Negative Mood Regulation Expectancies (NMRE) as a Moderator of the Association Between Stress and Treatment Outcomes in Interdisciplinary Chronic Pain Treatment

Larissa T. Blaettler, MS,*† Juan M. Goméz Penedo, PhD,‡ Kyrill Schwegler, MD,* Niklaus Egloff, MD,§ and Martin grosse Holtforth, PhD*†

Objective: Negative mood regulation expectancies (NMRE) describe the expectancies of an individual regarding his or her ability to regulate or reduce negative mood states by certain cognitive or behavioral strategies. NMRE are closely associated with the actual emotion regulation and potentially buffer the negative psychological and physical health consequences of stress. In the context of chronic pain, stress plays a central role, as long-term stress can have additional negative consequences regarding pain and its progression. The present study investigated the relationship of NMRE with treatment outcome, and more importantly, its buffering role in the association between stress and treatment outcomes.

Method: Two hundred six chronic pain inpatients (fulfilling the *International Classification of Diseases, 10th Revision* [ICD-10] diagnosis of F45.41) of an interdisciplinary treatment completed standardized self-report questionnaires at intake and discharge. Hierarchical linear regression analyses were used to test the main effects of the Negative Mood Regulation Scale—Short Form on pain intensity, pain-related disability, and psychological distress as treatment outcomes and its moderating role in the association of stress and the 3 outcome measures.

Results: A significant main effect of NMRE on treatment outcome was only found for psychological distress. However, for all 3 outcome measures, a significant moderating effect of NMRE on the association between stress level and treatment outcome was found.

Discussion: NMRE appear to play an important role for the outcome of inpatient treatment for chronic pain. Due to their buffering effect on the negative association between stress and therapy outcome, they should be targeted in the treatment of chronic pain.

Key Words: negative mood regulation expectancies, stress, chronic pain, moderation

(*Clin J Pain* 2022;38:351–359)

C hronic pain, defined as long-lasting (>3 mo) or reoccurring pain, affects about one third of the adult population in Europe and is, therefore, a highly prevalent

The authors declare no conflict of interest.

Reprints: Larissa T. Blaettler, MS, Divison of Psychosomatic Medicine, Department of Neurology, Inselspital, Bern University Hospital, Bern, 3010 Switzerland (e-mail: larissatatjana.blaettler@insel.ch).

Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved. DOI: 10.1097/AJP.000000000001020

condition.¹ Clinical experience shows that chronic pain is often associated with a combination of long-term physical, psychological, and social burdens and is frequently accompanied by negative affect, long-lasting distress, and comorbid affective disorders (depression and anxiety).²⁻⁴ While acute stress (defined as "a nonspecific response of the body to a demand") can have an analgesic effect, prolonged or recurring stress may contribute to an increase and a chronification of pain.5-8 Along with pain intensification, stress may also enhance pain perception, for example, a lower pain threshold and a higher pain sensitivity (so-called stress-induced hyperalgesia).7 Moreover, pain itself and its related biopsychosocial burdens can be sources of stress. While other sources of stress can be addressed and thus eliminated, the 2 aforementioned sources can rarely be completely eliminated in pain treatment. Both stress and pain are thus negative experiences that may compromise the body's homeostasis and may have a longer term negative impact on health and well-being. Stress and pain thus exhibit conceptual, physiological, and experiential overlaps. Nevertheless, there are crucial differences, eg, physiologically the role of the hypothalamic-pituitary-adrenal axis in pain remains unclear, and the brain endophenotype is different in pain compared with stress disorders (eg, posttraumatic stress disorder).⁹ Consequently, it is important to help affected individuals cope with stress more effectively and thereby also to modulate potential impacts of stress on pain and affect.

A factor that has been related to stress and its potential negative consequences are *Negative Mood Regulation Expectancies* (NMRE).¹⁰ NMRE are defined as expectancies of an individual to regulate or reduce negative moods by applying certain strategies.¹¹ NMRE are considered to be selfconfirming, that is, the mere expectation of being able to put oneself in a better mood may already improve one's mood.^{12,13} In addition, NMRE may also influence the effectiveness of coping attempts. Individuals with high NMRE apparently regulate negative moods better as they tend to use more adaptive regulation strategies. However, the relationship between NMRE and mood regulation can be assumed to be bidirectional, that is, experiences of successful regulation of negative mood likely fuel better NMRE, and low NMRE may reduce a person's attempts to regulate negative moods.^{13,14} Accordingly, low NMRE are related to maladaptive emotion-regulation *skills*.^{12,15} Unsurprisingly, low NMRE are also associated with depression and anxiety.^{16,17} NMRE has been shown to prospectively predict anxiety and depressive symptoms, symptom severity, and symptom change, ^{13,15,17–19} and accordingly different clinical populations report lower NMRE than healthy controls.13,17,20

Clin J Pain • Volume 38, Number 5, May 2022

www.clinicalpain.com | 351

Received for publication June 4, 2021; revised January 18, 2022; accepted January 22, 2022.

From the *Division of Psychosomatic Medicine, Department of Neurology, Inselspital, Bern University Hospital; †Department of Psychology; §Faculty of Medicine, University of Bern, Bern, Switzerland; and ‡Faculty of Psychology, University of Buenos Aires, Buenos Aires, Argentina.

High NMRE, in turn, seem to buffer the negative consequences of (dis-)stress (ie, anxiety, depression, somatic health problems). Empirical findings in different occupational and clinical populations show that the correlation between (occupational) (dis-)stress and psychological and somatic symptoms is particularly high when peoples' NMRE were low.^{15,20–22}

Although NMRE have been examined in the context of various disorders and their therapies, they have not been studied in the context of chronic pain. However, the ability to successfully regulate emotions has been found to be associated with pain-related impairment and negative affect.²³ Consequently, the aim of the present study was to investigate the association of NMRE with therapeutic outcomes in an interdisciplinary therapy for inpatients with chronic pain. Furthermore, we will test if NMRE moderate the association between stress and therapeutic outcome. We hypothesized that high NMRE (1) positively predicts therapy outcome (in the sense of buffering its effect, that is, higher NMRE will reduce the association between stress and posttreatment severity).

METHODS

Sample

Two hundred six inpatients of a Swiss tertiary psychosomatic university clinic diagnosed with a chronic pain disorder ("F45.41 Chronic pain disorder with somatic and psychological factors" in *International Classification of Diseases, 10th Revision* [ICD-10]; "chronic primary pain" in *International Classification of Diseases, 11th Revision* [ICD-11]; "307.89 Pain disorder with both psychological factors and a general medical condition" in *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* [DSM-5]) were investigated for the present study.^{24–26} Included were patients over 18 years of age who reported their NMRE at intake. Excluded from assessment and analyses were patients (1) who had insufficient German-language proficiency to correctly complete the questionnaires (2) who refused consent for the further use of their data.

Ethics Statement

The research has been approved by the ethics committee of the Canton of Bern, Switzerland (project ID 2018-00493) and is in accordance with the Declaration of Helsinki. All patients were informed about the use of their data for research purposes and provided informed general consent.

Interdisciplinary Pain Treatment (IPT)

At intake, physicians performed an elaborated interview exploring the main symptoms, recorded physical and psychological comorbidities, explained the diagnosis and treatment options in detail, and developed an individualized treatment plan together with the patient. Pharmacotherapy consisted of modifying the existing medication rather than starting new medications. Medication was mainly used to treat main symptom(s) as well as comorbid physical and mental disorders. (The main categories of drugs administered to the patients were paracetamol, novalgin, nonsteroidal anti-inflammatory drugs, tramadol, opioids, antidepressants, antiepileptics, and benzodiazepines. Antidepressants and antiepileptic drugs [pregabalin] were also used as coanalgesics.) The IPT consisted of individual and group therapies provide by specialized pain physicians, psychologists, physiotherapists, and occupational therapists and, where indicated, by social services. Average treatment duration was 25 days (mean = 25.25 d; SD = 5.29 d; range: 15 to 53 d).

Individual psychological treatment consisted of psychotherapy sessions scheduled twice a week, as well as biofeedback. Psychological group therapies included psychoeducation, pain management, mindfulness exercises, and relaxation.

Individual physiotherapeutic treatment consisted of individual sessions and medical training therapy. In group physiotherapy, patients could choose to attend water gymnastics, basic body awareness exercises, moving with the music, and/or nordic walking.

Occupational therapists offered individual sessions in work and household activities, as well as different expressive, musical, and/or artistic group therapies.

In case of limited work capacity, patients could attend social counseling including insurance and budget advice as well as a systematic analysis of working conditions.

Referrals came from primary care physicians, specialists, and other clinics. Indications were made by specialists with expertise in pain medicine. Indication for IPT was given (and covered by health insurances) if previous unimodal therapies had failed, outpatient medical care was no longer sufficient, there was a significant exacerbation in pain symptoms or an increase in medication consumption, and identifiable psychosocial factors or psychological comorbidities negatively affected the pain condition and its therapy.

Measures

In this research, NMRE (operationalized by the Negative Mood Regulation Scale—Short Form [NMR-SF]) and stress (operationalized by the Perceived Stress Scale [PSS-10]) were investigated as potential predictors of treatment outcome.

NMR-SF

The German version of the NMR-SF was used to measure NMRE.²⁷ For purposes of clarity, we called the investigated construct "NMRE" to emphasize expectancies. The NMR-SF consists of 15 items, where individuals have to indicate their beliefs about their ability to regulate negative mood states by applying general, cognitive or behavioral regulation strategies on a 5-point Likert scale from 1 (*strongly disagree*) to 5 (*strongly agree*). Higher scores in the NMR-SF scale thus indicate greater beliefs in successfully regulating negative mood states. Psychometric properties for the translated version are considered as good, and construct validity has been shown.²⁷ In the present study, Cronbach α was 0.81, which can be considered as good.

PSS-10

As a measure of perceived life stress at intake, the German version of the PSS-10 was used.²⁸ The PSS-10 measures the degree to which individuals perceive their lives as stressful. On a 5-point Likert scale from 0 (*never*) to 4 (*very often*), individuals indicated the extent to which they have experienced life as unpredictable, uncontrollable, and overloaded in the past month. Higher scores indicate greater perceived stress. The German version of the PSS-10 has shown good validity and reliability.²⁸ In the present study, the PSS had good internal consistency with Cronbach α of 0.86.

352 | www.clinicalpain.com

Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

Based on the recommendations of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT), treatment outcomes were defined as pain intensity (operationalized by the BPI_intensity scale), pain-related disability as a measure of physical functioning (operationalized by the BPI_interference scale), and psychological distress as a measure of emotional functioning (operationalized by the Hospital Anxiety and Depression Scale [HADS] total score).²⁹

Brief Pain Inventory (BPI)

The German version of the Brief Pain Inventory was used to measure pain intensity (BPI_intensity) and painrelated disability (BPI_interference).³⁰ The BPI consists of 11 items, which are evaluated from 0 to 10 on a rating scale. For BPI_intensity, 4 items were rated from 0 (*no pain*) to 10 (*pain as bad as you can imagine*) asking about the worst, least, and average pain during the past 24 hours as well as the current pain. For BPI_interference, 7 items were rated from 0 (*does not interfere*) to 10 (*completely interferes*) asking about how much pain has interfered with aspects of life. For the German version, the 2-factor structure was confirmed, and it showed similar psychometric properties as the original version.³⁰ In the present sample, both subscales showed good internal consistency with Cronbach α of 0.90 (BPI_intensity) and 0.81 (BPI_interference).

HADS

As a measure of emotional functioning, the German version of the Hospital Anxiety and Depression Scale (HADS-D) was used.³¹ In the HADS, individuals had to indicate the degree of depressive and anxious symptoms they had experienced in the past week using 4-level response alternatives from 0 to 3. In total, the HADS is comprised of 14 items, which can be divided into 2 subscales (Depression and Anxiety). The HADS was specifically designed for nonpsychiatric patient groups by explicitly excluding anxiety and depression-related symptoms associated with somatic disorders. This makes the HADS particularly suitable for the present sample of chronic pain patients. For the analyses of the present study, only the total score (HADS_total) was used as an indicator of the overall psychological distress. The translated version showed good reliability and validity indices.³² The internal consistency of the total score in the present sample was good with $\alpha = 0.87$.

Procedure

Patients completed the self-report questionnaires described above in maximally 3 appointments at intake (t_0) and 2 at discharge (t_1) supported by a research assistant. Number of appointments and scheduled duration for each may have varied between patients, as they were flexibly adjusted according to the patients' pain level and general condition, or patients canceling appointments on short notice, scheduling conflicts with already scheduled therapies, or patients leaving the clinic before the scheduled psychometric assessment. As a result, not all data was available for all patients at discharge, although all included patients had completed the treatment.

Data Analyses

Data analyses were performed using IBM SPSS Statistics (Version 26). Because not all patients for whom negative mood regulation (NMR) values were available at intake provided complete data (especially regarding outcome measures), listwise deletion was used for all analyses.

Descriptive analyses were first performed for demographic and clinical data. Paired t tests were used to calculate pre-post changes. The Pearson correlations were calculated to evaluate the association between the variables under investigation as well as control variables (age, sex, and duration of illness). The significance level was set at $\alpha = 0.05$.

To examine the statistical effects of PSS-10 and NMR-SF at to on BPI_intensity, BPI_interference, and HAD-S_total at t_1 , a hierarchical linear regression analysis was calculated. In a first step, we controlled for the baseline values of the outcome variables. For this purpose, the values of BPI_intensity, BPI_interference, and HADS_total at t_0 (pretreatment values) were included in the model as control variables. Since preliminary analyses showed a significant correlation of sex with BPI_intensity as well as age with HADS_total, these 2 factors were included in the corresponding models as additional control variables. In a second step, the PSS-10 and the NMR-SF were entered. To test for the moderation of NMR-SF on the relationship between PSS-10 and the 3 outcome variables, the interaction term between PSS-10 and NMR-SF values was added to the model in a third step.

For the hierarchical linear regression analyses, all variables were *z*-standardized. For the other analyses (descriptive statistics, t tests, and correlations), raw scores were used.

Based on the IMMPACT criteria, a reduction in pain intensity of $\geq 30\%$ was interpreted as an at least moderate clinically relevant decrease during treatment. For BPI_interference, a decrease of 1 point on the rating scale was considered clinically significant.³³ The reliable change index was used to evaluate changes in the HADS values.³⁴ In this study, a decrease of 8.18 of HADS total score was considered as a reliable and clinically significant change.

RESULTS

Descriptive Statistics

Demographic and Clinical Data

On average, patients were 47.04 years (SD = 13.56 y, range 18 to 81 y). The majority of patients were female (62.6%), married (37.4%), and had vocational training (eg, hairdresser, baker, locksmith) as the highest level of education (51.9%). The average pain intensity at intake was 5.3 (on a Numerical Rating Scale of 0 to 10). Forty-two percent of patients reported an average illness duration between 1 and 5 years. However, it should be noted that a significant proportion of patients (28.2%) also reported an illness duration of > 10 years. Slightly more than half of the patients (53.9%) also had a medically confirmed complete incapacity to work (partial or complete pain-related, medically certified inability to work is a specific Swiss regulation, indicating that, as a result of their pain condition, people are no longer able to carry out their previous occupational activity, or can only do so with restrictions or at the risk of aggravating their state of health). All demographic and clinical data is shown in Table 1. (Overall, NMR values were available for N = 284 patients at intake. However, after listwise deletion (using the predictor variables at intake as well as the outcome variables at intake and discharge) there remained a sample of N = 206 patients. To ensure that the N = 78 excluded patients did not differ from

Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

TABLE 1.	Demographic and	Clinical Characteristics
----------	-----------------	--------------------------

	n (%)
Age	
Mean (SD)	47.04 (13.56)
Range	18-81
Sex	
Female	129 (62.6)
Male	77 (37.4)
Marital status	
In a relationship	34 (16.5)
Married	82 (39.8)
Divorced/seperated	51 (24.8)
Widowed	5 (2.4)
Single	34 (16.5)
Education	
Mandatory school not completed	4 (1.9)
Mandatory school	36 (17.5)
Vocational training	107 (51.9)
High school	7 (3.4)
Community college degree	31 (15.1)
University or college degree	21 (10.2)
Illness duration	
0-3 mo	2 (1.0)
4-6 mo	13 (6.3)
7-11 mo	13 (6.3)
1-5 у	91 (44.2)
6-10 y	29 (14.1)
> 10 y	58 (28.2)
Inability to work	
0%	74 (35.9)
≤25%	4 (1.9)
≤50%	11 (5.3)
≤75%	6 (2.9)
≤100%	111 (53.9)

the patients included in the analyses, both χ^2 and t tests were performed for the descriptive and all variables under investigation.

The χ^2 tests showed that the 2 groups (included vs. excluded patients) did not differ significantly in their frequencies for patient sex ($\chi^2_{1, n=284} = 2.737$, P = 0.098), marital status $(\chi^2_{4, n=283}=3.677, P=0.452)$, education $(\chi^2_{8, n=283}=7.903,$ P = 0.443), illness duration ($\chi^2_{5, n=283} = 8.009$, P = 0.156), and inability to work ($\chi^2_{4, n=283} = 2.663$, P = 0.616).

Similarly, t tests showed no significant differences for age $(t_{282} = -0.714, P = 0.476)$, NMR-SF $(t_{282} = -0.936, P = 0.359)$, PSS-10 ($t_{268} = 1.285$, P = 0.200), HADS ($t_{278} = 1.010$, P = 0.313), BPI_intensity ($t_{272} = 1.810$, P = 0.071) and, BPI_interference $(t_{272} = 1.893, P = 0.059)$ at intake.

Pre-Post Changes

Table 2 shows means, SDs at intake and at discharge, t statistics for the paired t tests as well as effect sizes for the changes. All outcome variables showed significant improvements from intake to discharge. There was a small effect for pain intensity, a medium effect for pain-related disability, and a large effect for psychological distress.

According to the IMMPACT criteria, 36 patients (16.6%) showed an at least moderate clinically important decrease in pain intensity after an average of 3 to 4 weeks of inpatient treatment, 126 patients (51.2%) showed a clinically significant reduction in pain-related disability, and 49 patients (23.8%) showed a reliable change in psychological distress. Moreover, the number of patients who reached the clinical cutoff for significantly high levels of psychological distress (cutoff >13) decreased from 169 (82.0%) to 117 (56.8%), a reduction of 34.2%.

Correlation Analyses

All correlations are shown in Table 3 and are based on their pretreatment scores for all variables. Significant small to large correlations were found between perceived stress and all of the 3 outcome measures, as well as between NMRE and all outcome variables. The correlation between perceived stress and NMRE was also significant and large. Thus, higher perceived stress was slightly associated with higher levels of pain intensity, moderately associated with pain-related disability, and strongly associated with psychological distress; whereas higher NMRE were weakly related to lower levels in pain intensity, moderately related to lower levels in pain-related disability, and strongly related to psychological distress. Lower expectancies regarding NMR were strongly associated with higher levels of perceived stress.

Regression Analyses

Three hierarchical linear regression analyses were conducted to examine the prediction of pain intensity, painrelated disability, and psychological distress at t_1 by perceived stress and NMRE and their interaction at t_0 . Pain intensity, pain-related disability, and psychological distress values at t_0 were entered as control variables in step 1 (for pain intensity, sex was entered as a further control variable). In a second step of the regressions, perceived stress and NMRE were added.

As Table 4 shows, neither perceived stress nor NMRE predicted posttreatment scores (adjusted by intake scores) of pain intensity and pain-related disability. For psychological distress, both perceived stress and NMRE were significant

	Pretreatment		Posttrea	atment		
	Mean	SD	Mean	SD	t	d
BPI—Pain intensity	5.30	1.71	5.01	1.92	3.038**	-0.212
BPI—Pain interference	5.71	1.94	4.37	2.14	11.047***	-0.770
HADS—Total score	19.45	8.16	14.58	7.86	12.375***	-0.862
PSS-10—Total score	22.03	7.58				
NMR-SF—Total score	49.92	9.92				

*P<0.05. **P<0.01

***P < 0.001.

BPI indicates Brief Pain Inventory-German version; d, Cohen d; HADS, Hospital Anxiety and Depression Scale-German version; NMR-SF, Negative Mood Regulation Scale-Short Form (German version); PSS-10, Perceived Stress Scale-German version.

354 | www.clinicalpain.com

Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

TABLE 3. Cor	ABLE 3. Correlations of Psychometric and Demographic Variables at Intake										
	BPI— Intensity	BPI— Interference	HADS— Total Score	PSS-10— Total Score	NMR-SF— Total Score	Age	Sex	Education	Marital Status	Illness Duration	
BPI— Intensity	_										
BPI— Interference	0.492***	—									
HADS— Total score	0.296***	0.571***	_								
PSS-10— Total score	0.160*	0.475***	0.649***	—							
NMR-SF— Total score	-0.200**	-0.400***	-0.644***	-0.621***	—						
Age	0.047	0.054	0.006	-0.074	0.080						
Sex	-0.148*	-0.040	-0.038	-0.116	0.011	0.061					
Education	-0.049	0.015	-0.079	-0.102	0.181**	-0.044	0.014				
Marital status	-0.016	0.047	0.033	0.057	-0.001	-0.129	-0.024	-0.072			
Illness duration	0.105	0.050	-0.060	-0.013	-0.075	0.019	-0.104	-0.083	-0.014		

**P* < 0.05.

****P* < 0.001.

BPI indicates Brief Pain Inventory—German version; HADS-D, Hospital Anxiety and Depression Scale—German version; NMR-SF, Negative Mood Regulation Scale—Short Form (German version); PSS-10, Perceived Stress Scale—German version.

predictors. Hence, higher levels of psychological distress at discharge (ie, worse outcome) were associated with higher levels of perceived stress and lower NMRE at intake.

To test the hypothesized moderation of perceived stress by NMRE, an interaction term between PSS-10 and NMR-SF was entered in the third and final step (Table 5).

For all 3 outcome variables, a significant interaction emerged (Fig. 1). In the models with pain intensity as the outcome (Fig. 1A), patients with high levels of perceived stress (ie, 1 SD above mean) and lower levels of NMRE at intake presented greater posttreatment severity, while patients perceiving high levels of both, stress and NMRE at intake, presented lower pain intensity at posttreatment. In contrast, in patients with low levels of perceived stress at intake, NMRE were not associated with posttreatment outcome.

Similarly, in the models predicting pain-related disability, NMRE significantly moderated the association between perceived stress and posttreatment severity (Fig. 1B). Higher perceived stress levels in the context of low NMRE levels at intake were related to greater posttreatment severity, while

	b	SE _b	β	t	R^2	ΔR^2
BPI_intensity _{t1}						
Step 1: control variables					0.531	0.531
Ŝex	-0.094	0.100	-0.046	-0.944		
BPI_intensity ₁₀	0.727	0.051	0.706	14.358***		
Step 2: Perceived stress and negative mood regulation expectancies					0.536	0.005
PSS-10	-0.027	0.062	-0.026	-0.432		
NMR-SF	-0.117	0.063	-0.114	-1.851		
BPI_interference ₁						
Step 1					0.406	0.406
$\hat{B}PI_{interference_{t0}}$	0.547	0.061	0.539	8.913***		
Step 2					0.432	0.026
PSS-10	0.128	0.074	0.123	1.737		
NMR-SF	-0.111	0.072	-0.105	-1.539		
HADS_total ₍₁						
Step 1					0.564	0.564
$\hat{H}ADS_{total_{10}}$	0.479	0.059	0.500	8.079***		
Step 2					0.620	0.056
PSS-10	0.190	0.057	0.203	3.355***		
NMR-SF	-0.178	0.057	-0.187	-3.109**		

TABLE 4. Hierarchical Linear Regression Analyses Predicting Pain Intensity (BPI_intensity), Pain-related Disability (BPI_interference), and Psychological Distress (HADS_total) at Posttreatment

*P < 0.05

***P* < 0.01

****P* < 0.001.

b indicates unstandardized regression coefficient; β , standardized regression coefficient; BPI, Brief Pain Inventory—German version; HADS, Hospital Anxiety and Depression Scale—German Version; NMR-SF, Negative Mood Regulation Scale—Short Form (German version); PSS-10, Perceived Stress Scale—German version; R^2 , coefficient of determination; ΔR^2 , change in R^2 .

Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

www.clinicalpain.com | 355

^{**}P<0.01

TABLE 5.	Hierarchical L	inear Regression	Analyses With	Interaction	Predicting F	Pain Intensity	(BPI_inten	isity), Pain-relate	d Disability
(BPI_inter	ference), and	Psychological Dis	stress (HADS_to	tal) at Post	treatment	-			-

	b	SE _b	β	t	R ²	ΔR^2
BPI_intensity ₁						
Step 1: control variables					0.531	0.531
Ŝex	-0.102	0.098	-0.050	-1.042		
BPI_Intensity ₁₀	0.702	0.051	0.681	13.846***		
Step 2: Perceived stress and negative mood regulation expectancies					0.536	0.005
PSS-10	0.015	0.063	0.015	0.235		
NMR-SF	-0.118	0.062	-0.115	-1.896		
Step 3: Interaction effect					0.550	0.014
PSS-10×NMR-SF	-0.131	0.049	-0.134	-2.689 * *		
BPI_interference _{t1}						
Step 1					0.406	0.406
$\hat{B}PI_{interference_{t0}}$	0.559	0.060	0.551	9.309***		
Step 2					0.432	0.026
PSS-10	0.179	0.074	0.172	2.433*		
NMR-SF	-0.104	0.071	-0.098	-1.478		
Step 3					0.459	0.027
PSS-10×NMR-SF	-0.180	0.055	-0.177	-3.298**		
HADS_total ₁						
Step 1					0.564	0.564
HADS_total _{t0}	0.479	0.059	0.509	8.118***		
Step 2					0.620	0.056
PSS-10	0.212	0.058	0.226	3.675***		
NMR-SF	-0.177	0.057	-0.187	-3.091 **		
Step 3					0.624	0.004
PSS-10×NMR-SF	-0.071	0.041	-0.078	-1.752*		

b indicates unstandardized regression coefficient; β, standardized regression coefficient; BPI, Brief Pain Inventory-German version; HADS, Hospital Anxiety and Depression Scale-German Version; NMR-SF, Negative Mood Regulation Scale-Short Form (German version); PSS-10, Perceived Stress Scale-German version; R^2 , coefficient of determination; ΔR^2 , change in R^2 .

higher perceived stress levels were associated with lower severity at posttreatment when the patients had higher levels of NMRE at baseline.

The regressions on psychological distress, results showed another significant interaction between NMRE and perceived stress on the outcome. The association between



FIGURE 1. Graphical illustrations of the moderation models between NMR-SF and PSS-10 in relation to treatment outcomes BPI_intensity (A), BPI_interference (B), and HADS_total (C). BPI indicates Brief Pain Inventory; HADS, Hospital Anxiety and Depression Scale; NMR-SF, Negative Mood Regulation Scale—Short Form (German version); PSS-10, Perceived Stress Scale—German version.

356 | www.clinicalpain.com

Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

^{*}P < 0.05.**P < 0.01

^{***}*P* < 0.001.

stress and outcome was stronger in patients with low versus high NMRE at intake. This means that, irrespective of their stress level, patients reporting higher NMRE levels at intake experience lower psychological distress at posttreatment. Thus, NMRE might be able to buffer the negative influence of stress. Note that the division of the 2 predictor variables into high and low values was only done for better illustration in the moderation graphs, but not in the analyses.

DISCUSSION

The purpose of this study was to investigate the prediction of treatment outcome by NMRE as well as the hypothesized buffering role of NMRE on the relationship between perceived stress and treatment outcomes in the context of interdisciplinary inpatient treatment for with chronic pain.

Overall, pain intensity (BPI_intensity), pain-related disability (BPI_interference), and psychological distress (HADS_total) all significantly decreased across on average 3 to 4 weeks of IPT, with small effect sizes for pain intensity, medium effect sizes for pain-related disability, and large effect sizes for psychological distress. Correlation analyses showed significant correlations between NMRE and perceived stress. In addition, both NMRE and perceived stress correlated significantly with the 3 outcome variables.

Hierarchical regression analyses showed only a significant main effect of NMRE on HADS_total as outcome measure of psychological distress. Therefore, high expectancies to successfully regulate negative mood states (ie, high NMRE) predicted a more favorable outcome regarding psychological distress (ie, lower HADS_total values). With regard to pain intensity and pain-related disability, no significant main effect of NMRE on these 2 outcome variables could be found.

However, for all 3 outcome variables, significant moderating effects of NMRE on the relationship between perceived stress and the 3 therapy outcomes could be found. Therefore, it could be demonstrated that the negative influence of perceived stress on treatment outcome was lower for higher levels of NMRE (it is important to note that the main effect should be interpreted with caution and not be overinterpreted, given the significant interaction effects found).

The current study replicates and extends previous findings that high expectancies regarding NMR are able to buffer the negative effect of stress on the outcome.^{15,20-22} The present study extends previous research by investigating NMRE in patients with chronic pain. As already indicated, low NMRE are associated with maladaptive emotion regulation.^{12,15} In chronic pain, maladaptive responsefocused emotion regulation is considered a risk factor for the development and maintenance of chronic pain.³ It is related to a poorer adaptation to pain and its psychological comorbidities (poorer quality of life, increased negative affect, as well as higher anxiety and depression).^{3,23} In this context, it is encouraging that several previous studies have also shown that NMRE can be modified by psychological interventions and that these changes are related to better treatment outcome.14,35-37

Interventions to improve mood regulation expectancies might first focus on the improvement of emotion-regulation skills and related positive experiences. Better emotion-regulation skills may help to lower patients' stress reactions and thereby strengthen their general sense of self-efficacy.³⁸ Interventions targeting positive emotion-regulation *experiences* may then help to facilitate and emphasize experiences of

success (eg, by letting patients gain more and more control over their pain or by becoming aware of any experience of success in life that is not pain-related), facilitate vicarious experiences (eg, by enabling exchange with people with the same history of suffering in group therapies and thus seeing how others with similar problems successfully deal with their disease), use social persuasion (eg, by therapists repeatedly reinforcing patients' beliefs in their abilities to successfully deal with their pain), or teach patients to better regulate emotional arousal (eg, by relaxation or by different interpretations of uncomfortable sensations).³⁸ Thus, psychological interventions targeting emotion-regulation skills may strengthen patients' confidence in their own abilities to successfully regulate negative emotions and thereby improve their expectancies to successfully regulate negative emotions.

In addition to well-established psychological interventions such as acceptance and commitment therapy,39 mindfulness-based stress reduction,40 and emotional awareness and expression therapy,⁴¹ the integrative training of emotional competencies (ITEC),⁴² also focuses on the improvement of emotion-regulation skills. This group-based transdiagnostic training uses techniques from a wide variety of the previously mentioned therapeutic approaches and aims at teaching 7 emotion-regulation skills (psychoeducation, progressive muscle relaxation, breathing relaxation, nonjudgmental awareness, acceptance, and tolerance, effective self-support, analysis, and modification). Based on previous research, ITEC can be considered particularly helpful for handling of stressful emotions more adaptively.⁴³⁻⁴⁵ Compared with the other "therapy packages" mentioned, advantage of ITEC are that it can be implemented as an add-on to other psychotherapeutic treatments and that duration and intensity of the training can be adapted quite flexibly to the group size and the patients' levels of resilience and openness to experience. As such, ITEC may be particularly suitable for the treatment of chronic pain within a larger multidisciplinary multimodal therapy.

Limitations and Future Research

Several limitations characterize this study. The analyzed data are based on self-report questionnaires so that the influence of social desirability cannot be entirely ruled out. The reported effect sizes should not be overinterpreted, as only individuals who completed the questionnaires at posttreatment were included in the analyses. Furthermore, the high correlations between the predictors and the outcome HADS should be noted. Research is needed to investigate and substantiate the conceptual differences between the constructs further. Moreover, the present study did not include follow-up assessments so that statements about the sustainability of effects beyond the end of therapy are precluded. Future research should investigate the prediction of long-term outcomes by NMRE. Moreover, no conclusions can be drawn regarding the direction of causality, that is, it is also plausible that stress could reduce the beneficial effect of NMRE. However, previous studies support the hypothesized direction of influence. Futhermore, no intermediate measurements of the outcome variables were conducted during treatment but only the posttreatment severity adjusted for baseline levels, precluding the analysis of changes induced during treatment. Further, only patients with the chronic pain disorder "F45.41" were examined in this study. Future studies should also include patients with other specific pain conditions and thus support the generalizability of the results presented in this study. In addition, future research should examine the inclusion of

additional covariates to control for their effect on the prediction and moderation by NMRE in adequately sized samples. Because the present study focused on the prediction of outcome by factors measured at baseline, changes in NMRE and PSS-10 during interdisciplinary pain therapy were not included. However, future research will have to examine these changes in more detail (1) to provide evidence that these variables can be regarded as mechanisms of change in the context of chronic pain treatment, and (2) to identify interventions for the specific enhancement of NMRE during pain treatment.

CONCLUSIONS

In the present study, NMRE were identified as important predictors and moderators of outcome in the inpatient therapy of chronic pain. Higher NMRE were associated with better therapy outcomes and seem to buffer the negative effect of stress on outcome. The strengthening of these expectancies, for example, by the improvement of emotion-regulation skills, should be considered in treatment planning for patients with chronic pain.

REFERENCES

- Steingrímsdóttir ÓA, Landmark T, Macfarlane GJ, et al. Defining chronic pain in epidemiological studies: a systematic review and meta-analysis. *Pain*. 2017;158:2092–2107.
- Davis MC, Zautra AJ, Smith BW. Chronic pain, stress, and the dynamics of affective differentiation. J Pers. 2004;72:1133–1159.
- Koechlin H, Coakley R, Schechter N, et al. The role of emotion regulation in chronic pain: a systematic literature review. J Psychosom Res. 2018;107:38–45.
- 4. Lerman SF, Rudich Z, Brill S, et al. Longitudinal associations between depression, anxiety, pain, and pain-related disability in chronic pain patients. *Psychosom Med.* 2015;77:333–341.
- Butler RK, Finn DP. Stress-induced analgesia. Prog Neurobiol. 2009;88:184–202.
- Ferdousi M, Finn DP. Stress-induced modulation of pain: role of the endogenous opioid system. *Prog Brain Res.* 2018;239:121–177.
- Jennings EM, Okine BN, Roche M, et al. Stress-induced hyperalgesia. Prog Neurobiol. 2014;121:1–18.
- Selye H. Stress without distress. In: Serban G, ed. *Psychopa-thology of Human Adaptation*. Boston, MA: Springer US; 1976: 137–146.
- 9. Abdallah CG, Geha P. Chronic pain and chronic stress: two sides of the same coin? *Chronic Stress*. 2017;1:1–10.
- Catanzaro SJ. Mood regulation expectancies, affect intensity, dispositional coping, and depressive symptoms: a conceptual analysis and empirical reanalysis. *Pers Individ Dif.* 1997;23: 1065–1069.
- Catanzaro SJ, Mearns J. Measuring generalized expectancies for negative mood regulation: initial scale development and implications. J Pers Assess. 1990;54:546–563.
- Catanzaro SJ, Mearns J. Generalized expectancies for negative mood regulation development, assessment, and implications of a construct. In: Trusz S, Przemysław B, eds. *Interpersonal and Intrapersonal Expectancies*, 1st ed. London, UK: Routledge; 2016:67–76.
- Pfeiffer N, Kaemmerer A, Mearns J, et al. Generalized expectancies for negative mood regulation and major depressive disorder: the role of previous depressive episodes and comorbid mental disorders. *Psychopathology*. 2011;44:152–157.
- Backenstrass M, Schwarz T, Fiedler P, et al. Negative mood regulation expectancies, self-efficacy beliefs, and locus of control orientation: moderators or mediators of change in the treatment of depression? *Psychother Res.* 2006;16:250–258.
- 15. Kassel JD, Bornovalova M, Mehta N. Generalized expectancies for negative mood regulation predict change in anxiety

and depression among college students. *Behav Res Ther.* 2006; 45:939–950.

- Brockmeyer T, Grosse Holtforth M, Pfeiffer N, et al. Mood regulation expectancies and emotion avoidance in depression vulnerability. *Pers Individ Dif.* 2012;53:351–354.
- Sung SC, Porter E, Robinaugh DJ, et al. Mood regulation and quality of life in social anxiety disorder: an examination of generalized expectancies for negative mood regulation. J Anxiety Disord. 2012;26:435–441.
- Catanzaro SJ, Backenstrass M, Miller SA, et al. Prediction of symptoms of emotional distress by mood regulation expectancies and affective traits. *Int J Psychol.* 2014;49: 471–479.
- Catanzaro SJ, Wasch HH, Kirsch I, et al. Coping-related expectancies and dispositions as prospective predictors of coping responses and symptoms. J Pers. 2000;68:757–788.
- Thorberg FA, Lyvers M. Negative mood regulation (NMR) expectancies, mood, and affect intensity among clients in substance disorder treatment facilities. *Addict Behav.* 2006;31:811–820.
- Mearns J, Cain JE. Relationships between teachers' occupational stress and their burnout and distress: roles of coping and negative mood regulation expectancies. *Anxiety Stress Coping*. 2003;16:71–82.
- Mearns J, Mauch TG. Negative mood regulation expectancies predict anger among police officers and buffer the effects of job stress. J Nerv Ment Dis. 1998;186:120–125.
- Agar-Wilson M, Jackson T. Are emotion regulation skills related to adjustment among people with chronic pain, independent of pain coping? *Eur J Pain*. 2012;16:105–114.
- 24. World Health Organization. International Statistical Classification of Diseases and Related Health Problems, 10th ed. Geneva, Switzerland: WHO; 2016.
- World Health Organization. International Statistical Classification of Diseases and Related Health Problems, 11th ed. Geneva, Switzerland: WHO; 2019.
- American Psychiatric Assosiation. *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. Arlington, VA: APA; 2013.
- 27. Pfeiffer N, Krieger T, Brockmeyer T, et al. Die Kurzversion der NMR Skala (NMR-SF) zur Erfassung der selbsteingeschätzten Fähigkeit zur Regulation negativer Stimmungen: Überblick und Konstruktvalidierung [The Short Form of the NMR Scale (NMR-SF) as an Instrument for Measuring the Self-rated Ability. *Psychother Psychosom Medizinische Psychol.* 2014;64: 108–114.
- Klein EM, Brähler E, Dreier M, et al. The German version of the Perceived Stress Scale—psychometric characteristics in a representative German community sample. *BMC Psychiatry*. 2016;16:1–10.
- Turk DC, Dworkin RH, Allen RR, et al. Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. *Pain*. 2003;106:337–345.
- Radbruch L, Loick G, Kiencke P, et al. Validation of the German Version of the Brief Pain Inventory. J Pain Symptom Manage. 1999;18:180–187.
- Herrmann-Lingen C, Buss U, Snaith RP. Hospital Anxiety and Depression Scale, Deutsche Version (HADS-D), 3rd ed. Bern, Germany: Huber; 2011.
- Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale. J Psychosom Res. 2002; 52:69–77.
- Dworkin RH, Turk DC, Wyrwich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT Recommendations. J Pain. 2008; 9:105.
- Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J Consult Clin Psychol. 1991;59:12–19.
- Cloitre M, Stovall-McClough KC, Miranda R, et al. Therapeutic alliance, negative mood regulation, and treatment outcome in child abuse-related posttraumatic stress disorder. *J Consult Clin Psychol.* 2004;72:411–416.

358 | www.clinicalpain.com

Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

- Cloitre M, Stovall-McClough KC, Nooner K, et al. Treatment for PTSD related to childhood abuse: a randomized controlled trial. *Am J Psychiatry*. 2010;167:915–924.
- Ford JD, Steinberg KL, Zhang W. A randomized clinical trial comparing affect regulation and social problem-solving psychotherapies for mothers with victimization-related PTSD. *Behav Ther.* 2011;42:560–578.
- Bandura A. Self-efficacy: toward a unifying theory of behavioral change. *Psychol Rev.* 1977;84:191–215.
- Hann KEJ, McCracken LM. A systematic review of randomized controlled trials of acceptance and commitment therapy for adults with chronic pain: outcome domains, design quality, and efficacy. J Context Behav Sci. 2014;3:217–227.
- Robins CJ, Keng SL, Ekblad AG, et al. Effects of mindfulnessbased stress reduction on emotional experience and expression: a randomized controlled trial. *J Clin Psychol.* 2012;68: 117–131.

- Lumley MA, Schubiner H, Lockhart NL, et al. Emotional awareness and expression therapy, cognitive-behavioral therapy, and education for fibromyalgia: a cluster-randomized controlled trial. *Pain*. 2017;158:2354–2363.
- Berking M. Training Emotionaler Kompetenzen [Training of Emotional Competencies], 4th ed. Heidelberg, Germany: Springer; 2017.
- Berking M, Ebert D, Cuijpers P, et al. Emotion regulation skills training enhances the efficacy of inpatient cognitive behavioral therapy for major depressive disorder: a randomized controlled trial. *Psychother Psychosom.* 2013;82:234–245.
- Berking M, Wupperman P, Reichardt A, et al. Emotionregulation skills as a treatment target in psychotherapy. *Behav Res Ther.* 2008;46:1230–1237.
- 45. Ehret AM, Kowalsky J, Rief W, et al. Reducing symptoms of major depressive disorder through a systematic training of general emotion regulation skills: protocol of a randomized controlled trial. *BMC Psychiatry*. 2014;14:1–9.