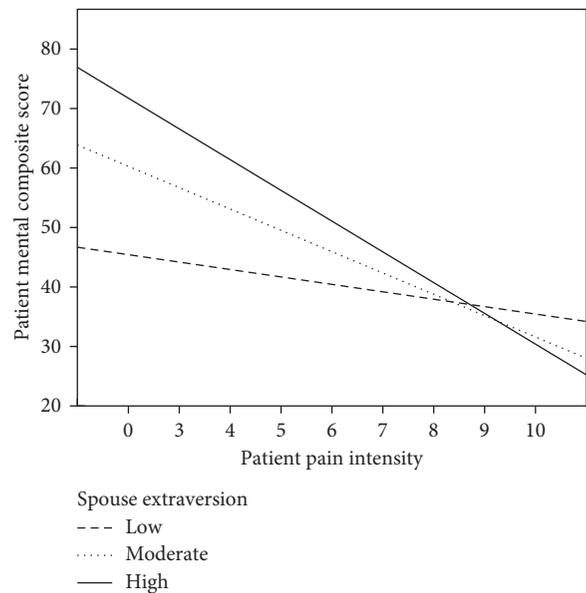


FIGURE 2: Extraversion as a moderator of the pain intensity to mental health relationship.

provided in accordance with the Transactional Model of Health. Specifically, it is possible that introverted spouses may add to the patients' mental burden when experiencing lower levels of pain by stimulating pessimistic thoughts about the disease and failing to promote the use of beneficial

coping efforts, such as social interactions and physical activity.

Regarding the other personality dimensions, our study revealed that spouse openness to experience, agreeableness, and conscientiousness did not moderate the pain-health

relationship in the pain patient. Research has previously shown that the contribution of openness and agreeableness to well-being is small when compared with that of neuroticism, extraversion, and conscientiousness [9, 55, 56]. The fact that conscientiousness did not emerge as a significant moderator of the pain-health relation is surprising in light of the role of this personality dimension in health settings [11]. However, its role in chronic pain settings has been argued to be modest [57–59], so its contribution might not be generalizable to all populations.

In our study, spouse neuroticism moderated pain-to-physical health associations, while the moderation of extraversion occurred for mental health. Extraversion is frequently associated with better physical and mental health in the general population [9]. However, its relation with physical health in pain settings appears to be less clear [57, 60], which might explain the results in our study. It is less clear why neuroticism of the spouse only correlated to physical and not to mental health. Most studies show a negative association between neuroticism and mental health [8, 57], so one would also expect a moderating effect neuroticism on pain-to-mental health associations. In fact, there is previous evidence to suggest that the relationship between a stressor (i.e., everyday problems) and both affective and physical problems are moderated by spouse neuroticism [19]. While the present study replicated this moderating effect of spouse neuroticism on physical health status, this was not the case for mental well-being.

The study of spouse personality, the inclusion of important covariates of patient health (i.e., patient personality and demographic factors), and the analysis of moderation are some of the strengths of the present investigation. Previous research had explored the association between spouse behaviors (i.e., response styles) and several outcomes in the patient, including pain intensity reports and physical and mental health status [16, 61, 62]. However, the role of spouse personality, as well as the moderating effect of spouse characteristics remained unexplored. The present study adds to the existent literature by showing that a possible mechanism by which spouse factors (i.e., personality) might contribute to patient health is by exacerbating or attenuating its relationship with pain intensity. Also importantly, moderation occurred even after controlling for patient demographic and personality characteristics.

The present study is not without limitations. Although some mechanisms explaining the moderation effects were proposed, they should be considered as hypotheses and need further investigation. Also, the effect sizes of the moderator were low. Although this is frequent in moderation studies, the power of the associations should not be overestimated. Additionally, some factors that might be important for the mental well-being of couples, such as length and quality of marriage, were not assessed in this investigation. In fact, while being married was a key eligibility factor in the study, the quality of the relationship, even without marriage, might be an interesting factor to be considered in the present study, as well as in future, similar investigations. Finally, there are methodological limitations in this study too. For example, the design used prevents us from drawing any causal

relationship from our findings and do not allow us to determine the direction of the associations. Also, the exclusion of unmarried couples inevitably affects the generalizability of findings.

5. Conclusions

While acknowledging the aforementioned shortcomings, our study might be important for applied settings: first, because patient and spouse characteristics in this study (patient health status and pain intensity and patient and spouse personality) were comparable to those of previous investigations, thus supporting the generalizability of the results; also, because the results revealed that the relationship between a chronic stressor (i.e., chronic pain) and health status may be complex. Specifically, our results suggest that this relationship may be influenced by contextual variables (i.e., spouse personality), as suggested in previous research [63, 64]. Therefore, it would be interesting to see whether a reduction of situational demands (i.e., pain intensity) before couple-oriented interventions maximizes the positive effects of treatments.

Abbreviations

FFM: Five-factor model
NEO-FFI: NEO five-factor inventory.

Data Availability

The datasets generated and analyzed during the current study are not publicly available due individual privacy but are available from the corresponding author on reasonable request.

Ethical Approval

The Ethics Committee of the Vall d'Hebron Hospital in Barcelona approved the current study.

Consent

All participants provided their written consent to participate in the study. The manuscript does not report individual participant's data.

Conflicts of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authors' Contributions

CSR and SSV designed the study. CSR collected the data. MS and CSR agreed on the analyses needed and CSR performed them. MS and SSV commented on the results and helped in their interpretation. CSR elaborated the first draft, which was then revised by MS and SSV. All authors read and approved the final manuscript.

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Review Article

Association of Depression/Anxiety Symptoms with Neck Pain: A Systematic Review and Meta-Analysis of Literature in China

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Background. Due to its high morbidity and prevalence, the potential relationships of depression/anxiety symptoms in neck pain (NP) are not well demonstrated. **Objectives.** This study aimed to conduct a comprehensive estimation of controlled trials of psychological problems and to test hypotheses concerning whether NP was statistically relative to anxiety/depression symptoms. **Methods.** Chinese literature databases such as the China National Knowledge Infrastructure (CNKI), VIP Information (VIP), Chinese Biomedicine (CBM), and Wanfang Data (WANFANG) were scientifically searched for reports published until February 5, 2018. Controlled trials incorporating NP patients with anxiety/depression versus healthy people were contained. Two researchers screened each article and extracted data, respectively, and blinded to the findings of each other. Meta-analysis was conducted by the Cochrane Collaboration's RevMan 5.3 and Stata 14.0 (Stata Corp LP, USA) software. **Results.** We identified 13 eligible studies involving 2339 patients and 3290 healthy people. Compared with healthy control participants, the findings indicated that depression/anxiety symptoms were more common or severe in NP patients (respectively, SMD = 0.89; 95% CI = (0.58, 1.20); $P < 0.01$ and SMD = 0.92; 95% CI = (0.65, 1.20); and $P < 0.01$), results from the pooled data demonstrated no statistical significance between depression/anxiety symptoms and gender in NP patients (resp., SMD = 0.16; 95% CI = (-0.18, 0.51); $P = 0.35$ and SMD = -0.08; 95% CI = (-0.42, 0.27); and $P = 0.67$), and the combined data of the incidence of depression or anxiety symptoms revealed significant difference between NP patients and healthy persons (resp., RR = 4.81; 95% CI = (3.30, 7.01); $P < 0.01$ and RR = 3.29; 95% CI = (2.16, 5.00); and $P < 0.01$). In addition, we did not find articles that met the inclusion criteria, which compared NP patients with other physical illnesses in terms of anxiety/depression symptoms. **Conclusions.** This meta-analysis suggests that anxiety/depression symptoms are associated with high morbidity in NP patients. We consider these reports support the viewpoint that nonspecific mechanisms mediate mental disturbances in NP. This study may have clinical value for NP, offering an underlying target for the prevention and treatment of anxiety/depression.

1. Introduction

Neck pain (NP) has become a common public health problem all over the world, with a high rate of disability, presents a negative impact on the health and quality of life in people, and exerts great pressure on individuals, families, health systems, and social economy [1–3]. Reportedly, NP was ranked the fourth leading cause of disability next to ischemic heart disease, cerebrovascular disease, and lower respiratory infection, with an annual prevalence rate exceeding 30% [4, 5]. In 2005, over a third of a billion had experienced neck pain

more than 3 months of duration [4, 5]. Preliminary statistics showed that the incidence of NP in China ranged between 3.8% and 17.6%, and it affected nearly 15% of the global population [6, 7]. NP has obvious financial problems and the annual economic losses caused by NP are as high as \$5 billion in America, while it can reach \$800 million just for the treatment cost per year in China [6]. The prevention and treatment of NP has attracted the wide attention of people from all walks of life and has important practical significance for the study of NP.

The clinical symptoms of NP are complicated, which mainly include neck, shoulder and back pain, stiffness and

weakness of upper limbs, numbness of fingers, dizziness, nausea, vomiting, and even blurred vision [8]. According to its clinical symptoms, it is divided into three syndromes, namely, cervical radiculopathy, cervical myelopathy, and axial neck pain [9]. By contrast, it contains seven types in China, including neck type, nerve root type, vertebral artery type, sympathetic type, spinal cord type, mixed type, and other type (mainly include esophageal compression type) [10]. The clinical diagnosis of NP is established on the basis of the identification of positive symptoms via diagnostic criteria and the exclusion of organic illness, for instance, unexplained dizziness and numbness [10]. Treatment for NP mainly depends on lifestyle intervention, medications, and physical therapies [11].

Research has found that mental health disorders are always connected with physical illness [12, 13] and is also more common in developing than developed countries [14]. What is particularly exciting here is the abundant description of depression/anxiety symptoms in NP. However, scholars differ in opinions on the nature of their relationships [15, 16]. In short, at present, it exists two opposing schools of thought: one considers that NP may be tied closely to depression/anxiety through some pathogenesis and the other considers the associations between NP and mental disorders as nonspecific or chance events.

Despite plentiful descriptions have been reported about mental disturbs in NP patients, no systematic evaluation of the relationship between NP and depression/anxiety symptoms has been found. This article is to systematically review prospective cohort or case-control studies and investigate the association between NP and anxiety/depression symptoms. We completed the quality assessment of included studies to analyze any inconsistencies in data. The research questions are (1) whether depression/anxiety symptoms are more common or serious in NP patients than in healthy people or patients with other medical diseases? and (2) does depression/anxiety symptoms differ from gender in NP patients?

2. Methods

2.1. Search Strategy. According to Cochrane Reviews' Handbook, we developed a study protocol for this systematic review and meta-analysis [17]. Electronic searches were systematically performed in CNKI, VIP, CBM, and WANFANG databases up to February 5, 2018, by two authors (Ting Fang and Mei Chen). Medical subject headings (MeSH) terms relevant to neck pain, anxiety, and depression was utilized in the search, and the same terms in Chinese databases. Then, we browsed the abstracts and full-text articles, respectively, and picked the eligible studies in line with the inclusion criteria. Additionally, we also manually searched the relevant lists of all eligible studies to identify further potential studies and contacted reference authors for additional data if necessary.

2.2. Criteria for Selecting Articles. Inclusion criteria include (1) prospective cohort or case-control studies that concerned

anxiety/depression symptoms measured at baseline and their relationship with neck pain; (2) population-based studies that have compared a group of persons with neck pain with another group of either healthy persons or persons with other medical illness; (3) studies that evaluated depression and anxiety symptoms via validated psychometric testings or a structured clinical interview; (4) people diagnosed with neck pain utilizing a certain diagnostic criterion and patients' gender, age, the source of the case, and duration of illness were not limited; and (5) studies must have provided reasonable data for estimating effect size and confidence intervals.

Exclusion criteria include duplicate studies, animal experiments, no clear diagnostic criteria for NP, the measures of anxiety/depression symptoms were not standardized, studies that included treatment measures; and studies that only included NP patients as a subgroup of a large sample and not compared, respectively, from the other participants.

2.3. Data Extraction. Data were independently extracted from the eligible studies by two authors (Ting Fang and Mei Chen) and cross checked. Any discrepancies were discussed among Fushui Liu, Meimei Zhao, and Fanyuan Zhou. The key information was collected systematically using a pre-defined Excel template. It mainly included first author, year of publication, case source, baseline characteristics for participants (age, sex, and number of participants), diagnostic criteria of NP, assessment standards of depression and anxiety symptoms, and outcome assessments. Where possible, we contacted the first author for clarifying the ambiguous information that provided in some studies.

2.4. Quality Assessment. For detecting bias of included studies, the methodological quality was assessed according to a validated rating scale [18], which was used in psychiatric case-control studies. For this meta-analysis, we regulated this scale and researched selection bias of cases (seven items), selection of bias of controls (six items), and information bias (one item). The quality assessments were completed independently by two reviewers (Ting Fang and Mei Chen). Disagreements would be settled by discussing and analyzing between reviewers.

2.5. Data Analysis. We used RevMan 5.3 statistical software (the Nordic Cochrane Centre, Copenhagen; the Cochrane Collaboration, 2014) for meta-analysis. We defined $P \leq 0.05$ as statistically significant between studies. We calculated combined risk ratio (RR) with 95% confidence intervals (CI) for the categorical data; as continuous variables, we estimated combined standard mean difference (SMD) with 95% CI. The studies' heterogeneity was evaluated by the chi-square test and Higgins I^2 test, and when $I^2 \leq 50\%$ and $P \geq 0.10$, the fixed effect model was used or else the random effect model was applied.

2.6. Ethical Statement. All analyses were based on previously published studies, and so ethical approval was superfluous.

3. Results

3.1. Search Results. Totally, 378 potential literature citations were initially obtained through database examinations. We removed 164 duplicates with EndNote software. 78 articles were ruled out through scanning the title and abstracts. And 118 articles were eliminated according to the exclusion and inclusion criteria. In the rest 18 articles, 3 of them did not compare with healthy people or patients with other medical disease, 2 studies failed to have assessment standards of depression and anxiety symptoms, and 13 eligible articles [7, 19–30] were included finally. The whole selection process is shown in Figure 1.

3.2. Basic Characteristics of Eligible Studies. The eligible studies were published between 2002 and 2017 in China, and 2339 patients and 3290 healthy controls were included. In these studies, regarding the source of cases, three studies [7, 22, 24] were multiple-center controlled trials, two studies [19, 26] were ambiguous, and the remaining studies were single-center controlled trials. Also, they were all completed in outpatients and inpatients, except one [29] which was completed in college students. As for the source of cases in control groups, seven groups [7, 19, 20, 25–28] were from domestic normal population, and the others were healthy people.

NP was diagnosed in 4 studies [22, 25, 29, 30] using the diagnostic criteria acknowledged in China, and the others used self-rating criteria which were validated and reliable. As for the diagnostic criteria of depression and anxiety symptoms, all the studies reported validated scale. Seven studies [7, 19–21, 23, 25, 26] utilized the symptom check list-90 (SCL-90), and 1 study [24] used the symptom check list-290 (SCL-290) to assess depression and anxiety symptoms levels; among them, one study [19] also used the state-trait anxiety inventory (STAI). One study [30] utilized generalized anxiety disorder-7 (GAD-7) and patient health questionnaire-9 (PHQ-9) as the evaluation standard, 4 studies [22, 24, 27, 28] utilized self-rating depression scale (SDS), 2 studies [24, 27] used self-rating depression scale (SAS), and the criteria in the last one [29] were unclear. Table 1 shows the key characteristics of the included studies: study design, sample sizes, design, mean ages, diagnosis criteria for NP, and scales utilized for assessments of the levels of anxiety and depression.

3.3. Quality Assessment. Table 2 reports the methodological quality of the included studies. The clinical setting used for recruitment was frequently reported eligible information, so were the inclusion/exclusion criteria for cases. As for controls, one item concerning the using of students or employees of the research institution was always rated as “no,” indicating good methodological practice. Few studies provided sufficient information about the using of advertising for recruitment. The rest questionnaire items for cases and controls were poorly described. Approximately half studies could not offer enough information on whether the investigators were “masked” or not.

3.4. Depression/Anxiety Symptoms Levels in NP Patients: Continuous. Depression and anxiety scores were, respectively, achieved in 13 and 10 studies that included SCL score and other depression rating scores. Data extracted from both reported significantly heterogeneity in the consistency of study results (respectively, $I^2 = 97\%$, $P < 0.01$, and $I^2 = 94\%$, $P < 0.01$), and the random effects model was applied. Overall, the depression and anxiety symptoms' scores were distinctly higher in NP patients compared to healthy control groups (resp., SMD = 0.89; 95% CI = (0.58, 1.20); $P < 0.01$ and SMD = 0.92; 95% CI = (0.65, 1.20); $P < 0.01$) (Figures 2 and 3).

3.5. Relationship between Anxiety/Depression Symptoms and Gender in NP Patients: Continuous. Only 2 studies [25, 30] reported the relationship between depression/anxiety scores and gender in NP patients. No heterogeneity exist in this analysis, and the fixed effects model was used. The overall results demonstrated no significant difference (resp., SMD = 0.16; 95% CI = (-0.18, 0.51); $P = 0.35$ and SMD = -0.08; 95% CI = (-0.42, 0.27); $P = 0.67$) (Figure 4).

3.6. The Incidence of Depression/Anxiety Symptoms in NP Patients: Categorical. 5 studies [22, 24, 27, 28, 30] provided categorical data for depression and anxiety, but only 2 of them [22, 24] presented categorical data in detail. The combined data revealed significant difference between NP patients and healthy persons, indicated that depression and anxiety were closely linked to NP patients (resp., RR = 4.81; 95% CI = (3.30, 7.01); $P < 0.01$ and RR = 3.29; 95% CI = (2.16, 5.00); $P < 0.01$) (Figure 5).

3.7. Sensitivity Analysis for Continuous Data. We completed the same meta-analysis for depression symptoms level in NP patients excluding 6 studies [22, 24, 27–30] whose psychiatric diagnostics were distinctly different from the remaining studies. The level of depression symptoms of NP patients was still higher than healthy control groups (SMD = 0.52; 95% CI = (0.45, 0.58); $P < 0.01$). More importantly, the I^2 showed no heterogeneity between studies ($I^2 = 0\%$, $P = 0.59$). We also conducted the same meta-analysis for anxiety level in NP patients excluding 3 studies [24, 27, 30], as the psychiatric diagnostics were different from the remaining studies. The I^2 drops from 95 to 44%, $P = 0.10$, and the level of anxiety remained practically stable (SMD = 0.73; 95% CI = (0.62, 0.84); $P < 0.01$). Totally, our different sensitivity analyses presented similar findings and indicated that the different psychiatric diagnostic criteria resulted high risk for the results.

4. Discussion

In this study, we identified 13 eligible studies involving 2339 patients and 3290 healthy people that intended to evaluate possible links between NP and mental disorders. According to our findings, compared to healthy control groups, the depression and anxiety symptoms scores were distinctly

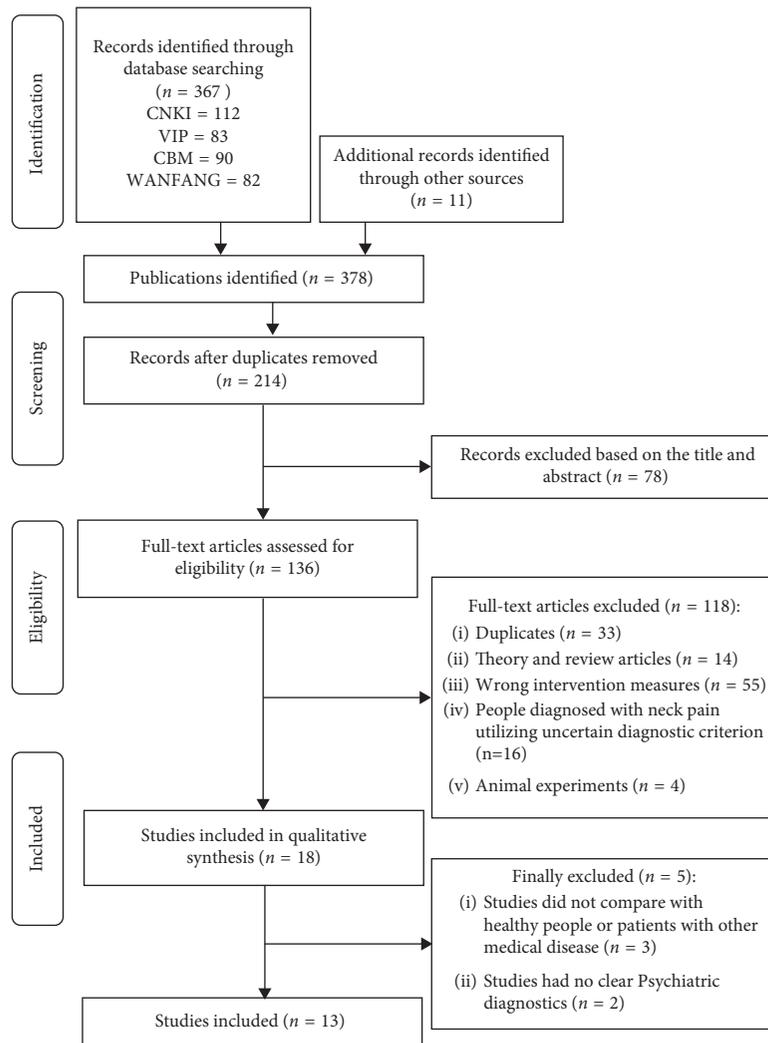


FIGURE 1: Flow diagram outlining the selection of studies for the review.

higher in NP patients. However, there was no significant difference between depression/anxiety symptoms and gender in NP patients. And we failed to obtain case reports to confirm whether NP patients differ from other chronic diseases in terms of anxiety and depression symptoms. But we found articles from PubMed which testified significant difference between NP patients and other chronic physical illnesses in terms of anxiety and depression symptoms [31, 32], and this conclusion deserved further exploration in future. Also, this study suggested that the morbidity of depression and anxiety symptoms was higher in NP patients. Wen and Liu [28] reported that the morbidity of depression symptoms in 336 cases of NP patients was 36.31%, Huang et al. [27] found that incidence of anxiety and depression symptoms in 38 NP patients was 60.53% and 92.11%, respectively, while it was 77% and 84%, respectively, in Sun's survey of 100 NP patients [30].

Neck pain is a common and frequently occurring disease with complicated clinical etiology, which is mainly related to people's bad living habits, such as long-term head bending posture. It is easy to relapse and lasts for a long time [33].

Long-term chronic pain has a profound impact on patients' mental health, and they are prone to negative emotions such as anxiety and depression, which seriously affect patients' quality of life. Reportedly, the longer the chronic pain lasts, the more severe it becomes and the more anxious or depressive it becomes [34]. Meanwhile, anxiety and depression can also promote psychological responses to chronic pain [34].

Some authors investigated the effects of depression and anxiety symptoms in NP patients and found NP and poor quality of life were two factors leading to depression and anxiety [35]. Instead, Galbusera and Gorter reported depression and anxiety symptoms were two major factors affecting the quality of life in patients with musculoskeletal pain [36, 37]. Relatively, few were currently known about causal mechanisms for depression and anxiety symptoms in NP patients. Different mechanisms perhaps could explain the relationship between pain and anxiety from different aspects of biology, psychology, and sociology [38]. Functional imaging studies showed the affective processing area of brain in patients with anxiety and depression symptoms

TABLE 1: Summary of studies included in the meta-analyses on anxiety and depression in NP.

Study	Sample sizes	Design	Group comparison	Mean age	NP diagnostics	Psychiatric diagnostics
He et al. [19]	58 vs. 1 388	Case-control	NP vs. Np	49.5	Self-rating	SCL-90/STAI
Wang et al. [20]	52 vs. 1 338	Case-control	NP vs. Np	48.25 ± 13.36	Self-rating	SCL-90
Lou et al. [21]	60 vs. 56	Case-control	NP vs. HC	54.31 ± 8.18	Self-rating	SCL-90
Chen et al. [22]	106 vs. 76	Case-control	NP vs. HC	51 ± 8 vs. 48 ± 7	Chinese acknowledged diagnostic criteria	SDS
Fang et al. [23]	89 vs. 60	Case-control	NP vs. HC	49.3 vs. 47.6	Self-rating	SCL-90
Yao et al. [24]	122 vs. 122	Case-control	NP vs. HC	58.86 ± 8.28 vs. 59.36 ± 7.04	Self-rating	SCL-290/SDS/SAS
Zhang et al. [25]	30 vs. 1 338	Case-control	NP vs. Np	52	Chinese acknowledged diagnostic criteria	SCL-90
Wei et al. [26]	217 vs. 1 338	Case-control	NP vs. Np	38.00 ± 5.67	Self-rating	SCL-90
Huang et al. [27]	38 vs. 1 340	Case-control	NP vs. Np	/	Self-rating	SDS/SAS
Wen and Liu [28]	336 vs. 1 340	Case-control	NP vs. Np	/	Self-rating	SDS
Wang et al. [29]	105 vs. 198	Prospective cohort	NP vs. HC	/	Chinese acknowledged diagnostic criteria	Self-rating
Chen et al. [7]	1 026 vs. 1 338	Case-control	NP vs. Np	/	Self-rating	SCL-90
Sun et al. [30]	100 vs. 100	Case-control	NP vs. HC	45.98 ± 8.54 vs. 45.86 ± 8.43	Chinese acknowledged diagnostic criteria	GAD-7/PHQ-9

NP, neck pain; HC, healthy controls; Np, normal population; SCL, symptom check list; STAI, state-trait anxiety inventory; SDS, self-rating depression scale; SAS, self-rating anxiety scale; GAD-7, generalized anxiety disorder-7; and PHQ-9, patient health questionnaire-9.

TABLE 2: Methodological quality of the case-control studies (N = 12).

Question	Answer		
	Yes N	No N	Unclear N
<i>Cases</i>			
Was the clinical setting used for recruitment made clear?	10	1	1
Was the denominator from which cases were recruited described?	8	1	3
Was duration of illness adequately described?	4	8	0
Was adequate information given on the total number of patients approached?	3	9	0
Was information given on participants and nonparticipants?	2	10	0
Was information given on the differences between participants and refusers?	0	12	0
Were the inclusion and exclusion criteria described well enough to be replicable?	10	2	0
<i>Controls</i>			
Did the study use controls who were students/employees of the research institution?*	0	11	1
Were controls selected from an explicit sampling frame?	9	2	1
Did the study recruit through advertisements?*	0	11	1
Were similar exclusion criteria applied for controls as for cases?	4	0	8
Was information given on number of controls approached?	6	6	0
Was adequate information given on differences between controls refusing and agreeing?	0	12	0
<i>Information bias</i>			
Were the investigators who rated the exposure masked to participants' status?	9	3	0

*"no" is the answer indicative of good methodological practice.

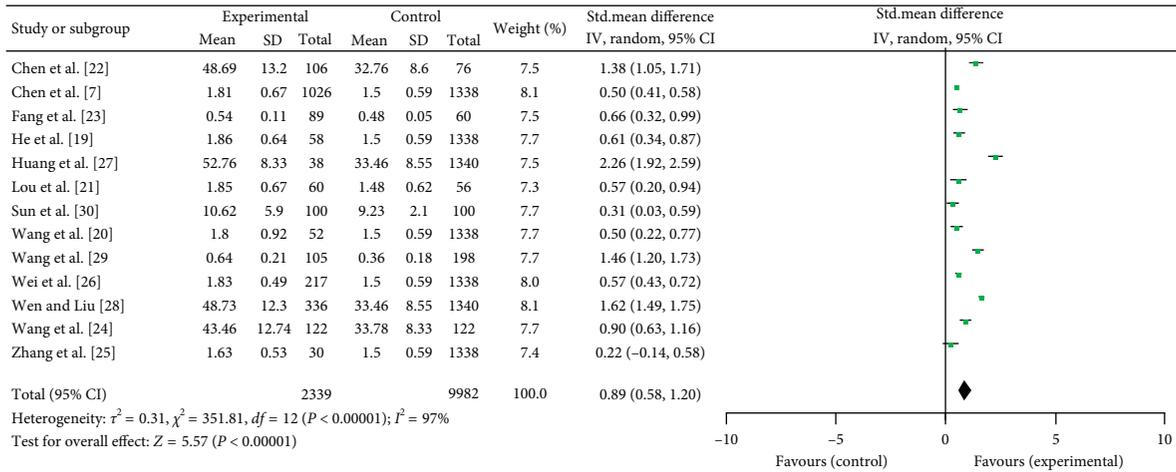


FIGURE 2: Meta-analysis of 13 studies about depression in NP.

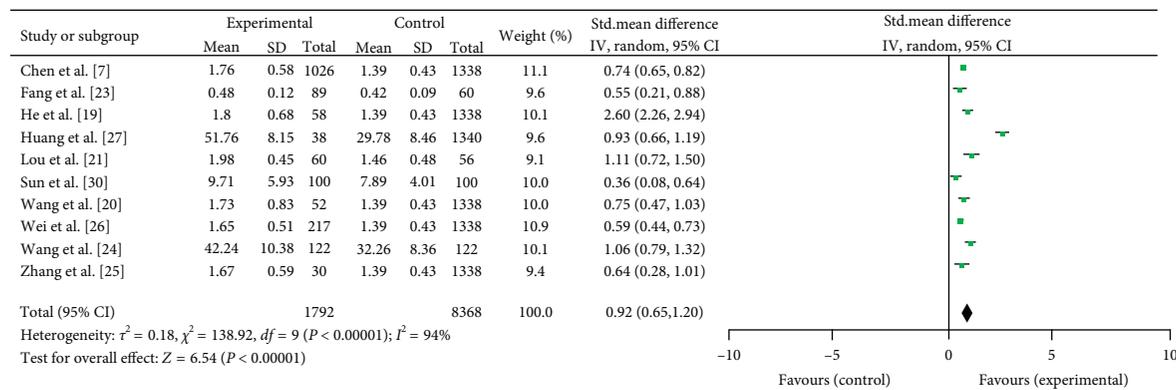


FIGURE 3: Meta-analysis of 10 studies about anxiety in NP patients.

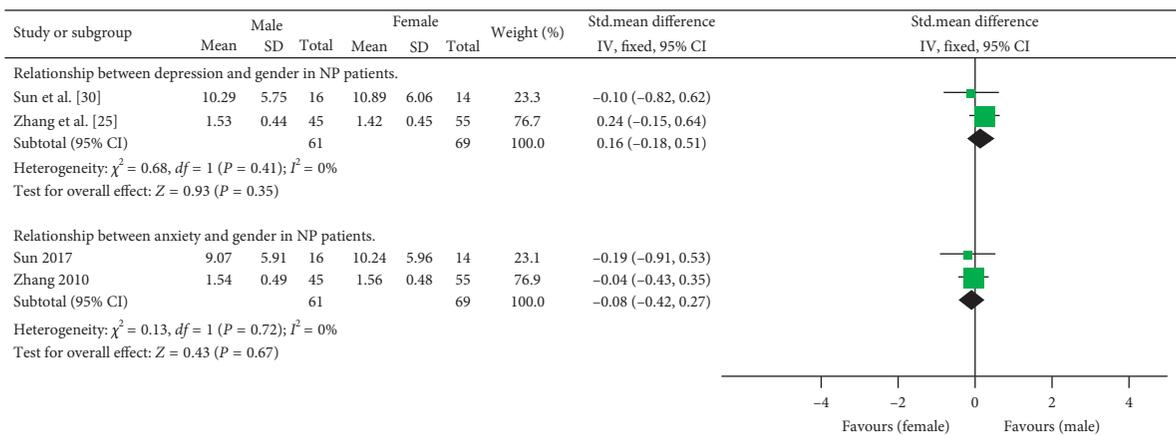


FIGURE 4: Relationship between depression/anxiety and gender in NP patients.

that changed from the insula topology to the prefrontal area of weight-bearing pain management [35]. Besides, it was also found patients with depression and anxiety symptoms had dysfunction of autonomic nervous function and inflammation and activity hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis [38–41]. Interestingly, when

neurotransmitters such as norepinephrine (NE) and 5-hydroxytryptamine (5-HT) decrease, the inhibitory mechanism of pain can be impeded and the development of affective disorders can be promoted [42]. Additionally, studies found an increase in systemic inflammatory markers in the blood of patients with pain disorders and affective

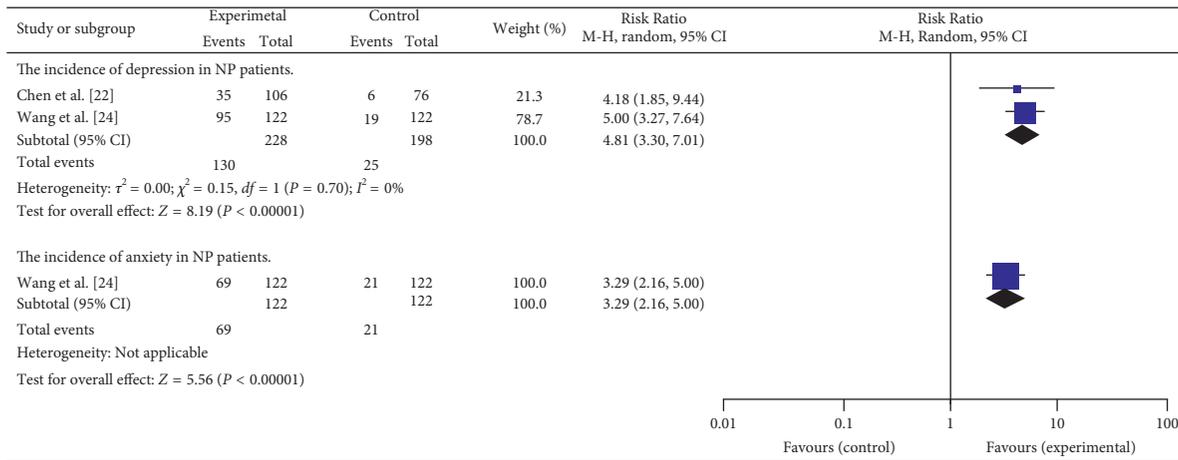


FIGURE 5: The incidence of depression/anxiety in NP patients.

disturbances, which suggests that there is the same basic pathogenetic pathway between the two diseases [43–45]. Similarly, consideration from the view of psychological sociology, pain, and mental disorders are also closely related. Many studies point out that psychological stress and potential obstacles caused by pain can possibly cause immunological changes that eventually results in depression and anxiety [40, 45–47]. In addition, a study had shown that both depression and pain might be risk factors for each other [48].

Anyhow, we should notice potential restrictions of this article. It included first that although we assessed the methodological quality of the included studies via a rating scale [18] for case-control studies, we cannot declare that the rating scale is valid even if the score presented high credibility. Second, few studies provided categorical data, despite 5 studies [22, 24, 27, 28, 30] had involved it, and none of them provided complete data except 2 [22, 24]. The incomplete data may not draw definite conclusion. Furthermore, there were no uniform inclusion and exclusion criteria, which may be a source of heterogeneity.

Despite these limitations, there are still many advantages in our study. In order to improve the accountability of the systematic procedure of this systematic review, we had taken several steps. Two reviewers (Ting Fang and Mei Chen) conducted the electronic searches and picked the suitable studies after browsing the abstracts and full-text articles, respectively, according to the inclusion criteria. Data extraction was also completed, respectively, by two authors. And the methodological quality of the included studies was still evaluated by two authors, and the results were counted.

5. Conclusions

Overall, NP is characterized as a kind of chronic degenerative disease, which has a series of serious influences on body and psychology and severely reduces the quality of life of patients. Therefore, attention should be cautiously attached to the psychological problems in the treatment of NP patients. And clinicians should give the necessary psychological counseling and psychological treatment, which may

help alleviate the mental pain of patients and relieve their physical pain at the same time. Moreover, clinicians who treat pain syndromes should not only improve the patients’ correct understanding of disease and treatment but also strengthen patients’ confidence to overcome the disease.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

All authors made substantial contributions to the conception and design of the work, acquisition, analysis, or interpretation of the data, drafting of the manuscript, and/or critical revision for important intellectual content. All authors approved the final version of the manuscript accepted for publication and agree to be accountable for the integrity of all aspects of the work.

Acknowledgments

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