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PAIN MANAGEMENT IN CLINICAL AND HEALTH PSYCHOLOGY,
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EDITORIAL
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Editorial: Pain Management in Clinical and Health Psychology

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Editorial on the Research Topic

Pain Management in Clinical and Health Psychology

According to a recent perspective article (Castelnuovo, 2017), the exclusive medical approach in clinical field would be considered "a soul without psychology" (TIME magazine—Dec. 24, 1956). Clinical and health psychology have improved the biopsychosocial framework (Engel, 1977, 1997) ensuring a deep attention to the psychosocial issues in treating different organic and psychosomatic disorders and counterbalancing the evidence based approach with the etiquette based one in the clinician-patient relationship and communication (Kahn, 2008; Castelnuovo, 2013). Nowadays clinical and health psychology has found solutions (protocols, treatments, evidences, etc.) in any medical area: psycho-cardiology, psycho-oncology, psycho-geriatrics, psycho-pneumology, psycho-endocrinology, neuropsychology, and psychology in pain management too. "No health without mental health" (Prince et al., 2007) and "No medicine without psychology" (Castelnuovo, 2010) are two messages still effective in the daily clinical practice.

About pain management, it is important to underline that chronic pain is a relevant health problem frequently associated with psychological distress, dysfunctions in physical and social functioning, reductions in quality of life and elevated direct and indirect costs. Medical approach is useful for treating chronic pain, but effects on pain are modest (Turk et al., 2011). Psychological contributions play an important role in pain management (Castelnuovo et al.; Williams et al., 2012; Veehof et al., 2016). In fact psychological treatments are recognized as generally effective for pain (Castelnuovo et al.).

Psychological approaches in managing pain have evolved considerably and now understanding and managing the cognitions, emotions, and behaviors that accompany the situation of discomfort can actually reduce the pain intensity and the interference of pain with daily life. Psychological therapies are highly indicated both for the treatment of painful conditions and for the treatment of pain related to several neurological diseases. Similar positive results about psychotherapy efficacy were reported in specific pain disorders such as low back pain, fibromyalgia, tension-type headache and migraine, pain associated with rheumatoid arthritis, chronic abdominal pain in adolescents, chronic orofacial pain, etc. (Castelnuovo et al.).

Another important contribution of clinical health psychology in pain management is the delivery of guidelines and best practices for more integrated clinical and impactful applications. One example to replicate is the Italian Consensus Conference on Pain in Neurorehabilitation that tried to fill in the gap between theory and practice providing practical recommendations for clinicians (Castelnuovo et al.;Aloisi et al., 2016; Tamburin et al., 2016; Castelnuovo et al., 2018).

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Clinical health psychology focuses also on the study of the psychological determinants in pain patients such as the role of depression, anxiety, pain-related disability, catastrophic thinking, psychological inflexibility, coping skills, beliefs, attitudes, expectations, self-efficacy, placebo, and nocebo effects, etc. Different psychological models of pain and disability (such as Fear-avoidance, Acceptance and commitment, Misdirected problem solving, Self-efficacy and Stress-diathesis models) have tried to highlight the psychological processes behind pain (McCracken and Morley, 2014).

A recent area of investigation is the study of attributions: how could comorbid symptoms worsen or improve each other? The central cognitive components of chronic pain are under investigation and could significantly influence the recovery process (Blågestad et al.).

Also measuring correctly and finely the pain phenomenon is relevant to understand the subjective experience in each patient (Boonstra et al.).

Moreover, to study the patient's life beyond pain is necessary: individuals with high perceived meaningfulness of life despite pain experienced less necessity to achieve pain control goals. Controlling pain is not necessary in order to be able to achieve non-pain goals (Crombez et al.).

Another key issue is the study of co-occurring disorders related to chronic pain, such as the sleep difficulties. ACT-based treatments for chronic pain, improving psychological flexibility, could reduce not only the level of pain, but the sleep disorders too (Daly-Eichenhardt et al.). Other ACT based protocols have been developed for pain management, for example in chronic debilitating pain for young patients (Kemani et al.) and delivering web-based psychosocial interventions (Trompetter et al.).

A typical psychological topic is the study of expectancies in pain management: optimism or pain catastrophizing can significantly shape pain experiences (Peerdeman et al.).

Further research is needed in the clinical health psychology and pain management area, also studying the role of mediators to understand the relationship between different variables, such as pain and functioning (Wicksell et al.) and the role of moderators to change in clinical psychology and psychotherapy (Holmbeck, 1997; Labus, 2007; Perz et al., 2011).

A focus on cost-analysis and cost-saving is also mandatory in the future clinical research (Giusti et al.).

AUTHOR CONTRIBUTIONS

GC and KS conceived of the presented idea and contributed to the final manuscript.

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OPINION
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The Economic Utility of Clinical Psychology in the Multidisciplinary Management of Pain

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INTRODUCTION

Chronic musculoskeletal pain is the leading sources of disability worldwide, imposing an enormous burden to both societies and healthcare systems (Vos et al., 2012). Direct medical expenses and indirect costs due to losses in work productivity exceed $200 billion in the US (Ma et al., 2014; Park et al., 2016) and are a major source of concern in Europe (Breivik et al., 2013). Mean *per capita* costs vary from country to country (see **Table 1**), but are estimated to double the expenses for the care of matched controls (Gore et al., 2012; Hong et al., 2013). Notably, their impact is directly linked both to the severity of the condition and to the presence of mental comorbidities, and can be inflated by concomitant opioid abuse (Baumeister et al., 2012; Manchikanti et al., 2013; Stockbridge et al., 2015; Rayner et al., 2016).

In the last decades, the biopsychosocial model has attempted to answer to the growing imperative need to identify the best practices for the prevention and treatment of chronic pain and related conditions. Scientific research shows that clinical psychology plays a key role within the multidisciplinary approach that is increasingly being suggested for pain management. Its added value is revealed not only by the improvement of the patient experience, but also with regards to economic savings and cost reduction of his care, which is an issue on which modern health services base their strategic decisions. These benefits have been corroborated by studies addressing psychological treatments for chronic musculoskeletal pain, which will be discussed later. However, we argue that the work of clinical psychologists can improve the economic sustainability of chronic pain management in all the stages of the care, from the assessment phase to the rehabilitation period, providing a differentiated contribution depending on the treatment course of the patient (i.e. conservative treatment, surgical intervention). In particular, we suggest that the cost-effectiveness of chronic pain management can be enhanced employing a psychometrically sound, computerized and integrated assessment. After the diagnostic process, psychological techniques and interventions can be useful for pain management or, in case of surgical interventions, to enhance their outcomes.

TABLE 1 | Direct and indirect annual cost per capita of musculoskeletal conditions.

Pain condition	References	Country	Type of cost	Cost per patient per year
Low back pain	Pasquale et al., 2014	US	Direct	$3,607
	Gore et al., 2012	US	Direct	$8,386
	Gustavsson et al., 2012	Sweden	Direct and indirect	$9,781
	Becker et al., 2010	Germany	Direct and indirect	€3,579
	Hong et al., 2013	UK	Direct	£1,074
Osteoarthritis	Pasquale et al., 2014	US	Direct	$5,344
	Xie et al., 2016	Various countries	Direct	From $1,442 to $21,335
			Indirect	From $238 to $29,935
	Gustavsson et al., 2012	Sweden	Direct and indirect	$77,98
Rheumatoid arthritis	Pasquale et al., 2014	US	Direct	$4,036
	Boonen and Severens, 2011	Various countries	Direct and indirect	€10,479
	Lundkvist et al., 2008	Various countries	Direct and indirect	From €2,825 to €24,688
Fibromyalgia	Rivera et al., 2009	Spain	Direct and indirect	€9,982
	Knight et al., 2013	US, France, Germany	Direct and indirect	From $9,199 to $13,518
	Pasquale et al., 2014	US	Direct	$1,755

ECONOMIC BENEFITS OF AN INTEGRATED ASSESSMENT OF PAIN AND TREATMENT OUTCOMES AND THE ROLE OF MODERN PSYCHOMETRIC METHODS

The multidimensional evaluation of pain and its correlates is crucial during the entire course of the care. Starting from the initial assessment phase, the aim of the pain specialist is to gather detailed information on pain characteristics and to ascertain how these characteristics are intertwined with biomedical, psychosocial and behavioral factors (Dansie and Turk, 2013; Aloisi et al., 2016; Castelnuovo et al., 2016a,b; Tamburin et al., 2016). An integrated assessment of these aspects may have an intrinsic positive clinical effect (Pietilä Holmner et al., 2013). In addition, accurate and objective measures are important for making correct decisions and to lead to a cost-effective management of the following pain management intervention. Standardized measures are fundamental for detecting the presence of contraindication for specific pain management options (Daubs et al., 2010). In this context, psychometrics may provide the tools for a reliable, sensitive and valid assessment of pain and of the outcomes of the treatment. Some authors advocate for the spread integrated and computerized assessment methods which exploit the potential of the most modern statistical models for the construction of valid, specific and user-friendly questionnaires which can be linked to automated dynamic pain assessment systems (Chang, 2013; El Miedany, 2013; Slover et al., 2015). Item Response Theory models can be used to calibrate these tools to assess the person's traits in a reliable and valid manner with the lowest possible amount of item, greatly reducing the administration time. These methods permit to evaluate the relevant aspects of the patient's experience and to easily store and access the acquired information throughout the different phases of the treatment and in the follow-up period. Models based on these principles have been specifically developed for musculoskeletal pain conditions with the aim to reduce costs and first proofs of their cost-effectiveness have been found (Wells et al., 2013; El Miedany et al., 2016).

ECONOMIC UTILITY OF THE ASSESSMENT OF THE PSYCHOLOGICAL VARIABLES ASSOCIATED WITH THE TREATMENT OUTCOMES IN THE SURGICAL MANAGEMENT OF PAIN

Surgery can be an option to relieve pain in rheumatoid arthritis, osteoarthritis and back conditions (Boonen and Severens, 2011; Gore et al., 2012; Xie et al., 2016). A large number of psychological aspects related to pain, such as anxiety, depression, cognitions, expectations and personality traits can be considered as strong predictors of the outcomes of these interventions (Schade et al., 1999; Trief et al., 2000; DeBerard et al., 2003; Kohlboeck et al., 2004; den Boer et al., 2006; Abbott et al., 2011; Judge et al., 2012; Block et al., 2013; Akins et al., 2015; Anderson et al., 2015; Kunutsor et al., 2016; Alattas et al., 2017; Lindberg et al., 2017; Mancuso et al., 2017). Each of these factors seems to differently affect the various outcomes of the treatment, leading to a boost of the direct and indirect costs of the care. Omitting to consider the psychosocial aspects which can interfere with the surgical intervention may lead to a worst patient experience in terms of pain intensity and quality of life, to a failure to return to work, to an increase in opioid consumption or to repeat other ineffective, potentially harmful and costly treatments. In this contexts, the contribution of

a psychologist can be essential. His role is not to decide whether an intervention should be implemented or discarded, but to help physicians to identify the patients at risk of poor outcomes and to suggest how the pain management strategies could be improved. Moreover, his work can be fundamental to prepare the patient for the surgical intervention, e.g., assessing unrealistic expectations or providing education, and to guide him in the post-operative period with the aim to foster his motivation, to facilitate his discharge, and to prevent the conditions which may cause a relapse of the symptoms and a readmission to the hospital (Childs et al., 2014; Louw et al., 2014).

THE ECONOMIC UTILITY OF CLINICAL PSYCHOLOGY FOR PAIN TREATMENT

Several psychological treatment options have been proven to be cost-effective and are available for the clinical management of pain both in traditional and in new technology-based scenarios (Kröner-Herwig, 2009; Trompetter et al., 2014, 2015, 2016; Veehof et al., 2016). In a recent meta-analysis, Pike et al. (2016) found that psychological interventions are successful in reducing the use of healthcare services by the patients. This finding extends the evidence for a positive effect of psychological interventions on pain intensity, pain disability and the quality of life of the treated subjects (Hoffman et al., 2007; Williams et al., 2012; Veehof et al., 2016).

Comprehensive pain programs administered by multidisciplinary teams which include the contribution of a psychologist or which use psychological techniques are associated with a substantial reduction in both the direct and indirect costs of the disease, with a cost saving which is estimated between 8,500$ to 13,000$ per patient per year (Gatchel et al., 2003; Gatchel and Okifuji, 2006). All the components of these programs are fundamental for a cost-effective care of the disease and "carving out" some of them may impair a satisfying recovery to the premorbid productivity levels, leading to an increase in the future use of the healthcare resources (Gatchel and Okifuji, 2006; Gatchel and Mayer, 2008). Moreover, these programs may be enhanced providing intensive psychological therapies for the management of pain. The research is increasingly showing that these interventions are highly effective and lead to considerable cost savings. A group treatment for musculoskeletal pain sufferers based on cognitive behavioral principles resulted in additional 0.0325 Quality Adjusted Life Years (QALY) with respect of the control condition, with an incremental cost per QALY of £5,786 (Taylor et al., 2016). Various RCTs evaluated the cost-effectiveness of group cognitive behavioral approaches for chronic low back pain, with estimates of additional cost per QALY ranging from £1,786 to $7,197 (Linton and Nordin, 2006; Lamb et al., 2010; Norton et al., 2015). An integrated care program for sick-listed back pain patients based on a workplace intervention and graded activity was found to provide work-related economic savings in the amount of £5744 (Lambeek et al., 2010), but graded activity was found to be less cost-effective than exposure *in vivo* in another trial (Goossens et al., 2015). Non-significant effects were found for a CBT program added to inpatient rehabilitation for chronic low back pain (Schweikert et al., 2006). With regards to the other syndromes, a telephone-delivered CBT for chronic widespread pain sufferers provided a 0.097 additional QALY with respect to a program of tailored exercise, with an incremental cost per QALY of £5917 (Beasley et al., 2015), an internet-delivered Acceptance and Commitment Therapy program for fibromyalgia patients provided cost savings which exceeded the costs of the treatment 2 months after its conclusion (Ljotsson et al., 2014) and a psychoeducational intervention for the same syndrome resulted in 0.12 additional QALY with respect to control (Luciano et al., 2013). Although a systematic evaluation of the cost-effectiveness of all the available programs is beyond the scope of this article, it is established that the costs of various psychological treatments are rapidly overtaken by direct and indirect savings. However, clinical psychologists are not required to indiscriminately implement their therapies. On the contrary, their role is to help the pain management team to identify the characteristics of the patient and to tailor their techniques accordingly. The importance of tailoring the interventions has been long advocated in the literature and some evidence of the benefit of such an approach the have been provided (Turk, 1990; Turk et al., 1996, 1998). In addition, in the clinical practice, the psychologist and the multidisciplinary pain team usually face very complex conditions accompanied by physical or mental comorbidities, which may prevent the use of standardized treatments. The future of the clinical psychology and of the biopsychosocial approach in the field of pain management seems therefore to reside in the possibility to deliver integrated interventions which are personalized in order to be more effective and, at the same time, less expensive (Castelnuovo, 2010a,b; Castelnuovo et al., 2016c).

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All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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CASE REPORT
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Exploring Changes in Valued Action in the Presence of Chronic Debilitating Pain in Acceptance and Commitment Therapy for Youth – A Single-Subject Design Study

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Objective: The objective of the study was to improve the understanding of processes of change in Acceptance and Commitment Therapy for youth with chronic debilitating pain by exploring the relation between individual change patterns in pain intensity and valued activities.

Method: A single-subject design across three adolescents suffering from longstanding debilitating pain was utilized. Pain intensity and participation in valued activities were rated daily. Visual analysis of the graphed data was performed to evaluate the effects of the intervention, and the relationship between pain intensity and values-based activity.

Results: The graphed data illustrated that pain levels did not decrease from the baseline period to the follow-up period. In contrast, compared to baseline ratings values oriented behaviors increased from the start of treatment to the follow-up period.

Conclusion: Results illustrate that increases in values-based behavior may occur without corresponding decreases in pain, and warrant further research on change processes in ACT for youth suffering from chronic pain.

Keywords: ACT, single-subject design, chronic pain, children, adolescents, change processes

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INTRODUCTION

A substantial number of children and adolescents suffer from longstanding pain, and previous studies report prevalence rates of 15–30% (El-Metwally et al., 2004). Among these a subset of persons suffer from pain related disability and reduced quality of life in addition to pain (Palermo, 2000; Miro et al., 2008; Hoftun et al., 2011). Importantly, several studies show that youth with longstanding pain enter adulthood with a substantial risk of chronicity (Walker et al., 1998; Brattberg, 2004).

Previous research provides empirical support for treatments based on a cognitive behavioral approach for pediatric longstanding pain (Eccleston et al., 2002; Hechler et al., 2015). Acceptance and Commitment Therapy (ACT) is a treatment within the cognitive behavioral field (Hayes et al., 1999). A number of studies illustrate the efficacy of ACT in improving pain related disability in adults with chronic pain (Hann and McCracken, 2014; Veehof et al., 2016), and a number of

studies suggest the utility of ACT for children and adolescents with longstanding pain as well (Wicksell et al., 2007, 2009). The objective in ACT is to increase engagement in behavior that is in accordance with personal goals and values (i.e., approach behavior governed by appetitive motivating functions), also in the presence of pain and related distress, by promoting a willingness to experience interfering thoughts, sensations (e.g., pain), and emotions (Hayes et al., 2006).

A few clinical studies have illustrated the relevance of values-based behavior in improving pain related disability following ACT for adults with chronic pain (e.g., Vowles et al., 2014). Also, other researchers in the field of chronic pain argue that structured and detailed assessments of the patient's personal overarching goals in important life domains would assist successful intervention (Schrooten et al., 2012). This underscores the relevance of clinical studies investigating values- and goal-based behavior. As a complement to clinical trials that use relatively few assessment points and group level data, single-subject studies that use frequent and idiographic assessments, of for example values-based action, may further enhance our knowledge of key processes of change in behavioral treatments for longstanding pain. This may in turn facilitate further development and improvement of treatment (Kazdin, 2009).

Thus, the present study aimed to explore the relationship between pain intensity and individualized assessments pertaining to pain related disability following ACT for youth with longstanding pain. This was done using a single-subject design including frequent assessments, before, during and after treatment, of pain intensity and values-based activities, that is, short- and long-term personally chosen behavioral goals in line with personal values.

METHOD

Design

A concurrent multiple baseline design across individuals was utilized (Kazdin, 1982), comprising a baseline (A), two intervention phases (B1 and B2) and a follow-up phase (C) replicated over three individuals. We randomized the order in which treatment was initiated for the patients (S1, S2, and S3). Baseline lengths of 12, 26, and 33 days were determined by taking into account the need for stable patterns in the assessment of pain intensity and valued activities (e.g., school attendance), as well as clinical considerations. One psychologist, a pain physician and a physiotherapist delivered the treatment. The psychologists and the pain physician had formal training in ACT, and all had clinical experience of using ACT with children and adolescents suffering from longstanding pain.

Recruitment

Three adolescents (S1, S2, and S3), two 14 year olds and one that was 18 years of age, with longstanding pain (i.e., a pain duration of more than 3 months) were included in the study. The patients were referred from county councils outside the Stockholm area to the Behavioral Medicine Pain Treatment Services (BMPTS), at the Karolinska University Hospital. Initial medical and psychological assessments at the clinic were conducted during 2–3 days (6–8 sessions). The medical assessment was based on a semi-structured interview focusing on the medical history of each patient. At this assessment pain intensity was rated using numeric scales ranging from 0–10 to 0–100 with the endpoints "no pain at all" to "worst pain imaginable." The psychological screening assessed the negative consequences of pain on different life domains based on a semi-structured interview, which also included clinical behavior analyses of relevant target behaviors. Also, valued activities (treatment goals) were defined for future assessment. Written consent to participate in the study was provided by both adolescents and parents and the Ethical Review Board in Stockholm approved the study.

Assessment

Activities deemed personally important by the participants were collaboratively formulated and rated individually on a daily basis. S1 rated the "Number of classes I attended today, of the total number of classes" (e.g., 4/5). S2 rated the "Number of minutes I bowled today" and the "Number of meters I jogged today." S3 rated the "Number of minutes I walked without support today," and the "Number of minutes I played tennis today." In addition, the item "How much pain have you experienced today," was rated daily on an 11-point numerical scale ranging from "no pain at all" (0) to "worst pain imaginable" (10). The participants were instructed to perform the ratings at the end of each day and parents were instructed to assist and ensure that the ratings were performed according to instructions. Pain was rated from baseline (A) to 7–14 days past follow-up (C).

Additionally, data was collected by the child version of the Functional Disability Inventory (FDI) (Walker and Greene, 1991). This version of the FDI measures the impact of sickness on physical and psychosocial functioning, and consists of 15 questions measuring ambulation; social interaction; ability to perform household tasks; ability to eat, sleep and rest, attend school; and mobility. The FDI was administered three times, at treatment start (B1), at the end of treatment (B2), and at follow-up (C), approximately two months following the end of treatment.

Data Analytic Approach

In single-subject designs the baseline data illustrates the trajectory of the variables over time under conditions that do not change (Boersma et al., 2004). And, if a change in the trajectory of a dependent variable occurs systematically following the intervention it increases the likelihood that the change is an effect of the intervention (Kazdin, 1982). Because each subject acts as his/her own control condition, and frequent assessments are made, these studies typically include a small number of participants. Multiple baselines across subjects increases the internal validity, and effects across subjects considerably builds a case for generality (Kazdin, 1982).

Visual non-statistical analyses of the graphed data within and between subjects were performed to evaluate if changes in the dependent variables (pain intensity and values-based behaviors, e.g., school attendance) were a consequence of treatment (Kazdin, 1982). More specifically, we evaluated the means and the

variability of the ratings across phases. Substantial changes in these regards (e.g., the range), after the introduction of treatment, were indicative of a treatment effect. We also analyzed the level, or degree, of change between phases and considered a shift or rupture in the trajectory, that is, a considerable drop or increase in the ratings, following the onset of treatment an expression of a treatment effect. Additionally, we took into account the latency of change, in other words, when in time a change in the slope occurred. The closer in proximity to treatment introduction that change occurred, the more likely we deemed this change to be an effect of treatment. Microsoft Excel 2010 was used to graph the data and to calculate means (M) and range (R).

Patient Characteristics

All patients lived with both parents. In addition to pain, two patients presented with psychiatric (S1) and somatic (S3) concurrent symptoms. Patient characteristics based on the initial clinical medical and psychological assessments are presented below. Previous medical investigations and treatments for the three patients are presented as Supplementary Material.

S1

S1 was a 14-year-old boy whose pain onset followed multiple minor foot injuries, such as sprains, at age 3. Over time pain gradually became more generalized and increased in intensity. At assessment S1 presented with generalized continuous spontaneous pain in his head, shoulders, back, knees, groin, and ankles, as well as recurrent pain in arms and wrists. He experienced his headache as the most disturbing. In addition, he reported that pain was triggered by brushing and touching of the skin, as well as by applying light pressure to the skin (i.e., mechanical and dynamic mechanical allodynia) of the shoulder area. Pain increased during and after physical activity, primarily in his feet and groin. Also, following physical activity he sometimes experienced a temporary brief loss of motor functioning in his legs. At the initial assessment S1 reported a current pain experience of 98 on a scale ranging from 0 ("no pain") to 100 ("worst pain imaginable"). Using the same scale, he reported that his pain was 100/100 when at its highest and 70/100 at its lowest.

Prior to assessment at the BMPTS, he was diagnosed with social phobia and Asperger's syndrome. S1 was also taking prescribed medication for anxiety and depression. S1 had been bullied in school during a period in the seventh grade. At assessment he attended the eighth grade and the bullying had ceased. A high level of pain related school absence was reported, and S1 was completely absent from school the past semester due to pain. He had stopped playing soccer and only sporadically played floorball (a type of field hockey), due to pain and social difficulties on the team.

S2

For S2, an 18-year-old male, pain debuted when he was 14 and the onset of pain could not be associated with any trauma or infection. Over time pain gradually generalized and increased in intensity, and at assessment S2 presented with continuous spontaneous back pain and mechanical dynamic allodynia in his back. He also experienced occasional shoulder and knee pain, especially during certain twisting movements of the knee. Walking was terminated after about 10 min due to pain. Pain was most intense in the mornings, and increased during physical activity. At assessment, S2 reported that his current pain intensity corresponded to a rating of 8.5 on scale ranging from 0 ("no pain") to 10 ("worst pain imaginable"). His pain corresponded to a 10 when it was at its highest and a 6 when it was at its lowest.

Also, he presented with recurrent muscle spasms, fatigue and widespread loss of muscle tonus that resulted in a temporary inability to stand up. S2 attended the 3rd year of high school and had only been absent a few days due to pain the past semester. He had not gone bowling or played soccer in several years, due to pain.

S3

Pain onset for S3, a 14-year-old girl occurred at age 13. This happened approximately 4 weeks after an ovarian torsion surgery, and was triggered by a strain in the groin during tennis play. Following a medical procedure at another university hospital, in which a tube with a camera was inserted through the urethra into the bladder (i.e., a cystoscopy) during epidural anesthesia (a regional anesthesia injected into the back), S3 lost all sensory and motor functioning in her legs. S3 presented with continuous spontaneous pain in the genital area and left groin as well as severe pain triggered by pressure to, or touch of, the skin (i.e., allodynia) in the left groin. She also experienced pain from the lower left abdomen and the center of her back. Pain intensity increased during and following physical activity.

S3 attended eighth grade and had a high level of school absence, and was completely absent from school the past semester. She had stopped playing floorball and tennis due to pain and loss of sensory and motor functioning in her legs. Key clinical characteristics for the three patients are presented in **Table 1**.

Treatment

The first treatment period (B1) consisted of 4 days, and was initiated directly following baseline. For all patients, sessions with a physician, psychologist and physiotherapist were included. All sessions promoted acceptance of pain and related distress as well as engagement in values-consistent behavior. During B1 the physician delivered 2–4 sessions; the physiotherapist one session; and the psychologist 7–15 sessions. The second treatment period (B2) also consisted of 4 days and was initiated 3–4 weeks after B1. During B2 the physician delivered 1–3 sessions; the physiotherapist one session; and the psychologist 5–7 sessions. Each session lasted 45–75 min. Three to 7 weeks following B2 there was a 1–2 days follow-up (C). The physician and the physiotherapist delivered one session each with the patient and the parents, and the psychologist 2–3 sessions.

First Treatment Period, B1

During initial assessment behavioral goals were operationalized based on the patients' values, in relation to for example family, school, leisure time, physical activity, and friends. At

TABLE 1 | Key patient characteristics for S1, S2 and S3 at the initial clinical assessment.

	Age	Sex	PainDur[a]	Prim. pain loc.(other pain loc.)	Concurrent symptoms	Diagnoses (secondary diagnoses)
S1	14	M	132	Head (wide-spread)	Recurrent loss of motor function in lower legs.	Unspecified generalized pain (Asperger's syndrome; Social phobia).
S2	18	M	48	Back (head)	Muscle spasms, widespread temporary loss of muscle tonus	Unspecified generalized pain.
S3	14	F	12	Groin (lower abdomen, back)	Loss of motor and sensory function in both legs	Unspecified generalized pain (unspecified pain in other areas of the lower abdomen; hyperesthesia; painful micturition; and unspecified paralytic syndrome).

[a]*Months.*

the start of B1 these values and goals were further discussed, as a way to motivate behavior change, and as a means to potentially reinforce behavioral patterns and direct behavior over extended periods of time, also in the presence of other aversive experiences such as pain and related distress. In conjunction with these discussions the physician and the psychologist provided information regarding the differences between acute and chronic pain, the complex and many times unclear etiology of longstanding pain, the high prevalence of such pain, and the potential downsides of a prolonged and extended search for an underlying and treatable pathophysiology. These discussions served to initiate a shift from seeking symptom reduction to increasing values-based action, even in the presence of pain.

To further motivate a shift from pain reducing behaviors to values-oriented behaviors, the short- and long-term workability of previously used behavioral strategies characterized by avoidance of pain and related distress (e.g., staying home from school) were collaboratively evaluated. This evaluation illustrated that avoidance strategies had led to a decrease in valued activities over time, without any corresponding decrease in pain and related distress. It also illustrated the difficulty of avoiding pain and related discomfort, while at the same time living an active and meaningful life.

In order to facilitate engagement in values consistent activities the psychologist introduced defusion and acceptance as alternative strategies to manage pain and related distress. Metaphors and experiential exercises were frequently used to enhance and elucidate the points addressed during sessions. The latter part of B1 focused on values-based behavior activation and the use of defusion and acceptance strategies while engaging in valued activities, such as attending classes in school and bowling. To facilitate in-session *in vivo* exposure to pain-inducing or distressing activities the psychologist and physiotherapist used various forms of physical activities, such as walking or pool exercises, depending upon type of symptoms and individually defined values. For S3, most sessions also included a focus on improving motor functioning in her legs. To achieve this, minimizing wheelchair use was promoted as a general strategy. Additionally, floor mobilization exercises (e.g., creeping) and tilt board exercises were utilized throughout treatment.

Second Treatment Period, B2

The second treatment period (B2) focused on the implementation of ACT strategies in everyday life. When needed, previously formulated behavioral goals were discussed and refined, such as increasing the time spent in school. The interaction with friends, parents and other significant adults was also addressed. For example, we discussed how the youth wanted to be coached toward increased valued living, and how this could be communicated to parents or friends. At follow-up (C), strategies to handle setback and relapse were discussed with both the patient and parents.

Parental Support

Broadly, over both treatment periods parent sessions were focused on improving coaching behaviors. Initially, parents were taught operant principles (contingency management), and how these principles applied to their child's values and goals. In addition, parental distress and ineffective coaching behaviors were discussed based on clinical behavior analysis of critical situations. Subsequently, alternative ways of dealing with parental distress to promote the child's behavioral activation were discussed. For example, the parents were encouraged to be accepting of their own distressing thoughts and emotions related to their child's pain, as a way to undermine the impact of these thoughts and feelings on effective coaching behaviors.

RESULTS

Notably, pain remained at similar levels throughout treatment for all patients. However, pain varied more for S1 compared to S2 and S3. Compared to baseline ($M = 3.6/5$), class attendance increased ($M = 4.3/5$) for S1 following B1. Shortly following B2, S1 attended five out of five classes for five consecutive weeks until the ratings were discontinued.

S2, did not bowl or jog during baseline, but shortly following B1 bowling increased in both duration ($M = 60$ min/week) and frequency ($M = 1$ occasion/week). Following B2, there was a continued increase in bowling, in both duration ($M = 210$ min/week) and frequency ($M = 2.8$ occasions/week). Also, jogging increased shortly following B1, in both distance ($M = 383$ m/week) and frequency ($M = 2$ occasions/week). This increase continued steadily following B2 ($M = 1419$ m/week; $M = 2.4$ occasions/week). After follow-up (C) there was a reduction in jogging ($M = 760$ min/week; $M = 1.5$ occasions/week).

S3 did not play tennis during baseline, but shortly following B1, there was an increase, both in duration ($M = 40$ min/week) and frequency ($M = 0.75$ occasions/week). Further increases shortly followed B2 ($M = 241$ min/week; $M = 2.6$ occasions/week). After follow-up (C) there was a decrease in playing tennis ($M = 143$ min/week; $M = 1$ occasion/week). S3 did not to walk without support during baseline, but this ability increased substantially following B2, in both duration ($M = 241$ min/week) and frequency ($M = 2.6$ occasions/week). There was a further increase in ability to walk without support ($M = 593$ min/week; $M = 5.5$ occasions/week) during the follow-up period. Means and ranges for the different variables, as well as the number of days for each phase, are presented in **Table 2** for each participant. Also, the individual daily assessments of the included variables are presented in graphs in **Figure 1**.

The results from the assessments made of pain related functional disability at the end of treatment and at follow up 2 months after treatment, indicated that functional disability had decreased for the participants, especially for S2 and S3. Please see **Table 3** for specifc scores at the different time points for the three particpants.

DISCUSSION

This study explored patterns of change in pain intensity and valued activities using daily assessments. Notably, pain reduction was not targeted in treatment, but is important to assess in order to evaluate the effects of treatment and the relationships between symptoms and improvements in disability. The pattern of results clearly suggests that changes in valued behaviors were independent of changes in pain intensity. The greatest increase in values oriented behaviors was seen following the second treatment phase (B2). The results align with results from previous studies on ACT for youth illustrating improvements in pain related disability (Wicksell et al., 2009). However, for adolescents the effect of ACT on pain intensity appears to vary across studies. In a study by Wicksell et al. (2009) results illustrated improvements in pain intensity following treatment, but in a study by Kanstrup et al. (2016) pain intensity was not reduced following treatment. Notably though, mediation analyses suggest that decreases in disability following ACT for adults as well as for youth are not primarily a function of pain reduction (Wicksell et al., 2010; Kemani et al., 2016), which the results from the current study also illustrate.

A number of methodological limitations should be noted. Limitations pertaining to the reliability of the visual analytic approach and to the generalizability of the results are of central concern. There is yet no clear consensus regarding the criteria for visual data analysis, particularly the interpretation of certain data patterns and how to establish the reliability of the effect (Deprospero and Cohen, 1979). Statistical methods have been suggested as a way to handle these problems (Kazdin, 2007), but it is yet unclear how statistical analyses should be conducted to be fully satisfactory given, for example, the usually small samples in these studies. Also, data collection relied heavily on self-report, which potentially undermines the reliability and validity of the results. In this regard, objective assessment, such as actigraphy, may complement self-ratings. Furthermore, the FDI was included mainly for comparisons with the daily ratings of values oriented behaviors. However, more frequent assessments using validated questionnaires that complement the individually formulated outcomes should be used, such as measures that assess emotional functioning and quality of life. Although treatment staff continuously discussed fidelity

TABLE 2 | Number of days for the respective phases, as well as means and ranges for the individual ratings, across all phases (A, B1, B2, and C) and participants (S1, S2, and S3).

		A		B1		B2		C	
	Variable	**Nr**	**Mean (Range)**	**Nr**	**Mean (Range)**	**Nr**	**Mean (Range)**	**Nr**	**Mean (Range)**
S1	Days[a]	12		13		20		13	
	Pain intensity[b]		8 (5)		8 (3)		7.3 (4)		8.3 (2)
	Class att. (att. classes/scheduled classes)		3.6/5 (0–4/5)		4.3/5 (0–5/5)		5/5		5/5
S2	Days	26		22		77		13	
	Pain intensity		8 (1)		7.5 (1)		7.6 (1)		7.5 (2)
	Bowling (minutes/week)		0		60 (60)		181 (330)		208 (380)
	Bowling (occasions/week)		0		1 (1)		2.8 (5)		2.9 (4)
	Jogging (meters/week)		0		383 (500)		1419 (2350)		760 (1800)
	Jogging (occasions/week)		0		2 (2)		2.4 (3)		1.5 (2)
S3	Days	33		23		74		6	
	Pain intensity		9 (2)		8 (1)		8.7 (2.5)		9 (0.5)
	Playing tennis (minutes/week)		0		40 (40)		241 (945)		143 (225)
	Playing tennis (occasions/week)		0		0.75 (2)		2 (6)		1 (1)
	Walking without support (minutes/week)		0		0		335 (600)		593 (605)
	Walking without support (occasions/week)		0		0		4.2 (7)		5.5 (6)

[a]*Phase length is reported as the number of days from the start of a specific phase (e.g., A) to the start of a new phase (e.g., B1).* [b]*The item was rated from "No pain at all" (0) to "Worst pain imaginable."*

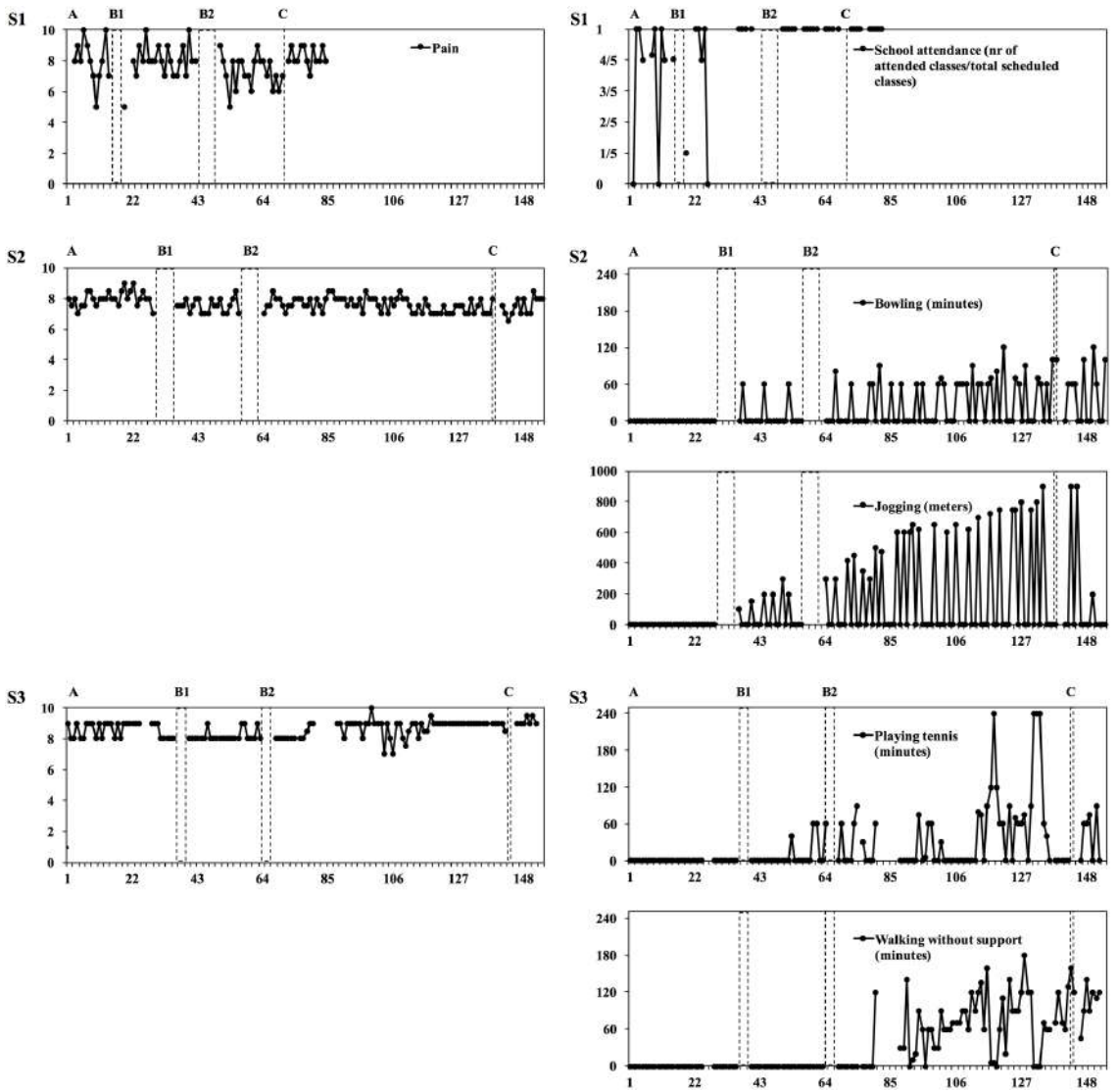

FIGURE 1 | Daily ratings of pain intensity and values-based behaviors are presented in graphs for S1, S2, and S3.

TABLE 3 | Functional Disability Inventory (FDI) scores for the three particpants (S1, S2, and S3).

	FDI pre[a]	FDI post	FDI 2mfu[b]
S1	29	26	–
S2	15	2	2
S3	50	27	36

A dash represents missing data. [a]*Data collected at assessment.* [b]*Data collected approximately 2 months after post-assessment.*

to treatment, adherence and therapist competence should be analyzed using recordings of the sessions and a standardized coding system.

More studies with larger samples are needed to determine the generalizability of the findings presented here. However, future studies should also consider the strengths of the current study, in essence, the focus on individual change in relation to personally important outcomes using multiple assessments during the course of the different phases related to treatment. Additionally, these studies should utilize designs with adequate experimental control that meet the requirements for adequate statistical analyses.

A number of studies on ACT for chronic pain have investigated the mediating role of core ACT processes, such as psychological inflexibility, in improving outcomes (Wicksell et al., 2010, 2013). However, only a few studies (Kemani et al., 2016) have modeled change more carefully using multiple assessments of the proposed process and outcome variables (e.g., acceptance and pain related disability), and evaluated the precedence of change in the process variable in

relation to the outcome. These aspects need to be further studied and single-subject designs provide a framework to explore both the specificity of these process variables and the temporal precedence of change in these variables in relation to the outcome variables.

Clinically, repeated assessments of individualized outcomes can be used concurrently with validated questionnaires or other means of data collection (e.g., actigraphy) to provide detailed feedback as to the efficacy of treatment, and as a basis for discussing potential adjustments to the treatment in cases when desired change does not occur. In conclusion, results indicate that values-based activity can improve even when reductions of pain do not occur. The study also points to the importance to further research the effects of ACT for patients with complex symptoms, as well as the circumstances under which desired change occurs.

ETHICS STATEMENT

The study was approved by the Ethical Review Board in Stockholm. The participants (and their parents) were informed that the data and results were going to be analyzed and that the results would be presented in a scientific publication, in such a way that they as individuals could not be identified. Thus, we have altered certain characteristics of the participants in order to ensure their anonymity.

AUTHOR CONTRIBUTIONS

MK, GO, and RW was involved in the design of the study, data preparation, visual analyses, and manuscript preparation. LH was involved in the data preparation, visual analyses and manuscript preparation.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: http://journal.frontiersin.org/article/10.3389/fpsyg.2016.01984/full#supplementary-material

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Pain Interference Mediates the Relationship between Pain and Functioning in Pediatric Chronic Pain

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Pediatric chronic pain is a major health problem commonly associated with impaired functioning. There is a great need for more knowledge regarding the complex interplay between demographic variables such as age and gender, pain, and functioning in pediatric chronic pain.

Objective: The objective of the study was to investigate if; (1) pediatric chronic pain patients with high and low levels of functioning differ in demographic variables, pain, and pain interference; (2) explore the mediating function of pain interference in the relationship between pain and functioning (i.e., depression and functional disability).

Method: The study includes a consecutive sample of children and adolescents referred to a tertiary pain clinic due to chronic pain ($n = 163$). Cross-sectional data was analyzed to investigate the interrelationships between variables. Analyses of indirect effects were used to assess the impact of pain interference on the relation between pain and depression.

Results: Findings illustrate high levels of depression, school absence and pain interference in this sample. Furthermore, pain interference mediated the relationship between pain and depression.

Conclusion: Thus, this study adds to the growing support of findings suggesting that functioning and pain interference should be routinely assessed in pediatric chronic pain and a central target in treatment. Particularly, these findings imply a need for interventions specifically aimed at improved functioning for patients with chronic debilitating pain.

Keywords: pain, chronic, pediatric, interference, functioning, depression

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INTRODUCTION

Longstanding pain is common among children and adolescents, with prevalence rates varying between 11 and 38% (1). Recent reports indicate that prevalence increases with age and the occurrence of chronic or recurrent pain is more often found in girls than boys (Roth-Isigkeit et al., 2005; Stanford et al., 2008; King et al., 2011). Headache, abdominal pain, back pain and musculoskeletal pain represent the most frequently reported types of chronic pain among children and adolescents (Stanford et al., 2008; King et al., 2011)- and a relatively large number of youths

report pain from multiple locations (Hoftun et al., 2011; King et al., 2011). For many children and adolescents, medical strategies are often ineffective or insufficient to alleviate symptoms and increase functioning.

A subsample of patients is severely affected by chronic pain, demonstrating low levels of functioning and quality of life. Functioning is a broad construct that can be subdivided into several different dimensions, such as physical, social, and emotional functioning (i.e., depression) (McGrath et al., 2008; Zernikow et al., 2012). More specifically, the presence of chronic pain can interfere with functioning with regard to quality of life (Huguet and Miro, 2008), sleeping, eating, and ability to pursue hobbies, as well as lead to absence from school and inability to lead an active social life (Konijnenberg et al., 2005; Simons et al., 2010).

The relationship between pain and functioning in children with chronic pain is complex, and information regarding factors associated with reduced functioning is still relatively scarce. However, some studies exist. For example, pain in multiple locations is associated with more disability (Hoftun et al., 2011; Holm et al., 2012), and depressive symptoms have been shown to predict school impairment (Gauntlett-Gilbert and Eccleston, 2007; Logan et al., 2009).

Importantly, existing research suggest that the ability to manage pain, in addition to pain intensity *per se*, is critical to functioning (Kashikar-Zuck et al., 2011; Kaczynski et al., 2013). From a behavior analytic (i.e., learning theory) perspective, anticipation of pain may result in avoidance of activities, even when perceived as important. Over time, such negatively reinforced behavior patterns, characterized by avoidance of pain, may result in a lowered level of functioning, without a corresponding decrease in pain.

Recent developments within Cognitive Behavior Therapy (CBT), particularly Acceptance and Commitment Therapy (ACT), has suggested the utility of pain management strategies based on acceptance and mindfulness to increase functioning (Wicksell et al., 2007, 2009). The treatment objective in ACT is to increase the ability to act in accordance with values and goals, also in the presence of interfering pain and distress (Hayes et al., 2006). In other words, treatment is not primarily aimed at reducing pain, but at reducing the impact of symptoms on behavior, i.e., pain interference. Thus, ACT and similar treatments may be particularly useful for a subgroup of individuals with avoidance and pain interference that result in low levels of functioning. However, more research is needed regarding factors (e.g., demographics, pain, pain interference) that characterize pediatric patients with chronic pain and low levels of functioning, and to explore the importance of these factors for the relation between pain and functioning.

Also, previous analysis have indicated that pain interference, as assessed by the pain interference index (PII), is tightly linked to pain intensity as well as functioning (Holmstrom et al., 2015). What distinguishes PII from other measures of functioning is that the PII was designed to specifically address the impact of pain on functioning, i.e., pain-related interference, whereas broader measures of functioning often take into account several different factors that can influence functioning, such as, developmental, social, and somatic problems other than pain. The scale includes questions such as; To what degree during the past 2 weeks has pain made it difficult for you to do schoolwork? Furthermore, the PII has been shown to independently predict variability in functioning above and beyond pain intensity (Holmstrom et al., 2015). Thus, the role of pain interference in the relation between pain and functioning should be further explored.

The purpose of the present study was to identify factors of importance for the relation between symptoms and disability. More specifically, the aims of the present study were to: (1) investigate if pediatric patients with chronic pain and high and low levels of functioning differ in demographic variables, pain, and pain interference; (2) explore the mediating function of pain interference in the relationship between pain and functioning (i.e., depression and functional disability).

MATERIALS AND METHODS

Procedure and Participants

The study sample consisted of 163 consecutively recruited pediatric patients and their parents, referred to a tertiary pain clinic due to longstanding pain. Some data from this sample have been published previously in a paper addressing insomnia in children with chronic pain and as part of the validation of the PII (Kanstrup et al., 2014; Holmstrom et al., 2015). Both parent and child gave informed written consent and the study was approved by the Regional Ethical Review Board in Stockholm.

Self-report questionnaires were administered just prior to a medical and psychological assessment. All patients between 7 and 18 years and with sufficient Swedish language skills referred to the clinic between June 2008 and October 2011 due to longstanding and/or recurrent pain (i.e., >3 months) were considered eligible for participation. Very few families (<5) declined participation, and statistical analyses of differences in characteristic are therefore not considered meaningful.

Assessments

The medical and psychological assessments consisted of two semi-structured clinical interviews conducted by a physician specialized in pediatric pain and a clinical psychologist trained in CBT or by self-report questionnaires (patients and parents) administered in conjunction with the interviews.

Interviews

Assessments focused on pain characteristics (e.g., pain intensity, location, and onset/duration), as well as the effects of pain on emotional, social, and physical functioning. For the present study, the following data were retrieved from the semi-structured interviews: (1) pain duration in months; (2) number of pain locations; (3) pain location/type, categorized as headache, abdominal pain, back pain, joint pain, complex regional pain syndrome (CRPS), wide spread pain (WSP) or other; (4) temporal pain patterns, categorized as continuous, daily, weekly, and monthly; (5) current school absence due to pain during the past month, classified as no absence (0), a few days of absence/month (1), >1 day/week of absence, (2), complete absence (3).

Pain Assessment

Current pain intensity, i.e., the patient's subjective amount of experienced pain at that particular moment (i.e., total amount of pain during the interview), was rated on a numerical rating scale (NRS) from 0 to 10, where 0 = no pain and 10 = the worst imaginable pain (von Baeyer, 2009). The NRS is validated for pediatric samples 8 years and older (Miro et al., 2009; von Baeyer et al., 2009). A measure of current pain intensity was used in the present study since retrospective ratings have been reported to show inflated rates in children and adolescents (Lewandowski et al., 2009).

Center for Epidemiological Studies-Depression Scale Children (CES-DC)

Symptoms of depression during the past week were measured by the Center for Epidemiological Studies-Depression Scale Children (CES-DC). The questionnaire consists of 20-items that are rated on a scale from 0 (not at all) to 3 (often), with a maximum score of 60. The Swedish version of the scale, with a high reliability coefficient alpha (0.91) and validated for children (6 years and older) and adolescents with a cut-off score of 24 as an indicator of major depression, was used in the present study (Fendrich et al., 1990; Olsson and von Knorring, 1997).

Functional Disability Inventory-Parent version (FDI-P)

This instrument comprises 15 questions regarding functioning in everyday activities, rated on a scale from 0 (no problems) to 4 (impossible). The maximum score is 60 and suggested cut-offs are; 0–12 (no disability), 13–20 (mild), 21–29 (moderate) and >30 (severe disability). Reports on the FDI-P has shown good correspondence between parent and child ratings in addition to satisfactory validity and reliability (Walker and Greene, 1991; Claar and Walker, 2006).

Pain Interference Index (PII)

The PII was developed as a brief instrument to specifically address pain related interference in everyday life. The Swedish version of the PII used in the present study has showed adequate statistical properties in a sample of children and adolescents 7–18 years (Holmstrom et al., 2015). Also, an English version of PII, including a parent version of the instrument, has recently been validated based on a sample of patients with neurofibromatosis aged 6–25 years (Martin et al., 2015). PII consist of six items rated on a scale from 0 (not at all) to 6 (very high) with a maximum total score of 36. The child is asked to what degree during the past 2 weeks pain has: (1) Made it difficult for you to do schoolwork, (2) Made it difficult for you to do activities outside school (leisure activities), (3) Made it difficult for you to spend time with friends, (4) Affected your mood, (5) Affected your ability to do physical activities (like run, walk upstairs, play sports), and (6) Affected your sleep.

Statistical Analyses

Patient Characteristics

Descriptive statistics were used to summarize sample characteristics (age, sex, pain locations, temporal pain pattern, pain duration over time, current pain intensity, and school absence). Student's *t*-tests were used to compare means between subgroups. Zero-order correlations were investigated with Pearson's *r* and internal consistency were investigated with Cronbach's alpha. Data is presented for the whole group, as well as divided into males and females.

Mediation Analyses

All analyses were conducted using SPSS version 22.

To explore the importance of pain interference for the relationships between pain and functioning (i.e., depression and functional disability), a mediation model was tested with pain intensity as the independent variable (X), PII as the mediator (M), and CES-DC or FDI-p as the dependent variables (Y). The product of coefficients approach was used, which is today widely viewed as the best overall test of mediation (MacKinnon et al., 2007). Also, although the Normal theory test may be used to assess the indirect effects of pain interference on the relationships between pain and functioning, recent methods have advocated bootstrapping, a non-parametric resampling procedure (Preacher and Hayes, 2004). In the present study, results from both the Normal theory test (parametric) and the bootstrapping approach (non-parametric) are presented. Furthermore, analyses were conducted to address the issue of directionality (i.e., if the functional relationship between M and Y variables is opposite to what is defined *a priori*). Specifically, the dependent variables (depression, functional disability) were entered into the analytic model as mediators, while the proposed mediator (pain interference) was used as dependent variable, essentially inverting the original analyses. Missing values were excluded listwise in all analysis. An α-level of $p < 0.05$ was chosen as threshold for statistical significance and two-tailed tests were used in all analyses.

Analyses of mediators should be based on theoretically relevant *a priori* hypotheses. In the present study, a conceptual model based on a behavioral analytic framework is tested. It is well known that chronic pain commonly results in disability, including reduced levels of physical, social, and emotional functioning. A wide variety of interventions exist to improve functioning, each with a more or less distinct treatment objective. For example, medical strategies are typically aimed at reducing pain intensity. In contrast, behavioral interventions such as ACT are not primarily aimed reducing pain but at reducing the impact of pain on behavior, i.e., pain interference. Thus, functioning may be increased by a reduction in pain interference, also when pain intensity remain relatively unchanged. This type of intervention is based on a conceptual model in which the relationship between pain and functioning is mediated by another, and modifiable, variable (i.e., pain interference). However, to our knowledge there are to date no studies that have evaluated the importance of pain interference as a mediator between pain and functioning in pediatric chronic pain. In the present study, it was hypothesized that pain interference mediates the relationship between pain intensity and depression, as well as between pain intensity and functional disability.

RESULTS

Sample Characteristics

The mean age in this sample ($n = 163$) was 14.1 years ($SD = 2.6$), 121 girls (74.2%) were included in the sample.

A large proportion (75.3%) of the patients reported pain from multiple locations and the most frequently reported type of pain was headache (65.9%), while 40.6% reported stomach pain, 30.6% back pain and 22.9% pain from joints, 12% widespread pain and 12% were diagnosed with CRPS. Over 55% of total the sample reported to have continuous pain, and 22% reported episodes of pain on a daily basis.

The total sample mean for current pain intensity was 4.4 ($SD = 2.8$, range 0–10), with 15% ($n = 23$) of the sample reporting a pain intensity of >7. The mean pain duration in the total sample at the time for data collection was 51.4 months ($SD = 43$, range 3–192 months) or approximately 4 years. Current pain intensity was significantly correlated with the PII ($r = 0.39$, $p < 0.01$) and the CES-DC ($r = 0.21$, $p < 0.01$), but not with the FDI-P.

The mean score on the CES-DC for the total group was 23.1 ($SD = 12.1$), with 44% of the sample scoring above the suggested cut-off for major depression (see Materials and Methods). The mean score on FDI-P was 16.5 ($SD = 11.7$) for the total sample, indicative of overall mild disability according to suggested cut-offs (see Materials and Methods), and 15% of the sample had a score higher than the suggested cut-off for severe disability. The sample mean for pain interference (PII) was 18.3 ($SD = 9.4$) of a maximum 36. The PII correlated significantly with the CES-DC ($r = 0.68$, $p < 0.01$) and the FDI-P ($r = 0.55$, $p < 0.01$). There was also a significant but weaker relationship between the CES-DC and FDI-P ($r = 0.33$, $p < 0.01$). The internal consistency of the scales, as measured by Cronbach's alpha, was found to be high in the present sample, 0.82 for the CES-DC, 0.86 for the PII and 0.91 for the FDI-P.

School absence due to pain was frequently reported within the sample, with over 70% of the patients staying home from school or missing classes due to pain at least once a week. Also, 13% of the children/adolescents that reported school absence due to pain were not attending school at all (**Table 1**).

Differences in Pain and Functioning between Subgroups of Patients

Subgroups of patients based on gender and number of pain locations were compared to evaluate possible differences in age, pain (intensity, duration and interference) and functioning (functional disability, depression).

TABLE 1 | Pain related school absence.

Pain related school absence ($N = 161$)	Frequency	Percent
No absence	43	26.7
A few days of absence/month	49	30.4
>1 day/week of absence	48	29.8
Complete absence	21	13
Total	161	100

Gender

In this sample, girls experienced significantly more depression than boys. In contrast, boys illustrated longer pain duration than girls, however, this difference did not reach statistical significance. No significant differences were found between boys and girls in pain intensity, disability or pain interference, see **Table 2**.

Single or Multiple Pain Locations

Children with pain from multiple locations ($n = 122$) were compared to the group of children with pain from a single location ($n = 41$). No significant differences between these two subgroups were found, showing that children/adolescents with pain from multiple sites were not more impaired (as measured by PII, CES-DC, and FDI-P), not experiencing higher levels of pain and had not been experiencing pain for a longer period of time, see **Table 2**.

Comparing Patients With and Without Depression

A series of analyses were conducted to compare patients with scores above and below the cut-off for major depression (24) on age, pain intensity, pain duration, pain interference, and functional disability. Patients with a score indicative of major depression (>23, $n = 78$) had significantly higher scores on the PII and FDI-P and were significantly older when compared to the patients with CES-DC scores below the suggested cut off. However, no significant difference could be found between subgroups with higher/lower depression scores regarding pain duration, see **Table 2**.

Functional Disability

Similarly, a subgroup analysis was carried out to compare patients ($n = 25$) scoring above and below the suggested cut-off for severe disability on the (FDI-P > 30). The subgroup with severe disability displayed significantly higher levels of depression and pain interference, compared to patients with lower scores on disability (i.e., no disability to moderate disability. There were no significant differences in age, pain duration, or pain intensity between the disability subgroups.

Pain Interference as a Mediator between Pain and Functioning

The influence of pain interference on the relation between pain and functioning was evaluated by analyzing the indirect effect of PII in the association of (1) pain intensity and CES-DC, and (2) pain intensity and FDI-p (**Figure 1**).

The Relation between Pain and Depression

Significant indirect effects ($p < 0.01$) of pain interference in the relationship between pain intensity and depression was seen in the Normal Theory Test as well as when using a bootstrap approach. The Normal Theory Tests revealed that both the a and b paths were significant. Furthermore, the relation between the predictor (pain) and outcome variable (depression) changed from significant to non-significant when controlling for the indirect effects (mediator), suggesting that the relationship between pain and depression is strongly influenced by the pain interference.

TABLE 2 | Pain and functioning in subgroups of patients.

	Gender			Multiple pain locations			CES-DC			FDI-P		
	Girls (*N* = 121)	Boys (*N* = 42)	*p*	Single (*N* = 41)	Multiple (*N* = 122)	*p*	Low (*N* = 85)	High (*N* = 78)	*p*	Low (*N* = 138)	High (*N* = 25)	*p*
Age (years)*M* (*SD*)	14.3 (2.5)	13.5 (2.9)	0.09	13.78 (3.4)	14.2 (2.4)	0.42	13.3 (2.9)	14.9 (2.1)	0.00*	13.9 (2.7)	14.9 (2.1)	0.8
Pain duration*M* (*SD*)	47.0 (41.2)	63.9 (46.0)	0.04	40.3 (38.2)	55.3.2 (44.2)	0.06	51.9 (39.7)	50.9 (46.6)	0.89	51.8 (42.6)	49.2 (45.8)	0.02
Pain (NRS)*M* (*SD*)	4.5 (2.7)	4.0 (3.2)	0.34	3.8 (3.0)	4.6 (2.8)	0.115	3.8 (2.8)	4.9 (2.9)	0.02	4.1 (2.8)	5.6 (3.1)	0.80
PII*M* (*SD*)	19.2 (9.3)	16.1 (9.5)	0.09	17.2 (11.9)	18.7 (8.8)	0.35	13.0 (8.0)	24.1 (7.3)	0.00*	17.0 (9.3)	25.2 (7.1)	0.00*
CES-DC*M* (*SD*)	24.7 (12.2)	18.3 (10.3)	0.00*	21.7 (12.0)	23.6 (12.1)	0.45	13.6 (6.3)	33.4 (7.4)	0.00*	22.0 (12.2)	29.3 (9.6)	0.00*
FDI-P*M* (*SD*)	16.6 (11.4)	16.5 (12.8)	0.96	14.9 (13.5)	17.1 (11.2)	0.26	13.3 (10.8)	19.9 (11.8)	0.00*	12.7 (8.3)	36.1 (6.6)	0.00*

*Significant at the $p < 0.01$ level. *M*, Mean; *SD*, Standard deviation; N, Number of subjects; NRS, numerical rating scale. Pain duration is presented in months. PII, Pain Interference Index; CES-DC, Center for Epidemiological Studies-Depression Scale Children; FDI-P, Functional Disability Inventory-Parent version. Low = below cut off; High = above cut off.

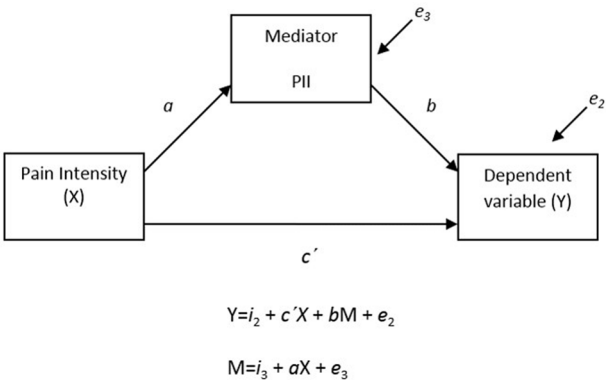

FIGURE 1 | Mediation analysis; The influence of pain interference on the relation between pain and functioning was evaluated by analyzing the indirect effect of PII in the association of (1) pain intensity (X) and CES-DC (Y), and (2) pain intensity (X) and FDI-P (Y).

The Relation between Pain and Functional Disability

Consistent with the findings on depression, both the Normal Theory Test and the bootstrap method illustrated a significant indirect effect ($p < 0.01$) of pain interference on the relation between pain and functional disability. Results are summarized in **Table 3**.

Examining Directionality

To examine the issue of directionality, two analyses were performed with each of the dependent variables (depression or functional disability) entered as mediator of the relation between pain intensity and pain interference (essentially reversing the original mediation analyses). Neither of these results were significant, providing incremental yet tentative support for the directionality of the meditational effect illustrated in the original analyses.

DISCUSSION

An increasing number of studies have illustrated that chronic pain is commonly associated with low levels of functioning. However, little is yet known about how specific factors influence the complex interplay between pain and functioning. To investigate if pediatric chronic pain patients with high and low levels of functioning differed in demographic variables, pain, and pain interference and to explore the mediating function of pain interference in the relationship between pain and functioning (i.e., depression and functional disability) a series of analysis was carried out in a sample of pediatric patients referred to a tertiary care pain clinic.

Findings from the present study showed that, older participants presented with higher levels of depression and pain interference, corresponding with a previous study showing that decreased functioning in daily life may be related to age (Roth-Isigkeit et al., 2005). In line with previous research (Piccinelli and Wilkinson, 2000), girls reported higher levels of depression. However, girls and boys reported similar levels

TABLE 3 | The mediating role of pain interference in the relationships between pain intensity and depression, as well as between pain intensity and functional disability.

The effects of pain interference on the relation between pain and depression				
		Normal theory test		
Path	**Coefficient**	***SE***	***t*[a]**	***p***
a	1.28	0.25	5.14	<0.0001
B	0.90	0.08	11.05	<0.0001
Total *(c)*	0.90	0.33	2.68	0.0081
Direct *(c′)*	−0.25	0.27	−0.92	0.3602
*a*b*	1.14	0.24	4.68	<0.0001
		Non-parametric bootstrap approach		
			CI (95%)[b]	
Mediator	**Mean indirect effect**	***SE***	**Lower**	**Upper**
Depression	1.14	0.23	0.60	1.78
The effects of pain interference on the relation between pain and functional disability				
		Normal theory test		
Path	**Coefficient**	***SE***	***t*[a]**	***p***
1-5 *a*	1.29	0.26	4.97	<0.0001
B	0.70	0.09	7.63	<0.0001
Total *(c)*	0.66	0.34	1.95	0.0533
Direct *(c′)*	−0.24	0.31	−0.77	0.4444
*a*b*	0.90	0.22	4.18	<0.0001
		Non-parametric bootstrap approach		
			CI (95%)[b]	
Mediator	**Mean indirect effect**	***SE***	**Lower**	**Upper**
Functional disability	0.90	0.20	0.42	1.47

of pain intensity, pain interference and disability. In contrast to previous studies reporting that pain in multiple locations is associated with more severe disability, participants with pain from multiple sites did not demonstrate higher levels of pain, pain interference, disability or depression than those experiencing pain from a single location in the present sample (Hoftun et al., 2011; Holm et al., 2012) and the patients displaying the most impaired functioning (depression, high pain interference and decreased physical functioning) were not the patients that had experienced pain over the longest period of time, nor where they the patients that were experiencing the highest levels of pain.

The association between pain and depression is well established in adults, and this study provides further support that these variables are strongly correlated also in youths with chronic pain. Scores above the suggested cut-offs for depression were found in almost half of the total sample, with a mean score on the depression measure significantly higher in girls compared to boys. These findings further emphasize the close relationship between chronic pain and depression found in several recent studies (Claar and Walker, 2006; Zernikow et al., 2012).

Previous research has shown that the relationship between pain intensity and functioning is less direct than expected (Claar and Walker, 2006), pointing at a need to further explore how these and other related variables are associated. It can be argued that pain interference is a critical factor in the development of depression in youths with chronic pain. The avoidance of physical and social activities that are perceived as meaningful although associated with pain may reduce pain and distress in the short run, but may over time result in a less active and meaningful life. Results from the present study indicated that pain interference is a key factor in the complex relationship between pain and functioning. Although tentative due to the cross-sectional data set, results from the present study suggest that the mediating role of pain interference should be further evaluated in longitudinal studies and clinical trials. Thus, the present findings support the notion that pain interference might be a more important factor in relation to functioning than levels or duration of pain. This is line with recent research, emphasizing

the need for a shift in focus to the behavioral aspect of pain (Palermo, 2009). It is of utmost importance to adequately capture the impact of chronic pain in children, and the present findings suggests that pain interference is a highly relevant dimension. In addition, the alarming prevalence of chronic debilitating pain calls for further development of interventions that reduce pain interference among children and adolescents where symptoms may remain, such as CBT and ACT (24).

Although the empirical support for this type of treatment is relatively strong, more research is needed to clarify individual characteristics of treatment responders, particularly in pediatric chronic pain. For example, it is possible that patient characteristics (i.e., age, pain duration) moderate the effects of treatment. If we can identify patient characteristics (e.g., demographics, pain, pain interference, depression) of individuals with low levels of functioning, this will improve the ability to tailor treatment to meet the individual needs of each patient which may improve effect sizes.

A number of limitations should be taken into account when interpreting the results from this study. It should be noted that the sample in this study was selected on the basis of referral to a tertiary pain clinic and it is thus possible that the included children and youths represent a sub group of individuals that are particularly affected by their chronic pain. The use of cross-sectional data obviously prevents any causal conclusions. Furthermore, it is important to emphasize, that a cross sectional design only provides a pattern of results that suggest the importance of pain interference for the relationship between, e.g., symptoms and depression. Longitudinal studies are needed to confirm these findings in addition to studies investigating the relative importance of different hypothesized mediators. Although the child and parent version of the FDI has shown to correlate well, it is possible that the use of the child version had provided different results on disability, and it may be argued that including both versions would have facilitated a relevant comparison between parent and child reports, as well as between PII and FDI. In addition, more information regarding pain, e.g., average pain intensity over the past weeks, would have been useful to validate the correlations between, e.g., pain and depression. Also, it would have been desirable to have data on the current pain management of the included children since this could have added another dimension to the findings, however, this was not assessed in a structured way in the present study. Furthermore, data for the present study was collected in clinical interviews or by self-report questionnaires. Thus the present study used self-reports only and it is suggested that future studies include objective measures of functioning, such as actigraphic monitoring or records of school absence provided by teachers and the results in the present study should be cross-validated in a study with a different, and ideally larger, sample.

CONCLUSION

Thus, this study adds to the growing support of findings suggesting that functioning and pain interference should be routinely assessed in pediatric chronic pain and a central target in treatment. Particularly, these findings imply a need for interventions specifically aimed at improved functioning for patients with chronic debilitating pain.

ETHICS STATEMENT

The study sample consisted of 163 consecutive pediatric patients and their parents, referred to a tertiary pain clinic due to longstanding pain. Both parent and child gave informed written consent and the study was approved by the local ethics committee. A written copy of the study information sheet was given to the families when arriving at the hospital. Families were given sufficient time to read the information and ask any question they might have. Consent was then obtained prior to data collection (at the first visit to the clinic). Both parents and child were given written and oral information prior to accepting the invitation to partake in the study, and informed consent was obtained from both parties.

AUTHOR CONTRIBUTIONS

LH has been responsible for the study design, analysis and manuscript preparation (in collaboration with RW). RW has been responsible for the study design, analysis and manuscript preparation (in collaboration with LH). MaK has been responsible for data collection and setting up the data base, taken part in analysis and have commented on the manuscript through out the writing process. MiK has taken part in study design, data collection and analysis and have commented on the manuscript through out the writing process.

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How Perceived Pain Influence Sleep and Mood More Than The Reverse: A Novel, Exploratory Study with Patients Awaiting Total Hip Arthroplasty

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Objectives: Attributions about how comorbid symptoms worsen or improve each other are central cognitive components of chronic pain that are shown to facilitate or impede the recovery process. Still, these attributions have been poorly illuminated in chronic pain patients. The present study explored perceptions of how sleep, pain, and mood influence each other in patients awaiting total hip arthroplasty (THA).

Design and Methods: In this cross-sectional study, 291 patients (mean age 67.8, 65.3% female) rated 12 statements about how much a given symptom (pain, sleep, mood) changed when another symptom (pain, sleep, mood) worsened or improved on a response scale ranging from much worse (−2) via no change (0) to much better (2). Sleep (Bergen Insomnia Scale), pain (McGill Pain Questionnaire), anxiety and depression (Hospital Anxiety and Depression Scale) were assessed as background variables.

Results: Of the patients in the study, 56% reported symptoms indicating insomnia. Anxiety and depression were indicated in 16 and 10%, respectively. Over 80% rated their pain as horrible/unbearable and reported that pain occurred always/daily. When experiencing increased pain, a majority perceived that sleep (90%) and mood (70%) worsened, whilst experiencing reduced pain improved sleep and mood in 50%. Poor sleep increased pain and worsened mood in 45 and 60% of the patients, respectively. Better sleep was perceived to reduce pain and improve mood in 50%. Worsened mood increased pain (46%) and worsened sleep (52%). Improved mood decreased pain and improved sleep in 25 and 35%, respectively.

Discussion: In this study, a novel approach was used to investigate perceptions of reciprocal relationships between symptoms. We found that THA patients perceived interrelationships between pain, sleep and mood. These perceived interrelations were stronger when symptoms worsened than when symptoms improved. They also held stronger beliefs about the effect of pain on sleep and mood, than the effect of sleep and

mood on pain. Attributions are central in illness perception and ultimately affect illness behavior. For patients who perceive symptoms to interrelate, the door has already been opened to utilize these attributions in treatments aiming to disrupt vicious cycles, hence supporting the use of multimodal treatments.

Keywords: chronic pain, sleep, mood, attribution, reciprocal relationships between symptoms

INTRODUCTION

Pain in patients eligible for total hip arthroplasty (THA) is normally caused by arthritis (Hamel et al., 2008). The experience and expression of such pain is commonly modulated by the presence of comorbid conditions like sleep and mood disturbances (Chiu et al., 2005; Lautenbacher et al., 2006; Roehrs et al., 2006; Haack et al., 2007; Smith et al., 2007; O'Brien et al., 2011; Blagestad et al., 2012) as well as expectancies and appraisals about these conditions (Tracey, 2010; Bjorkedal and Flaten, 2012). Chronic pain patients often attribute specific causal relationships in terms of how these conditions influence each other (Morin et al., 1998; Hawker et al., 2008; Tang et al., 2009; Theadom and Cropley, 2010). Shown to shape symptom expression, such attributions also influence a person's overall perceived symptom load (Petrie et al., 2007). Attributions typically enable a person to predict and influence future events, and are, accordingly, found to predict thoughts and behavior aimed at getting well, or motivation to perform preventive health behavior (Michela and Wood, 1986). In chronic pain specifically, such attributions are found to be central cognitive facilitators or impediments to the recovery process (Dean, 1986; Michela and Wood, 1986; DeGood and Kiernan, 1996; Roesch and Weiner, 2001).

Sleep and mood disturbances are frequently experienced as a consequence of pain in chronic pain patients (Brennan and Lieberman, 2009), and often interact to worsen pain (Chiu et al., 2005; Zautra et al., 2005; Vitiello et al., 2009; Ong et al., 2010; Theadom and Cropley, 2010; Sivertsen et al., 2015). Conversely, there is also recent research highlighting the amplifying effect of improvements of sleep and mood involved in the recovery from chronic pain (Zautra et al., 2005; Davies et al., 2008; Ashworth et al., 2010; Ong et al., 2010). Sleep and mood are therefore central components both in expression of illness, and as part of the multimodality treatment of chronic pain patients. There is emerging evidence that chronic pain patients with comorbid sleep problems are aware of the bidirectional relationship between the constructs (Tang et al., 2009; Ramlee et al., 2016). Hence, there is great potential in assessing and utilizing attributions to aid accurate understanding and treatment of chronic pain and its comorbid conditions.

Attributions about the perceived relationship between pain, sleep and mood have been poorly illuminated empirically. A few studies have explored the perceived effect of pain on sleep and mood and found, first, that good sleep and emotional well-being are rated as very important for chronic pain patients (Turk et al., 2008). Furthermore, many pain patients are convinced that their sleep problems result from their pain (Morin et al., 1998; Hawker et al., 2008), and consequently when they experience severe pain, it is difficult for them to sleep (Edwards et al., 2011; Tang et al., 2012a). In line with this, chronic pain patients often believe that their sleep problem will disappear when their pain is gone (Morin et al., 1998). Of the studies to date, only one has explored this reciprocal relationship from the perspective of sleep, finding that fibromyalgia patients directly associate poor sleep with feelings of pain and fatigue, in addition to reduced coping abilities (Theadom and Cropley, 2010). Knowledge of attributions about the perceived mutual influence of mood, pain and sleep is lacking in chronic pain patients. Also missing are studies exploring attributions about how improvements, and not only worsening, of symptoms, are perceived to influence other symptoms. Finally, in order to investigate whether bidirectional relationships exist in how patients attribute reciprocal symptom influence, these multidirectional attributions need to be explored within the same individuals.

To improve our understanding of attributions of symptoms in chronic pain patients, we developed an instrument to explore how patients waiting to undergo THA perceived pain, sleep and mood to influence each other. The questionnaire contained 12 statements assessing two main aspects of symptom influence: (1) how levels of pain influence sleep and mood, but also, conversely, the influence of sleep and mood on pain, and (2) the perceived effect on pain, sleep and mood both when symptoms are worse than usual and when symptoms are better than usual. Based on the responses to these statements, bidirectional relationships between pain, sleep and mood were investigated.

MATERIALS AND METHODS

Study Design

This questionnaire-based study was part of a prospective, multi-center study that evaluated pain, sleep, anxiety, depression and symptom attribution in patients 6–0 weeks before THA. These results are reported elsewhere.

Participants

Participants were recruited from four different orthopedic departments in hospitals across Norway (Haukeland University Hospital, Diakonhjemmet Hospital, Coastal Hospital Hagevik and Sørlandet Hospital Arendal) between May 2014 and November 2015. A total of 643 patients who entered the waiting lists for THA were invited to participate and 314 patients accepted. The response rate differed between the hospitals, with response rates of 75.2, 72.0, 58.7, and 23.2%, respectively. Due to the low response rate in the last hospital, sensitivity analyses were performed whereby results with all hospitals included were compared to results from all hospitals without the hospital

with the lowest response rate. In all cases, the results did not significantly differ, with differences in effect (measured by Cohen's *d* effect size) of less than 0.1. Hence, including data from the hospital with low response rate had negligible effects on the results. Eighteen participants were excluded from the analysis due to missing signed consent form pre-operatively, and five because their THA was canceled. Thus, the final sample consisted of 291 participants.

Procedure

The participants were recruited consecutively from the waiting lists for THA. When sending the notice of the date for their operation, an administrative staff member at the respective hospital enclosed information about the study, provided a questionnaire consisting of several validated scales as well as an informed consent form. Patients willing to participate were asked to complete the questionnaire at home and return the questionnaire and signed consent form when arriving at the pre-operative consultation. At one hospital, the patients were asked to return the questionnaire in a prepaid return envelope. Date of surgery was extracted from the Norwegian Arthroplasty Register via the participant's unique identifying code provided in the questionnaire. The participant's address was provided by the respective hospitals.

The study was approved by The Regional Committee for Medical and Health Research Ethics in Western Norway (2014/63/REK Vest) and was also approved at each of the hospitals involved.

Materials

The questionnaire contained a selection of measures that registered the participant's name, identifying code and data on the participant's demographics (age, sex, ethnicity, education level, employment, income, marital status, and number of children) and self-reported health. The following clinical background variables were assessed; pain intensity and frequency [from the McGill Pain Questionnaire (Melzack, 1975), in addition to reporting additional pain in the hip being replaced], sleep [Bergen Insomnia Scale (BIS; Pallesen et al., 2008)], symptoms of anxiety and depression [Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983)], and specific hip-related outcomes [Hip Osteoarthritis Outcome Scale (Nilsdotter et al., 2003)]. In addition, the participants completed a questionnaire assessing attribution of symptoms specifically designed for this study. These questionnaires are briefly described in the following paragraphs.

General pain was assessed using two verbal descriptor scales from the McGill Pain Questionnaire (Melzack, 1975), validated in Norwegian (Kim et al., 1995). The magnitude of pain was assessed by the phrase: "place a cross in the box fitting your pain," with the response alternatives "no pain," "weak," "unpleasant," "bothersome," "terrible" or "unbearable." The frequency of pain was assessed by the phrase: "How often do you have pain?" The response alternatives were "constantly," "daily," "several times a week," "about once a week," "several times a month," "about once a month," "less than once a month" and "never." Patients were also asked whether the pain was chronic (> 3 months), if they had additional pain to the hip being replaced and whether they felt that analgesics relieved their pain.

Sleep was assessed using the BIS which measures self-reported symptoms of insomnia corresponding to the criteria for insomnia in the Diagnostic and Statistical Manual of Mental Disorders-IV-TR (American Psychiatric Association, 2000). The scale includes six items that are scored on an eight-point scale indicating the number of days per week for which a specific symptom is experienced (0–7 days, total scores ranging from 0 to 42). The BIS is validated using subjective as well as polysomnographic data and is found to possess good psychometric properties (Pallesen et al., 2008). Participants were categorized as insomniacs if scoring 3 or more on at least one of items 1–4, and 3 or more on at least one of items 5 and 6. The scale provided a Cronbach's alpha of 0.91 in the present study.

The Hospital Anxiety and Depression Scale (HADS) was used to assess the presence of anxiety and depression. The HADS contains 14 items describing non-vegetative symptoms of anxiety and depression (scoring range 0–21 for both anxiety and depression subscales) (Zigmond and Snaith, 1983). Higher scores indicate greater symptom severity. A score of 8 or higher on the HADS subscales of anxiety and depression respectively is considered a clinical cut-off. A validated Norwegian version of the HADS was used in the present study (Bjelland et al., 2002), for which the Cronbach's alpha for each subscale was 0.86.

The Hip Osteoarthritis Outcome Scale (HOOS) evaluated hip related outcomes through 5 subscales [pain, symptoms, functioning in activities of daily living (ADL), functioning in sport and recreation, and hip-related quality of life]. Standardized response alternatives are provided on a 5-point Likert scale (0–4). Then, a normalized score from 0 to 100 is calculated for each subscale (100 indicating no symptoms, and 0 indicating extreme symptoms) (Nilsdotter et al., 2003). The Cronbach's alpha coefficient was 0.96 in the present study.

The main outcome variable was symptom attribution. In order to assess how participants perceived symptoms of pain, sleep and mood to influence each other, a questionnaire was developed containing 12 statements about how much a given symptom (pain, sleep, mood) changed when another symptom (pain, sleep, mood) worsened or improved. Six statements explored the effect on the other two symptoms when a given symptom worsened, and six statements explored the effect on the other two symptoms when a given symptom improved. The participants were asked to provide responses on a 5-point scale (from 1 to 5) for each statement. **Table 1** presents the 12 statements together with the response alternatives.

Data Analysis

Analyses were performed using SPSS, version 21. For the symptom attribution questionnaire, the rating scale was recoded in order to display the positive or negative properties of the perceived influence. *Much worse* was recoded to −2, *a bit worse* was recoded to −1, *as usual* was recoded to 0 (indicating no change), *a bit better* was recoded to 1 and *much better* was recoded as 2. Descriptive statistics were used to characterize symptom attributions and the difference of the mean from 0 (no change) was measured through one-sample

TABLE 1 | Symptom attribution questionnaire.

	Response alternatives				
	Much better	**A bit better**	**No change**	**A bit worse**	**Much worse**
When my pain is worse than usual, my sleep becomes...					
When my pain is worse than usual, my mood becomes...					
When my sleep is worse than usual, my pain becomes...					
When my sleep is worse than usual, my mood becomes...					
When my mood is worse than usual, my pain becomes...					
When my mood is worse than usual, my sleep becomes...					
When my pain is weaker than usual, my sleep becomes...					
When my pain is weaker than usual, my mood becomes...					
When my sleep is better than usual, my pain becomes...					
When my sleep is better than usual, my mood becomes...					
When my mood is better than usual, my pain becomes...					
When my mood is better than usual, my sleep becomes...					

t-tests. A paired sample *t*-test was used to compare items in bidirectional relationships in order to assess the directionality of symptom attribution. All statements are listed in **Table 1**. For example, whether pain influences sleep more than sleep influences pain was assessed by comparing statements 1a and 2a for the worsening relationships between symptoms, and statements 1c and 2c for the improving relationships between symptoms. For the pain-mood relationship, statements 1b and 3a and statements 1d and 3c were compared for the worsening and improving effect of symptoms, respectively. For the sleep-mood relationship, statements 2b and 3b and statements 2d and 3d were compared for the worsening and improving effect of symptoms, respectively. Pairs with one or more missing values were removed from analyses (excluded pairwise). To measure the magnitude of the effect, effect sizes (Cohen's *d*) were estimated using DSTAT (Johnson, 1995). An effect size of 0.2 is regarded as a small, 0.5 a medium, and effect sizes of 0.8 or higher are regarded as large (Cohen, 1988). A Bonferroni-correction was applied due to multiple comparisons, setting the new critical *p*-value to 0.002.

RESULTS

Description of Baseline Characteristics

Table 2 presents the participants' characteristics. The mean age was 67.9 years and 65.3% were female. The majority were retired, married/cohabiting, and had 2 or 3 children. The majority had an income between 100 000 and 399 999 NOK (equivalent to approximately 12 000–50 000 USD). Clinical background variables are presented in **Table 3**. On the PPI, most participants rated their pain to be horrible (66.3%) or unbearable (16.2%), and over 90% rated their pain to occur daily or be present constantly. Over 70% also reported additional pain in the hip being replaced. In total, 54.0% reported symptoms indicating insomnia (the average BIS score was 16.4, $SD = 12.0$). Symptoms indicating caseness of anxiety or depression were reported by 16.2 and 10.3%, respectively. According to the hip-specific outcome measure (HOOS), the self-reported hip-related pain, function, quality of life, ADL and sports and recreation were poor (between 40 and 24 on a scale of 100–0 where 100 indicates no symptoms, and 0 indicates extreme symptoms).

Attributions between Pain, Sleep and Mood When Symptoms Worsened

A substantial portion of patients perceived that worsening of symptoms influenced their pain, sleep and mood (**Table 4**, **Figure 1**). Ninety per cent of the patients reported that sleep worsened in the presence of increased pain and 70% reported mood to worsen with increased pain. Close to 45% perceived their pain to worsen with poorer sleep, and almost 60% perceived mood to worsen with poorer sleep. Worse mood was perceived to have the least influence on pain (64.3% perceived there to be no change), but 51.9% reported mood to influence sleep. As displayed in **Table 5**, the mean on all subscales differed significantly from 0 (all *t*-values significant on the 0.002-level) with effect sizes ranging from 0.6 to 2.3 (medium to very large effect size).

Attributions between Pain, Sleep and Mood When Symptoms Improved

Patients reported improvement of one symptom to influence the other symptoms to a smaller degree than did worsening of it (**Table 4**, **Figure 1**). Still, reduced pain was perceived to improve sleep and mood in 56.7 and 51.8% of the patients, respectively. Improved sleep was also perceived to improve pain

in 35.4% of the patients. Improved sleep had a strong influence on improvements of mood and was reported by 47.2% of the patients. Again, mood was perceived to have the least influence on pain and sleep; improved mood was perceived not to have an effect in 74.9% for pain and 63.2% for sleep. Regardless, all variables differed significantly from 0 (all t-values significant on a 0.002-level). **Table 5** displays the effect sizes (ranging from 0.3 = small effect size to 0.9 = large effect size).

Directionality of Attributions When Symptoms Worsened

When symptoms worsened, pain was significantly perceived to influence sleep more than sleep influenced pain ($t = -19.2$, $df = 279$). The effect size was large ($d = 1.1$) (**Table 6**, **Figure 2**). Increased pain was also perceived to influence mood significantly more than worsened mood influenced pain ($t = -10.5$, $df = 269$). This effect size was medium ($d = 0.6$). There was no significant difference to which degree the participants perceived sleep and mood to influence each other.

Directionality Attributions When Symptoms Improved

Reduced pain significantly influenced sleep more than improved sleep influenced pain (**Table 6**, **Figure 3**, $t = 5.7$, $df = 272$). The effect size was small to medium ($d = 0.4$). Reduced pain also influenced mood more than improved mood influenced pain ($t = 10.3$, $df = 268$) with a medium effect size ($d = 0.6$). Lastly, improved sleep was perceived to influence mood more than improved mood influenced sleep ($t = 8.0$, $df = 269$) with a medium effect size ($d = 0.5$).

TABLE 2 | Demographics (*N* = 291).

Age	67.9 (*SD*: 11.1), range 23–96
Sex	65.3% female
Education (%)	
No schooling completed	0.3
Nursery school	15.8
High school graduate	16.2
Trade/technical/vocational training	29.2
Bachelor's degree	25.4
Master's degree	10.1
Doctorate degree	1.0
Work status (%)	
Full time 100 %	15.1
Part time	3.4
Homemaker	0.7
Unemployed	0.7
Student	0.3
On sick leave 100%	7.6
On sick leave <100%	1.7
Work assessment allowance	1.4
Disability benefit	8.6
Retired	59.8
Marital status (%)	
Married/cohabitant/partner	74.6
Single/separated/divorced/widow/widower	24.7
Number of children (%)	
None	9.9
1–2	48.1
3–4	36.4
5 or more	5.2
Income (NOK, %)	
0–199 999	15.4
200 000–399 999	44.7
400 000–599 999	25.1
600 000 or more	8.6

TABLE 3 | Clinical background variables (*N* = 291).

Pain	
Magnitude (%)	
Weak, unpleasant or bothersome	14.5
Horrible	66.3
Unbearable	16.2
Frequency (%)	
Constant or daily	89.3
Once or multiple times a week	7.2
Once or multiple times a month	0.6
Less than once a month	1.0
Chronic (pain lasting <3 months, %)	96.9
Experiencing additional pain to the replaced hip (%)	70.4
Effect of analgesics (%)	
None or to a small degree	56.0
To a large degree or completely	34.7
Health (%)	
Excellent or very good	24.0
Good or quite good	64.3
Poor	10.7
Health compared to a year ago (%)	
Much or a bit better than a year ago	7.2
About the same as a year ago	31.3
A bit or much worse than a year ago	59.1
Insomnia (BIS)	
Sum (mean)	16.4
Cutoff-insomnia* (%)	54.0
Anxiety (HAD–A < 8, %)	16.2
Mean (*SD*)	4.3 (*SD*: 3.9)
Depression (HAD–D < 8, %)	10.3
Mean (*SD*)	3.5 (*SD*: 3.19)
Hip related measures - HOOS	
Symptoms	34.35
Pain	39.22
ADL	40.05
Sportrec	23.02
QoL	24.78

**As defined by DSM-IV; BIS, Bergen Insomnia Scale; HADS, Hospital Anxiety and Depression Scale; HOOS, Hip Osteoarthritis Outcome Scale. Normal scores from 0–100, (100 indicating no symptoms, and 0 indicating extreme symptoms).*

DISCUSSION

In contrast to the number of studies that aim to disentangle the relationship between chronic pain, sleep and mood, limited effort has been devoted to investigating how patients themselves perceive how these symptoms influence each other. The present study explored perceived bi-directional influences of pain, sleep and mood when symptoms worsened or improved in patients awaiting THA. We found that a large majority perceived sleep and mood to worsen when experiencing worse pain than usual and less intense pain than usual was perceived to improve sleep and mood. A significant proportion of the patients perceived pain to worsen with poorer sleep, and better sleep was perceived to reduce pain. Overall, pain stood out as the symptom with the largest perceived influence on the other symptoms, while mood was the symptom perceived by the fewest patients as influencing the other symptoms.

Worsening Symptom Attribution

We found that almost all of the patients in the present study perceived increased pain to lead to poorer sleep, corroborating the impact of pain on sleep in previous qualitative and quantitative studies (Smith et al., 2000; Breivik et al., 2006; Hawker et al., 2008; Ashworth et al., 2010; Theadom and

TABLE 4 | Description of attributions of the effect between pain, sleep and mood ($N = 291$).

Attributions when symptoms worsen			Level of effect (%)				
	Mean (from −2 to 2)	*SD*	Much worse	A bit worse	No change	A bit better	Much better
When my pain is worse than usual, my sleep becomes…	−1.4	0.6	49.1	40.9	6.5	0.0	0.0
When my pain is worse than usual, my mood becomes…	−0.9	0.6	14.4	56.4	24.1	0.3	0.0
When my sleep is poorer than usual, my pain becomes…	−0.6	0.7	11.3	32.6	51.9	0.3	0.0
When my sleep is poorer than usual, my mood becomes…	−0.7	0.7	11.3	45.7	37.5	0.3	0.0
When my mood is worse than usual, my pain becomes…	−0.4	0.6	7.9	22.0	64.3	0.0	0.0
When my mood is worse than usual, my sleep becomes…	−0.7	0.7	13.4	38.5	41.2	0.3	0.0
Attributions when symptoms improve			**Level of effect (%)**				
	Mean (from −2 to 2)	***SD***	**Much better**	**A bit better**	**No change**	**A bit worse**	**Much Worse**
When my pain is weaker than usual, my sleep becomes…	0.7	0.9	17.5	39.2	30.6	6.5	0.3
When my pain is weaker than usual, my mood becomes...	0.8	0.8	21.6	30.2	40.5	1.4	0.3
When my sleep is better than usual, my pain becomes…	0.4	0.7	7.6	27.8	56.4	2.7	1.4
When my sleep is better than usual, my mood becomes…	0.7	0.8	18.9	28.2	46.4	1.0	0.3
When my mood is better than usual, my pain becomes…	0.2	0.5	2.7	13.7	74.9	2.1	0.7
When my mood is better than usual, my sleep becomes…	0.3	0.6	4.5	23.4	63.2	3.1	0.0

TABLE 5 | Strength of relationships between symptoms

Attributions when symptoms worsen	Difference from 0 (indicating no change)					
	t	***df***	**95% CI of the difference**		**Sig**	**Effect size**
When my pain is worse than usual, my sleep becomes…	−39.0	280	−1.5	−1.4	0.000	2.3
When my pain is worse than usual, my mood becomes…	−23.2	276	−1.0	−0.8	0.000	1.4
When my sleep is poorer than usual, my pain becomes…	−13.7	279	−0.7	−0.5	0.000	0.8
When my sleep is poorer than usual, my mood becomes…	−17.8	275	−0.8	−0.6	0.000	1.1
When my mood is worse than usual, my pain becomes…	−10.4	273	−0.5	−0.3	0.000	0.6
When my mood is worse than usual, my sleep becomes…	−16.1	271	−0.8	−0.6	0.000	1.0
Attributions when symptoms improve	**Difference from 0 (indicating no change)**					
	t	***df***	**95% CI of the difference**		**Sig**	**Effect size**
When my pain is weaker than usual, my sleep becomes…	13.7	273	0.6	0.8	0.000	0.8
When my pain is weaker than usual, my mood becomes...	15.1	273	0.7	0.9	0.000	0.9
When my sleep is better than usual, my pain becomes…	8.9	278	0.3	0.5	0.000	0.5
When my sleep is better than usual, my mood becomes…	13.8	275	0.6	0.8	0.000	0.8
When my mood is better than usual, my pain becomes…	5.2	273	0.1	0.2	0.000	0.3
When my mood is better than usual, my sleep becomes…	8.4	273	0.2	0.4	0.000	0.5

CI, Confidence Interval. Effect size, Cohen's d.

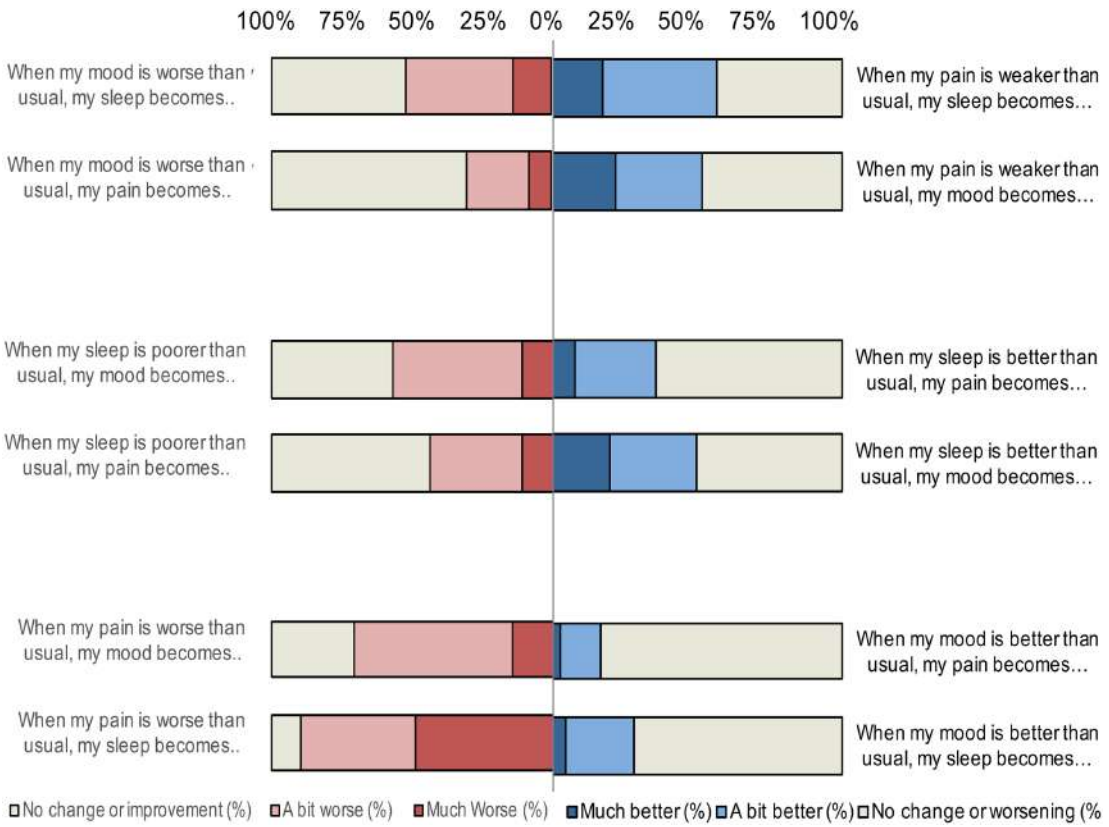

FIGURE 1 | Percentages of patients attributing changes in their pain, sleep, and mood when symptoms worsen or improve.

TABLE 6 | Directionality of symptom attribution between pain, sleep and mood (*N* = 291).

When symptoms worsen	95 % CI		*t*	df	Sig	Effect size
Pain affects sleep (1a) Sleep affects pain (2a)	−1.0	−0.8	−19.2	279	0.000	1.1
Pain affects mood (1b) Mood affects pain (3a)	−0.6	−0.4	−10.5	269	0.000	0.6
Sleep affects mood (2b) Mood affects sleep (3b)	−0.1	0.1	−0.17	267	0.868	
When symptoms Improve	**95 % CI**		***t***	**df**	**Sig**	**Effect size**
Pain affects sleep (1c) Sleep affects pain (2c)	0.2	0.4	5.7	272	0.000	0.4
Pain affects mood (1d) Mood affects pain (3c)	0.5	0.7	10.3	268	0.000	0.6
Sleep affects mood (2d) Mood affects sleep (3d)	0.3	0.5	8.0	269	0.000	0.5

CI, Confidence Interval. Effect size, Cohen's d.

Cropley, 2010; Henderson et al., 2013; Thomazeau et al., 2014). For example, many chronic pain patients firmly believe that when they are in pain, it is simply impossible for them to get comfortable and go to sleep (Edwards et al., 2011; Tang et al., 2012a). The rate of patients perceiving pain to negatively impact sleep was higher in the present study than found in chronic pain patients in general (90% vs. 65%) (Breivik et al., 2006); also, the intensity and frequency of pain was higher in the present

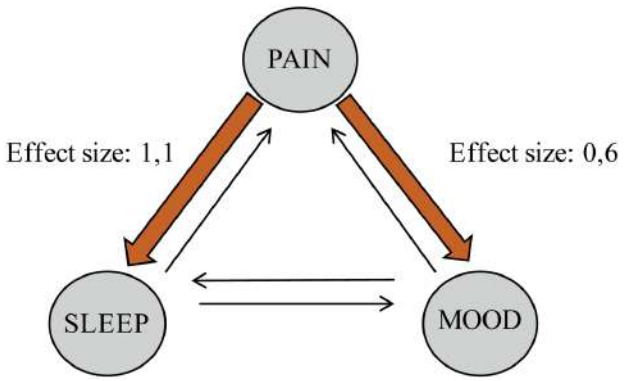

FIGURE 2 | Perceptions about reciprocal relationships when symptoms worsen.

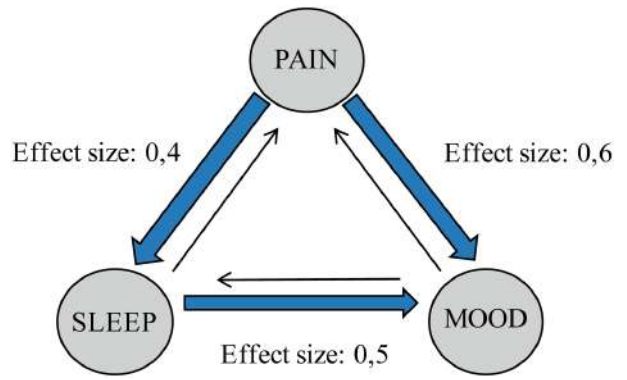

FIGURE 3 | Perceptions about reciprocal relationships when symptoms improve.

sample. The present study highlights the importance of effective treatments for chronic pain.

One third of our patient's perceived pain and mood to worsen with poorer sleep, mirroring one qualitative study where a poor night's sleep was found to be directly associated with increased pain (Theadom and Cropley, 2010). Our results are also in line with increasing numbers of observational and experimental studies establishing an effect of sleep on pain. However, more than half of the patients in our study did not perceive poorer sleep to increase pain. One of the most distressing features of chronic pain is the unpredictable fluctuation in its type and intensity (Hawker et al., 2008), and it may thus be difficult for patients to perceive how these symptoms are influenced by sleep and mood. This is supported by a recent daily process study that reported the pain-relieving effect of good sleep to be short-lived. Although sleep quality showed an inverse relationship with pain upon waking and during the first half of the day, no association was found during the second half of the day (Tang et al., 2012c). The authors suggest that for some patients, reduced pain might actually lead to over-extending activity. This would cause even more pain during the night, consequently masking the positive effect of good sleep on pain. Hence, perceived improvement of pain as a result of good sleep might be masked by the fluctuations or other sources of increasing pain. In addition, many clinicians do not regularly assess, diagnose or treat comorbid sleep problems in pain patients, since they are under the false impression that treatment of the underlying organic /psychiatric condition will resolve any residual sleep complaints (Ozminkowski et al., 2007). This lack of focus might contribute to these patients' perception of illness.

Although depression, anxiety and negative mood are closely related to chronic pain (Lin et al., 2003; Argoff, 2007; Montin et al., 2007; O'Brien et al., 2010; Wylde et al., 2011; Hoogeboom et al., 2012), worse mood than usual was perceived by the fewest patients to impact pain and sleep in our study. In a study of middle-aged women with chronic pain, an increase in negative affect during the previous week predicted greater pain during subsequent weeks (Zautra et al., 2005). One could assume that patients would perceive this same effect to a larger degree than what we found. Our results might indicate, as suggested by Lavigne (2005), that negative mood affects sleep and pain in a more indirect way. Alternatively, if the perception about reciprocal relationships between symptoms depend on the presence of the symptom in question, our results might simply reflect lower rates of anxiety and depression compared to pain and sleep complaints in the present study. Future investigations of symptom attributions in chronic pain patients with larger samples of comorbid anxiety and depression would clarify this matter.

Improving Symptom Attribution

The present study is to the authors' knowledge the first to explore how improvement in one symptom (pain, sleep, or mood) is perceived to influence other symptoms. We found that a majority of our patients perceive reduction of pain to improve sleep and mood. Although chronic pain is intractable by definition, this underlines the importance of optimal pain management, whereby reducing pain may also improve comorbid symptoms (Turk and Cohen, 2010). More noteworthy is the finding that one third perceived better sleep than usual to improve pain. The role of sound sleep is key in chronic pain patients. Firstly, restorative sleep is shown to be involved in the resolution of chronic pain (Davies et al., 2008), and chronic pain patients that are "good sleepers" report less pain at night, less negative consequences from their pain and less depression or pain-related anxiety (Ashworth et al., 2010). Accordingly, the concurrent treatment of pain-related sleep problems is found either to reduce pain itself, or to reduce pain interference, which might be an important aspect of pain in chronic pain patients (Edinger et al., 2005; Vitiello et al., 2009; Jungquist et al., 2010; Tang et al., 2012b). Furthermore, positive emotions are seen as resilience factors decreasing the negative impact of chronic pain conditions (Zautra et al., 2005; Ong et al., 2010). In a study investigating positive and negative affect in women with chronic pain, people who tend to have higher levels of positive affect also had less pain over time (Zautra et al., 2005). Hence, adequate sleep and positive mood seems to be a buffer involved not only in the biological foundation of pain perception (Davies et al., 2008), but also in the ability to cope with daily pain

(Theadom and Cropley, 2010). Positive emotions and good sleep may therefore play an important role in fostering recovery after episodes of severe pain (Zautra et al., 2001).

Taken together, the present findings have implications for the assessment and treatment of chronic pain and pain-related sleep and mood disturbances. That symptoms interact to worsen and improve each other forms the basis of multimodality treatments. This emphasizes the benefit of interventions aiming at disrupting vicious circles between symptoms (Argoff, 2007; Smith et al., 2009). The results of the present study support the use of interventions that target sleep and mood in addition to pain. Furthermore, attributions are found to be central cognitive facilitators or impediments to the recovery process (Dean, 1986; DeGood and Kiernan, 1996; Roesch and Weiner, 2001). According to attribution theory, individuals with chronic illness who make internal, unstable and controllable attributions also believe they can do something to minimize the impact of their illness. This leads directly to certain motivated coping cognitions and behavior, and ultimately to more positive psychological adjustment (Weiner, 1985). For chronic pain patients who perceive symptoms to interrelate, the door has already been opened to utilize these attributions in the treatment of chronic pain and its comorbid conditions. For our patients awaiting THA specifically, these attributions might aid a positive reinforcing cycle of symptom improvement when pain is reduced after surgery.

The limitations of the study should be noted. Firstly, due to the lack of previous studies that include the key attribution elements aimed at in the present study, a questionnaire was constructed for this purpose. It is therefore not previously validated. The questions used for assessing reciprocal relationships between pain, sleep and mood should be validated in other types of samples (e.g., normal subjects as well as in patients suffering from sleep and mood disorders). In the process of developing the questionnaire, mood was intentionally chosen as a general symptom-effector instead of specifying anxiety and depression, for several reasons. By broadening the term into "mood," we are convinced that aspects of disturbed mood such as "helplessness" or "frustrations" often experienced by these patients would be included in addition to aspects of anxiety and depression. Furthermore, there is no equivalent positive category to diagnoses such as anxiety and depression, and we also wanted to capture eventual positive attributions of improved mood, beyond the absence of negative symptoms. Another limitation is that since the patients completed the questionnaires without assistance from the researchers we had no way to ensure that participants understood the intention of the attribution questionnaire. Third, it is important to note that one of the hospitals included in the study had a very low response rate (22%), due to unknown factors. In order to ensure representativeness of our data, sensitivity analyses were performed and showed no major changes in results when the respective hospital was removed from analyses.

Despite the limitations, there are several strengths of this novel study. It places itself in a line of studies focusing on obtaining wider knowledge about the sleep-pain domain from the patient's perspective (Hawker et al., 2008; Turk et al., 2008), but it extends the scope to also explore attributions about sleep and mood, and to illuminate both the attributions related to worsening as well as improvement of symptoms. The natural path forward is to extend this newly acquired perspective into different chronic pain populations or populations where pain is a frequently experienced comorbid symptom.

CONCLUSION

The present study found that patients awaiting THA perceive pain, sleep and mood to influence each other when symptoms worsen or improve. Pain was perceived to have a stronger influence on sleep and mood, than sleep and mood had on pain. Attributions of symptom dynamics as investigated in the present study may play a key role in overall pain experience and illness behavior.

AUTHOR CONTRIBUTIONS

TB designed the study, developed the main questionnaire, recruited the hospitals participating in the study and collected the data. She also analyzed the data and wrote the manuscript. SP supervised the project, including participating in the design of the study and developing the main questionnaire. He also took part in deciding the choice of analyses, and critically reviewed the manuscript. JG also supervised the project, including participating in the design of the study and developing the main questionnaire. she also took part in deciding the choice of analyses, and critically reviewed the manuscript. NT took part in deciding the choice of analyses, the interpretation of the results and critically reviewed the manuscript. IN was the main supervisor of the project and participated in the design of the study and the development of the main questionnaire. She also took part in deciding the choice of analyses, and critically reviewed the manuscript. All authors have approved of the final version of the manuscript to be published.

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frontiers in Psychology

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Cut-Off Points for Mild, Moderate, and Severe Pain on the Numeric Rating Scale for Pain in Patients with Chronic Musculoskeletal Pain: Variability and Influence of Sex and Catastrophizing

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Objectives: The 0–10 Numeric Rating Scale (NRS) is often used in pain management. The aims of our study were to determine the cut-off points for mild, moderate, and severe pain in terms of pain-related interference with functioning in patients with chronic musculoskeletal pain, to measure the variability of the optimal cut-off points, and to determine the influence of patients' catastrophizing and their sex on these cut-off points.

Methods: 2854 patients were included. Pain was assessed by the NRS, functioning by the Pain Disability Index (PDI) and catastrophizing by the Pain Catastrophizing Scale (PCS). Cut-off point schemes were tested using ANOVAs with and without using the PSC scores or sex as co-variates and with the interaction between CP scheme and PCS score and sex, respectively. The variability of the optimal cut-off point schemes was quantified using bootstrapping procedure.

Results and conclusion: The study showed that NRS scores $\leq$5 correspond to mild, scores of 6–7 to moderate and scores $\geq$8 to severe pain in terms of pain-related interference with functioning. Bootstrapping analysis identified this optimal NRS cut-off point scheme in 90% of the bootstrapping samples. The interpretation of the NRS is independent of sex, but seems to depend on catastrophizing. In patients with high catastrophizing tendency, the optimal cut-off point scheme equals that for the total study sample, but in patients with a low catastrophizing tendency, NRS scores $\leq$3 correspond to mild, scores of 4–6 to moderate and scores $\geq$7 to severe pain in terms of interference

with functioning. In these optimal cut-off schemes, NRS scores of 4 and 5 correspond to moderate interference with functioning for patients with low catastrophizing tendency and to mild interference for patients with high catastrophizing tendency. Theoretically one would therefore expect that among the patients with NRS scores 4 and 5 there would be a higher average PDI score for those with low catastrophizing than for those with high catastrophizing. However, we found the opposite. The fact that we did not find the same optimal CP scheme in the subgroups with lower and higher catastrophizing tendency may be due to chance variability.

Keywords: musculoskeletal pain, numeric rating scale, pain interference, classification, chronic pain

INTRODUCTION

Assessment of pain intensity is considered one of the core outcome domains in clinical pain research (Dworkin et al., 2005), and is thus very commonly applied. The Numeric Rating Scale (NRS) is regarded as one of the best single-item methods available to estimate the intensity of pain (Jensen et al., 1999; Breivik et al., 2000). The NRS assesses pain intensity using a 0–10 ranking scale with 0 representing "no pain" and 10 "unbearable pain" or comparable statement. Clinicians, including psychologists, often use the categories of mild, moderate, and severe to simplify communication between patients and health care professionals. However, translating continuous measures such as NRS into discrete categories is not straightforward. Simply dividing an NRS into mild, moderate, and severe pain by dividing the scale into three equal parts is not a valid method (Serlin et al., 1995). Serlin et al. (1995) tried to solve this problem by correlating pain intensity to the level of interference of the pain with the daily functioning of patients with pain due to cancer, using a specific statistical technique, i.e., estimating how much of the variance in pain-related disability can be explained by different possible pain intensity classifications. Their statistical approach has been repeated for the same patient population, i.e., cancer patients (Paul et al., 2005) as well as being applied to other patient populations (e.g., Zelman et al., 2005; Hirschfeld and Zernikow, 2013; Oldenmenger et al., 2013; Boonstra et al., 2014). Results from the literature (Hirschfeld and Zernikow, 2013; Oldenmenger et al., 2013) show that the cut-off between mild and moderate pain, in terms of pain-related interference with functioning, is mostly placed between 3 and 4, and the cut-off between moderate and severe pain between 6 and 8. The differences may be caused by differences in study samples, pain definitions, and/or measures of functioning. Difference in diagnoses is generally accepted as one of the main causes of differences in cut-off points between studies (Zelman et al., 2003), while differences between study samples may also be explained by chance variation (Hirschfeld and Zernikow, 2013).

An unresolved issue is the influence of psychological factors on cut-off points. Catastrophizing (expecting or worrying about major negative consequences from a situation, even one of minor importance) is associated with pain severity and disability in patients with several chronic pain conditions (Wertli et al., 2014a,b). Another issue is the influence of the patient's sex on the cut-off points. There are clear, though incompletely understood, differences in pain perception between men and women (Rollman and Lautenbacher, 2001; Racine et al., 2012). Only Fejer et al. (2005) have studied the association between sex and the cut-off points for interference with functioning in individuals with neck pain, and found a small difference between male and female patients.

Most studies have classified pain intensity using the statistical method described by Serlin et al. (1995) to estimate how much of the variance in pain-related disability can be explained by different possible pain intensity classifications. The cut-off point scheme explaining the highest proportion of the variance is then chosen as the optimal scheme. Although this method may have shortcomings, its use facilitates comparisons between studies. Hirschfeld and Zernikow (2013) used a bootstrap resampling procedure and found a very large variability in the cut-off points in their sample of children and adolescents with chronic pain. They recommended that studies to define cut-off points include measures of variability for the optimal cut-off points.

The aims of the present study were to determine the optimal cut-off points for mild, moderate, and severe pain in terms of pain-related interference with functioning for patients with chronic musculoskeletal pain, as well as to measure the variability of the optimal cut-off points, and to determine the association between these cut-off points and patients' catastrophizing tendency and their sex.

MATERIALS AND METHODS

Patients

The patients included in the study participated in a nationwide survey of patients with musculoskeletal pain, who were referred or admitted to rehabilitation treatment in one of the cooperating rehabilitation centers. The patients were included when they first consulted their rehabilitation physician or started multidisciplinary inpatient or outpatient rehabilitation treatment. The study included patients from five rehabilitation centers, each with one (rehabilitation centers a, b, e), two (rehabilitation center d), or five (rehabilitation center c) treatment sites in the Netherlands. Some of these centers were departments of a university or general hospital, others were stand-alone rehabilitation centers. The centers are located in different parts of the Netherlands, with patients from rural or semi-industrialized areas, living in villages or medium-sized

to large towns and cities. Patients were included between the early months of 2012 and mid-2014; the exact time of inclusion differed between the participating rehabilitation centers. Inclusion criteria were: age over 18 years and having had musculoskeletal pain for longer than 3 months. Exclusion criteria were inability to understand Dutch, current major psychiatric disorder (active psychosis, severe depression with risk of suicide attempt, addiction, etc.), unwillingness to provide data for research purposes, a score of "no pain" or missing data on the NRS and more than 3 missing values on the Pain Disability Index (PDI-DV, see measurements).

Ethics Statement

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. The data were collected in a setting of usual care, in order to measure the outcome of the treatment. The patients were asked to indicate if they did not allow their anonymous data to be used for the nationwide survey and/or for scientific studies. Because the data were collected during usual care, no approval of a Medical Ethics Committee was needed.

Study Design

Cross-sectional study in the context of care as usual.

Measurements

Characteristics of the Sample

The following background characteristics were assessed: age, sex, marital status, duration of current pain period, and localization of pain (mainly back pain, neck pain including cervicobrachialgia, widespread pain including fibromyalgia, pain in an extremity including shoulder pain, other).

Pain Intensity and Catastrophizing

The NRS for pain is an 11-point numeric rating scale, with 0 representing "no pain" and 10 "unbearable pain." The patients were asked to assign a number to their average pain in the last week. We decided to ask the patients to report their average pain, as two studies found no differences in the cut-off point schemes of the NRS for average and worst pain (Paul et al., 2005; Zelman et al., 2005) and one study found only a small difference (Fejer et al., 2005). Zelman et al. (2003) also preferred the average pain measure for cut-off point derivation, because in their view average pain better reflects the experiences regarding the interference of pain with daily activities and is more stable than worst pain.

Catastrophizing was evaluated by the Pain Catastrophizing Scale (PCS; Osman et al., 1997). In this questionnaire the patients were asked to reflect on past painful experiences and indicate the degree to which they experienced each of 13 thoughts or feelings when in pain, on a 5-point scale from 0 (not at all) to 4 (all the time). Three or less missing values per patient were replaced by the mean score of the other values. Pain catastrophizing affects how individuals experience pain: ruminating about their pain (e.g., "I can't stop thinking about how much it hurts"), magnifying their pain (e.g., "I'm afraid that something serious might happen"), or feeling helpless to manage their pain (e.g., "There is nothing I can do to reduce the intensity of my pain"). A higher score means greater dominance of the subscale. The total score on the PCS was used in the analyses.

Functioning

Interference with functioning was assessed with the Pain Disability Index, Dutch Version (PDI-DV; Soer et al., 2013). The PDI is a 7-item questionnaire to investigate the magnitude of self-reported disability in different situations such as work, leisure time, self-care, and social activities. Each item is scored on an 11-item numeric rating scale in which 0 means no disability and 10 maximum disability. Three or less missing values per patient were replaced by the mean score of the other values. A higher score means greater disability and therefore greater interference with functioning.

Procedure

All data were collected prior to the start or in the first 2 weeks of the rehabilitation program.

Statistical Analysis

Descriptive statistics were used to analyze the characteristics of the study sample. Marital status was dichotomized into living alone vs. being married or living with a partner.

Cut-Off Points on the NRS in Relation to Interference of Pain with Functioning

Each patient's pain intensity rating on the NRS was classified into three categories, viz. mild, moderate, and severe interference. We analyzed all 28 possible classification schemes, ranging from 2,3 to 8,9. The cut-off points in these classification schemes were named after the upper values for the mild and moderate categories, in accordance with Serlin et al. (1995). For example, a 3,7 CP scheme means that the first category ranges from 1 to 3, the second from 4 to 7 and the third from 8 to 10. The first number, i.e., 3, is thus the upper value of the mild category and the second number, i.e., 7, the upper value of the moderate category. Other examples of schemes are: the 2,5 CP scheme with 1–2 classified as mild, 3–5 as moderate, and 6–10 as severe; the 3,5 CP scheme with 1–3 classified as mild, 4–5 as moderate, and 6–10 as severe; the 5,6 CP scheme with 1–5 classified as mild, 6 as moderate, and 7–10 as severe; and the 5,8 CP scheme with 1–5 classified as mild, 6–8 as moderate, and 9–10 as severe.

In order to determine which CP scheme best distinguished between mild, moderate and severe pain, we used the method introduced by Serlin et al. (1995). We conducted one-way ANOVAs (using the Generalized Linear Model in SPSS, version 22) for each of the 28 classification schemes, using NRS scores recoded as 1, 2, or 3 (depending on the CP scheme) as the independent variable and PDI-DV scores as the dependent variables. A significant F-value of the CP scheme indicated that there were significant differences between the three pain severity categories in terms of pain-related interference. In accordance with Serlin et al. (1995), we interpreted the highest F-value as indicating the classification scheme that maximized

the differences between the groups and was therefore the most useful for distinguishing between mild, moderate, and severe pain-related interference.

The variability of the optimal CP scheme was quantified using a bootstrap resampling procedure (STATA, version 13.1). In this procedure the distribution is estimated using the information based on a number of resamples from the total sample. One thousand (1000) repetitions of samples of the patients were used to yield sufficiently stable estimates for the variability of the optimal cut-off points. The optimal CP scheme for each of the 1000 randomly chosen samples was determined, using the above-mentioned method introduced by Serlin et al. (1995).

Association of Catastrophizing and Patient's Sex with the Cut-Off Points for Mild, Moderate, and Severe Pain in Terms of Pain-Related Interference with Functioning

The associations between the cut-off point schemes and the patients' catastrophizing tendency and sex were determined by once again conducting ANOVAs (using the Generalized Linear Model in SPSS, version 22) for each of the 28 CP schemes. In the two series of additional analyses (i.e., with PCS total score and sex), the NRS (recoded as 1–3) was again used as the independent variable and the PDI-DV score as the dependent variable, while the total score on the PSC and the patient's sex were respectively included as co-variates, as was the interaction between CP scheme and PCS score and sex, respectively. In view of the results of the analyses with the PCS score, we decided to conduct separate analyses, firstly for the patients with a PCS score equal to or lower than the median of the PCS scores and the patients with a PCS score higher than the median of the PCS scores (dividing the population into two groups by the median split method), and secondly for patients in the lower and higher quartiles and the middle group of scores (dividing the population into three groups by the quartile split method). In total, therefore, 7 times 28 (196) ANOVAs were conducted. Again, the *F*-values of the CP schemes were used to determine which scheme fitted best. In these two (median split method) and three (quartile split method) patient subgroups we also conducted the bootstrap resampling procedure described above.

RESULTS

A total of 2854 patients enrolled in the study. Patient characteristics are presented in **Table 1**. The results of the ANOVAs for the total population are presented in **Table 2**, which lists only the mid-range of CP schemes. The *F*-values of the CP schemes not presented here were lower than the *F*-value with ranking 6 as indicated in **Table 2**. The 5,7 CP scheme had the highest *F*-value, indicating that this scheme provided the best fit for distinguishing pain into three categories, i.e., mild, moderate, or severe pain, in terms of interference with functioning. This means that an NRS score in the 1–5 range corresponds to mild interference with functioning, while scores of 6 and 7 represent moderate interference and a score in the 8–10 range corresponds to severe interference with functioning. The mean PDI scores of the patients with NRS scores in the range of 1–5, 6–7, and 8–10 were 30.3 (*SD* 11.8), 39.7 (*SD* 10.6), and 45.4 (11.5), respectively.

Bootstrapping analysis identified the optimal CP scheme (5,7) in 90.2% of the bootstrapping samples. The 3,6 scheme was identified as the optimal CP scheme in 3.4% of the samples and the 4,6 scheme in 3.3%.

The patients' sex did not influence the optimal CP scheme: in the analyses in which sex and the interaction variable sex*CP scheme were entered as co-variates, neither of these covariates contributed significantly to the model. In the analyses in which the PCS score and the interaction variable PCS score*CP scheme were entered as co-variates in catastrophizing, the PCS score contributed significantly to the model in all analyses, while the interaction variable PCS score*CP scheme contributed sometimes (i.e., in 2 of the 28 analyses). The latter finding was explained as chance variation because only 2 of the analyses found a significant contribution. To explore the finding of the significant contribution of the PCS scores to the models, we conducted more analyses, as described above. First we split the total group into patients with low and with high catastrophizing tendency, and since the median of the PCS score was 29, we performed the analyses separately for patients with a PCS score equal or lower than 29 and for those with a PCS score higher than 29. For the patients with low catastrophizing tendency, i.e., a PCS score $\leq$ 29, the optimal CP scheme proved to be 3,6 and for the patients with high catastrophizing tendency, i.e., a PCS score $>$ 29, the optimal CP scheme was 5,7 (see **Table 2**). In the subgroup with low catastrophizing tendency, bootstrapping analysis identified the optimal CP scheme as 3,6 in 29% of the bootstrapping samples, while the 5,7 scheme was identified as the optimal CP scheme in 23% of the samples and the 4,6 scheme in 21%. In the subgroup with high catastrophizing tendency, bootstrapping analysis identified the optimal CP scheme as 5,7 in 87% of the bootstrapping samples, while the 4,7 scheme was identified as the optimal CP scheme in 11% of the samples and the 4,6 scheme in 10%.

Secondly, we split the total group into patients with low, moderate, and high catastrophizing tendencies, and since the lower quartile of the PCS score was below 21 and the higher quartile was above 37, we performed the analyses separately for patients with a PCS score equal to or lower than 21, for PCS scores between 21 and 37, and for those with a PCS score higher than 37. For the patients with low catastrophizing tendency, i.e., a PCS score $\leq$ 21, the optimal CP scheme proved to be 3,6. For the patients with moderate catastrophizing tendency, i.e., $>$ 21 and $\leq$ 37, and for those with high catastrophizing tendency, i.e., a PCS score $>$ 37, the optimal CP scheme was 5,7 in both cases. In the subgroup with low catastrophizing tendency, bootstrap analysis identified the optimal CP scheme as 3,6 in 42% of the bootstrapping samples, while the 4,6 scheme was identified as the optimal CP scheme in 19% of the samples and the 5,7 scheme in 18%. In the subgroup with moderate catastrophizing tendency, bootstrapping analysis identified the optimal CP scheme as 5,7 in 87% of the bootstrapping samples, while the 4,6 scheme was identified as the optimal CP scheme in 3% of the samples and the 4,7 scheme also in 3%. In the subgroup with high catastrophizing tendency, bootstrapping analysis identified the

TABLE 1 | Characteristics of patients with chronic musculoskeletal pain, Pain Disability Index (PDI) scores, numeric rating scale (NRS) for pain scores and Pain Catastrophizing Scale (PCS) scores, for total sample (*n* = 2854) and for each rehabilitation center (*n* total = a:435, b:539, c:840, d:683, e: 357).

	All patients		Rehab center a		Rehab center b		Rehab center c		Rehab center d		Rehab center e	
	n		*n*		*n*		*n*		*n*		*n*	
CHARACTERISTICS												
Age (years, mean (*SD*))	2794	43 (12.5)	435	44 (11.5)	539	42 (12.2)	840	43 (12.8)	679	43 (13.1)	301	43 (12.2)
Sex (% male)	2789	28	431	30	539	24	840	31	678	28	301	29
Marital status (% single)	2746	30	434	29	535	35	817	29	674	30	286	30
Work (%)	2657		319		531		835		673		299	
• Employed or self-employed		51		47		62		50		50		43
• Student		4		2		6		5		4		4
• Without work, or homemaker		29		28		24		28		31		40
• Retired		4		4		2		4		5		4
• Other/mixed		12		19		7		14		10		10
Location of pain (%)	2854		435		539		840		683		357	
• Widespread pain		18		10		36		26		7		
• Neck pain		8		1		21		13		2		
• Back pain		18		4		24		35		10		
• Pain in extremity		7		0		9		18		2		
• Others		4		1		4		7		4		
• Unknown		45		84		6		1		75		100
Duration of complaints (%)	2503		154		533		836		679		301	
• 3–6 months		5		1		8		4		5		3
• 6–12 months		11		9		12		12		12		10
• 1–2 years		20		20		18		24		18		19
• 2–5 years		25		19		25		23		27		27
• >5 years		39		52		37		38		38		42
FUNCTIONING												
PDI (mean, *SD*)	2854	39 (12.6)	435	37 (12.7)	539	41 (11.8)	840	37 (12.7)	683	36 (13.2)	357	40 (12.4)
PAIN												
NRS (median, quartiles)	2854	7 (5–8)	435	6 (5–7)	539	7 (6–8)	840	6 (5–7)	683	6 (5–7)	357	7 (6–8)
CATASTROPHIZING												
PCS	2846		435		535		840		679		357	
• Total score												
Median, quartiles		29 (21–37)		22 (13–30)		21 (14–30)		31 (25–38)		33 (25–41)		35 (27–43)
Mean, *SD*		30 (11.9)		22 (10.8)		22 (10.9)		32 (9.6)		34 (10.6)		36 (11.2)

optimal CP scheme as 5,7 in 35% of the bootstrapping samples, while the 2,6 scheme was identified as the optimal CP scheme in 22% of the samples and the 2,5 scheme in 12%.

DISCUSSION

The aim of the current study was to find the optimal cut-off points for mild, moderate, and severe pain in terms of pain-related interference with functioning in patients with chronic musculoskeletal pain, as well as to measure the variability of the optimal cut-off points and determine the association between these cut-off points and patients' catastrophizing tendency and sex. The NRS score cut-off points (CPs) of 5 and 7 (i.e., a 5,7 CP scheme) were found to provide the best model fit, indicating that an NRS score $\leq$5 corresponds to mild interference of pain with functioning, 6 and 7 to moderate interference and 8–10 to severe interference. The variability of the optimal CP scheme was low, as bootstrapping found the 5,7 CP scheme to be optimal in $\sim$90% of the samples. This makes it unlikely that our findings were due to chance fluctuations.

No clear association was found between the cut-off points and patients' sex. In clinical practice, therefore, interpreting the NRS as mild, moderate or severe pain in terms of interference with functioning is independent of the patient's sex. By contrast, the level of catastrophizing influenced the optimal CP scheme: the optimal scheme for patients with low catastrophizing tendency was 3,6, indicating that an NRS score $\leq$3 corresponds to mild interference of pain with functioning, 4–6 to moderate interference, and 7–10 to severe interference, whereas the optimal scheme for patients with high catastrophizing tendency was the same as for the total patient sample, i.e., 5,7, indicating that an NRS score $\leq$5 corresponds to mild interference of pain with

TABLE 2 | Comparison of different cut-off point (CP) schemes for classifying Numeric Rating Scale (NRS) scores as mild, moderate or severe pain in terms of interference with functioning: *F*-value in ANOVA using the CP scheme as independent variable and the Pain Disability Index (PDI) scores as dependent variables, for all patients and for the subgroups with low and high catastrophizing tendency (i.e., Pain Catastrophizing Scale (PCS) scores ≤ or > the median of the scores, 29).

	CP 3,6	CP 3,7	CP 4,5	CP 4,6	CP 4,7	CP 4,8	CP 5,6	CP 5,7	CP 5,8	CP 5,9	CP 6,7
ALL PATIENTS (*N* = 2854)											
CP scheme–PDI	332.63	306.15	317.17	337.60	334.67	253.48	337.63	369.65	324.08	306.96	291.35
Ranking	5			3	4		2	1	6		
PATIENTS WITH PCS TOTAL SCORE ≤ 29 (*N* = 1461)											
CP scheme–PDI	173.14	140.30	163.10	172.20	152.79	122.50	170.00	172.34	157.38	154.46	136.35
Ranking	1		5	3			4	2	6		
PATIENTS WITH PCS TOTAL SCORE > 29 (*N* = 1385)											
CP scheme–PDI	124,57	129.58	121.62	130.02	143.46	101.41	132.35	156.76	130.55	121.63	123.61
Ranking		6		5	2		3	1	4		

Rankings are given below the F-values, from the highest (1) to the lowest (6) rank.
CP: cut-off points, figures refer to highest scores in the first and second categories, for example CP 4,7 means a CP scheme where the first category includes the NRS scores 1–4, the second category NRS 5–7 and the third category NRS 8–10.

functioning, 6 and 7 to moderate interference and 8–10 to severe interference. In terms of the cut-off points between mild and moderate, this finding implies the following: among patients with low catastrophizing tendency, the interpretation of an NRS score of 4 or 5 is that the patients with these scores experience moderate interference of their pain with functioning, while among patients with high catastrophizing tendency, the interpretation of the NRS score 4 or 5 is that the patients with these scores experience mild interference of their pain with functioning.

Moderate interference with functioning would theoretically imply a higher PDI score than mild interference. However, as can be seen in **Figure 1**, the PDI scores of the patients with low catastrophizing tendency were lower for each NRS score than those of the patients with high catastrophizing tendency, thus including the group of patients with NRS scores 4 and 5. This contradicts the cut-off point schemes and their interpretation. Two possible explanations may be given. Firstly, the optimal CP scheme for patients with a low catastrophizing tendency may actually also be 5,7 and our finding of the 3,6 scheme was a matter of chance variability. In the subgroup with lower catastrophizing tendency (both the subgroup with a PCS score lower than the median and the subgroup with PCS scores in the lower quartile), the variability was much higher than in the subgroup with higher catastrophizing tendency. The probability that the correct optimal CP scheme was not found is therefore rather high (type 1 error). Secondly, the statistical method introduced by Serlin et al. (1995), which uses the highest *F*-value to indicate the classification scheme that maximizes the differences between the groups and is therefore the most useful for distinguishing between mild, moderate, and severe pain-related interference, may not be the best method for finding the optimal CP scheme.

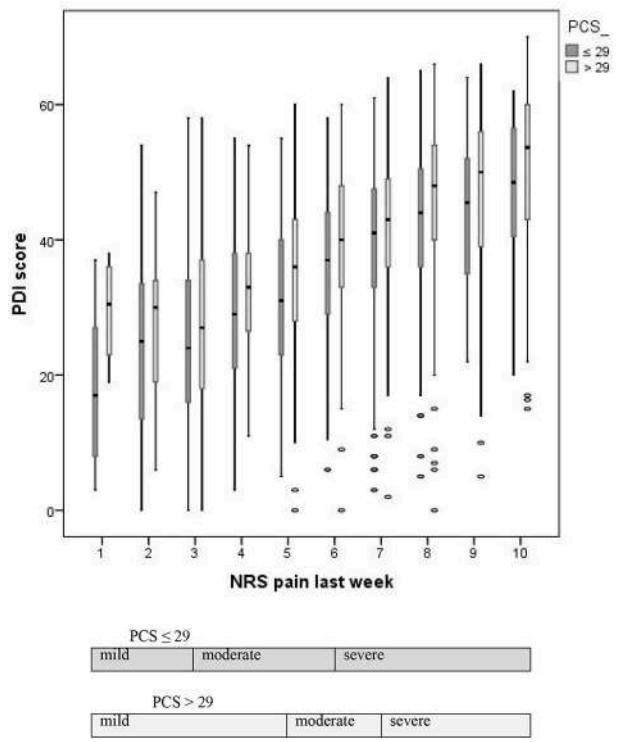

FIGURE 1 | Boxplots of the Pain Disability Index (PDI) scores by Numeric Rating Scale (NRS) score for average pain during the last week for the patients with low and high catastrophizing tendency (i.e., lower or higher than the median of the total scorer on the Pain Catastrophizing Scale (PCS), viz. 29).

Optimal cut-off points of 5 and 7 were only mentioned in the literature by Zelman et al. (2003), for patients with osteoarthritis. That this particular CP scheme was found in only one other study may be due to the fact that it was not assessed by most other authors (see **Table 3**). Our previous study (Boonstra et al., 2014) in a comparable population (not including patients of the present study), but with a smaller sample, found 3 and 6 to be the optimal cut-off points between mild, moderate, and severe interference with functioning, whereas the present study found this 3,6 scheme to be only the fifth best CP scheme. Our previous study used domains of the SF-36 (Aaronson et al.,

TABLE 3 | Published studies about optimal cut-off point schemes for mild, moderate, and severe pain in terms of interference with functioning.

Study, authors	Type of pain/diagnosis	Pain measurement	*n*	Optimal cut-off points found in the study		Range of values studied by the authors for the lower cut-off point (between mild and moderate), and the higher cut-off point (between moderate and severe)
				Lower	Higher	
Serlin et al., 1995	Cancer pain	NRS, worst pain	470	4	6	Lower cut-off point: 3–4 Higher cut-off point: 6–7
Jensen et al., 1999	Leg amputation patients:	NRS, average pain				
	Phantom pain		74	4	7	Lower cut-off point: 3–4
	Back pain		29	4	6	Higher cut-off point: 6–7
	General pain		102	3	6	
Zelman et al., 2003	Low back pain	NRS, average pain	96	5	8	Lower cut-off point: 4–6
	Osteoarthritis		98	5	7	Higher cut-off point: 6–8
Turner et al., 2004	CTS	NRS, average pain		No superior		Lower cut-off point: 3–5
	Low back injuries			scheme	6	Higher cut-off point: 6–7
				4		
Zelman et al., 2005	Diabetic peripheral neuropathy	NRS, worst and average pain	255	4	7	Lower cut-off point: 4–6 Higher cut-off point: 6–8
Paul et al., 2005	Cancer pain	NRS, average pain	160	4	7	Lower cut-off point: 3–5 Higher cut-off point: 5–7
Fejer et al., 2005	Neck pain	NRS, average, worst, and characteristic pain	1385	4	7	14 categories between 3 and 8
Hanley et al., 2006	Spinal cord injury	NRS, (a) overall pain or (b) current pain at worst location	a: 307 b: 174	a and b: 3	a: 7 b: 6	Lower cut-off point: 3–4 Higher cut-off point: 6–7
Li et al., 2007	Cancer pain, patients with bone metastases	NRS, (a) worst, (b) average, and (c) current	199	a and b: 4, c: 2	a, b, and c: 6	Lower cut-off point: 2–8 Higher cut-off point: 3–9
Kapstad et al., 2008	Osteoarthritis of the hip	NRS, average pain	224	4	6	Lower cut-off point: 3–5
	Osteoarthritis of the knee		94	4	7	Higher cut-off point: 5–7
Kalyadina et al., 2008	Cancer pain, hematological malignancies or solid tumors	NRS, worst pain	221	4	6	Lower cut-off point: 3–4 Higher cut-off point: 6–7
Ferreira et al., 2011	Cancer pain	NRS, worst pain	143	4	7	Lower cut-off point: 3–5 Higher cut-off point: 5–7
Hoffman et al., 2010	Diabetic peripheral neuropathy	NRS, average pain	401	3	6	Not mentioned
Hirschfeld and Zernikow, 2013	Children and adolescents with chronic pain	NRS, maximum pain				Lower cut-off point: 2–7 Higher cut-off point: 3–8
	Whole sample		2249	4	8	
	Constant pain		650	5	8	
	Chronic headache		430	4	8	
	Musculoskeletal pain		295	2	8	
Boonstra et al., 2014	Musculoskeletal pain	VAS, average pain	456	3	6	Lower cut-off point: 3–5 Higher cut-off point: 5–7
Brailo and Zakrzewska, 2015	Nondental orofacial pain	NRS, average pain	245	4	7	Lower cut-off point: 3–5 Higher cut-off point: 5–9
Present study	Musculoskeletal pain	NRS, average pain	2854	5	7	Lower cut-off point: 2–8 Higher cut-off point: 3–9

Cut-off points (CP): figures refer to highest scores in the first and second categories, for example CP lower 4, higher 7 means: first category includes the NRS scores 1–4, second category NRS 5–7, third category NRS 8–10.
NRS: numeric rating scale; VAS: visual analog scale.

1998) to measure interference with functioning, and the Visual Analogue Scale (VAS) for pain, instead of the PDI and NRS, respectively. These different measures may be the reason why we found a different CP scheme in the present study. Other reasons may be chance variability and a possible difference in the distribution of the PCS scores, as the CP scheme is the same as that found in the subgroup of patients with low catastrophizing tendency.

The association between catastrophizing and cut-off points has not been studied before, so no comparison with other studies is possible. As far as we are aware, only Fejer et al. (2005) studied the influence of patients' sex on the cut-off points for interference with functioning, and their analysis of CP schemes for average pain found a small difference between the sexes, viz. a lower cut-off point between mild and moderate pain interference for women (4) than for men (6). Their other analyses, with the worst and what they called characteristic pain as independent variables, found no or other differences between women and men, and they finally concluded that the differences were small.

The main strength of our study was the large study sample, the largest sample used until now in studies of this topic. It was also the first study taking patient's catastrophizing into account and the second to examine the influence of sex on the CP schemes.

LIMITATIONS

One weakness of our study is the way the patients were included, i.e., using data from a nationwide survey, which meant that response rate and hence selection bias were unknown. In some rehabilitation centers, the localization of pain complaints was not recorded in the survey questionnaire for most patients (see **Table 1**). Moreover, none of the rehabilitation centers comprehensively recorded the diagnoses in the survey.

Secondly, our study used the PDI to measure interference with functioning. It is possible that other instruments, such as the BPI, would have given different results. Finally, we explored the effect of catastrophizing by splitting the population using the median split and quartile split methods. Although these are common methods to split a population, they may have influenced the results.

Conclusion

In conclusion, we found that NRS scores $\leq$5 correspond to mild pain-related interference with functioning, scores of 6 and 7 to moderate interference and scores $\geq$8 to severe interference. This interpretation of the NRS in terms of mild, moderate and severe interference with functioning is independent of the patient's sex, but seems to be influenced by their catastrophizing tendency. However, the difference in CP schemes we found for patients with lower and higher catastrophizing tendencies contradicts what is theoretically plausible. The reason why we did not find the same optimal CP scheme in the subgroups of patients with lower and higher catastrophizing tendencies may be chance variability.

AUTHOR CONTRIBUTIONS

AB, contributed to the design of the work; and the acquisition, analysis, and interpretation of data; drafted the work, approves final version to be published; agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. RS contributed to design of the work; analysis, and interpretation of data for the work; revised the work critically for important intellectual content; approved final version to be published; agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. HS, AK, RO, JS, KS, contributed to design of the work; and interpretation of data for the work; revised the work critically for important intellectual content; approved final version to be published; and agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Changes in Sleep Problems and Psychological Flexibility following Interdisciplinary Acceptance and Commitment Therapy for Chronic Pain: An Observational Cohort Study

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Aims: Cognitive and behavioral treatments (CBT) for sleep problems and chronic pain have shown good results, although these results could improve. More recent developments based on the psychological flexibility model, the model underlying Acceptance and Commitment Therapy (ACT) may offer a useful addition to traditional CBT. The aim of this study was to examine whether an ACT-based treatment for chronic pain is associated with improved sleep. Secondly, we examined the associations between changes on measures of psychological flexibility and sleep-related outcomes.

Methods: The study used an observational cohort methodology. Participants were 252 patients (73.8% female) attending a 4-week, interdisciplinary, pain management program in London, United Kingdom. Participants completed standard self-report measures of pain and functioning, sleep outcomes, and processes of psychological flexibility. Pre- to post-treatment, and pre-treatment to follow-up measures were examined for statistically significant differences using paired samples *t*-tests. Secondarily, hierarchical multiple regression analyses were conducted to examine change in process measures in relation to change in treatment outcome.

Results: Participants showed statistically significant improvements (all $p < 0.001$) at post-treatment on measures of insomnia severity ($d = 0.45$), sleep interference ($d = 0.61$), and sleep efficiency ($d = 0.32$). Significant improvements in insomnia severity and sleep interference were also observed at 9-month follow up. Small to medium effect sizes were observed across the sleep outcomes. Statistically significant changes were also observed on measures of psychological flexibility, and these improvements were significantly associated with improvements on sleep-related outcomes, independently contributing up to 19% of unique variance.

Conclusion: This study supports the potential usefulness of ACT-based treatments for chronic pain for addressing co-occurring sleep difficulties. Further research is needed to determine how to improve the impact of this treatment for co-morbid pain and sleep difficulties, possibly using a randomized-controlled trial design.

Keywords: chronic pain, insomnia, acceptance and commitment therapy

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INTRODUCTION

Sleep is clearly an important factor in the experience of chronic pain. When people with chronic pain are asked to identify the most important areas of their life impacted by pain, sleep is rated among their top five (Turk et al., 2008). The prevalence of insomnia in people with chronic pain is at least twice as high as in those without chronic pain (Silverstein et al., 2009). In people seeking treatment for chronic pain, 53% in secondary care (Tang et al., 2007) and 79% in tertiary care (McCracken et al., 2011) screen positive for significant insomnia. Pain appears to contribute to sleep disorders (Fishbain et al., 2010) and poor sleep appears to increase pain and emotional distress (Haack and Mullington, 2005; Bonvanie et al., 2016). There is likely a bi-directional relationship between chronic pain and insomnia (Koffel et al., 2016). Given that both chronic pain and sleep difficulties are independently linked to reduced quality of life, a greater focus on addressing insomnia in the context of chronic pain is needed (Currie et al., 2002; Smith and Haythornthwaite, 2004; Tang et al., 2007; Fishbain et al., 2010; McCracken et al., 2011).

Cognitive and behavioral treatments (CBT) for insomnia appear to produce significant and lasting improvements in sleep (e.g., Morin et al., 2006). Thus, CBT presents a natural opportunity for addressing insomnia in the context of chronic pain. An earlier review of 13 longitudinal studies of CBT related to insomnia and chronic pain, suggested that CBT may offer benefits for reducing pain and improving sleep (Smith and Haythornthwaite, 2004). An early study of CBT for insomnia in people with chronic pain showed 57% of participants achieved a reliable improvement, although only 18% fully recovered from sleep problems (Currie et al., 2002). In another pilot study, CBT designed to address both pain and insomnia in people with chronic pain appeared feasible and possibly superior to CBT for either pain or insomnia alone, but only in terms of sleep outcomes (Pigeon et al., 2012). A much larger trial of combined CBT for pain and insomnia ($N = 367$ older adults with osteoarthritis) similarly showed favorable outcomes for insomnia severity but not for pain (Vitiello et al., 2013). In a more recent pilot trial of a "cognitive behavioral pain management program" compared to a waiting list condition the former produced better results for anxiety, depression, and kinesiophobia; however, on most of the sleep measures it did not produce a better result (Blake et al., 2015). In analyses of long terms effects of combined CBT for pain and insomnia there were no differences between combined CBT, CBT for pain alone, or an education only control condition at 18-month follow-up in older adults with osteoarthritis (McCurry et al., 2014). Only in an *ad hoc* analysis of selected participants with severe pain and insomnia did an effect of the combined treatment emerge, and only for pain severity. Hence, there appears to be a lack of reliable effects in trials of CBT for chronic pain or insomnia, or both, when considering both measures of insomnia and other pain-related outcomes.

A newer generation of CBT may improve the ways we treat the collateral problems of chronic pain and insomnia. These treatments include processes of mindfulness and acceptance (Ong et al., 2008, 2012) or a related broader process, psychological flexibility (McCracken et al., 2011; Hayes et al., 2012). Psychological flexibility includes a set of behavioral capacities, including acceptance, present moment awareness, and goal-directed or values-based activation skills. The current treatment approach most specifically focused on increasing psychological flexibility is Acceptance and Commitment Therapy (ACT; Hayes et al., 2012). ACT is a form of CBT that includes experiential, exposure-based, awareness-focused, and activation and motivation focused methods directed toward building behavior that is "open, aware, and active," the essential qualities of psychological flexibility (Hayes et al., 2011).

Results from previous cross-sectional studies show that acceptance, mindfulness, and values-based action correlate significantly with measures of insomnia severity, and daytime rest (McCracken et al., 2011; Bothelius et al., 2015). The benefits for sleep from acceptance, mindfulness, and values-based action processes may derive from the ways they coordinate less struggling with feelings, less entanglement in arousing and distressing thoughts, and less daytime rest and disengagement, thus facilitating improved patterns of nighttime sleep and daytime activity (McCracken et al., 2011). While there has been published treatment development work focusing on adding mindfulness methods to CBT for insomnia (Ong et al., 2008), as far as we are aware there is not yet a published prospective or treatment outcome study of psychological flexibility and insomnia or sleep outcomes in people with chronic pain. Such a study would be a next logical step for exploring the potential role of this set of "newer generation" processes in this area.

The primary purpose of the current study was to investigate changes in insomnia and sleep-related difficulties following interdisciplinary treatment for chronic pain. A secondary purpose was to examine associations between changes in processes of psychological flexibility and changes in sleep outcomes following treatment. A relatively large cohort of participants in a service for complex chronic pain problems received treatment based on ACT. Patients received two formal sessions aimed at addressing sleep problems—the specific treatment content aimed at improving sleep was therefore minimal. Standard pain treatment outcomes as well as insomnia severity, sleep interference, estimated sleep efficiency, and sleep medication use were assessed before and after treatment and at a 9 month follow-up. At the same assessment intervals, facets of psychological flexibility, including pain acceptance, cognitive fusion, decentering, and committed action, were also assessed. It was predicted that both standard pain and functioning outcomes and sleep-related outcomes would improve significantly. In the secondary analyses, it was predicted that psychological flexibility processes would improve significantly, and that changes in psychological flexibility would account for significant variance in improvements in sleep outcomes.

METHODS

Participants and Procedures

Participants were recruited from 299 consecutive patients attending a 4-week, interdisciplinary, pain management program between August 2014 and September 2015 in London, United Kingdom. Patients were screened and selected for treatment by

a physiotherapist and a psychologist using the following criteria: pain lasting more than 6 months that significantly impacted on day to day living. Patients were excluded if they had any poorly controlled psychiatric condition or neurocognitive impairment that might interfere with treatment or if they were unwilling to attend a group-based treatment program. A semi-structured interview was carried out by a psychologist and a physiotherapist to assess pain-related distress and disability. The physiotherapist also conducted a physical examination or performance tests as needed. These methods are the routine assessment and selection process within the service. Selection for treatment was at the discretion of the assessing clinicians on a case-by-case basis, rather than on the basis of scores on standardized measures of distress and disability.

A total of 299 patients began treatment. Thirteen patients did not consent to have their data used for research purposes and, therefore, were excluded from the analyses. A further 28 people (9.4%) did not complete treatment and were likewise excluded from the current study. Another six people completed treatment, but did not complete post-treatment questionnaires. Therefore, the final sample included in the pre- to post-treatment analyses consisted of 252 participants. Of these 252 people, 153 (61%) returned for their 9 month follow-up assessment and completed questionnaires. Therefore, follow-up data analyses were computed on this subsample of 153 people.

Participants completed a standard baseline assessment on the first day of treatment, during which they reported their sex, age, ethnicity, pain location and duration, living situation, and employment status. The pre-treatment assessment also included measures of pain intensity, pain interference, depression, insomnia severity, sleep efficiency, sleep interference, and measures of processes of psychological flexibility. Participants completed the same measures during the final week of treatment and at a 9 month follow-up assessment. Use of hypnotic and anxiolytic medications, as categorized by the British National Formulary (BNF; Royal Pharmaceutical Society of Great Britain, 2011), was recorded by a nurse on the first day and the final week of treatment. Hypnotic and anxiolytic medications were selected for analysis as these are the drug groups currently recommended for management of insomnia in the UK (NICE, 2015). These data were gathered using prescription records and self-report, and recorded in the database as taking or not taking. The research database and study were granted ethics and National Health Service Research and Development approvals prior to commencing data collection.

Measures

Pain Intensity

Participants rated their pain intensity on average over the last week on a standard scale from 0 (no pain) to 10 (extremely intense pain).

Pain Interference

The Brief Pain Inventory (BPI) is a measure of pain severity and interference (Cleeland and Ryan, 1994). In the current study we used the seven-item interference scale from this measure. The interference scale includes items related to general activity, mood, walking, work, relations with others, sleep and enjoyment of life, each rated with regard to how much pain interferes, from 0 (does not interfere) to 10 (completely interferes). The interference score is calculated as a mean of the seven interference item ratings. For the purpose of this study, the sleep interference item was also used as an individual rating. The BPI is widely used and recommended in consensus guidelines as a measure of pain clinical trials (Dworkin et al., 2005). The BPI demonstrated good internal consistency in the current sample (Cronbach's $\alpha = 0.85$).

Insomnia Severity

The Insomnia Severity Index (ISI; Bastien et al., 2001) is a seven item screening measure of insomnia severity. Participants are asked to consider the last 2 weeks and rate the severity of their difficulties falling asleep, staying asleep, sleep quality and its impact on daily functioning, as well as their concerns on a scale of 0 (not at all) to 4 (extremely). Higher scores indicate more severe sleep problems. Items are summed to produce a total score, with higher scores reflecting greater severity of insomnia. Total scores are categorized as not clinically significant (0–7), sub threshold (8–14), moderate insomnia (15–21), and severe insomnia (22–28; Morin et al., 2011). The ISI has been validated and shows good internal consistency in clinical samples (Cronbach's $\alpha = 0.74$) (Bastien et al., 2001) including in the current sample (Cronbach's $\alpha = 0.87$).

Sleep Efficiency

Participants reported on their total time spent in bed and total sleep time on a "typical night in the past 2 weeks." A sleep efficiency rating was calculated by multiplying the ratio of total sleep time to total time spent in bed by 100 (McCracken et al., 2011).

Depression

The Patient Health Questionnaire (PHQ-9, Kroenke et al., 2001) was used to measure depression. Participants rated how frequently they experienced nine common symptoms of depression in the last 2 weeks using a scale of 0 (not at all) to 3 (nearly every day). Higher total scores indicate greater severity. The measure has been well validated among people with chronic health conditions (Kroenke et al., 2001) and demonstrated good internal consistency in the current sample (Cronbach's $\alpha = 0.83$).

Pain Acceptance

The eight-item Chronic Pain Acceptance Questionnaire (CPAQ-8) was used to measure acceptance of chronic pain. It reflects the engagement in normal daily activities with pain and cessation of ineffective avoidance or control strategies (McCracken et al., 2004; Fish et al., 2010). Each item is rated on a scale of 0 (never true) to 6 (always true) and higher total scores indicate greater acceptance of pain. The CPAQ-8 has been validated and shown to have good reliability in people with chronic pain (Fish et al., 2010). The CPAQ-8 showed acceptable internal consistency in the current sample (Cronbach's $\alpha = 0.71$).

Cognitive Fusion

Cognitive fusion, the failure to experience a distinction between the content of thoughts and direct experience, was measured

using the self-report seven item measure, the Cognitive Fusion Questionnaire (CFQ-7; Gillanders et al., 2014). Cognitive defusion in contrast, is similar to mindfulness processes in which participants see their thoughts as transient events that may or may not reflect reality, with the aim of reducing their impact. Participants are asked to rate how true a list of statements are for them using a scale of 1 (never true) to 7 (always true). When summed, higher total scores indicate greater cognitive fusion. The CFQ-7 has previously been validated among people with chronic pain (McCracken et al., 2013a) and demonstrated excellent internal consistency in the current sample (Cronbach's $\alpha = 0.95$).

Decentering

The 12-item decentering scale from the Experiences Questionnaire (EQ; Fresco et al., 2007; McCracken et al., 2013b) was used here. It reflects the ability to observe one's thoughts and feelings as temporary, objective events in the mind and not necessarily true reflections of oneself or one's circumstances. Each statement is rated on a scale of 1 (never) to 5 (always). Higher total scores suggest greater decentering. The EQ has been validated among people with chronic pain (McCracken et al., 2013b). The decentering scale showed good internal consistency in the current sample (Cronbach's $\alpha = 0.85$).

Committed Action

The Committed Action Questionnaire (CAQ-8; McCracken, 2013; McCracken et al., 2015) was used to measure flexible, goal-oriented behavior. The measure consists of eight items and asks participants to rate how true a list of statements are for them, using a scale of 0 (never true) to 6 (always true). The item pool consists of four positively and four negatively phrased items. Negatively phrased items are reverse scored before the total score is calculated, with higher scores indicating greater committed action. The reliability and validity of the CAQ is supported by previous research in a chronic pain population (McCracken et al., 2015) and this good internal consistency was evident in the current sample (Cronbach's $\alpha = 0.83$).

Treatment Program

The treatment here used principles and methods of ACT within a multidisciplinary rehabilitation context comprised of psychologists, occupational therapists, physiotherapists, nurses, and physicians. Treatment was provided in a group format, of up to 12 participants, for four days a week over four weeks. All professionals had received extensive training in and routinely worked within an ACT model, and attended continuing professional development training to facilitate further improvement in treatment delivery. As part of routine clinical practice, regular team meetings, and clinical development sessions were held to ensure treatment fidelity and promote clinical competency. Participants were expected to attend all sessions, although attendance data are not available. Treatment sessions lasted one hour on average and were divided among all professions, with the largest proportion including psychology, physiotherapy, and occupational therapy. Treatment sessions were designed to develop key processes of psychological flexibility: openness to experiencing pain and unwanted feelings; present moment awareness; and values-guided behavior. Pain reduction and controlling unwanted thoughts and feelings were not an explicit focus of treatment. Instead, the emphasis of treatment was on experiential exercises, use of metaphor, mindfulness practice, cognitive defusion techniques, and values-based methods in order to promote improved daily functioning and general wellbeing. These were used across disciplines in addition to goal-setting and educational approaches.

The sleep component of the treatment was based on a cognitive behavioral approach for treating insomnia and was routinely delivered by an occupational therapist. The therapist had the relevant clinical experience and had a particular interest in this area. Occupational therapists are well placed to deliver interventions that are empowering and facilitate behavioral change. The sleep component was delivered over two, hour-long, group sessions in the second and third week of the treatment program. The two group-based sessions were followed up with individual sessions, if necessary.

The first group-based sleep session focused on exploring beliefs the patients held about their sleep and provided information to assist them to reframe their experience of sleeplessness. Patients were asked to keep a 7-day sleep diary to examine their current pattern of sleep and their perception of quality of sleep (Carney et al., 2012). The second group-based sleep session incorporated practice of ACT-based techniques covered in the treatment program and relating them to struggles with sleep, such as defusion from insomnia-related thoughts and mindfulness skills. Participants were invited to practice the psychological flexibility skills in relation to sleep problems during the evenings both in the residential setting and at home. This was reviewed in the structure of the sleep session during the 4 weeks and also at the 1 and 9 month follow-up session. The completed sleep diary was used to highlight individuals who could benefit from individual sessions focusing on scheduling a new sleep pattern. Patients were invited to attend two individual sessions if the diary highlighted a particularly poor sleep routine or poor sleep efficiency, for example 10 h in bed and 5 h asleep = 50% efficient.

The individual work focused on a sleep compression approach with the aim of establishing an improved sleep pattern and efficiency (Espie, 2012). The completed sleep diary was used to establish an average amount of time spent in bed compared to time spent sleeping. A new sleep pattern was planned with the getting up time remaining the same, getting into bed at a later time and the amount of time in bed reduced to a minimum of 6 h. This usually involved two individual sessions up to 1 h each with progress reviewed at a 1 month follow up. Again, skills covered in the 4 week treatment course were also applied to struggles related to sleep. The number of patients who received 1:1 session was not recorded.

Statistical Analyses

Data analyses were conducted using SPSS version 22. Means and standard deviations were computed for all measures for pre- and post-treatment and follow-up. Across the pre- and post-treatment assessments, the largest percentage of missing data

attributable to a single item within a given questionnaire was 1.2%. At the follow-up assessment, the largest percentage of missing responses attributable to a single item on a questionnaire was 2.6%. Therefore, missing item-level data were considered to be missing completely at random. For questionnaires with 7 or more items (i.e., the BPI, ISI, PHQ-9, CPAQ-8, CFQ-7, EQ, and CAQ-8), person mean substitution was used to impute missing values for participants missing only a single item. Scores were not imputed for participants missing two or more items on these questionnaires, or for individual assessment items (i.e., pain intensity, sleep interference, estimated sleep time, and total time in bed). Following imputation, the range of participants with missing data at pre- or post-treatment on the questionnaire total scores was 0–4%. At follow-up, there was a range of 0–5% missing data across the questionnaire total scores.

Medication use was categorized as the proportion of patients taking hypnotic and anxiolytic medication (yes/no) at pre- and post-treatment. Participants' total scores on the ISI were categorized according to previously established clinical cut-offs for severity at pre-, post-treatment, and follow-up. Sleep efficiency was calculated as participants' estimated sleep time divided by their total reported time in bed, and multiplied by 100. Sleep efficiency was not computed for participants with missing data on either (or both) estimated sleep time or total time in bed. Since a sleep efficiency of greater than 100 percent is not interpretable, participants for whom sleep efficiency scores were >100 were removed from this analysis (number of cases removed was six, four, and one for pre-treatment, post-treatment, and follow-up, respectively). Independent samples *t*-tests and Chi-square tests were computed to examine differences on pre-treatment assessment and demographic variables for treatment and follow-up completers and non-completers.

The clinical significance of changes for the following treatment outcome variables were also examined: pain intensity, pain interference, insomnia severity, sleep interference, sleep efficiency, and depression. For these analyses, raw change scores greater than one half of a standard deviation from baseline score for each respective outcome variable were coded as "clinically improved" (Norman et al., 2003). All participants whose scores did not improve by one half of a standard deviation were coded as "not clinically improved," while those who worsened by greater than half of a standard deviation were coded as "clinically worsened." Frequencies were tabulated for the proportion of individuals with change scores in each of these categories.

A series of paired-samples *t*-tests were computed to examine differences on assessment measures between pre- to post-treatment and pre-treatment to follow-up. Normality was assessed through examination of skewness and kurtosis values (between −2 and +2), and inspection of histograms and normal q-q plots. For the pre- to post-treatment analyses, all of the paired differences were considered to be normally distributed except for sleep efficiency. For the pre- to follow-up analyses, the paired differences were considered to be normally distributed for all variables except sleep efficiency. Cases with raw change scores that were more than three standard deviations from the mean change in either direction were considered as outliers and removed from the analysis. Following this procedure, 2 cases were removed for the pre- to post-treatment, and pre- to follow-up paired comparisons for sleep efficiency. Following removal of these outliers, the paired differences for these variables were considered to be normally distributed. Within-subjects effect sizes (Cohen's d) were calculated as the difference between pre- and post-treatment means, and pre-treatment and follow-up means divided by the pooled standard deviation. Effect sizes were interpreted as small (>0.20), medium (>0.50), or large (>0.80) in accordance with Cohen's guidelines (Cohen, 1992). McNemar tests were used to compare the proportion of participants who were and were not taking hypnotic and anxiolytic medications before and after treatment.

A correlation analysis of changes on psychological flexibility processes and changes in treatment outcomes was calculated using residualized change scores. Residualized change scores were used rather than raw change scores as they account for the influence of baseline scores on subsequent assessment values, whereas raw change scores do not. Residualized change scores were computed using the baseline score of a variable to predict the post-treatment or follow-up value of the variable in a regression analysis; the residualized change score was computed as the difference between the predicted and actual post-treatment or follow-up score with the baseline covaried out. Pearson correlations using residualized change scores were then computed to examine the relationship between changes on psychological flexibility processes and treatment outcomes.

Hierarchical multiple regression analyses were computed to examine the shared and unique contributions of change in psychological flexibility variables to change in sleep outcomes from pre- to post-treatment and pre-treatment to follow-up. Changes in pain intensity were controlled for in the first step of each regression analysis. Psychological flexibility processes (i.e., pain acceptance, cognitive fusion, decentering, and committed action) were entered in the second step of the regression equations. To maximize sample size for all analyses, pairwise deletion was used to address missing values on study variables. Therefore, the sample size varies slightly across the *t*-tests, correlations, and regression analyses, depending on the variables being examined. Degrees of freedom and sample sizes are reported throughout the analyses to reflect these minor differences.

RESULTS

Sample Demographics

The majority of the sample was female (73.8%) and white European (74.0%). The sample had an average age of 45.3 years (SD = 12.2), and median pain duration of 102.0 months (IQR = 164.0). The most frequent pain site was generalized pain (41.8%), followed by pain in the lower back (38.2%). The majority of the sample (53.2%) was unemployed at the time of assessment. Further demographic characteristics of the sample are presented in **Table 1**.

People who completed more years of education ($M = 14.0$; $SD = 4.0$) were more likely to complete treatment than those who completed less ($M = 12.5$; $SD = 3.4$), $t_{(281)} = 2.03$, $p < 0.05$. Treatment completers and non-completers did not differ

TABLE 1 | Characteristics of study sample.

Variable	*n* (%) or *M* (SD)
GENDER	
Male	66 (26.2)
Female	186 (73.8)
Age (years)	45.34 (12.24)
Pain duration (months)*	102.00 (164.00)
MAIN PAIN SITE	
Head	5 (2.0)
Neck	6 (2.4)
Upper limbs	9 (3.6)
Chest	2 (0.8)
Abdominal	5 (2.0)
Lower back	96 (38.2)
Lower limbs	21 (8.4)
Pelvic	2 (0.8)
Generalized	105 (41.8)
Missing	1 (0.4)
ETHNIC GROUP	
White	185 (74.0)
Black	28 (11.2)
Asian	17 (6.8)
Latin/Hispanic	6 (2.4)
Mixed	14 (5.6)
Missing	2 (0.8)
LIVING STATUS	
Alone	60 (23.8)
With partner	57 (22.6)
With child/children	34 (13.5)
With partner and child/children	72 (28.6)
With other relatives	22 (8.7)
With friends/flatmates	7 (2.8)
EMPLOYMENT STATUS	
Full-time	37 (14.7)
Part-time	27 (10.7)
Unemployed	134 (53.2)
Volunteer	10 (4.0)
Student	6 (2.4)
Homemaker/Carer	16 (6.3)
Retired	21 (8.3)

**Pain duration reported as median and interquartile range.*

significantly in terms of other demographic variables or any pre-treatment assessment variable. Compared to follow-up non-completers, follow-up completers scored significantly higher on chronic pain acceptance at post-treatment ($M = 24.61$; SD = 7.38 vs. $M = 21.62$; SD = 7.85), $t_{(248)} = 3.04$, $p < 0.01$, and on committed action at post-treatment ($M = 28.72$; SD = 6.84 vs. $M = 26.71$; SD = 7.32), $t_{(250)} = 2.22$, $p < 0.05$. Participants who did and did not complete the follow-up assessment did not differ significantly on any other post-treatment assessment or demographic variables.

At the beginning of treatment, the sample reported spending an average of 9.01 h (SD = 3.31) in bed between going to bed at night and getting up in the morning. The average estimated sleep time of the sample was 5.30 h (SD = 2.27). Based on established clinical cut-offs for interpreting the ISI, ∼81.3% of the sample scored in the clinically significant range (i.e., moderate or severe) in terms of the severity of their insomnia symptoms (Morin et al., 2011).

Treatment Changes on Sleep and Psychological Flexibility Variables

Table 2 summarizes descriptive statistics for scores on pain intensity and the sleep and psychological flexibility measures at pre- and post-treatment and follow-up. Paired-samples *t*-tests indicated that pain intensity, pain interference, depression, insomnia severity, sleep interference, and sleep efficiency showed significant improvements from pre- to post-treatment. Large effect sizes were observed for improvements in pain interference and depression. A medium effect size was observed on pain intensity and sleep interference. Small effect sizes were seen for insomnia severity and sleep efficiency. Each of the psychological flexibility variables likewise showed statistically significant improvements from pre- to post-treatment. The magnitude of changes in cognitive fusion and committed action were near small and small, while the changes for decentering and pain acceptance were medium and large, respectively. At the end of treatment 67.0% of participants met criteria for clinically significant insomnia on the ISI, compared to 81.3% before treatment (**Table 3**).

Pre- and post-treatment hypnotic and anxiolytic medication use was recorded for 249 participants. At the beginning of treatment 22 (8.8%) participants were taking 1 or more hypnotic medication, while 227 (91.2%) of participants were taking none. At post-treatment, 17 (6.9%) were taking hypnotic medication, while 229 (93.1%) were not. A McNemar's test revealed that this difference in proportions was not statistically significant $p = 0.06$. At the beginning of treatment 48 (19.3%) participants were taking 1 or more anxiolytic medication, while 201 participants (80.7%) of participants were not. At post-treatment, 38 (15.4%) were taking anxiolytic medication, while 208 (84.6%) were not. A McNemar's test revealed that this difference in proportions was statistically significant $p = 0.006$.

From pre-treatment to follow-up, significant improvements were seen for all of the variables with the exception of sleep efficiency. Pain acceptance showed a large effect size from pre-treatment to follow-up. Effect sizes were medium for follow-up changes in pain interference, depression, and decentering. The follow-up changes in pain intensity, insomnia severity, sleep interference, cognitive fusion, and committed action were small to near small. At the 9 month follow-up, 72.2% of the sample met criteria for clinically meaningful insomnia.

Table 4 shows the proportion of patients reporting clinically significant improvements on outcome measures from pre- to post-treatment, and pre-treatment to follow-up. Across the outcome measures, 58.8% of patients showed clinically meaningful improvement from pre- to post-treatment on average. The proportion of patients reporting clinically

TABLE 2 | Changes in sleep and psychological flexibility process variables.

	Pre-treatment	Post-treatment	*t (df)*	*d*	Follow-up	*t (df)*	*d*
Pain intensity	7.84 (1.65)	6.62 (1.73)	$t_{(249)} = 10.78^{***}$	0.72	7.33 (1.94)	$t_{(150)} = 3.08^{**}$	0.25
Pain Interference (Average)	7.81 (1.51)	5.85 (2.04)	$t_{(247)} = 15.16^{***}$	1.09	6.60 (2.17)	$t_{(144)} = 6.66^{***}$	0.62
Depression	17.50 (5.53)	11.71 (5.71)	$t_{(243)} = 16.41^{***}$	1.03	13.95 (6.49)	$t_{(145)} = 7.22^{***}$	0.60
Insomnia severity	20.03 (5.82)	17.20 (6.75)	$t_{(249)} = 7.62^{***}$	0.45	17.81 (6.20)	$t_{(145)} = 4.68^{***}$	0.36
Sleep Interference	8.05 (2.21)	6.53 (2.73)	$t_{(251)} = 9.36^{***}$	0.61	7.25 (2.59)	$t_{(152)} = 3.83^{***}$	0.33
Sleep efficiency	60.03(19.84)	66.30 (19.60)	$t_{(228)} = -4.72^{***}$	0.32	60.74(19.87)	$t_{(138)} = -0.47$	0.04
Pain acceptance	17.22 (7.54)	23.44 (7.70)	$t_{(248)} = -12.09^{***}$	0.81	24.55 (8.10)	$t_{(148)} = -10.95^{***}$	0.91
Cognitive fusion	30.41 (11.26)	28.54 (10.54)	$t_{(247)} = 3.23^{***}$	0.17	25.01 (10.64)	$t_{(143)} = 5.62^{***}$	0.43
Decentering	35.39 (7.69)	39.41 (7.48)	$t_{(241)} = -7.60^{***}$	0.53	39.52 (7.90)	$t_{(141)} = -5.48^{***}$	0.52
Committed action	26.30 (8.47)	27.96 (7.08)	$t_{(246)} = -3.42^{***}$	0.21	28.78 (7.37)	$t_{(143)} = -2.02^{*}$	0.17

$^{***}p \leq 0.001$; $^{**}p < 0.01$; $^{*}p < 0.05$.

TABLE 3 | Proportion of participants with clinically meaningful scores on the Insomnia Severity Index at pre- and post-treatment and follow-up.

Insomnia severity category	Pre-treatment *n* (%)	Post-treatment *n* (%)	Follow-up *n* (%)
Not clinically significant	7 (2.8)	24 (9.5)	7 (4.8)
Sub-threshold	40 (15.9)	59 (23.4)	34 (23.1)
Clinically significant: Moderate	86 (34.1)	89 (35.3)	58 (39.5)
Clinically significant: Severe	119 (47.2)	80 (31.7)	48 (32.7)
Missing	0 (0)	0 (0)	6 (3.9)

ISI, Insomnia Severity Index; Not clinically significant, ISI = 0–7; Sub-threshold, ISI = 8–14; Moderate, ISI = 15–21; Severe, ISI = 22–28. Pre- and post-treatment N = 252; Follow-up N = 147.

meaningful improvements over this time period ranged from 42.7% for sleep efficiency to 84.5% for pain interference. At follow-up, an average of 47.3% of patients reported significant improvement compared to pre-treatment. The proportion of patients showing clinically meaningful improvements during this interval ranged from 28.8% for sleep efficiency to 69.0% for pain interference.

Correlations between Changes on Psychological Flexibility Processes and Sleep Outcomes

Pearson correlations between residualized change scores for sleep outcomes and psychological flexibility variables are displayed in **Table 5**. Changes in the sleep outcome variables were all significantly inter-correlated. Improvements in pain intensity, pain interference, and depression were significantly correlated with improvements in insomnia severity and sleep interference. Improvements on all of the psychological flexibility processes were significantly correlated with improvements in insomnia severity and sleep interference. The same pattern of correlations was observed between changes in these variables from pre-treatment to follow-up. Pre- to post-treatment changes in sleep efficiency were significantly correlated with pre- to post-treatment changes in pain intensity, pain interference, depression, cognitive fusion, decentering, and committed action; changes in sleep efficiency at follow-up were significantly correlated with changes in pain interference, depression, and committed action.

Regression Analyses Examining Contributions of Change in Psychological Flexibility Variables to Change in Sleep Outcomes

Hierarchical multiple regression analyses were conducted to examine the shared and unique contributions of changes in psychological flexibility processes to improvements in sleep outcomes for the pre- to post-treatment interval (**Table 6**). Change in insomnia severity was the dependent variable for the first set of analyses. Change in pain was entered in the first step of this analysis, and significantly contributed 11% of the variance to change in insomnia severity. Changes in psychological flexibility processes (i.e., pain acceptance, cognitive fusion, decentering, and committed action) were entered in the second step and together contributed an additional 15% of the variance to change in insomnia severity, above and beyond that accounted for by changes in pain. Examination of the beta weights from the final regression equation indicated that changes in pain intensity, $\beta = 0.22$, $t_{(240)} = 3.72$, $p < 0.001$, pain acceptance, $\beta = -0.18$, $t_{(240)} = 2.65$, $p < 0.01$, and cognitive fusion, $\beta = 0.24$, $t_{(240)} = 3.46$, $p < 0.001$ each contributed significant unique variance to the prediction of change in insomnia severity. In the pre-treatment to follow-up regression analysis (**Table 7**), changes in psychological flexibility processes likewise significantly contributed an additional 13% of the variance to changes in insomnia severity, above and beyond the variance accounted for by changes in pain intensity (10%). For this follow-up analysis, changes in pain intensity and pain acceptance each contributed uniquely to changes in insomnia severity in the final regression equation, $\beta = 0.24$, $t_{(116)} = 2.77$, $p < 0.01$, and $\beta = -0.25$, $t_{(116)} = -2.62$, $p = 0.01$, respectively.

For the second set of analyses, change in sleep interference was the dependent variable. Change in pain was entered in the first step of this analysis, and significantly contributed 15% of the variance to change in sleep interference. Changes in psychological flexibility processes were entered in the second step and together contributed an additional 5% of the variance to

TABLE 4 | Clinically significant change on outcome variables.

	Pre- to post-treatment *n* (%)			Pre-treatment to follow-up *n* (%)		
	Significantly worse	No change	Significantly improved	Significantly worse	No change	Significantly improved
Pain intensity	30 (12.0)	62 (24.8)	158 (63.2)	37 (24.5)	48 (31.8)	66 (43.7)
Pain interference	35 (13.9)	4 (1.6)	213 (84.5)	41 (28.3)	4 (2.8)	100 (69.0)
Depression	15 (6.1)	53 (21.7)	176 (72.1)	21 (14.4)	40 (27.4)	85 (58.2)
Insomnia severity	38 (15.2)	100 (40.0)	112 (44.8)	24 (16.4)	53 (36.3)	69 (47.3)
Sleep interference	16 (6.3)	122 (48.4)	114 (45.2)	17 (11.1)	80 (52.3)	56 (36.6)
Sleep efficiency	45 (19.8)	85 (37.4)	97 (42.7)	33 (23.7)	66 (47.5)	40 (28.8)

TABLE 5 | Correlations between change in sleep and psychological flexibility process variables.

	Pre- to post-treatment change			Pre-treatment to follow-up change		
	Insomnia severity	Sleep interference	Sleep efficiency	Insomnia severity	Sleep interference	Sleep efficiency
Pain intensity	0.34***	0.38***	−0.17*	0.37***	0.58***	−0.13
Pain Interference	0.57**	0.76***	−0.34***	0.45***	0.75***	−0.21*
Depression	0.58***	0.45***	−0.33***	0.57***	0.40***	−0.33***
Pain Acceptance	−0.37***	−0.30***	0.12	−0.34***	−0.51***	0.14
Cognitive Fusion	0.44***	0.26***	−0.20**	0.27**	0.16*	0.03
Decentering	−0.30***	−0.20**	0.20**	−0.25**	−0.25**	0.14
Committed Action	−0.31***	−0.16*	0.15*	−0.35***	−0.26**	0.20*

*Pre- to post-treatment N = 227–252; Pre-treatment to follow-up N = 130–151; ***p ≤ 0.001, **p ≤ 0.01, *p ≤ 0.05.*

change in sleep interference, above and beyond that accounted for by changes in pain. Examination of the beta weights from the final regression equation indicated that changes in pain intensity, $\beta = 0.31$, $t_{(240)} = 5.15$, $p < 0.001$, and pain acceptance, $\beta = -0.17$, $t_{(240)} = -2.50$, $p < 0.05$, each contributed significant unique variance to the prediction of change in sleep interference. For the pre- to follow-up regression analysis, changes in psychological flexibility processes significantly contributed 19% of the variance to changes in sleep interference, beyond the variance accounted for by changes in pain intensity (32%). In the final regression equation for the follow-up analysis, changes in pain intensity, $\beta = 0.48$, $t_{(121)} = 7.24$, $p < 0.001$, and pain acceptance, $\beta = -0.47$, $t_{(121)} = -6.39$, $p < 0.001$, both contributed significant unique variance to changes in sleep interference.

For the third analysis, change in sleep efficiency was the dependent variable. Change in pain intensity significantly contributed to the prediction of change in sleep efficiency; however, change in pain only accounted for 3% of the variance in this outcome. Changes in psychological flexibility variables did not significantly contribute additional variance to the prediction of change in sleep efficiency above and beyond the variance accounted for by change in pain. Given the non-significant change in sleep efficiency for the pre-treatment follow-up period, regression analyses were not computed for sleep efficiency over the follow-up period.

DISCUSSION

There is still relatively little known about the best ways to treat sleeping problems in the context of chronic pain. Producing good outcomes for both sets of problems appears particularly difficult. Here we examined the outcomes and process changes obtained in an intensive, interdisciplinary, pain management course based on ACT for chronic pain in adults. First, a high rate of participants in this treatment reported clinically significant insomnia at pre-treatment, 81.3%. Outcomes on standard pain management outcomes were good, including large effects for pain interference and depression at post-treatment and medium effects at follow-up. Insomnia severity, sleep interference, and sleep-efficiency also improved significantly with a medium effect for sleep interference and small effect for the other two a post treatment. A significant reduction in the proportion of participants taking anxiolytic medication, which are often also used for sleeping problems, was observed at post-treatment. At follow-up, however, only small effects for insomnia severity and sleep interference remained. Furthermore, 42.7–84.5% of participants showed clinically meaningful improvements across outcomes at post treatment, while 6.1–19.8% of participants showed clinically meaningful worsening on post treatment outcomes. At follow-up, 28.8–69.0% of participants showed clinically meaningful improvements across treatment outcomes, while 11.1–28.3% of participants appeared to show clinically meaningful worsening.

A secondary aim of this study was to examine changes in ACT process measures and whether these changes correlated with changes in sleep outcome measures. Pain acceptance, cognitive fusion, decentering, and committed action each improved at post-treatment and follow-up with near small to large effect sizes, including somewhat larger effect sizes at follow-up for pain acceptance and cognitive fusion. Moreover,

TABLE 6 | Regression analyses examining contributions of change in psychological flexibility processes to change in sleep variables from pre- to post-treatment.

	ΔR^2	*F*change *(df)*	*p*	β
DV: INSOMNIA SEVERITY				
Step 1	0.11	30.93 (1, 244)	<0.001	
Pain intensity				0.22***
Step 2	0.15	12.56 (4, 240)	<0.001	
Pain acceptance				−0.18**
Cognitive fusion				0.24***
Decentering				−0.02
Committed action				−0.07
DV: SLEEP INTERFERENCE				
Step 1	0.15	42.04 (1, 244)	<0.001	
Pain intensity				0.31***
Step 2	0.05	3.73 (4, 240)	<0.01	
Pain acceptance				−0.17*
Cognitive fusion				0.09
Decentering				−0.02
Committed action				0.01
DV: SLEEP EFFICIENCY				
Step 1	0.03	6.71 (1, 223)	=0.01	
Pain intensity				−0.13
Step 2	0.03	1.99 (4, 219)	*ns*	
Pain acceptance				−0.01
Cognitive fusion				−0.09
Decentering				0.12
Committed action				0.01

***$p \leq 0.001$, **$p \leq 0.01$, *$p < 0.05$.

TABLE 7 | Regression analyses examining contributions of change in psychological flexibility processes to change in sleep variables from pre-treatment to follow-up.

	ΔR^2	*F*change *(df)*	*p*	β
DV: INSOMNIA SEVERITY				
Step 1	0.10	13.10 (1, 120)	<0.001	
Pain intensity				0.24**
Step 2	0.13	4.90 (4, 116)	=0.001	
Pain acceptance				−0.24**
Cognitive fusion				0.09
Decentering				0.06
Committed action				−0.16
DV: SLEEP INTERFERENCE				
Step 1	0.32	58.43 (1, 125)	<0.001	
Pain intensity				0.48***
Step 2	0.19	11.80 (4, 121)	<0.001	
Pain acceptance				−0.47***
Cognitive fusion				0.01
Decentering				0.05
Committed action				−0.03

***$p \leq 0.001$, **$p \leq 0.01$, *$p < 0.05$.

pre- to post treatment changes in pain acceptance, cognitive fusion, decentering, and committed action correlated in the expected therapeutic direction with improvements in insomnia severity and sleep interference. Only pre- to post-treatment changes in cognitive fusion, decentering, and committed action correlated with improved sleep efficiency and these correlations were quite small. A similar pattern of results as those at post treatment were obtained in the follow-up analyses for correlations between changes in psychological flexibility process variables and improvements in insomnia severity and sleep interference. However, only changes in committed action correlated significantly with sleep efficiency changes, which is perhaps unsurprising given that there was no longer a significant improvement in this variable at follow-up. Taken together, the outcome and process evidence suggest that an ACT-based treatment, even one with minimal sleep treatment content, is associated with improvements in sleep for people with chronic pain, and it appears that improvements in the specific processes targeted within this therapy are related to improvements in treatment outcomes.

The rate for screening positive for possible clinically significant insomnia here is very high and similar to the rate found in previous specialty treatment contexts in the UK where a rate of 79% was found (McCracken et al., 2011). Given the known adverse health impacts of poor sleep (Tang et al., 2007) these rates are startling. While we demonstrate significant effects on sleep outcomes here, the fact that the positive screening rate of insomnia only reduced from 81.3% at pre-treatment to 72.7% at follow-up indicates the need for further treatment developments. This partial recovery rate is similar to the results of Currie et al. (2002). Unlike previous studies of treatments explicitly focused on chronic pain and fatigue (Vitiello et al., 2009; Pigeon et al., 2012) the current treatment appeared to successfully address both pain and sleep-related outcomes, although it may have addressed the pain-related outcomes more successfully.

The improvements in general clinical outcomes and process changes observed here are consistent with those produced in previous studies of ACT for chronic pain (Wicksell et al., 2008; McCracken and Gutiérrez-Martínez, 2011; Wetherell et al., 2011; Trompetter et al., 2015; see Hann and McCracken, 2014 and A-Tjak et al., 2015 for reviews). The support found here for the role of psychological flexibility facets in relation to sleep also is consistent with previous findings (McCracken et al., 2011; Bothelius et al., 2015), particularly the finding that these facets correlate more highly with ratings of sleep quality than directly measured sleep efficiency. In multiple regression analyses of changes in outcomes and process measures, pain acceptance appeared as the strongest unique predictor of sleep outcome change. This may mean that the role of pain acceptance is more important compared to the other process changes when it comes to generating improvements in sleep. Previous studies of ACT for chronic pain also reflect this pattern (Vowles and McCracken, 2008). An alternative explanation is that we are generating smaller effects on the other process measures and this places a ceiling on their apparent role

in the regression analyses. Of all of the current facets of psychological flexibility now available to target, acceptance likely is the most familiar and perhaps easiest to engage in an interdisciplinary treatment context. We suggest that our ability to address the other facets, such as cognitive fusion/defusion and committed action, requires greater focus, refinement, and empirical investigation.

It is increasingly recognized that better interdisciplinary treatments for chronic pain will not come from treatment packages that address a little bit of everything, but rather a greater focus and impact on a few key processes and outcome domains, and perhaps from better matching of patients to specific, customized treatments (Williams et al., 2012; McCracken and Morley, 2014). Although the results of the present study seem promising, the outcomes could be better. We suggest that ways to improve upon the results include the following: (a) selection of people with significant insomnia, (b) a greater focus on processes of change that show a significant role in sleep improvement, and (c) a greater targeting of these processes specifically to sleep-related behavior patterns. The issues of greater focus or targeting could mean increased time, intensity, or dosage. It has been suggested that combining psychological flexibility and conventional sleep improvement methods, such as sleep compression, may represent a particularly potent way to address sleep problems (Lundh, 2011; McCracken et al., 2011). To capitalize on this synergy, a more structured and intensive application of the sleep methods would be needed than was done here. Finally, we do not know the full potential role of cognitive defusion and committed action processes in sleep. Greater therapeutic impact on these may yield a larger impact on sleep, but this remains to be further studied.

Another relevant point is that the analyses here are based on group data. When a more specific process like acceptance of pain appears more important than a more general process like committed action or defusion, for example, this does not mean that this applies to every individual. Instead this arises as a pattern in the group. We assume that the barriers for sleep, or skills and capacities to achieve good sleep, are somewhat different for each individual. Thus, it may be useful for future research to examine subgroups for which more specific processes like pain acceptance play a more important role in sleep outcomes than the more general "open, aware, and engaged" processes of psychological flexibility, and vice versa. Greater tailoring of treatment to the specific and general barriers to sleep on a more individualized basis may enhance the treatment effects seen here. In general, we recommend that more "single-subject" research to understand processes of change (e.g., Villatte et al., 2016) combined with user-involvement in method design may improve on the treatment methods and therefore the results here.

There are limitations in the current study. It is not a controlled trial. The study shows changes over time in sleep outcomes and process measures, but we cannot definitively say that ACT produced these improvements in sleep via increased psychological flexibility. It is possible that other components of the treatment contributed to the changes observed. A randomized controlled trial (RCT) design and formal mediation analyses are required to more definitively test this question. Furthermore, clinician competency, treatment and protocol fidelity were not formally monitored, as this study was conducted in routine clinical care and not as a part of a funded RCT, nor was participant session attendance recorded. Within the subsample of participants we analyzed at follow-up, there was considerable attrition. We also know the follow-up completers differed from non-completers in that they reported greater pain acceptance and committed action at post treatment. Therefore, we cannot rule out some biasing effect on the follow-up data. Further, the sample here is highly selected, appearing as they do in a specialty service in central London. Future research is needed to examine the generalizability of the current results to patients with characteristics that differ from the current sample. Finally, the sleep measures used here are retrospective and indirect, and this allows for the influence of recall bias and other sources of inaccuracy. Certainly in the future sleep diaries and perhaps automatic monitoring could improve the quality of data.

In summary, a convincing pattern of significantly disturbed sleep appears in around 8 out of 10 of adult participants in specialty treatment for chronic pain. An intensive, interdisciplinary, ACT-based treatment course with minimal methods to address disturbed sleep here was associated with decreased insomnia severity and interference with sleep both immediately post-treatment and at a 9-month follow-up. Facets of psychological flexibility also improved during this treatment and changes in these were correlated with improvements in sleep, with pain acceptance appearing to play a relatively larger role. There appears to be an opportunity here to follow-up from these results with both a greater focus on sleep methods and a more intensive focus on psychological flexibility to improve sleep outcomes even further, particularly in RCT designs.

AUTHOR CONTRIBUTIONS

All authors helped to conceive and plan the study and prepared and approved the final manuscript. AD conducted the data collection and analyses, the latter supervised by WS. MH devised and conducted the treatment methods related to sleep. TN conducted preliminary analyses of the data and produced the first draft for parts of the final manuscript. LM supervised the research and treatment, formalized the rationale for the study, and led on the interpretation of findings.

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An Integrative Review of the Influence of Expectancies on Pain

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Expectancies can shape pain experiences. Attention for the influence of expectancies on pain has increased particularly due to research on placebo effects, of which expectancy is believed to be the core mechanism. In the current review, we provide a brief overview of the literature on the influence of expectancies on pain. We first discuss the central role of expectancy in the major psychological learning theories. Based on these theories, different kinds of expectancies can be distinguished. Pain experiences are influenced particularly by response expectancies directly pertaining to the pain experience itself, but can also be affected by self-efficacy expectancies regarding one's ability to cope with pain, and possibly by stimulus expectancies regarding external events. These different kinds of expectancies might interact with each other, and related emotions and cognitions, as reflected by various multifaceted constructs in which expectancies are incorporated. Optimism and pain catastrophizing, in particular, but also hope, trust, worry, and neuroticism have been found to be associated with pain outcomes. We conclude with recommendations for further advancing research on the influence of expectancies on pain and for harnessing expectancy effects in clinical practice.

Keywords: pain, expectancy, self-efficacy, optimism, hope, trust, worry, pain catastrophizing

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INTRODUCTION

Pain is an unpleasant experience, in which not only sensory input but also psychological factors such as cognitions and emotions are at play. One important cognitive factor that can shape pain experiences is expectancies (i.e., cognitions regarding the probability of future experiences, events, and behavior; Mondloch et al., 2001; Rasmussen et al., 2009; Haanstra et al., 2012). The influence of expectancies on pain gained scientific interest especially due to research on placebo effects. A sham treatment such as a sugar pill or saline injection may relieve pain due to the mere expectation that a treatment will be helpful (i.e., placebo effect), or worsen pain when harmful treatment effects are expected (i.e., nocebo effect; Kirsch, 1985, 1997; Benedetti, 2014; Horing et al., 2014). Similarly, expectancies about treatment outcomes can enhance or reduce the analgesic effects of active treatments (e.g., Kam-Hansen et al., 2014; Aslaksen et al., 2015). Besides expectancies about the effects of treatment on pain, people can hold other kinds of expectancies. For example, someone might have high expectations about his/her ability to tolerate pain, and this might actually result in higher pain tolerance (Bandura, 1977; Litt, 1988). Different expectancies are likely to interact with each other, and with related emotions and cognitions. An understanding of the influence of expectancies on the experience of pain is crucial for both clinicians and researchers who treat or study pain, in order to obtain a comprehensive picture of the factors that determine pain and to optimize analgesic interventions via expectancy interventions.

In the current review, we provide a brief overview of the literature on the influence of expectancies on pain. First, we discuss the major psychological learning theories concerning expectancies. Based on these theories, different kinds of expectancies are distinguished, and we evaluate the influence of each of these on pain. Subsequently, we discuss multifaceted constructs (e.g., optimism, trust, and worry) in which expectancies are incorporated, and explore the evidence for their associations with pain. We conclude with recommendations for further research on the influence of expectancies on pain and for harnessing expectancy effects in clinical practice.

EXPECTANCIES IN PSYCHOLOGICAL LEARNING THEORIES

Expectancies are seen as important determinants of behavior, events, and experiences in many psychological theories of learning. Here we describe the most influential learning theories chronologically to gain an understanding of the conceptualization of expectancies.

One of the oldest and most systematically studied learning phenomena in psychology is conditioning. Classical conditioning is generally described as learning that results from pairing an initially neutral stimulus or event with a biologically relevant stimulus or event (Rescorla, 1988). In operant (or instrumental) conditioning, an association is made between a particular behavior and its consequence (e.g., reward or punishment; Bolles, 1972). According to most contemporary learning theorists, what is learned from these contingencies is outcome expectancies (although conditioning can also be automatic, i.e., not mediated cognitively; Pavlov, 1927; Bolles, 1972; Rescorla, 1988; Kirsch et al., 2004; Stewart-Williams and Podd, 2004). These expectancies indicate the perceived likelihood of a stimulus (e.g., receiving food) as the outcome of another stimulus or event (e.g., flashing of a light; in case of classical conditioning), or as the outcome of a specific behavior (e.g., pulling a lever; in case of operant conditioning; Pavlov, 1927; Bolles, 1972; Rescorla, 1988; Kirsch et al., 2004). These outcome expectancies are seen as important determinants of behavior. Since most of the expected outcomes described in conditioning research were external stimuli or events, these expectancies have been more specifically referred to as stimulus expectancies, to distinguish them from expectancies of other kinds of outcomes (specifically response expectancies regarding internal experiences, see below; Kirsch, 1985, 1997). In relation to pain, stimulus expectancies could for example entail expectations of the timing of a painful event, or of receiving a prescription for an analgesic on consulting a doctor.

Social learning theories were developed to address learning in interpersonal contexts and suggested that learning takes place not only via direct experiences (i.e., conditioning), but also via observation of others (i.e., observational learning), and verbal instructions (i.e., instructional learning; Bandura, 1977; Kirsch, 1985). Moreover, these theories postulate that not only outcome expectancies, but also other cognitions influence behavior. In the first major social learning theory, Rotter (1954) stated that the crucial determinant of behavior is the expected outcome of that behavior, in concert with the value a person places on that outcome. This theory had a major impact and has been further developed by many researchers. One of the most influential extensions is Bandura's self-efficacy theory (Bandura, 1977). Bandura theorized that behavior is determined not only by expected outcomes, but also by expectancies regarding the ability to perform the behavior, i.e., self-efficacy expectancies. For example, someone with high self-efficacy expectations of tolerating pain might engage in physical activities despite pain (e.g., lifting heavy bags despite lower-back pain).

The theories described above focus mainly on expectancies of external outcomes and behavior (Rotter, 1954; Bolles, 1972; Bandura, 1977), expectancies of automatic, non-volitional responses – i.e., internal experiences such as emotions, and physical sensations such as pain – were largely overlooked. This was addressed by Kirsch (1985, 1997) in response expectancy theory. The hypothesis underlying response expectancy theory is that the expectation of one's own automatic response to a certain behavior or situation (i.e., response expectancy, a form of outcome expectancy) not only influences behavior, but also directly influences one's actual non-volitional response, and is as such directly self-confirming (Kirsch, 1985, 1997). These response expectancies are thought to be acquired through conditioning, instructional learning, and observational learning (Kirsch, 1985, 1997). An example of response expectancy is a patient's expectation of pain relief upon taking an analgesic.

Based on these learning theories, in line with Kirsch's conceptualization (Kirsch, 1985, 1997), we distinguish different kinds of expectancies: (1) outcome expectancies, which can be further subdivided into (a) stimulus expectancies, i.e., expectancies regarding external stimuli or events and (b) response expectancies, i.e., expectancies regarding internal non-volitional experiences; and (2) self-efficacy expectancies, i.e., expectancies regarding the ability to perform behavior. Several other, largely overlapping, typologies of expectancies have been proposed in the literature (e.g., Thompson and Sunol, 1995; Atlas and Wager, 2012), but since stimulus, response, and self-efficacy expectancies have the strongest theoretical foundation and empirical support, we focus only on these three kinds of expectancies in the current review.

THE INFLUENCE OF DIFFERENT KINDS OF EXPECTANCIES ON PAIN

The different kinds of expectancies may influence pain in unique ways. Response expectancies probably exert the strongest and most direct influence on pain, since they can directly pertain to pain experiences. It is these kinds of expectancies that are generally believed to be the core mechanism of placebo and nocebo effects and that are consequently thought to greatly contribute to the efficacy of active treatments (Kirsch, 1997; Benedetti, 2014; Horing et al., 2014). When placebo or nocebo effects are induced, pain expectations are modified, and these response expectations predict changes in the intensity and

unpleasantness of both experimental and clinical pain (Atlas et al., 2012; Schmid et al., 2013; Kirsch et al., 2014; Colagiuri et al., 2015; Peerdeman et al., 2016). Stimulus expectancies may exert an indirect influence on pain experiences, e.g., by affecting behavior, but could possibly also influence pain directly. Stimulus expectancies have received little scientific attention in the context of pain. There are indications that induced expectations regarding the timing of a painful event can reduce pain unpleasantness but not pain intensity (Price et al., 1980), but further research is needed. Self-efficacy expectancies have received much more scientific interest. They have consistently been found to predict pain coping efforts and pain tolerance (e.g., Litt, 1988; Jensen et al., 1991). Furthermore, self-efficacy expectancies have been found to be robust correlates of chronic pain severity (Jackson et al., 2014), and inducing self-efficacy can reduce experienced pain (e.g., Vancleef and Peters, 2011).

Thus, empirical research supports the independent effects of response, stimulus, and self-efficacy expectancies on pain. These different kinds of expectancies may also interact with each other. For example, when inducing self-efficacy expectancies, response expectancies may also be enhanced (e.g., Vancleef and Peters, 2011), and effects of outcome expectancies may be mitigated if one has low self-efficacy expectancies, e.g., when one expects that a physical exercise will reduce neck pain, but also expects that one is not able to perform the exercise (e.g., Bandura, 1977). A schematic overview of the influence of the different kinds of expectancies on pain is depicted in **Figure 1**.

MULTIFACETED EXPECTANCY CONSTRUCTS AND THEIR INFLUENCE ON PAIN

The co-occurrence of different kinds of expectancies with related emotions and cognitions is captured in multifaceted constructs, in which expectancies are incorporated. Here we provide an overview of the most common multifaceted expectancy constructs and their associations with pain.

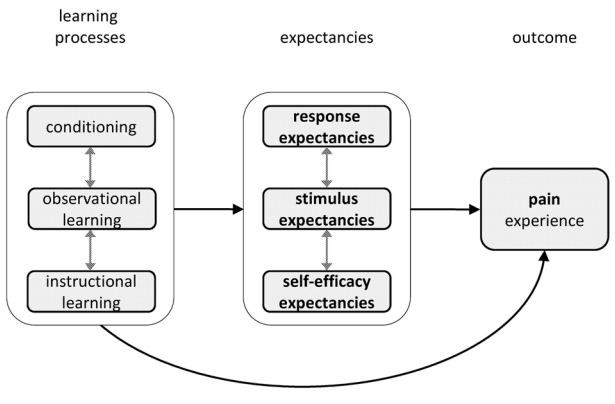

FIGURE 1 | Schematic depiction of the influence of expectancies on pain, including the learning processes that influence these expectancies. Probable mediators and/or moderators are behavior, emotions, and cognitions. All elements in the model may also feed back to preceding elements.

Optimism and hope are perhaps the most commonly considered multifaceted expectancy constructs. Optimism entails generalized positive expectancies of both stimulus and response type outcomes and is generally seen as a dispositional characteristic, although it can also vary depending on specific situations (Scheier and Carver, 1987). High levels of optimism are reliably associated with better health, including less severe acute and chronic pain (Rasmussen et al., 2009; Goodin and Bulls, 2013). The experimental induction of optimism can reduce pain sensitivity and pain interference (Hanssen et al., 2013; Boselie et al., 2014). Furthermore, optimism has been found to be associated with larger placebo analgesic effects (Geers et al., 2007, 2010; Morton et al., 2009; but see e.g., Hanssen et al., 2014). Hope is a related concept that is described as goal-directed thinking based on constructs that resemble outcome and self-efficacy expectancies (i.e., agency and pathway thinking, respectively) as well as motivational constructs (Snyder et al., 1991). Hope can pertain to specific situations or goals, but people also vary in their general tendency to be hopeful (Snyder, 2002). Several studies indicate that more hope is associated with using more pain-coping strategies, with higher pain tolerance, and with lower pain intensity (Snyder, 2002; Snyder et al., 2005; Rawdin et al., 2013). In addition, a hope-based intervention has been found to increase pain tolerance, though it did not affect pain intensity or pain threshold (Berg et al., 2008).

At an interpersonal level, trust is a multifaceted expectancy construct that is especially relevant in a medical context in which one has to entrust care of one's health to another person (Hall et al., 2001). In the majority of definitions of trust, trusting is seen as entailing expectations that someone, e.g., the physician, will act in a benevolent manner, and that one can rely on this person and his/her intentions (Rotter, 1967; Pearson and Raeke, 2000; Hall et al., 2001). Trust takes on an emotional quality that extends beyond mere estimations of the likelihood of another person's behaviors (Hall et al., 2001). Trust has been found to be associated with health behaviors such as adherence to treatment recommendations (Hall et al., 2001). In addition, trust in the physician has been associated with higher tolerance for treatment-induced pain (Caterinicchio, 1979).

Other constructs in which expectancies play a role and that can affect pain are constructs related to negative expectancies and the related emotions of fear and anxiety, such as worrying, pain catastrophizing, and neuroticism. Worrying is a repetitive thinking style that concerns a negative future (Borkovec et al., 1983). A person's expectation that the event worried about will happen appears to be an important component of worrying (Butler and Mathews, 1983; Macleod et al., 1991). Furthermore, worrying has been suggested to heighten vigilance to threat, such as pain (Borkovec et al., 1983; Aldrich et al., 2000). Worrying about pain and worry intensity have been associated with higher pain levels and more frequent pain complaints, respectively (Verkuil et al., 2012; Davis et al., 2014). One interventional study,

for example, found that a worry postponement intervention reduced somatic health complaints, including pain (Brosschot and van der Doef, 2006). The related construct of pain catastrophizing has frequently been a focus in pain research. Individuals who catastrophize often have negative response expectancies (e.g., that the pain may not go away), feel helpless about controlling their pain (i.e., low self-efficacy expectancies), are anxious, and worry and/or ruminate about their pain (Sullivan et al., 1995; Quartana et al., 2009). Pain catastrophizing is thus a comprehensive construct that involves different kinds of negative expectancies and related cognitions and emotions. Pain catastrophizing has consistently been linked to higher acute and chronic pain intensity, pain-related disability, and distress (e.g., Quartana et al., 2009; Wertli et al., 2014). The manipulation of pain catastrophizing has been found to affect experimental and chronic pain (both intensity and unpleasantness), though the findings are not fully consistent (Severeijns et al., 2005; Terry et al., 2015; Kjøgx et al., 2016). A last related construct is neuroticism. People high on neuroticism tend to be preoccupied with things that might go wrong (i.e., they tend to have negative expectancies, particularly negative outcome expectancies), to be easily frightened, and to feel despondent (Sanderman et al., 1995). Higher levels of neuroticism have been found to predict pain (Vassend et al., 2013; Wilner et al., 2014). Neuroticism has also been associated with placebo responses, but the results are equivocal (van Laarhoven et al., 2011; Darragh et al., 2014; Peerdeman et al., 2015).

IMPLICATIONS OF CURRENT FINDINGS

In the current review we set out to provide a brief overview of the literature on the influence of expectancies on pain. We found that different kinds of expectancies can be distinguished, which illustrates the complexity of the construct of expectancy. Nonetheless, it is clear that expectancies have an important influence on pain. Pain is influenced particularly by response expectancies that directly pertain to the pain experience itself. In addition, pain can be affected by self-efficacy expectancies regarding one's ability to cope with pain and possibly also by stimulus expectancies regarding external events. The co-occurrence of various expectancies, and related emotions and cognitions, is captured by multifaceted constructs in which expectancies are incorporated. Optimism and pain catastrophizing, in particular, but also hope, trust, worry, and neuroticism have been found to be associated with pain.

To truly grasp the influence of expectancies on pain and to harness these effects, we recommend to refine existing theoretical models of expectancies by also addressing the interplay between different kinds of expectancies. Studies testing the predictions following from these models, should then assess multiple kinds of expectancies and expectancy constructs to determine their independent and interactive influence on pain. In this research the expectancy constructs of interest should be carefully determined, and clearly operationalized and reported. Since no single study can assess all kinds of expectancies, meta-analytic research can ultimately be used to make overarching inferences about the relative, and possible additive and interactive effects of the various kinds of expectancies on pain.

When addressing the effects of expectancies on pain in research and clinical practice, several additional considerations are of importance. First, it is important to take into account the strength and valence of the expectancy, as well as the intensity, nature, and duration of pain (Bandura, 1977; Kirsch, 1985, 1997; Peerdeman et al., 2016). For example, negative expectancies may exert larger effects on pain than positive expectancies (Baumeister et al., 2001), and acute pain is more sensitive to expectation interventions than chronic pain (Peerdeman et al., 2016). Second, research has generally focused on short-term effects in artificial laboratory situations. Although there are indications that expectancies can have an enduring clinical impact (e.g., Rodriguez-Raecke et al., 2010), further research into long-term effects is required. Third, expectancies are generally hypothesized and observed to have congruent effects on experiences: one experiences what one expects (Mondloch et al., 2001; Rasmussen et al., 2009; Haanstra et al., 2012; Peerdeman et al., 2016). However, in the case of a large discrepancy between what is expected and what is observed, expectancies may actually have detrimental effects, resulting in disappointment and experiences that contrast rather than mirror prior expectancies (Wilson et al., 1989; Thompson and Sunol, 1995; Geers and Lassiter, 1999; Shepperd et al., 2015). Importantly, if there is a large discrepancy between the expected and the actual outcome, the current experience may have a larger impact on learning (and thus on future expectancies and experiences), than if the actual experiences are in line with what was expected (Rescorla and Wagner, 1972). Thus, physicians should be wary of inducing either overly positive or overly negative expectancies regarding analgesic treatment outcomes in their patients.

Clinical applications of expectancy interventions are very promising for optimizing analgesic treatment effects. Several interventions tap into the learning processes that have been described in the learning theories (i.e., conditioning, observational, and instructional learning). Instructional learning via positive verbal suggestions of analgesic treatment outcomes, in particular, has been found to effectively reduce pain in clinical samples (Peerdeman et al., 2016). This demonstrates the significance of the information a physician provides when administering an analgesic treatment. A physician can address conditioning processes by assessing previous treatment experiences. If a treatment has previously been experienced as effective, current treatment outcomes could be enhanced by using the same route of treatment administration, while a switch (e.g., from topical to oral administration) may be beneficial if a patient's previous experiences have been negative (Hofmann et al., 2014). Beneficial social learning may be facilitated via, for example, meetings with fellow or former patients or online video tutorials (Hunter et al., 2014). Furthermore, interventions evoking indirect experiences of pain reduction via mental imagery appear promising for inducing analgesia (Peerdeman et al., review). Experimental research suggests that

the combination of multiple strategies, tapping into multiple learning processes (e.g., both conditioning and instructional learning), may be most beneficial (e.g., Amanzio and Benedetti, 1999; Peerdeman et al., review).

CONCLUSION

The theoretical and empirical literature indicates that expectancies are an important determinant of pain, and that expectation interventions can effectively reduce pain. Future research requires the simultaneous study of different expectancy constructs in experimental and long-term interventional research, to further enhance our understanding of expectancies and their potential for optimizing analgesic interventions.

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Goal Pursuit in Individuals with Chronic Pain: A Personal Project Analysis

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Objectives: In individuals with chronic pain (ICPs), controlling pain often is a salient goal, despite the difficulty to achieve it. This situation may bring along frustration and distress. Yet much remains unknown about the content, appraisal, and structure of goals that ICPs pursue. Here, we explore these goals, and specifically focus upon possible differences and interrelations between pain control goals (e.g., "to control my pain") and non-pain goals (e.g., "to go to work").

Design and Methods: "Personal Project Analysis" was used in 73 ICPs (48 females; 25 males; M_{age} = 49.85 years; SD = 9.72) to elicit goals and goal appraisals. Interrelations between pain and non-pain goals, namely interference (i.e., negative influence), facilitation (i.e., positive influence), and necessary condition (i.e., conditional relation between pain control goal and non-pain goals) were measured with three items. Self-report measures of pain intensity, pain catastrophizing, problem solving and acceptance were completed.

Results: Participants reported a variety of goals. Appraisals of pain control goals were less favorable than appraisals of non-pain goals. ICPs with higher acceptance and meaningfulness of life reported more control over pain goals, and more progress in reaching pain control goals. These individuals also reported an overall much more positive appraisal of non-pain goals (i.e., less stress, difficulty, more progress, control). In contrast, high catastrophizing and the need to solve pain were negatively related to goal appraisals. Importantly, ICP's with high perceived meaningfulness of life despite pain experienced less necessity to achieve pain control goals in order to achieve non-pain goals. This was opposite for individuals with high levels of catastrophizing.

Discussion: An understanding of why ICPs may become stuck in attempts to control their pain does not only require an understanding of how individuals appraise their pain, but also requires an understanding of how pain and non-pain goals interrelate. In particular, the view that controlling pain is necessary in order to be able to achieve other goals seems detrimental.

Keywords: chronic pain, goals, catastrophizing, problem solving, acceptance

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INTRODUCTION

Some individuals with chronic pain (ICPs) adjust well to their pain. Others report high levels of interference of their daily activities by pain, and experience distress and despair (McCracken and Eccleston, 2003, 2005; Viane et al., 2003). Research has attempted to understand why these individuals are stuck in a vicious circle of enduring pain, disability and suffering. It has been proposed that distress and suffering result from a rigid search for a solution with regard to an experience that (unfortunately) cannot be controlled (McCracken and Eccleston, 2003; Eccleston and Crombez, 2007). Indeed, medical treatments often cannot provide satisfying pain relief for ICPs. Nevertheless, ICPs may remain searching for a solution, and this search may start to dominate their life at the expense of the pursuit of other valued activities.

Trying to solve the problem of chronic pain, or at least reducing it to an acceptable level, is typically the first response to pain-induced goal disturbance (Eccleston and Crombez, 2007; Van Damme et al., 2008). ICPs may then engage in a variety of behaviors, such as looking up information on the internet, visiting healthcare providers, taking medication, resting in bed, or avoiding pain-inducing activities. A second possible response is accepting the problem of chronic pain as insoluble. ICPs may then disengage from trying to solve the problem of chronic pain, and reengage in other valued goals despite the presence of pain (McCracken and Eccleston, 2003). In line with this view, acceptance has been related to favorable outcomes in the context of chronic pain (McCracken and Eccleston, 2003, 2005; Viane et al., 2003). Problems may arise when ICPs persist in futile attempts to solve or control pain at the expense of the pursuit of other valuable life goals. Such attempts have been dubbed 'misdirected problem solving' (Aldrich et al., 2000; Eccleston and Crombez, 2007). In line with this view, attempting to solve the problem of chronic pain has been linked to unfavorable outcomes (De Vlieger et al., 2006; Crombez et al., 2008). Adhering to an agenda of pain control is also believed to more readily occur in those who catastrophize about their pain (De Vlieger et al., 2006), i.e., excessively worry about pain and its possible consequences.

As yet, we do not have a broad understanding of why ICPs may become stuck in attempts to control pain. We also do not have a broad view on how ICPs experience the pursuit of pain control amidst the other goals that often are simultaneously pursued (Crombez et al., 2012). Overall, the assessment of goals in the context of chronic pain is not a well-studied area. Most of these studies focus on the assessment of non-pain goals in chronic pain (Karoly and Ruehlman, 1996; Karoly and Lecci, 1997; Affleck et al., 1998, 2001; Karoly et al., 2008; Hardy et al., 2011), but do not assess how ICPs construct and appraise their pain control goals. Therefore, this study focuses upon pain goals, in particular the goal to control pain, and their interrelations with other, non-pain, goals.

The present study adopts the "Personal Project Analysis" (PPA, Little, 1983) to assess personal goals and their characteristics. According to PPA, personal projects are "extended sets of personally salient action" (Little and Gee, 2007, p. 25). Typically, a PPA requires respondents to list goals that are currently important to them, to rate these goals on a number of dimensions or appraisals, and to report on the interrelationships between the goals (goal structure). For goal structure, we were particularly interested how working on a pain control goal facilitates the pursuit of other goals (goal facilitation: e.g., "to control pain" allows me "to go to work"), or interferes with the progress on other goals (goal interference: e.g., "to control pain" hinders me "to go out with friends") (Riediger and Freund, 2004). Although the characterization of goal interrelations in terms of facilitation and interference is theoretically well established (Riediger and Freund, 2004), we found that one particular characteristic was lacking. Clinical practice learns that patients often frame their attempts to control pain as a necessary condition to be able to continue with their life (Malec et al., 1977). We believed that this characterization was insufficiently captured under the constructs of goal facilitation and interference (Riediger and Freund, 2004). For that reason, we asked ICPs directly about this feature, which we dubbed "necessary condition" (e.g., "to be able to control pain" is necessary in order "to spend time with family").

Given the current state of research, we opted for an exploratory approach (Rozin, 2009), in which the content, appraisals and structure of the goals that ICPs pursue, were broadly assessed. We sought answers to 4 questions: (1) What types of goals are spontaneously elicited by ICPs?; (2) How do ICPs appraise their pain control goals, and how does this compare with non-pain goal appraisals?; (3) How do pain control goals relate to other, non-pain goals?; (4) Finally, we were interested in whether the goal appraisals and interrelationships were related to some key constructs involved in misdirected problem solving, such as catastrophic thinking about pain, attempts to solve pain and acceptance.

MATERIALS AND METHODS

Participants

The present study was part of the GPD-I study consisting of three studies on chronic pain and functioning. More information and details about this study can be found on http://hdl.handle.net/1854/LU-3050986. Participants were recruited from Flemish patient associations from December 2010 onward over a 4-month period. Inclusion criteria were (a) being aged between 18 and 65 years, (b) having sufficient Dutch language skills to fill out self-report measures, and (c) having pain for at least 6 months. Exclusion criteria were (a) reporting headache as a primary complaint, (b) reporting a psychiatric disorder (other than pain disorder) as primary complaint, and (c) physical limitations that made it impossible to participate in computer tasks. Three hundred and fifteen ICPs agreed that they could be contacted for the GPD-I study. Of these 315, 267 ICPs were contacted by phone and invited to participate. Eighty-one ICPs were eligible and agreed to participate in the study. However, 7 ICPs refrained from participation owing to health problems, and one participant was excluded because he/she did not report pain at the moment of testing.

The final sample consisted of 73 participants (48 females; 25 males; mean age = 49.85 years; *SD* = 9.72). Most ICPs were married or living together (69.9%), 39.4% had a higher education (longer than the age of 18 years). Only 18.1% was in paid employment or followed education, 7% was in unpaid employment, 13.9% was retired, and 4.2% was unemployed. All others received disablement insurance benefits (55.5%) or were legally trying to receive one (1.4%). The mean pain duration was 14.04 years (*SD* = 9.37). Back pain was the most reported pain location (90.4%). Participants also frequently reported pain in other body sites, such as the legs (67.1%), neck (67.1%), arms (46.6%), and head (32.9%). On average, participants reported pain on at least three different locations (*M* = 3.84, *SD* = 1.88). Socio-demographic information on non-participants was not available. The Local Ethics Committee of the University approved the study protocol.

Measures

Personal Project Analysis

We followed the guidelines of the Personal Project Analysis (Little, 1983) and conducted a semi-structured interview in which clarification, prompts and feedback were provided to elicit goals. Participants were asked to list all their current goals. We asked participants to report as many personal goals as possible that they had for the near future, currently judged to be important, and still expected to be important in the upcoming months. Whenever ICPs did not spontaneously mention a pain control goal during the free-elicitation phase, we required participants to identify one. We asked participants to write down their goals with a few words or short sentences (Ogilvie et al., 2001).

Goals were coded into 12 categories. We followed a standard coding procedure. Two independent raters were asked for the initial coding. Whenever there was disagreement, a third rater was assigned and recoded until consensus was achieved. The coding was based on existing taxonomies of goals (Chulef et al., 2001) and consisted of the following categories: interpersonal goals (e.g., to keep in touch with friends), intrapersonal goals (e.g., to be loving), health/physical domain goals (e.g., to lose weight), work/education goals (e.g., to do voluntary work), financial goals (e.g., to be financially independent), leisure/entertainment-related goals (e.g., to travel more), and psychological/mental well-being goals (e.g., to be full of energy). When we examined the list of goals participants provided, we decided to add three other categories: one related to household (e.g., cleaning the house), one related to exercise (e.g., to walk on a daily basis), and one related to social validation of one's pain (Hamilton et al., 2005) (e.g., to be believed that the pain is real). Individuals' pain goal, i.e., the goal to control pain was classified separately as pain control (e.g., to have less pain). Finally, there was a rest category, consisting of all goals that could not be classified into one of the 11 categories above. The inter-rater reliability was high (Cohen's Kappa = 0.77, $p < 0.001$) and there was an overall simple agreement coefficient of 79.5% (421-86/421).

In line with PPA guidelines (Little, 1983), participants were asked to select their two most important non-pain goals, and their pain control goal. Then, they were asked to rate these goals on a number of appraisal dimensions. A standard set of goal appraisals has been identified (Little, 1989, 1998; Austin and Vancouver, 1996). These usually include the following: meaning (e.g., importance, value congruency, self-identity), structure (e.g., control, time), efficacy (e.g., satisfaction with progress), or stress (e.g., stress, difficulty) (Little and Chambers, 2004). We selected a limited number of dimensions, mainly to avoid mental overload in participants. The following dimensions were included: (1) importance ("This goal is important to me"); (2) difficulty ("I find it hard to achieve this goal"); (3) control ("I feel I am in control of this goal"); (4) stressfulness ("I find it stressful to pursue this goal"); (5) time ("I spend a lot of time in pursuing this goal"); (6) progress ("I am satisfied with the progression I made in achieving this goal"); (7) self-identity ("This goal says a lot about who I am"); and (8) value ("This goal is highly valuable to me"). Each appraisal had to be rated on a 7-point Likert scale, ranging from 0, *not at all*, to 6, *completely*.

Goal interrelationships were measured by three items. Items were formulated during an iterative process, and piloted for comprehensibility with ICPs. Participants were instructed to rate the interrelationships of each possible pair of goals from their selected set of three goals, i.e., their pain control goal [C]) and their two most important non-pain goals [A and B], There were six possible pairs (A-B, B-A, A-C, C-A, B-C, C-B). For each pair of goals, participants rated three items, one item reflecting intergoal interference (e.g., "To what extent does the pursuit of goal C have a negative influence on the pursuit of goal B?"), one item reflecting intergoal facilitation (e.g., "To what extent does goal C have a positive influence on the pursuit of goal B?"), and one item reflecting goal necessity (e.g., "To what extent is it necessary to achieve goal C in order to be able to achieve goal B?"). As such, participants responded to a total of 18 items. All items were rated on a 5-point Likert scale, ranging from 1, *not at all*, to 5, *very much*. Of importance for this study were the goal interrelationships between the pain control goal and the non-pain goals.

Questionnaires

Pain severity was measured by means of the two-item pain severity subscale of the Dutch version of the Multidimensional Pain Inventory (MPI; Lousberg et al., 1999) (i.e., "Rate the level of your pain at the present moment", and "On average, how severe has your pain been during the last week"). Ratings are made on a 7-point scale (from 0 to 6). The sum score of the two items may range between 0 and 12. The MPI has been shown to have good reliability and validity. Test–retest reliability ($r = 0.71$) and Cronbach's alpha ($\alpha = 0.74$) of the pain severity subscale are both adequate. Data on construct validity are also adequate (Lousberg et al., 1999). Cronbach's alpha in this study was $\alpha = 0.80$.

We used the Pain Solutions Questionnaire (PaSol; De Vlieger et al., 2006) to assess efforts at changing, solving or accepting pain and the problems associated with pain. The PaSol has 14 items grouped into four interrelated scales: (1) solving pain (four items; e.g., "I try everything to get rid of my pain"); (2) meaningfulness of life despite pain (five items; e.g., "Even when I have severe pain, I still find my life meaningful"); (3) acceptance of the insolubility

of pain (three items; e.g., "I can live with the idea that there is no solution for my pain"); and (4) belief in a solution (two items; e.g., "I am convinced that there is a treatment for my pain"). Participants are instructed to describe the degree to which each statement applies to them. Each item is answered on a 7-point Likert scale, ranging from 0, *not at all applicable*, to 6, *highly applicable*. Although the original PaSol has demonstrated good reliability and validity (De Vlieger et al., 2006), subscale scores tend to be heavily skewed in ICPs (Crombez et al., 2008). Therefore, we decided to slightly adjust the wording of 13 out of 14 items and formulated them in a more extreme way, i.e., (1) solving pain; e.g., "I would try *really* everything to get rid of my pain"; (2) meaningfulness of life despite pain; e.g., "*Even when in pain*, I still find my life meaningful"; (3) acceptance of the insolubility of pain; e.g., "I can live with the idea that there *exists* no solution for my pain"; (4) belief in a solution; e.g., "I am *truly* convinced that there is a treatment for my pain". Cronbach's alpha's in this study were $\alpha = 0.85$, 0.86, 0.78, and 0.86, respectively, for the four scales. Subsequent analyses showed that three (i.e., solving pain, acceptance of the insolubility of pain, and belief in a solution) out of the four subscales met criteria for normal distribution.

The Dutch version of the Pain Catastrophizing Scale (PCS-; Sullivan et al., 1995; Crombez et al., 1998) was used to measure catastrophic thinking about pain. It is a 13-item scale for both non-clinical and clinical populations. Participants are asked to reflect on past painful experiences and to indicate the degree to which they experienced each of the 13 thoughts or feelings during pain on a 5-point scale (e.g., "I can't seem to keep it out of my mind", or "I become afraid that the pain may get worse"). Scores range from 0 to 4. The PCS has shown to be valid and highly reliable (Osman et al., 2000; Van Damme et al., 2002). Cronbach's alpha in this study was $\alpha = 0.90$.

Procedure

A self-report assessment and a semi-structured interview were employed. First, participants were invited to fill in a set of questionnaires at home. These could be completed online (i.e., Limesurvey, $n = 62$) or on paper ($n = 11$). Next, participants were invited to the university. Participants were further informed about the study and provided a written consent. They were then requested to provide socio-demographic information and completed some brief questions about their pain. Subsequently, participants responded to the Personal Project Analysis through a semi-structured interview format.

Statistical Strategy

Data were analyzed using the Statistical Package for Social Sciences (SPSS 20.0) and Microsoft Excell 2007 for Windows (Microsoft® Office Excell® 2007). Counting the number of times a participant mentioned at least one goal of a specific category and calculating relative percentages, enabled us to investigate the frequency of goal types reported by our sample.

As we were only interested in the effects of the pain control goal (Goal C) on the other two goals (goal A en B), we averaged the ratings of the two non-pain goals for all further statistical analyses. Descriptive statistics (mean, *SD*) were calculated for each of the goal appraisals of both the pain as well as non-pain goals. Further, a series of pairwise *t*-tests or non-parametric Wilcoxon signed-rank tests was conducted to examine whether there was a significant difference in how ICPs appraised their pain control goal compared to their non-pain goals. To obtain a standardized measure of the magnitude of the observed effects, i.e., a standardized difference between two means, effect sizes (Cohen's *d*) for independent samples were calculated using Morris and DeShon's formula (Borenstein et al., 2009). The 95% confidence interval (95% CI) was also calculated. Cohen's *d* is an effect size that is not design-dependent and conventional norms are available (Field, 2005). We determined whether Cohen's *d* was small (0.20), medium (0.50), or large (0.80) (Cohen, 1988). Lastly, Pearson correlations or non-parametric Kendall's tau correlations were calculated to describe the association between goal appraisals on the one hand and problem solving, acceptance, and catastrophizing about pain on the other hand.

In order to examine whether participants reported high levels of pain goal interference, facilitation and necessity, we focused upon the effects of the pain control goal (Goal C) on the other two goals (goal A en B). We calculated descriptive statistics (mean, *SD*), frequencies and proportions of response options across the sample. We used response options ≥ 4 as indicators of high levels (Riediger and Freund, 2004). Furthermore, Pearson or Kendall's tau correlations were calculated to assess associations between intergoal variables. Lastly, Pearson or Kendall's tau correlations were calculated to examine associations between pain control goal interference, facilitation and necessary condition on the one hand and solving pain, acceptance and catastrophizing on the other hand.

RESULTS

Type of Goals

Participants listed an average of 5.76 goals ($SD = 2.01$; range 3–12). We found that 41.1% of the participants spontaneously reported at least one pain control goal. Also, participants frequently reported one or more goals in the following life domains: interpersonal (80.82%), work/education (49.32%), leisure time (46.58%), exercise (45.21%), and health/physical well-being (41.10%). The least mentioned were goals related to social validation for one's pain (6.85%). **Table 1** shows examples of goals reported within each domain.

Goal Appraisals

Tables 2 and **3** display descriptive statistics on goal appraisals. A series of pairwise *t*-tests or non-parametric Wilcoxon-signed rank tests was conducted to examine whether there were significant differences in goal appraisals between one's pain and non-pain goals. Results indicated that participants rated the pain control goal as more difficult to achieve, $t(72) = -2.80$, $p = 0.007$, Cohen's $d = 0.38$, 95% CI [0.11, 0.66], and more stressful while pursuing, $t(72) = -2.09$, $p = 0.04$, Cohen's $d = 0.27$, 95% CI [0.01, 0.52] than the non-pain goals. Participants also reported to spend more time in achieving the pain control goal than the non-pain goals, $Z = -2.48$, $p = 0.013$, Cohen's $d = 0.29$,

TABLE 1 | Examples of goals provided by participants.

Life domains	Sample goals
Pain Control	To have less pain To live without pain
Interpersonal	To build up social contact To maintain contact with friends
Intrapersonal	To get to know and live with my limitations To be less anxious in contact with other people
Health/Physical Well-being	To lose weight To sleep better
Work/Education	To be able to work again To volunteer in helping students pass their language courses
Finances	To have no financial worries To save money to be able to buy a car
Leisure Time	To travel To do cultural stuff (e.g., concerts, musicals, expositions)
House holding	To clean the house To be able to do the cooking
Psychological/Mental Well-being	To be able to enjoy pleasant things (e.g., watching kids play together) To feel useful again
Exercise	To be able to keep on doing exercise (e.g., swimming, walking) To improve my walking condition
Social Validation	To have others to know what pain is about To be believed by other people
Other	To grow old To wish everybody a good future

95% CI [−0.01, 0.58]. Of note, the pain control goal was rated to be related less to one's identity, $t(72) = 2.85$, $p = 0.006$, Cohen's $d = -0.38$, 95% CI [−0.65, −0.11] than the non-pain goals. No significant differences between the pain control goal and the non-pain goals were found for importance, $Z = -0.90$, $p = 0.367$, control, $Z = -0.64$, $p = 0.523$, satisfaction with progress, $Z = -1.84$, $p = 0.07$, and value, $Z = -0.53$, $p = 0.595$.

Pearson or Kendall's tau correlations were calculated to investigate the association between goal appraisals and measures of problem solving, acceptance and catastrophic thinking about pain (see **Tables 2** and **3**). Higher levels of attempts to solve pain (PaSol) were related to rating the pain control goal as more important ($r = 0.26$) and more valuable ($r = 0.29$), and to a higher investment of time in the pain control goal ($r = 0.32$). Acceptance, i.e., acceptance of the insolubility of pain (PaSol) and meaningfulness of life despite pain (PaSol), were found to be positively related to satisfaction with progress in achieving both the pain control goal ($r = 0.28$ and $r = 0.38$, respectively) and non-pain goals ($r = 0.43$ and $r = 0.41$, respectively). Also, acceptance was found to be associated with lower ratings of stress in pursuing non-pain goals ($r = -0.40$). Finally, catastrophizing about pain (PCS) was related to more stress while pursuing the

TABLE 2 | Descriptive statistics and correlation coefficients between the appraisals of the pain control goal on the one hand, and pain severity, attempts to control pain, meaningfulness of life despite pain, acceptance, and catastrophizing on the other hand.

	N	*M* (SD)	Pain Severity (MPI)	Solving pain (PaSol)	Meaning-fulness[b] (PaSol)	Acceptance (PaSol)	Catastrophizing (PCS)
Importance[b]	73	5.66 (0.67)	0.02	0.26*	0.12	−0.09	−0.07
Difficulty[a]	73	4.08 (1.57)	0.29*	0.09	−0.12	−0.20	0.19
Control[b]	73	2.92 (1.67)	−0.08	−0.03	0.20*	0.24**	−0.16
Stress[a]	73	3.37 (1.70)	0.07	0.11	−0.18**	−0.20	0.35**
Time[b]	73	4.32 (1.51)	0.25**	0.32***	0.04	−0.03	0.06
Progress[b]	73	2.74 (1.90)	−0.18*	−0.17	0.38***	0.28**	−0.28**
Self-Identity[a]	73	3.78 (1.79)	−0.12	0.06	0.17	0.17	−0.20
Value[b]	73	5.51 (0.99)	0.04	0.29**	0.16	0.10	−0.02

[a]*Pearson Correlations;* [b]*Kendall's tau correlations; PaSol, Pain Solutions Questionnaire; PCS, Pain Catastrophizing Scale. *p < 0.05. **p < 0.01. ***p < 0.001.*

TABLE 3 | Descriptive statistics and correlation coefficients between appraisals of the non-pain goals (averaged) on the one hand, and pain severity, attempts to solve pain, meaningfulness of life despite pain, acceptance, and catastrophizing on the other hand.

	N	*M* (*SD*)	Pain Severity (MPI)	Solving pain (PaSol)	Meaningfulness[b] (PaSol)	Acceptance (PaSol)	Catastrophizing (PCS)
Importance[b]	73	5.61 (0.47)	0.05	0.08	0.08	−0.01	−0.06
Difficulty[a]	73	3.50 (1.44)	0.17	0.25*	−0.18*	−0.30*	0.37**
Control[a]	73	3.08 (1.40)	−0.14	−0.21	0.25**	0.30*	−0.15
Stress[a]	73	2.92 (1.68)	0.30**	0.19	−0.32***	−0.40***	0.43***
Time[a]	73	3.95 (1.01)	0.10	0.13	0.16	0.12	0.05
Progress[a]	73	3.21 (1.50)	−0.17	−0.16	0.41***	0.43***	−0.39***
Self-Identity[a]	73	4.37 (1.17)	−0.11	−0.18	0.21*	0.25*	−0.21
Value[b]	73	5.62 (0.49)	0.07	0.00	0.12	−0.04	−0.02

[a]*Pearson correlations;* [b]*Kendall's tau correlations; MPI, Multidimensional Pain Inventory; PaSol, Pain Solutions Questionnaire; PCS, Pain Catastrophizing Scale. *p < 0.05. **p < 0.01. ***p < 0.001.*

pain control goal ($r = 0.35$) and the non-pain goals ($r = 0.43$), and to lower ratings of satisfaction with progress in achieving both the pain control goal ($r = -0.28$) and the non-pain goals ($r = -0.39$). Catastrophizing was also related to higher ratings of difficulty in achieving non-pain goals ($r = 0.37$).

Intergoal Relationships

Table 4 presents the descriptive statistics (mean, *SD*) of the intergoal variables. High levels (response options ≥4) of pain control goal interference were reported by 50% of the participants, 80.15% reported high amounts of pain control goal facilitation, and 59.55% showed high need to control pain before pursuing other goals (necessary condition). Pain goal interference was found to be unrelated to pain goal facilitation ($r = 0.09$). No significant association was found between pain goal facilitation and necessary condition ($r = 0.08$).

Table 4 presents the results of the correlational analyses between intergoal variables on the one hand, and problem solving, acceptance, and catastrophizing. Attempting to solve pain (PaSol) was associated with higher levels of facilitation of pain control goals on non-pain goals ($r = 0.26$). Acceptance of the insolubility of pain (PaSol) and meaningfulness of life despite pain (PaSol), were related to lower levels of necessity of achieving the pain control goal upon pursuing one's non-pain goals ($r = -0.31$ and $r = -0.20$, respectively). Catastrophizing about pain (PCS) was related to higher levels of necessity of achieving the pain control goal upon pursuing one's non-pain goals ($r = 0.40$).

DISCUSSION

This study investigated (1) which goals are spontaneously elicited by ICPs, (2) how ICPs appraise their pain control goals, and whether these differ from non-pain goal appraisals, (3) how the pursuit of pain control goals affects the working on non-pain goals, and (4) whether the goal appraisals and interrelations are related to some key constructs involved in misdirected problem solving, such as attempts to solve pain, acceptance and catastrophic thinking about pain.

Individuals with chronic pains pursued a wide array of personal goals, and although we did not perform an in-depth analysis of their content, they seem to be quite similar to the goals that other individuals report (PPA, Little, 1983). Surprisingly, pain control goals, i.e., goals related to the control and management of pain, were not overly salient in our sample. Only about 40% spontaneously provided a goal related to attempts to control pain. One may have expected a larger percentage. However, several reasons may account for this finding. First, we mainly focused upon the goal to control pain. When categorizing the content of the goals, it became apparent that other pain-related goals were also pursued. The content of about 7% of goals were related to social validation. It seems that next to attempting to try to control pain, being believed by others that the pain is real, is a concern for a subgroup of ICPs (Kool et al., 2013). More research on this largely neglected topic is warranted (Hamilton et al., 2005; De Ruddere and Craig, 2016). Second, the study took place in a research context and not in a clinical setting, in which pain control may be more salient. Relatedly, participants were recruited from a patient association group, and not from a specialist clinic or rehabilitation center. It is likely that not all these individuals show tenacity in trying to solve their pain (Crombez et al., 2008). Third, in the instructions regarding the goal elicitation procedure, ICPs were not prompted with the example of a pain control goal.

Overall, the pattern of results indicates that attempting to control pain is a time-consuming and frustrating enterprise in ICPs (McCracken and Eccleston, 2003, 2005; Eccleston and Crombez, 2007). Participants indicated that their pain control goal was more difficult to achieve, more stressful, and required more of their time than their non-pain goals. They also experienced their pain control goal as less representative for their identity than the non-pain goals. Also, the pattern of correlations is in line with this picture. ICPs who report to be more engaged in solving pain, rated the goal to control pain as more important and valuable, and invested more time in it. Not accepting that pain is insoluble and not believing that life is meaningful despite pain were both associated with being less satisfied with the progress on pain control goals.

A noteworthy finding is that individual differences in attempts to solve pain were not only related to appraisals of the pain control goal, but also to appraisals of the non-pain goals. ICPs who reported to be more engaged in solving pain also reported more difficulties in achieving their non-pain goals. This was

TABLE 4 | Results of correlational analyses between pain goal interference, facilitation and necessary condition, and solving pain, meaningfulness of life despite pain, acceptance, and catastrophizing.

	M (*SD*)	2	3	4	5	6	7	8
1. Pain Goal Interference[a]	3.16 (1.04)	0.08	0.16	0.10	0.23^{+}	−0.08	−0.21	0.09
2. Pain Goal Facilitation[b]	4.00 (0.84)		0.08	0.05	0.26**	0.04	−0.02	0.05
3. Necessary Condition[a]	3.58 (1.04)			0.16	0.07	−0.20*	−0.31**	0.40***
4. Pain intensity (MPI)	11.78 (2.73)				0.38**	−0.32**	−0.28*	0.35**
5. Solving pain (PaSol)[a]	16.53 (5.62)					−0.08	−0.31	0.34**
6. Meaningfulness (PaSol)[b]	20.88 (5.60)						0.55**	−0.35**
7. Acceptance (PaSol)[a]	8.78 (4.56)							−0.39**
8. Catastrophizing (PCS)[a]	23.25 (10.06)							

[a]*Pearson correlations;* [b]*Kendall's tau correlations; PaSol, Pain Solutions Questionnaire; PCS, Pain Catastrophizing Scale.* $^{+}p = 0.05$. *$p < 0.05$. **$p < 0.01$. ***$p < 0.001$.

also the case for ICPs who do not accept that their pain is insoluble and do not believe that life is meaningful despite pain. The latter two variables were also related to experiencing more stress and less progress during the pursuit of the non-pain goals. There are several avenues to make sense of these data. First, it may be that attempts to solve pain come along with costs in pursuing other goals (Riediger and Freund, 2004). If this is the case one would expect that ICPs also report that working on the pain control goal interferes with the pursuit of non-pain goals. Further data of our study seem to corroborate this interpretation. ICPs who cannot accept pain as insoluble and do not believe that life is meaningful despite pain, report that solving pain is necessary in order to pursue their non-pain goals. Likewise, ICPs who engage more in attempts to solve pain also report more interference of their pain control goal with non-pain goals, although this effect failed to reach statistical significance. Second, it may be that attempts to solve pain are fueled by the interfering effect of pain on goal-related activities. Indeed, in many self-regulation models (Karoly, 1993; Carver and Scheier, 1998; Brandtstädter and Rothermund, 2002) coping and problem solving are triggered by goal interference, an experience that is highly prevalent in ICPs (Karoly and Ruehlman, 2007).

An important objective of this study was to investigate the goal structure or how ICPs experience the relationships between pain and non-pain goals. More specifically, we explored whether working on pain control goals facilitated working on non-pain goals (pain goal facilitation), whether working on pain control goals interfered with working on non-pain goals, and whether achievement of pain control goals is deemed necessary to attain non-pain goals (necessary condition). Despite the extensive piloting with the precise format of the items, some methodological issues remain. First, necessary condition is logically a part of the larger construct of pain goal facilitation. We would then expect a positive association between both, which, however, was not the case. Second, participants reported that the questions on goal interrelations were difficult. It is our impression that overall, the necessity item made more sense than the items on facilitation and interference. Notwithstanding, the pattern of results on the goal structure is intriguing, especially related to the necessity to solve pain in order to pursue non-pain goals. Most notable was our finding that perceiving one's pain control goal as necessary for achieving other goals, was related to accepting less that pain is insoluble and believing less that life is meaningful despite pain. These findings resonate with the idea of Conditional Goal Setting (CGS; Street, 2002; Street et al., 2007). CGS refers to the mechanism of goal linking, which means that a lower order goal (e.g., to control my pain) is conditionally linked to a higher order value (e.g., be happy). Through goal linking, the lower order goal gains significant importance, and will become difficult to disengage from. As a result, depression and distress may increase (Street, 2002; Street et al., 2007). As such, CGS theory may help explaining tenacious efforts to achieve pain control and resulting distress. Solving pain may become a necessary mean to continue with their life. Individuals may then become stuck in their attempts to solve pain, as an easy solution is not at hand.

Our results challenge some current understandings of catastrophizing about pain, and call for a conceptual broadening. Catastrophizing has been found a robust predictor of pain-related distress and disability in cross-sectional and longitudinal studies (Peters et al., 2007). Traditionally, catastrophizing is defined as an exaggerated negative mental set brought to bear during actual or anticipated pain experience (Sullivan et al., 2001). This is also evidenced in the influential fear-avoidance model. According to this model, those who catastrophize about pain develop erroneous fears about their pain [fear of (re)injury], which lead to avoidance of pain-evoking activities (Vlaeyen and Linton, 2000). Our results indicate that more might be at stake. Individuals who catastrophized about pain reported also elevated levels of stress in pursuing non-pain goals and less satisfaction with progress toward these goals. Those individuals also perceived their pain control goal as a necessary condition for pursuing their non-pain goals. Catastrophizing may thus not be limited to the mere experience of pain, but may extend to the experienced interference of daily goals by pain, possibly resulting in worrying and attempts to problem solving (Eccleston and Crombez, 2007; Crombez et al., 2012).

There are some limitations to this study. First, we adopted a goal and self-regulation perspective (Karoly, 1993; Little, 1998; Crombez et al., 2012) to frame our research and interpret our findings. However, our data are also compatible with other theoretical perspectives, amongst which the psychological flexibility (PF) model (Kashdan and Rottenberg, 2010; McCracken and Morley, 2014). PF could be described as the capacity to be fully in contact with the present moment without needless defense against pain, and to persist or change behavior in function of one's goals despite pain. For example, our findings on the potential negative effect of seeing pain control as necessary to allow pursuit of other non-pain goals, could be easily translated to PF language. (Hayes et al., 2012; Trompetter et al., 2015; Yu and McCracken, 2016). Second, results of this study are based on cross-sectional data, so we cannot infer causality. The use of moment-to-moment assessment by, for instance, diary approaches and the use of longitudinal designs will be necessary to allow causal inferences. A third limitation relates to sample characteristics. Within this study, we have explored goals in a self-defined chronic pain population, which may not be a representative sample of patients. Fourth, only a limited number of standard goal appraisals were assessed. Other dimensions are possible and may be of further relevance to help understand how patients juggle between the pain and non-pain goals. Fifth, we limited our focus to the goal of controlling pain. However, other pain-related goals, such as being believed by others that the pain is real, may also be at stake and important to assess (Karoly and Jensen, 1987; Hamilton et al., 2005).

AUTHOR CONTRIBUTIONS

GC has initiated and developed research ideas and design, and finalized paper. EL was involved in developing research ideas and design, collected and analysed the data, and made a first draft of the paper. LG was involved in developing the research design, and providing feedback on the paper. SD was involved in

developing the research design and ideas, and provided feedback on the paper.

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REVIEW
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Psychological Considerations in the Assessment and Treatment of Pain in Neurorehabilitation and Psychological Factors Predictive of Therapeutic Response: Evidence and Recommendations from the Italian Consensus Conference on Pain in Neurorehabilitation

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Background: In order to provide effective care to patients suffering from chronic pain secondary to neurological diseases, health professionals must appraise the role of the psychosocial factors in the genesis and maintenance of this condition whilst considering how emotions and cognitions influence the course of treatment. Furthermore, it is important not only to recognize the psychological reactions to pain that are common to the various conditions, but also to evaluate how these syndromes differ with regards to the psychological factors that may be involved. As an extensive evaluation of these factors is still lacking, the Italian Consensus Conference on Pain in Neurorehabilitation (ICCPN) aimed to collate the evidence available across these topics.

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Objectives: To determine the psychological factors which are associated with or predictive of pain secondary to neurological conditions and to assess the influence of these aspects on the outcome of neurorehabilitation.

Methods: Two reviews were performed. In the first, a PUBMED search of the studies assessing the association between psychological factors and pain or the predictive value of these aspects with respect to chronic pain was conducted. The included papers were then rated with regards to their methodological quality and recommendations were made accordingly. In the second study, the same methodology was used to collect the available evidence on the predictive role of psychological factors on the therapeutic response to pain treatments in the setting of neurorehabilitation.

Results: The first literature search identified 1170 results and the final database included 189 articles. Factors such as depression, anxiety, pain catastrophizing, coping strategies, and cognitive functions were found to be associated with pain across the various conditions. However, there are differences between chronic musculoskeletal pain, migraine, neuropathy, and conditions associated with complex disability with regards to the psychological aspects that are involved. The second PUBMED search yielded 252 studies, which were all evaluated. Anxiety, depression, pain catastrophizing, coping strategies, and pain beliefs were found to be associated to different degrees with the outcomes of multidisciplinary programs, surgery, physical therapies, and psychological interventions. Finally, sense of presence was found to be related to the effectiveness of virtual reality as a distraction tool.

Conclusions: Several psychological factors are associated with pain secondary to neurological conditions and should be acknowledged and addressed in order to effectively treat this condition. These factors also predict the therapeutic response to the neurorehabilitative interventions.

Keywords: pain management, clinical psychology, health psychology, chronic pain, neurorehabilitation

INTRODUCTION

Within neurorehabilitation programs, knowledge of the psychological factors associated with pain is crucial for its treatment. In fact, the differential impact of various pathologies on the patient as well as the way in which subjective features can affect the course of the disease and the treatment effectiveness are recognized as important factors that should be assessed in order to successfully treat pain conditions (Castelnuovo, 2010a,b, 2013; Cipolletta et al., 2014). What the research clearly highlights is that there is a set of psychological variables that are common to different disorders, but also that each pathology is characterized by some specific psychological issues. In this sense, pathologies that result in the experience of neuropathic pain are similar to pathologies associated with nociceptive pain as regard to anxiety, depression, and cognitions, but different if we consider the subjects' responses to and representations of the disease (Daniel et al., 2008). Several psychological variables may contribute to a better or worse outcome to pain treatment. These issues have a direct influence on the treatment itself. In both cases it is necessary to assess and address concerning changes in mood. However, while patients suffering from chronic musculoskeletal pain should be helped not to avoid movements and exercises that are associated with pain, the treatment of patients suffering from neuropathic pain instead should focus on the management of allodynia, for example.

METHODS

The Italian Consensus Conference on Pain in Neurorehabilitation (ICCPN) is a multidisciplinary board formed in October 2012, aimed at creating the updated guidelines for the treatment of pain in the field of neurorehabilitation (Castelnuovo et al., 2016). A systematic literature review was conducted by the ICCPN, given the importance of psychological factors in the genesis, maintenance, and resolution of pain conditions as well as on the patient's experience of illness. The study was divided in two parts: in the first part we considered the psychological issues associated with pain. We conducted a PubMed search using the keywords: "pain" (restricted to the title), various disorders that are targets of neurorehabilitation (stroke, cerebral palsy, Parkinson's disease, brain injury, multiple sclerosis, post-polio syndrome, Guillain-Barré syndrome, amyotrophic lateral sclerosis, spinal cord injury, concussion, vestibular disorder, neuropathies, neuropathic pain) and a range

of psychological variables (depression, anxiety, anger, cognitions, beliefs, catastrophizing, fear avoidance, emotions). The search was conducted in November 2013 and yielded 794 articles. Two upgrades, which were conducted in June 2014 (considering only articles from 2013 to 2014) and in May 2015 (considering articles from 2013 to May 2015), identified, respectively, 169 and 207 more articles. Abstracts or, if necessary, full-text articles were consulted to assess whether studies adhered to the inclusion criteria, namely the presence of at least one psychological factor associated with or predictive of pain in at least one disorder treated in neurorehabilitation services. The final database was composed of 189 articles. The methodological quality of the articles was then evaluated using a checklist specifically created, and assigned a high, medium, or low quality rating. The checklist considered the number of patients included in the study, drop-out rate, risk of bias with regard to the original studies, and the presence of systematic procedures, the comprehensiveness of research and bias risk assessment as regard to the review and meta-analysis. Each article was assigned a level of evidence, on the basis of an adaptation of the SIGN grading system (**Table 1**) and then recommendations were formulated accordingly (**Table 2**; Harbour and Miller, 2001).

In the second part we considered the psychological factors predictive of the therapeutic response using the same methodology. We conducted a PubMed search in November 2013, using the terms: "pain" (restricted to the title), the names of various disorders that are treated by neurorehabilitation services, the names of psychological factors and the following terms: moderator, mediator, prognostic factor, impact, predictor, outcome. The search identified 159 articles. An update conducted in May 2015 was restricted to the period from 2013 to 2015 and yielded another 93 articles. All these studies were included and were evaluated with the procedure previously outlined.

RESULTS

As noted before, several psychological factors are commonly associated with pain across different pathologies. Among them, depression has been identified as a crucial factor in a large number of studies. For some disorders, the relationship between depression and pain is correlational, thus it is difficult to identify the direction of the relationship; in other cases, depression can be considered predictive of the occurrence of secondary painful symptoms. Depression is a predictive factor of pain in pathologies such as chronic musculoskeletal pain (Wasserman et al., 2014), multiple sclerosis (Brochet et al., 2009; Harrison et al., 2015), post-stroke pain (O'Donnell et al., 2013), and Parkinson's disease (Wen et al., 2012). A correlation between pain and depression has been highlighted in patients with traumatic brain injuries (Dobscha et al., 2009; Garden and Sullivan, 2010), complex regional pain syndrome (CRPS) type I and II (Lohnberg and Altmaier, 2013; Rewhorn et al., 2014), spinal cord injury (Craig et al., 2013; Avluk et al., 2014; Van Gorp et al., 2015), peripheral diabetic neuropathies (Yoshida et al., 2009; Rekleiti et al., 2013), muscular dystrophies (Alschuler et al., 2012), Parkinson's disease (Zhang et al., 2014; Kass-Iliyya et al., 2015; Mao et al., 2015; Rana et al., 2016), fibromyalgia (Scheidt et al., 2014), and post-herpetic neuralgia (Drolet et al., 2010). Moreover depression is associated with anxiety in patients with headache (Kröner-Herwig et al., 2008; Wieser et al., 2012). The presence of neuropathic components in the pain experienced by the patient correlates with higher values for depressive and anxious symptomatology (Radat et al., 2013; Shaygan et al., 2013; Uher and Bob, 2013); in case of complex conditions the comorbidity with major depressive disorder is high (Proctor et al., 2013). Together with anxiety, alexithymia is also frequently associated with depression (although it can occur without the latter) in influencing the quality of perceived pain, mainly on the affective component and, to a lesser degree, on its sensory component in a relationship mediated by perceived psychological stress (Lumley et al., 2002; Huber et al., 2009; Hosoi et al., 2010). Although it has been studied to a lesser extent compared to depression, anxiety has a high rate of comorbidity with chronic pain conditions and is associated with pain intensity (Ligthart et al., 2013; Radat et al., 2013; Subramaniam et al., 2013). In particular, anxiety is exacerbated by the occurrence of headaches following traumatic brain injuries (Weyer Jamora et al., 2013), predicts chronic musculoskeletal pain following traumas (Castillo et al., 2013), increases in intensity concurrently with post-herpetic neuralgia (Drolet et al., 2010), is associated with diabetic neuropathy (Gore et al., 2005), is correlated with intensity and frequency of headache attacks (Nicholson et al., 2007; Kröner-Herwig et al., 2008) and it is a factor associated with and predicting CRPS (Dilek et al., 2012; Rewhorn et al., 2014) and chronic widespread pain (McBeth et al., 2014). Studies have been conducted on specific aspects of anxiety; in particular, research that has focused on constructs such as *anxiety sensitivity* (autonomic anxiety linked to the activation of the body) and anxious perception of pain (Wood et al., 2011; Yamaguchi et al., 2013) seems promising. Also, different sets of beliefs are associated with pain in relation to the various disorders that are treated by neurorehabilitation. Among these, pain catastrophizing has been studied in association with different neurological pathologies. In most cases, catastrophic thinking seems predictive of the emergence of painful conditions (Jensen et al., 2011). It is associated with or predicts pain in cerebral palsy (Engel et al., 2013), in lumbar or musculoskeletal pain (Hasenbring et al., 2012; Nakamura et al., 2014), in multiple sclerosis (Osborne et al., 2007; Hirsh et al., 2011; Harrison et al., 2015), in migraine (Radat et al., 2009), in diabetic neuropathy, post-herpetic neuralgia, and post-surgical neuropathic pain (Sullivan et al., 2005), in neuropathic pain due to HIV (Lucey et al., 2011) and in phantom limb pain (Vase et al., 2011). The importance of catastrophizing, in conditions associated with chronic pain, also lies in its mediation effect between the pain intensity and related emotions (Sturgeon et al., 2014). Along with pain catastrophizing, research also identified cognitive variables or maladaptive coping strategies that patients with pain related to neurological diseases tend to use. In particular, self-efficacy is correlated with the presence of pain in the case of stroke (Miller et al., 2013) and mediates the effect of pain on depression in the case of spinal cord injury (Craig et al., 2013). With regard to the coping strategies, both the tendency to avoid moving the painful part in an attempt

TABLE 1 | Levels of evidence (Harbour and Miller, 2001).

Level of evidence	Type of evidence
1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1–	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort or studies; high quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2–	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g., case reports, case series
4	Expert opinion

TABLE 2 | Grades of recommendations (Harbour and Miller, 2001).

Grade of recommendation	Evidence
A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or extrapolated evidence from studies rated as 2+
GPP	Recommended best practice based on the clinical experience of the guideline development group

to prevent increase in pain and the tendency to excessively exercise it are associated with a worse adaptation to the condition (Engel et al., 2000; Jensen et al., 2011; Andrews et al., 2012). A final note on factors associated with pain concerns the bidirectional relationship with the cognitive functions. Different lines of evidence underline the association between the two factors: patients that report chronic pain have lower scores in attentional and learning skills, delayed recall, reaction times, prospective memory, psychomotor skills, recognition of mental and emotional states, and executive functions (Hart et al., 2000; Jongsma et al., 2011; Moriarty et al., 2011; Beaupré et al., 2012; Shin et al., 2013; Miller and Radford, 2014; Zhang et al., 2014). However, it should be noted that a) there are differences between different diseases, b) not all studies have found these associations, c) factors linking pain and cognitive decline are still unclear, d) the direction of the cause-effect relationship is still unclear (Apkarian et al., 2004, 2005, 2013; Berger et al., 2014), e) results can be partly explained by comorbidity with other disorders or the use of drugs, in particular antidepressants (Moriarty et al., 2011; Pickering et al., 2014). Recent evidence indicates that lower scores on cognitive tests may represent a risk factor for the occurrence of post-operative pain and may predict its intensity and the presence of neuropathic components (Attal et al., 2014). As noted earlier, along with the factors that seem to be associated with pain in most diseases, the variables that differentiate between various diseases should be considered. In general, depending on psychological variables involved, the following macro-categories of diseases can be identified: chronic musculoskeletal pain, headache, neuropathic pain, conditions associated with complex and highly disabling pathologies. Musculoskeletal chronic pain conditions are often associated with high levels of depression, and uncertainty regarding the diagnosis and prognosis of the disorder (Daniel et al., 2008), avoidance of activities and exercise (Andrews et al., 2012), and anger (Fernandez and Turk, 1995). Despite being considered a musculoskeletal chronic pain, fibromyalgia has peculiar features, since it is accompanied with even more markedly depressive episodes, and the perceived pain, which is generally more intense compared to other musculoskeletal disorders, has long been considered to overlap with neuropathic pain (Koroschetz et al., 2011; Scheidt et al., 2014). Several studies report a high incidence of physical, emotional and sexual abuses among patients suffering from different forms of musculoskeletal chronic pain (Bailey et al., 2003; Kosseva et al., 2010), which may be associated with post-traumatic symptoms (Ruiz-Párraga and Lopez-Martinez, 2013). Two clarifications are necessary: on the one hand, the presence of previous abuse does not reduce the probability that psychotherapy will be effective (Bailey et al., 2003); on the other hand, the profile of patients suffering from musculoskeletal chronic pain is extremely variable and knowledge of the psychological factors associated with these diseases does not replace the need to assess the individual circumstances of the patient and provide personalized treatment. Research aimed at subgrouping patients according to their psychological characteristics and the risk of pain chronification is still in progress (Hasenbring et al., 2012). Psychological factors associated with migraine and tension-type headache should be considered separately from those of other disorders because the

underlying mechanisms are different. Researchers have focused mainly on the association between intensity and frequency of headache attacks and anxiety, depression and anger, as well as on cognitions, attributions and coping styles (Nicholson et al., 2007). In particular, an external locus of control (perception of not having control over the headache) together with high levels of anxiety, depression and pain catastrophizing are associated with a higher probability of chronification of attacks (Radat et al., 2009). Contrary to musculoskeletal pain, dysfunctional coping strategies such as avoidance of social activities, are not always associated with worsening of the patient's condition (Wieser et al., 2012). Neuropathic pain conditions are characterized by discomfort due to pain intensity and allodynia. In this condition, pain avoidance appears as fear of the painful sensation itself and the perception of dangerousness of different activities thereby leading to social withdrawal. This is in contrast to the fear of pain associated with movement which is typical of CRPS and causes increased irritability (Rommel et al., 2005; de Jong et al., 2011). Treatments must address these issues and consider that neuropathic pain is characterized by a significant association between psychosocial factors and pain intensity (Yoshida et al., 2009; Hirsh et al., 2010; Vase et al., 2011). Highly disabling pathologies, such as lateral amyotrophic sclerosis, multiple sclerosis and muscular dystrophies, are also frequently associated with pain. Central and peripheral pain components weave together and strengthen mutually (Seifert et al., 2013). These pathologies are hard to manage and the related pain condition can be associated with higher levels of fatigue and depression, which together significantly affect patients' quality of life (Pagnini et al., 2012; Fernández-de-Las-Peñas et al., 2014; Amtmann et al., 2015). A recent literature review underlined that psychosocial variables, in particular pain catastrophizing, may have medium to great effects on the level of psychological and physical functioning and on the intensity of perceived pain (Jensen et al., 2011). Also, the social support perceived by the patient, and some coping strategies have a core role in the experience of pain: task persistence (the ability to persist in performing hard and effort-requiring actions) can decrease its influence while the tendency to rest and stay alert after painful sensations increases it. The importance of the psychosocial factors listed above is not only based on their direct impact on pain but also on their influence on the therapeutic response to various interventions. The effectiveness of pharmacological treatments, surgery and psychotherapy is mediated by subjective characteristics that may predict worse (or better) outcome. The psychological predictors of the therapeutic response studied so far are both emotional, such as anxiety and depression, and cognitive, in particular pain catastrophizing, coping strategies and beliefs regarding the disease. There is evidence on the role of emotional factors in pain outcomes. Several studies documented the role of depression in influencing outcome of treatments for chronic pain conditions through multidisciplinary programs (Hill et al., 2007; Glombiewski et al., 2010; Miles et al., 2011; Morlion et al., 2011; de Rooij et al., 2013) and in spinal and orthopedic surgeries (Arpino et al., 2004; Celestin et al., 2009; Judge et al., 2012). The role of anxiety in multidisciplinary therapies (McCracken et al., 2002; Flink et al., 2010), physical therapies (Hill et al., 2007) and spinal and orthopedic surgeries (Celestin et al., 2009; D'Angelo et al., 2010; Judge et al., 2012), and that of anger suppression in chronic pain treatment (Burns et al., 1998) have also been demonstrated. Different cognitive factors seem also to have a crucial role, in particular pain catastrophizing in multidisciplinary (Smeets et al., 2006; Vowles et al., 2007; Desrochers et al., 2010; Heutink et al., 2013; Litt and Porto, 2013) and pharmacological treatments (Toth et al., 2014), cognitive flexibility in psychotherapy (Wicksell et al., 2010, 2013), acceptance in multidisciplinary programs and psychotherapy (Vowles et al., 2007; Samwel et al., 2009; Day et al., 2014), self-efficacy in multidisciplinary programs (Kores et al., 1990; Buckelew et al., 1996; Turner et al., 2007; Miles et al., 2011) and in the prognosis of tension-type headache (Holroyd et al., 2009), stress in Internet-based cognitive-behavioral therapies (DasMahapatra et al., 2015), dysfunctional coping strategies in spinal surgeries (Gross, 1986) and multidisciplinary interventions (Nicassio et al., 1997; Rhee et al., 2000; Nielson and Jensen, 2004; Hechler et al., 2010), expectations on the result of the therapies or on the course of the disease in psychotherapies or in multidisciplinary programs (Goossens et al., 2005; Milling et al., 2006, 2007; Galli et al., 2010; Bostick et al., 2015) and in headache treatment (Goldstein et al., 2011), and fear of movement in treatments for musculoskeletal chronic pain (den Boer et al., 2006). It should be underlined that not all the studies agree on the association between these factors and the outcomes and that it is not possible to exclude the presence of publication bias. Moreover, although these studies demonstrate that the conditions pre-existing before treatment may have an influence on the result or that a change of the considered variables is associated with a change in the outcome, a cause-effect relationship between the groups of variables cannot be assumed. Finally, although there is evidence that changes in levels of pain catastrophizing, anxiety and helplessness related to pain can enhance treatment outcomes, it is still unclear whether changes in cognitions correspond to better outcomes (Burns et al., 2003a,b). In relation to the use of virtual reality as a distraction technology a recent systematic review (Triberti et al., 2014) underlined the importance of different psychological factors in the effectiveness of the analgesic distraction. While sense of presence (Riva and Mantovani, 2012; Villani et al., 2012) influence the effectiveness of VR as a distraction tool, anxiety as well as positive emotions directly affect the experience of pain.

Further, issues that need to be considered among the factors that influence the results of treatment results include, on one hand, the core role of professionals, their listening, and communication skills, which are fundamental to maximize both treatment compliance and the therapeutic alliance (Butow and Sharpe, 2013; Farin et al., 2013; Raichle et al., 2014), and, on the other hand, the features of the context in which the patient lives, including the social and work situation and the perceived support received from their own family (Jamison and Virts, 1990; Becker et al., 1998). Further, studies are necessary to reach firm conclusions on the mediating role of these factors and to understand which factors can be seen as contraindications for specific treatments. As previously noted, the treatment for these pain conditions should be aimed at taking care of the individual in the context of their relationships in a wholistic

TABLE 3 | Summary of evidence and recommendations.

In different neurological conditions, various psychological components may be related to pain, represent risk factors, or have an influence on pain treatment. It is necessary to consider both shared factors, particularly depression, anxiety, and pain catastrophizing, and factors that are specific to different pathologies. Musculoskeletal chronic pain is associated with avoidance, anger, and uncertainty about the future and frequently with previous childhood abuse. Chronic headaches are influenced by both emotional and cognitive factors; coping strategies otherwise dysfunctional, such as the avoidance of activities, can have adaptive characteristics in this condition. Neuropathic pain, especially if associated with allodynia, is mostly correlated with fear and discomfort and characterized by a strong relation between psycho-social factors and pain intensity. Pain associated with highly disabling pathologies is highly correlated to psychological factors (mainly pain catastrophizing) and may have a different impact, depending on the perceived social support and the coping strategies. Emotional factors, such as depression, anxiety, and anger, and cognitive factors, such as self-efficacy and pain catastrophizing, influence the response to treatment. The treatment is more effective if it takes care of the person as a whole, taking into consideration the life environment and the relationships with caregivers and family.	
Depending on the different neurological conditions, various psychological factors may be related to pain, represent risk factors or have an influence on pain treatments. It is necessary to consider both common factors, particularly depression, anxiety, and pain catastrophizing, and factors that are specific to different pathologies. Emotional and cognitive factors influence the response to treatment. The treatment is more effective if it takes care of the whole person, taking into consideration the life environment and relationships with caregivers and family.	GPP
Depression is a predictive factor of pain associated with neurological conditions and the two factors are correlated.	B
Anxiety and pain catastrophizing are predictive factors of pain associated with neurological conditions and these aspects are correlated.	C
Musculoskeletal chronic pain is associated with avoidance, anger, and uncertainty about the future and frequently with previous abuses.	C
The chronification of migraine and tension-type headache is influenced by anxiety, depression, and anger, as well as an external locus of control. Coping strategies, which are dysfunctional in other conditions, can have adaptive characteristics in headache patients.	C
Neuropathic pain, especially when associated with allodynia, is highly correlated with fear and discomfort and is characterized by a strong relation between psycho-social factors and pain intensity.	C
Pain associated with highly disabling pathologies is strongly correlated to psychological factors (mainly pain catastrophizing) and may have a different impact, depending on the perceived social support and the coping strategies used.	GPP
Depression, anxiety, anger, and cognitive factors, such as self-efficacy and pain catastrophizing, predict worse outcomes for multidisciplinary, surgical, physical, and psychological treatments and are mediating factors in pain reduction.	B

*Legend: for B, C, and GPP please check the previous **Table 2**—Grades of recommendations (Harbour and Miller, 2001).*

sense, as opposed to simply intervening at a symptom-level. Each of the factors listed above must be seen in the context of their interaction with the person's living environment. Caregivers' responses to the disease can be significantly influenced by the presence of anxiety and depression (Ennis et al., 2013) and, as noted by Syed Hassan et al. (2013), their condition may be particularly distressing because of the need to cope with their own difficulties in the context of providing potentially exhausting care to the named patient. For this purpose, educational interventions have been designed to give patients and caregivers necessary information regarding the characteristics of the pathologies and treatment options, and providing details on potential positive effects on variables related to the family functioning and patient behavior (Daviet et al., 2012).

CONCLUSIONS

In conclusion, it is clear that an effective pain treatment in neurorehabilitation must consider both the specific and non-specific psychological factors of various diseases, including the environment in which the person lives and relationships with caregivers and family (see **Table 3**).

THE ITALIAN CONSENSUS CONFERENCE ON PAIN IN NEUROREHABILITATION

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All authors listed, have made substantial, direct and intellectual contribution to the work, and approved it for publication.

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Aerobic Exercise As a Potential Way to Improve Self-Control after Ego-Depletion in Healthy Female College Students

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Purpose: To test whether aerobic exercise can help build self-control stamina in healthy female young adults. Stamina in this context is defined as the capability to endure ego depletion, which can be measured with a self-control task following another activity also requiring self-control.

Methods: Forty-five healthy undergraduate women were randomized to either an experimental group or control group. Participants in the experimental group were required to run in their campus running field for 30 min for a period of 5 weeks. Individuals in the control group were required to do diary entries regarding self-control in their daily lives, also for a period of 5 weeks. Before and after the 5-week intervention, participants completed a pain threshold test, a color word Stroop task and the following Cold Pressor Task (CPT) (with and without a distraction component).

Results: There was significant decrease of pain tolerance in session 2 relative to session 1 in the control group, but no such decline was found in the experimental group (though the improvement of pain tolerance was not significant), possibly suggesting successful self-control against this kind of decline.

Conclusions: Five weeks of aerobic exercise increased self-control after ego depletion in terms of pain tolerance. These findings suggest that aerobic exercise may serve as a potential effective intervention for enhancing self-control in a college female population.

Keywords: aerobic exercise, self-control, stamina, pain tolerance, cold pressor task (CPT)

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INTRODUCTION

Self-control involves the ability to filter irrelevant environmental information, the ability to override a pre-potent response, or stop an ongoing response, and plays a vital role in daily life (Barkley, 1997; Davidson et al., 2006). Recently, Berkman et al. (2012) put forward a multi-dimensional perspective of self-control. According to their theory, self-control can be subdivided into three parts: behavioral control (e.g., stopping at a green light for a jaywalking pedestrian), emotional control (e.g., controlling one's anger at a demeaning superior at work), and cognitive control (e.g., focusing one's thoughts on the task at hand instead of daydreaming). Exerting self-control brings people's responses into line with certain standards such as ideals, values, morals, and social expectations, and supports the pursuit of long-term goals. On the contrary, many

behavioral problems such as drug addiction, eating disorders, and domestic violence involve a lack of self-control (Baumeister and Heatherton, 1996; Baumeister, 2002).

Another related and important theory is the "strength model" of self-control. According to this model, all self-control activities depend on a limited resource, and when a situation demands two consecutive acts of self-control, performance on the second one is frequently impaired. This is usually referred to as ego depletion (Baumeister, 2002; Baumeister et al., 2007). Based on the strength model, there are two forms of self-control abilities that can be trained: power (the baseline capacity), and stamina (the capability to endure depletion) (Muraven et al., 1999). In daily life, binge eating, crime, violent acts and addictive relapses tend to occur later in the day, a phenomenon possibly attributed to a depletion of self-control resources after completion of daytime activities (Baumeister, 2002).

Given the vital role of self-control, identifying proper ways to promote it can be of great value, especially ways to improve self-control stamina. In the long run, both self-control power and stamina can be trained and enhanced through small but regular exercise. For example, Muraven et al. (1999) found that 2 weeks of regulating mood or monitoring posture could build self-control stamina, as reflected by improved performance on the hand-grip task after depletion from a former thought-suppression task. Muraven (2010) also found that 2 weeks of cutting back on sweets could improve the overall power of self-control ability measured by a stop signal task.

Among various training protocols, aerobic exercise has been suggested as an effective intervention. Aerobic exercise has been found to have robust (but selective) benefits for executive-control processes in aged people (Colcombe and Kramer, 2003), children, and schizophrenia patients and patients suffering from disease (Franco-Martin et al., 2013; Sollerhed et al., 2013; Li et al., 2014; Yau et al., 2014).However, little is known whether long-term aerobic exercise training can modulate cognitive inhibition in healthy young adults, a population particularly at risk for a variety of impulsive behaviors. Oaten and Cheng (2006a) showed that participants who did physical exercise (aerobic exercise, free-weights or resistance training) had significant improvements in cognitive stamina (enhanced performance) as measured by a visual tracking test following a thought-suppression task. Later, Baker et al. (2010) found that 6 months of high intensity aerobic exercise improved women's baseline self-control performance. However, Baker et al. (2010) did not test self-control after depletion. Overall, there is a need for more empirical studies regarding self-control *after* depletion in order to verify the influence of physical exercise on self-control stamina.

Furthermore, previous studies tend to only test the cognitive component of self-control, and not other kinds of self-control despite this faculty being multi-dimensional in nature that also includes emotional control and behavioral control besides cognitive control. Up to now, possible improvements in behavioral and emotional self-control through physical exercise remain unknown. However, some research hints at possible benefits of physical exercise on emotional and behavioral control. For example, some clinical studies have reported that exercise training can help increase pain tolerance ability in patients with chronic pain (Hayden et al., 2005; Hoffman et al., 2005). As we know, pain is not simply a sensation detected by receptors, but is rather a complex phenomenon accompanied by a series of reactions. Pain tolerance is closely related to emotional (fear of pain) and behavioral (automatic avoidance from pain) self-control (Fernandez and Turk, 1992). Thus, pain tolerance may be a good index to test whether physical exercise can modulate emotional and behavioral self-control in a healthy population.

A recent report of the benefits of aerobic exercise on pain tolerance seems promising (Jones et al., 2014). That study found that 6 weeks of structured aerobic exercise training increased ischemic pain tolerance in healthy individuals. Though the Jones study provided evidence that aerobic exercise could lead to increased pain tolerance, several limitations confined the generalization of their findings. Firstly, the sample size was relatively small (12 in the training group and 12 in the control group), and the sample spanned a large age range (18–50 years old). Secondly, there was no intervention for the control group, which could have enlarged the effect of the manipulations because of potential placebo effects. Thirdly, the author only investigated pain tolerance at baseline to test for self-control ability, lacking the stamina component of self-control revealed after depletion.

In the present study, we intended to explore whether aerobic exercise could improve pain tolerance (as an index of behavioral and emotional self-control) after ego-depletion in healthy young adults. In order to measure stamina, we used the color word Stroop task (Stroop, 1935), a well-established and effective method for causing depletion (Wallace and Baumeister, 2002). Pain tolerance was measured with the Cold Pressor Task (CPT), which indexes people's self-control ability to retain their hand immersed in cold water (Kanfer and Seidner, 1973). Shorter immersion duration on this task has been associated with poor self-control (Oosterman et al., 2010). We hypothesized that compared to the control group, the experimental group would have higher pain tolerance in the CPT following ego-depletion.

MATERIALS AND METHODS

Participants

Forty-five sophomore female volunteers from Southwest University (Chongqing, China) were recruited from a general psychology course with 50 Yuan RMB for their participation. They were randomly assigned to two groups, with the experimental group containing 22 participants and the control group 23. There were no significant differences between the two groups in age, or years of education (all sophomore students).

The final experimental group only contained 18 participants, and the control group 18, due to 6 participants (two from the experimental group, and four from the control group) giving up during the intervention, and three participants (two from the experimental group, and one participant from the control group) not taking part in post-training tests. Reasons reported for stopping included lack of time/time constraints, academic burden, and absence from school.

Only female students were recruited in the present study due to the following concerns. First, physical exercise frequency, duration, and intensity of Chinese female students has been reported to be significantly lower than those of male students (Zhang et al., 2009).This diversity of physical exercise baseline would make it hard to discern appropriate exercise intensity for each gender during the training. Second, females tend to have shorter pain tolerance during performance of the Cold Pressor Task (CPT), thought to be due to a decrease in pain threshold when reaching puberty (Fillingim et al., 2009; Schmitz et al., 2013; Sollerhed et al., 2013). Thus, only female participants were recruited to attain a more homogeneous sample in order to minimize individual differences. Last but not the least, gender is a factor needed to be considered in the CPT because it may influence the pain tolerance performance in CPT (Fillingim, 2000). For instance, Levine and De Simone (1991) found a significant interaction of experimenter gender and subject gender on pain tolerance; subjects tolerated pain longer when tested by an experimenter of the opposite sex. The experimenters of this study were females, and so only female subjects were recruited in order to avoid an interaction of gender.

Ethics Statement

This study was approved by the review board and Ethics Committee of Southwest University. Written informed consent was obtained from all participants. All participants were informed that their participation was completely voluntary and that they may withdraw from it at any time. All participants were over 18 years of age.

Materials and Tasks

Physical Activity Rating Scale (PARS-3)

The PARS-3(Hashimoto, 1990) evaluates one's physical activity by the multiplication of exercise intensity, frequency and time, with the resulting score ranging from 0 to 100. The Chinese version of the PARS-3 has a high reliability and validity in Chinese samples (Liang and Liu, 1994).

Color Word Stroop Task

The color word Stroop task, a well-established cognitive test of inhibition, was used to create depletion. Color words presented included RED, GREEN, BLUE, and YELLOW ("红," "绿," "蓝," "黄" in Chinese, respectively). Print colors in which the words could be displayed were the same as the traditional task. A non-color word, "ke" (棵), printed with the above four colors, was treated as the neutral word. Such a task conducted with Chinese words maintains the essence of the original task, and is widely used by local Chinese psychologists (Li et al., 2009).

After practice, 216 trials were presented in random order, including 72 congruent trials (e.g., the word RED printed in red), 72 incongruent trials (e.g., the word RED printed in green), and 72 control trials (e.g., the Chinese word "ke" printed in red). In each trial, a central fixation lasting for 300 ms, a black screen for 300 or 500 ms randomly, and stimuli for 1200 ms, were presented in sequence. Participants were required to respond accordingly to the color of the ink, while ignoring the words' semantic meaning (i.e., if the word BLUE appeared in red, they should respond "red"). They were required to respond as quickly as possible by pressing "F," "G," "H," or "J" on the keyboard, for red, yellow, green, and blue, respectively. As the subjects' tendency is to name the word itself (rather than the color of the text), the Stroop task requires cognitive control and an ability to focus one's attention, causing self-depletion (Wallace and Baumeister, 2002).

Pain Threshold Test

We measured the pain threshold of participants with a pain threshold test. Participants were instructed to immerse their non-dominant hand in a circulating bath of cold water (5°C), and were given the following instructions:

> *The water temperature is very low, and the sensation may be somewhat unpleasant. However, I would like to emphasize that this procedure is in no way harmful. First, you will immerse your non-dominant hand into the cold water. At the moment you feel pain, please shout out and withdraw your hand out of the water.*

The duration of immersion (in milliseconds, recorded by a stop watch), from the time the hand was placed into the water to the moment of pain perception, was used as the index for baseline pain threshold.

Cold Pressor Task I

We measured the pain tolerance of participants using the Cold Pressor Task (CPT). Participants were instructed to immerse their non-dominant hand in a circulating bath of cold water (5°C), and to hold it there for as long as possible with the following instruction (von Baeyer et al., 2005):

> *Now, you will try the cold water one more time. This time, please try your best to keep your hand in the cold water as long as you can or until you are required to withdraw. The longer you keep your hand in the water, the more information we can gather, and the more valuable your participation will be. However, when you cannot tolerate the cold any longer, you should withdraw your hand.*

The Cold Pressor Task (CPT) provides a useful measure of pain tolerance (Kanfer and Seidner, 1973). The duration of immersion (in milliseconds, recorded by a stop watch), from the time the hand was placed in the water to when it was voluntarily withdrawn, was the index of pain tolerance. We set 2 min as the time limit in order to not cause physical discomfort to subjects for an extended period of time. Furthermore, after the participants had withdrawn their hand or reached the 2 min limit, they were asked to rate the pain intensity on a Visual Analog Scale (VAS), measuring 100 mm-long anchoring at one end with "0, no pain at all" and "10, unbearable pain" at the other. Ratings of these kinds are regarded as a fast and reliable way to record self-reported pain sensitivity (Turk et al., 1983).

Cold Pressor Task II

The Cold Pressor Task II was designed to test pain tolerance while participants are less focused on pain, compared to the Cold Pressor Task I. Here, participants were required to do the same thing as in Cold Pressor Task I, but were additionally asked to complete the color word Stroop task at the same time. Thus, they

had to modulate their attention from pain tolerance toward the demands of the Stroop task.

Procedures and Interventions

This was a longitudinal study with two sessions. Before training (i.e., Session 1), all participants were required to complete the baseline tests, including the PARS-3, color word Stroop task followed by the pain threshold test, pain Cold Pressor Task I and Cold Pressor Task II. Presentation of the two pain cold pressor tasks was counter-balanced between subjects. Upon completion, both the experimental group and control group were intercepted by a 5 weeks long intervention after which, all participants were required to come back to the lab to complete the post-training test (i.e., Session 2), which was the same as Session 1.

We chose physical running exercise as the intervention for the experimental group to see whether aerobic training could build self-control ability. The control group was required to keep a diary of exerted self-control in their daily lives. This method was adopted as the intervention for the control group from Muraven's study, where keeping such a diary was shown to increase the saliency of self-control, without actually exerting it (Muraven, 2010).

To be more specific, exercise involves planned, structured, and repetitive activity, improvement in cardiopulmonary fitness, and is performed at least 2 to 3 times a week, for at least 15–20 min on each occasion (Turk et al., 1983). Participants in the experimental group spent 20–30 min running together with the experimenter every evening. The physical training lasted 5 weeks. On the other hand, participants in the control group completed the diary of successful self-control every day. Enough details enclosed were required. For example, wanting a sweet but choosing to not have one, or resisting the thought of giving up on memorizing few vocabulary words, were some examples. Every evening, they handed in their diary and got a new sheet of paper for their next entry from the experimenter.

Furthermore, in Session 2, all participants were required to answer a question, "To what extent do you believe the assigned task could help you build self-control strength?," on a Likert scale (0 "not at all" and 10"extremely yes"). This question was intended to examine whether our manipulation was successful in letting both groups believe that their assigned intervention could help them build self-control abilities to the same extent.

Data Analysis

Pain sensitivity and pain tolerance were treated as the dependent variables. Pain sensitivity was indexed by the pain threshold and pain rating scores in the Visual Analog Scale (VAS).The pain tolerance was indexed by the duration of immersion that participants kept their hand in the cold-water bath. We set 2 min as the longest limit to prevent potential harm to participants. For those people who did not withdraw their hands from the cold water until 2 min, we set 2 min as their immersion duration when doing the analysis. As the data of tolerance time in this study violated key assumptions of normality, Log transformation was conducted before further analysis (von Baeyer et al., 2005).

We first analyzed the performance of the Cold Pressor Task I and Cold Pressor Task II, respectively. A repeated measures ANOVA was used for the pain tolerance in both sessions. After that, we also conducted a two-sample *t*-test of pain tolerance change across sessions (change = Pain tolerance$_{_post-training}$− Pain tolerance$_{_pre-training}$) to test for group differences. Then, an ANOVA was used to compare the difference between Cold Pressor Task I and Cold Pressor Task II. At last, a Pearson correlation analysis was used to test the correlation between pain tolerance and PARS-3 scores.

RESULTS

Manipulation Check

The intervention stage lasted for 5 weeks. However, owing to rainy weather, female students' physiological cycle, and holidays, the average number of times the experimental group engaged in aerobic exercise was 12.89 ($SD = 4.35$), whereas the control group handed in an average of 22.6 ($SD = 4.77$) sheets of diaries. Thus, there was a difference between the number of times the two groups engaged in the assigned activities due to some objective factors [$t_{(36)} = 6.53$, $p < 0.01$, $d = 2.18$].

The scores of the PARS-3showed that the two groups did not differ in their pre-training levels of physical activity [$t_{(34)} = 0.949$, $p = 0.350$),while after intervention, participants in the experimental group scored much higher than those in the control group [$t_{(34)} = 4.94$, $p < 0.001$], indicating that the control group did not engage in as many physical activities as the experimental group did during the intervention (see **Table 1**). Repeated measures ANOVA of PARS-3 verified the significant group × session interaction [$F_{(1, 34)} = 20.73$, $p < 0.001$]. Furthermore, simple effect analysis showed that the PARS-3 score increased significantly [$F_{(1, 34)} = 21.913$, $p < 0.001$, $\eta^2 = 0.392$] in the experimental group but declined significantly in the control group [$F_{(1, 34)} = 3.090$, $p > 0.05$, $\eta^2 = 0.083$].

Furthermore, no difference on the question "To what extent do you believe the assigned task could help build your self-control strength" was found between the two groups [$t_{(34)} = 1.56$, $p = 0.13$, $d = 0.51$]. This indicated that participants in the control group also believed they could build their self-control abilities through diary keeping, without actually exerting self-control.

Pain Threshold

The pain threshold was measured before cold pressor tasks in both sessions. A repeated measures ANOVA analysis showed no significant main effect or interaction (*F*s < 1), which

TABLE 1 | Mean and SD of demographics and PARS-3 score of participants.

	Exp. Group		Control Group		*t*	*p*
	M	*SD*	*M*	*SD*		
N	18		18			
Age	20.5	1.01	20.6	1.20	−0.22	0.82
PARS-3 (pre)	11.72	8.96	14.78	10.32	−0.95	0.35
PARS-3 (Post)	25.33	11.2	9.67	7.45	4.94	0.000

PARS-3, Physical Activity Rating Scale.

indicated the two groups' sensation of pain were similar, pre-(Exp. group: 8.24 ± 0.51; Control group: 8.57 ± 0.43) and post intervention(Exp. group: 8.34 ± 0.45; Control group: 8.40 ± 0.64).

Pain Intensity Rating

Pain intensity was measured by VAS rating for the cold pressor tasks across sessions. ANOVA analysis showed no significant main effects nor interactions ($Fs < 1$), which showed that the two groups had similar subjective pain experiences pre-(Exp. group: 7.11 ± 0.37; Control group: 8.19 ± 0.33) and post intervention (Exp. group: 7.33 ± 0.29; Control group: 6.97 ± 0.25).

Pain Tolerance in Cold Pressor Tasks

The mean and SD of pain tolerance in CPTs are shown in **Table 2**. For Cold Pressor Task I, a repeated measures-ANOVA analysis showed no significant main effect of session (Pre vs. Post) and intervention (Running vs. Daily writing), while the interaction was significant [$F_{(1, 34)} = 6.57$, $p = 0.015$, $\eta^2 = 0.162$]. A further simple effect analysis showed that the control group had a significant decline of pain tolerance across sessions [$F_{(1, 34)} = 6.80$, $p = 0.013$, $\eta^2 = 0.167$]. However, improvement of pain tolerance in the experimental group across sessions was not significant ($F_{(1, 34)} = 1.03$, $p = 0.317$, $\eta^2 = 0.029$]. Furthermore, we did an independent samples t-test for the changes of pain tolerance across sessions and verified that the control group had significantly more deterioration [$t_{(34)} = 2.56$, $p = 0.015$], (see **Figure 1**).

We performed the same analysis to pain tolerance scores in Cold Pressor Task II and got very similar results (see **Table 2**) though the effect size was much smaller. The session in (Pre vs. Post) × intervention (Running vs. Daily writing) interaction was significant [$F_{(1, 34)} = 4.25$, $p = 0.047$, $\eta^2 = 0.111$]. The group difference of changes of pain tolerance across sessions was also significant [$t_{(34)} = 2.06$, $p = 0.048$], (see **Figure 1**).

A 2 (task: CPT I vs. CPT II) × 2 (group: Exp. vs. Control) × 2 (session: Pre vs. Post) repeated measures ANOVA analysis was used to find differences between Cold Pressor Task I and Cold Pressor Task II. We found a significant main effect of task [$F_{(1, 36)} = 68.549$, $p < 0.001$, $\eta^2 = 0.656$], showing longer pain tolerance in CPT II in both pre ($p < 0.001$, $\eta^2 = 0.598$) and post training sessions ($p < 0.001$, $\eta^2 = 0.584$). We also found significant session × group interaction [$F_{(1, 36)} = 7.172$, $p = 0.011$, $\eta^2 = 0.166$], similar as shown above.

TABLE 2 | Mean and SD of pain tolerance in cold pressor tasks (Log_e transformed).

		Exp. group			Control group		
		N	*M*	*SD*	*N*	*M*	*SD*
CPT I	Pre-training	18	10.01	0.92	18	10.38	1.00
	Post-training	18	10.18	0.94	18	9.95	0.88
	Change(post-pre)	18	0.17	0.15	18	−0.43*	0.17
CPT II	Pre-training	18	10.71	0.87	18	10.85	0.79
	Post-training	18	10.83	0.95	18	10.59	0.86
	Change(post-pre)	18	0.12	0.12	18	−0.26*	0.13

*$p < 0.05$.

Correlations between Pars-3 and Pain Tolerance Change

Pearson Correlation analysis showed that the pain tolerance change (Pain tolerance$_{_post}$ − Pain tolerance$_{_pre}$) was significantly positively correlated with the change of PARS-3 scores. In CPT I and CPT II, the correlation coefficient was 0.494 ($p = 0.002$) and 0.333 ($p = 0.047$), respectively.

DISCUSSION

Previous research studies have supported that aerobic exercise can help with cognitive executive control abilities in elderly, children, and some clinical populations, yet little evidence is given in healthy populations. Furthermore, previous studies focus on the effect of physical exercise on cognitive self-control, with little attention paid to other aspects (emotional and behavioral components) of self-control. Additionally, physical exercise has been shown to improve overall self-control ability, but little is known about its effect on the stamina of self-control. To our knowledge, this is the first study investigating the possible effects of aerobic exercise on the stamina of self-control (pain tolerance as an emotional and behavioral aspect of self-control) in healthy adults.

Our data suggest that after 5 weeks of running, the sensation of pain (Pain threshold and Pain intensity rating) did not

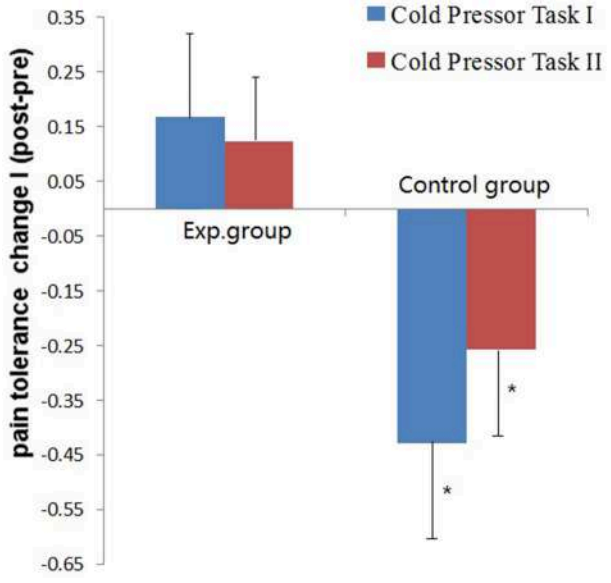

FIGURE 1 | Mean pain tolerance scores change and S.E.M. of the two groups (Exp. vs. Control group) in the two Cold Pressor Tasks. Pain tolerance was calculated by the Log_e transformation of immersion duration in cold water. Change = Pain tolerance$_{_post-training}$ − Pain tolerance$_{_pre-training}$. *$p < 0.05$.

change in both groups, but pain tolerance (index of self-control ability) changed significantly. There was significant decrease of pain tolerance in session 2 relative to session 1 in the control group, but no such decline was found in the experimental group (though the improvement of pain tolerance was not significant), possibly suggesting successful self-control against this kind of decline. Furthermore, a significant positive correlation was found between the change of PARS-3 scores and the change of pain tolerance across sessions. These findings suggest that the stamina of self-control may be improved with 5 weeks of aerobic exercise.

Self-Control and Pain Tolerance

Theoretically, pain can be understood as a subjective, unpleasant experience with both sensory and emotional components [IASP (International Association for the Study of Pain Task Force on Taxonomy), 1994]. Painful stimulation produces general autonomic arousal such as changes in respiration rate, muscle tension, intensification of electro dermal activity, and dilation of the pupils, resulting in behavioral escape from the painful stimuli (Kyle and McNeil, 2014). To combat this "bottom-up" process, the individual must deliberately use central cognitive resources to execute pain control or redirect attention away from pain (Legrain et al., 2009). Self-control is thus vital for this "top-down," intentional, goal-directed, and effortful process.

Studies have shown that the experience of pain can be influenced by behavioral inhibition (Karsdorp et al., 2014; Pulvers et al., 2014), as in Karsdorp's et al. (2014) study that measured response inhibition with the stop-signal task, along with pain-related fear with the Fear of Pain Questionnaire. Their findings suggest that individuals with stronger response inhibition abilities are better able to inhibit escape/avoidance responses elicited by pain. Verhoeven et al. (2014) found similar results when investigating the role of executive function on pain control in children. Moreover, high self-efficacy regarding the ability to exert control over pain has been shown to result in a significant reduction in anticipated pain intensity, anticipated pain unpleasantness, and experienced pain intensity ratings (Vancleef and Peters, 2011).

Besides behavioral inhibition, studies have also confirmed that the experience of pain can be influenced by emotional factors, such as anxiety (Liang and Liu, 1994), emotional regulation (Tang et al., 2008; Hampton et al., 2015), and emotional intelligence (Ruiz-Aranda et al., 2011). Tang et al. (2008) for example, showed that experimentally induced negative mood increases self-reported pain and decreases tolerance for a pain-relevant task. Ruiz-Aranda et al. (2011) found that participants with higher Emotional Intelligence rated pain as less intense and perceived it as less unpleasant. More recently, Hampton et al. (2015) showed positive effects of emotion regulation strategies for improving pain tolerance, potentially due to the process of reducing the level of negative affect generated by the experimental task. All of this evidence supports that the ability to control the perception of pain requires cognitive strength, and that pain tolerance is closely related to emotional self-control during induced pain.

Moreover, an individual's past experience with pain, the memory of that pain, and the recurrence of pain can lead an individual to anticipate more pain, can impact the amount of fear felt, and can greatly increase pain–avoidance behaviors (Lethem et al., 1983; Turk and Wilson, 2010; Crombez et al., 2012; Vlaeyen and Linton, 2012). According to the fear-avoidance model (or FA model) of pain (Lethem et al., 1983), if an individual experiences acute discomfort and delays the situation by using avoidant behavior, a lack of pain increase reinforces this behavior. Increased vulnerability provides positive feedback to the perceived level of pain, and rewards avoidant behavior for removing unwanted stimuli. If the individual perceives the pain as non-threatening or temporary, he or she feels less anxious and confronts the pain-related situation. In 1993, Waddell et al. developed a Fear-Avoidance Beliefs Questionnaire (FABQ) which showed that fear-avoidance beliefs about physical activities are strongly related to work loss (Waddell et al., 1993).

Thus, the significant decline of pain tolerance in Session 2 for the control group may be attributed to the negative experience of the Cold Pressor Task (CPT) felt in Session 1. However, no such decline was found in the experimental group, possibly suggesting successful self-control against this kind of decline.

Physical Exercise As a Way to Improve Self-Control

Overall, the present findings support previous findings that self-control ability can be improved through physical exercise (Taylor et al., 1985). For instance, Smiley-Oyen found that 10 months of aerobic exercise training significantly improved older adults' (65–79 years-old) performance on the Stroop task (Smiley-Oyen et al., 2008), and a similar study found that 6 months of high intensity aerobic exercise improved women's performance on multiple executive function tests, including the Stroop task (Baker et al., 2010). In comparison to previous studies, the present study helped look for potential benefits of physical exercise beyond measures of baseline cognitive self-control.

In terms of the strength model of self-control, self-control is energized by the same metaphorical resource or strength for which the capacity is limited (Baumeister et al., 1998). After a primary act of self-control, this resource can be temporarily depleted (a state termed *ego depletion*). It is important to note however, that ego depletion is not domain specific, meaning that exerting self-control in one domain (e.g., cognitive control in Stroop task) can have an effect on self-control on seemingly unrelated domains (e.g., emotional regulation in Cold Pressor Task) (Baumeister et al., 1998). For example, a series of studies conducted by Megan Oaten showed that after people exercised self-control through financial monitoring or after forcing themselves to study for extended periods of time (e.g., 2 weeks to 4 months), they showed less depletion after completing an unrelated self-regulatory task (Oaten and Cheng, 2006b, 2007).Thus, improvements gained within one domain may be transferable to another (Berkman et al., 2012). The present findings support that improvement gained from aerobic exercise may help enhance self-control in pain tolerance.

Previous studies provide hints to the effect that physical exercise can have on pain tolerance. A school-based study comprised of 206 Swedish children 8–12 years old, showed that

physically active children had higher fitness levels and reported less pain symptoms than inactive peers (Sollerhed et al., 2013). Similarly, meta-analyses of studies reveal that athletes possess higher pain tolerance compared to normally active controls (Tesarz et al., 2012). However, only one study directly explores the causality between physical exercise and pain tolerance. Jones et al. (2014), found that pain tolerance in healthy individuals increased after 6 weeks of structured aerobic exercise training. However, our results did not show significant improvement of pain tolerance as Jones et al. (2014) did. We in fact found a significant decline of pain tolerance across sessions in the control group but not in the experimental group.

This inconsistence might be attributed to several factors. The first contributor is the different tasks used in the studies. What Jones et al. (2014) tested was baseline self-control (power), but what we tested was stamina of self-control (i.e., pain tolerance after depletion from the Stroop task). There is no such evidence of the effect of exercise on pain tolerance after ego-depletion. Thus, more empirical studies are needed to confirm our findings. Another factor is that the negative experience of pain may cause shorter pain tolerance in CPT, which is discussed above in terms of the fear-avoidance model of pain(Lethem et al., 1983).The last potential factor that may have contributed to the decline of pain tolerance in the control group was the cold weather. The present study was conducted in winter. The training session began in November and ended in December. With the weather getting colder, the subjects in the control group engaged in less physical exercise in their daily lives, which led to a decline in self-control ability. Whatever, the causes of the decline of pain tolerance in the control group, our findings overall supports the positive effect that physical exercise can have on self-control ability.

The underlying mechanism of the positive effect of physical exercise may be related with specific changes in the brain. For example, it has been shown that increased aerobic fitness in childhood is associated with greater dorsal striatum volume, a region that facilitates cognitive control ability (Chaddock et al., 2010). However, research directly testing the mechanism underlying these effects could help answer questions of how long, how frequently, and what kinds of aerobic exercise should be performed in order to achieve optimal effects from physical exercise.

Pain Tolerance and Modulation of Attention

Previous studies have consistently shown that distractors are often good methods for improving pain tolerance in both clinical pain and lab-induced pain in both children and adults. Verhoeven et al. (2011) had 91 undergraduate students randomly assigned to (1) a distraction group, in which an attention-demanding tone-detection task was performed during the CPT, and (2) a control group, in which no distraction task was performed. Results showed that participants in the distraction group reported significantly less pain during the CPT. Swee and Schirmer (2015) provided evidence that even vocalization can help individuals cope with pain, and suggest that motoric processes more so than other processes, contribute to this effect. Jameson et al. (2011) suggested electronic gaming as a pain distraction method for children to improve pain tolerance, because an interactive distraction task (playing a game) includes greater central cognitive processing demands. Similarly, Wohlheiter and Dahlquist (2013) examined 3- to 6-years-old children who underwent three cold-pressor trials: one while receiving no intervention, one while playing a video game (interactive distraction), and one while watching a video game (passive distraction). Their findings suggest that young preschoolers can benefit from interactive distraction to manage acute pain.

In the present study, we found people had longer pain tolerance in CPT II than in CPT I, which may be caused by distraction effects. In CPT II, participants were instructed to complete the Stroop task while their hand was immersed in the cold water bath, having to modulate their attention between the two tasks. Thus, the Stroop task proved to be a good distractor for sensory pain, which may have led to the significant longer pain tolerance in CPT II than in CPT I.

We found a very similar effect of aerobic exercise on pain tolerance in both CPT I and CPT II (though relatively smaller effect size), suggesting that aerobic exercise could also improve self-control ability even in the less attention focused condition.

Implications and Shortages

Successful persistence in the CPT requires efforts and self-control. Pain tolerance can be facilitated by greater self-control abilities, especially in terms of emotional and behavioral self-control. Our results indicate that physical exercise can help train self-control to be less vulnerable to depletion in the pain condition.

The current study had some practical implications. Among various physical sports, running is a traditional form of aerobic exercise and has received widespread popularity across all ages, for it can be easily implemented and requires no special skills. Our results demonstrated that running may serve as a way to reduce people's vulnerability to depletion of self-control. Improved self-control stamina could help one to become more efficient in their daily life by improving the ability to deal with forthcoming affairs that call for self-control. Thus, future research studies are needed to explore physical exercise as a potential treatment for impulsive behavior stemming from compromised self-control, such as that seen in drug abuse, eating disorders, violence, and so on.

Moreover, for populations suffering from chronic pain, aerobic exercise may serve as an approach to help build both physical strength and self-control ability at the same time, helping to improve pain tolerance in daily life (Eccleston et al., 2014).

Despite interesting results, there is much work needed due to various limiting factors. First, the present study suffered from a small sample size. Future studies with larger samples are needed to verify our findings. Second, the participant pool in the current study contained only Chinese female college students. Similar studies with other populations are important in order to better generalize the findings. Third, we were unable to match intervention times for the two groups due to factors such as inclement weather, and participants from the control group completed the assigned exercises more frequently than those in the experimental group. Thus, we could perhaps postulate

that the improvement in stamina found in the experimental group may be magnified if the two groups exercised with similar frequency in a future study. Last, we did not directly investigate the neural mechanisms underlying the effect of physical exercise on emotional and behavioral self-control after ego-depletion. Future research using functional magnetic resonance imaging (fMRI) and/or electroencephalography (EEG) techniques are necessary in order to address this need.

AUTHOR CONTRIBUTIONS

ZZ, Substantial contributions to the conception or design of the work, interpretation of data for the work, revising it critically, Final approval of the version to be published. YL, acquisition, data analysis, interpretation of data, drafting the work. JX, preparation of materials, acquisition, analysis of data, interpretation of data. XH, contributions to the conception or design of the work, contributions to the interpretation, revising, Final approval of the version to be published.

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Positive Psychological Wellbeing Is Required for Online Self-Help Acceptance and Commitment Therapy for Chronic Pain to be Effective

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The web-based delivery of psychosocial interventions is a promising treatment modality for people suffering from chronic pain, and other forms of physical and mental illness. Despite the promising findings of first studies, patients may vary in the benefits they draw from self-managing a full-blown web-based psychosocial treatment. We lack knowledge on moderators and predictors of change during web-based interventions that explain for whom web-based interventions are especially (in)effective. In this study, we primarily explored for which chronic pain patients web-based Acceptance and Commitment Therapy (ACT) was (in)effective during a large three-armed randomized controlled trial. Besides standard demographic, physical and psychosocial factors we focused on positive mental health. Data from 238 heterogeneously diagnosed chronic pain sufferers from the general Dutch population following either web-based ACT ($n = 82$), or one of two control conditions [web-based Expressive Writing (EW; $n = 79$) and Waiting List (WL; $n = 77$)] were analysed. ACT and EW both consisted of nine modules and lasted nine to 12 weeks. Exploratory linear regression analyses were performed using the PROCESS macro in SPSS. Pain interference at 3-month follow-up was predicted from baseline moderator (characteristics that influence the outcome of specific treatments in comparison to other treatments) and predictor (characteristics that influence outcome regardless of treatment) variables. The results showed that none of the demographic or physical characteristics moderated ACT treatment changes compared to both control conditions. The only significant moderator of change compared to both EW and WL was baseline psychological wellbeing, and pain intensity was a moderator of change compared to EW. Furthermore, higher pain interference, depression and anxiety, and also lower levels of emotional well-being predicted higher pain interference in daily life 6 months later. These results suggest that web-based self-help ACT may not be allocated to chronic pain sufferers experiencing low levels of mental resilience resources such as self-acceptance, goals in life, and environmental mastery. Other subgroups are identified that potentially need specific tailoring of (web-based) ACT. Emotional and psychological wellbeing should receive much more attention in subsequent studies on chronic pain and illness.

Keywords: chronic pain, moderator, predictor, psychological wellbeing, Acceptance and Commitment Therapy, web-based, online, resilience

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INTRODUCTION

Chronic pain is a prevalent, disabling and difficult-to-treat condition that affects both individual pain sufferers and society (Breivik et al., 2006). Where biomedical oriented treatment modalities focus on pain removal, psychosocial treatments based on a cognitive behavioral framework try to effectively restore functioning and enhance pain management (Williams et al., 2012). The last decade has seen an expansion in studies exploring *web-based* delivery of psychosocial interventions for chronic pain and an additional, broad range of physical and mental health problem. First review studies indicate that web-based Cognitive Behavioural Therapies (CBT) are effective for chronic pain and other disorders (Cuijpers et al., 2010; Bender et al., 2011). Advantages that are associated with web-based psychosocial interventions are its cost- and time-effectiveness and its ability to reach physically disabled, stigmatized, or isolated patient groups. Furthermore, online interventions enable individuals to follow an intervention at their own pace (Andersson and Cuijpers, 2008). Even minimal improvements during self-help interventions that can be easily disseminated through the Internet to many individuals may contribute to alleviate the general disease burden of chronic pain and illness. Despite the promising findings of first studies, patients may vary in the benefits they draw from self-managing a full-blown web-based psychosocial treatment. At present, however, studies are lacking that specify for whom web-based cognitive behavioral interventions can be more or less profitable (Macea et al., 2010; Bender et al., 2011).

In general, to explore what, how, why and for whom psychosocial treatment does or does not work is a promising pathway to increase the effectiveness of psychosocial interventions for chronic pain and other physical and mental health problems (Kraemer et al., 2002; Morley and Keefe, 2007). Knowledge on moderators of change ('for whom') can inform future allocation of patients to treatment and guide tailoring of interventions to patient characteristics, thereby potentially enhancing both treatment effectiveness and efficiency (Morley et al., 2013). Such knowledge would be especially helpful in the area of chronic pain, as effects of both biomedical and psychosocial interventions are small to moderate and not all patients can be helped effectively at present (Turk et al., 2011; Eccleston et al., 2013). Unfortunately, there is a paucity of knowledge in this area. Factors that have been identified in *face-to-face* CBT for chronic pain to be negatively associated with treatment response include baseline levels of high psychological distress, low perceptions of pain control, high levels of negative thinking (e.g., catastrophizing) toward the pain, and stress (McCracken and Turk, 2002; Turner et al., 2007). No consistent relationships were found in previous CBT-studies between patient outcomes and demographic variables (McCracken and Turk, 2002).

The present study explores moderators (baseline characteristics that interact with treatment to affect outcome) and non-specific predictors (baseline characteristic that do not interact with treatment, but predict outcome regardless of treatment) of treatment change during a large, three-armed randomised controlled trial (RCT) on the efficacy of a guided, self-help web-based program based on Acceptance and Commitment Therapy (ACT) (Hayes et al., 2012; Trompetter et al., 2014). ACT is a distinct form of CBT that teaches pain patients to recognize and abandon unfruitful and narrowing attempts to avoid the pain experience itself and related thoughts and feelings (Hayes et al., 2006). Overall, therapeutic processes that are targeted in ACT – including pain acceptance, cognitive defusion and mindfulness – promote psychological flexibility, the ability to behave in accordance with personal, meaningful values from an open, accepting and present-moment stance toward the pain experience. ACT is an effective treatment for both chronic pain and a broader range of mental and physical health problems (Powers et al., 2009; Veehof et al., 2011; A-Tjak et al., 2015). Outcomes of the RCT generally showed small to moderate effects for the ACT-program Living with Pain compared to two (minimal intervention and waiting-list) control conditions in improving several disability-related processes and outcomes (Trompetter et al., 2014).

Of specific interest is *positive mental health* in addition to standard demographic, physical and psychosocial domain factors in chronic pain and psychosomatic research (Keyes, 2002). Positive mental health is a state of optimal mental functioning that consists of the aspects emotional, psychological and social wellbeing (Keyes, 2002). While emotional wellbeing relates to hedonic aspects of happiness, psychological wellbeing relates to eudemonic aspects of functioning that, for example, include feelings of personal growth and environmental mastery (Ryff, 1989, 2014). Social wellbeing pertains to feelings of social coherence, integration and social contribution (Keyes, 2002). Positive mental health and especially psychological wellbeing is related to resilience, the ability to maintain wellbeing despite life adversities such as enduring pain or to bounce back after adversities (Fava and Tomba, 2009; Ryff et al., 2012). We included a measure of positive mental health in our trial since the focus of ACT on commitment to personal goals that are intrinsically motivated, acceptance and mindfulness, is intrinsically and empirically supportive of increasing an rich, full and engaged life (Fledderus et al., 2012; Kashdan and Ciarrochi, 2013; Bohlmeijer et al., 2015). Also, psychological wellbeing is an underrepresented, but important and independent factor in relation to outcomes such as distress, chronic pain and physical frailty (Ruini et al., 2003; Schleicher et al., 2005; Gale et al., 2014).

Based on previous studies on face-to-face CBT for chronic pain, we predicted that psychosocial domain factors (depression, anxiety and positive mental health), and not physical domain factors (pain intensity, pain disability and pain interference) or demographic characteristics would function as moderators and predictors of change in pain interference in daily life during the RCT.

MATERIALS AND METHODS

Participants and Procedure

The sample for the current study stems from the original sample in the RCT on the effectiveness of web-based ACT (Trompetter et al., 2014). The original RCT protocol was approved by

the Dutch Medical-Ethical Review Board (METC, trial number NL38622.044.11), which operates under the Dutch Central Committee for Research involving human participants (CCMO). All subjects gave written informed consent in accordance with the Declaration of Helsinki. Participants were a heterogeneously diagnosed group of pain sufferers recruited from the general Dutch population through advertisements in Dutch newspapers and online patient platforms. Study inclusion criteria were (a) 18 years or older, (b) momentary pain intensity Numeric Rating Scale (11-point NRS) score > 4, (c) having pain for at least three days per week, (d) for at least 6 months. Exclusion criteria were partly based on the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) and Psychological Inflexibility in Pain scale (PIPS) (Wicksell et al., 2010), and were (a) severe psychological distress (HADS > 24), (b) extremely low levels of psychological inflexibility (PIPS < 24), (c) current participation in another CBT-based treatment, (d) having no internet or e-mail address, (e) reading problems due to insufficient Dutch language skills or illiteracy, and (f) an unwillingness or inability to invest approximately 30 min per day. The primary reason for exclusion prior to randomization was severe psychological distress.

Participants in this study followed either the ACT-condition ($n = 82$) or were allocated to one of both control conditions, being either Expressive Writing (EW) ($n = 79$) or Waiting List (WL) ($n = 77$). EW was included as a control condition to control for general, non-specific effects (i.e., receiving attention from a counselor, working actively to reduce pain-related complaints). Small improvements in EW were expected as a large meta-analysis showed that EW has small effects on physical and mental health outcomes in chronic pain (Frattaroli, 2006). Those allocated to ACT or EW followed a 9-week web-based self-help program. WL-participants were not offered any intervention, but were free to access any other form of treatment. These participants could follow the ACT-intervention 6 months from baseline.

Intervention

Each participant in ACT and EW received weekly minimal guidance and support on a fixed day of the week by trained clinical psychology students. In the ACT-condition, modules mainly consisted of text, metaphors and exercises based on the six ACT-therapeutic processes (pain acceptance/experiential avoidance, cognitive defusion, self-as-context, present-moment awareness, values and committed action) (Hayes et al., 2012). Two extra modules were included that did not explore ACT-processes, but focused on psycho-education regarding chronic pain (first module) and communicating about pain complaints with one's social context (eight' module). Following the first module on psychoeducation, the next four modules primarily explored favorite ways to experiential avoid pain, and explored acceptance of pain as an alternative strategy. Simultaneously, participants explored their values and subsequent goals in different life domains. The following two modules mainly explained and explored the two ACT-processes cognitive defusion and self-as-context, to learn to relate differently to oneself, one's thinking states and one's context. The final module again focused on committed action, and it was explored how one would cope with setbacks and failure in the long term. Participants were encouraged to download new mindfulness exercises weekly (e.g., 'body scan,' 'breathing toward pain' or 'observe your thinking'), and practice mindfulness daily for 10–15 min. Participants were advised to spend approximately 30 min each day, or 3 h per week in total, on the course. In EW, the general assignment was to emotionally disclose (write) on a regular basis about experiences and emotions either related to chronic pain or to other situations. These emotions could be either negative or positive, depending on specific weekly assignments. Additionally, each module started with some short psycho-education about emotions and emotion regulation. Participants were asked to invest 2 h or more per week, or 15 min per day on the course. In both ACT and EW, participants could keep an online diary. The average time-investment was self-assessed at multiple times throughout the course. 48% and 47% of participants in ACT and EW respectively adhered to the intervention, which meant they both completed the intervention and invested the advised amount of time interacting with the course [*adherence* is the extent to which individuals experience the content of an intervention. This is different from *drop-out,* which refers to the number of people who did not follow the research protocol (i.e., did not fill in questionnaires; Kelders et al., 2012)].

Measures

The primary outcome was measured at 3-month follow-up, 6 months after baseline assessment (T1). All other measures functioned as possible moderators/predictors of change and were assessed at baseline, prior to randomization (T0).

Outcome

Pain interference in daily life

The Multidimensional Pain Inventory (MPI), subscale *pain interference* consists of nine items and measures the degree to which pain interferes with different life domains, such as work, household work and social activities (Kerns et al., 1985). Higher scores indicate more pain interference (range 0–54). Internal consistency in the present study was at baseline $\alpha = 0.87$, at T1 $\alpha = 0.89$.

Moderator/Predictors

Demographic variables

Demographic variables that were assessed as possible moderators/predictors were age, gender, educational level, employment status, and duration of pain complaints.

Pain intensity

Pain intensity was measured with a 11-point Numeric Rating Scale (NRS), ranging from 'no pain' (0) to 'pain as bad as you can imagine' (10). Item formulation and response categories were consistent with IMMPACT recommendations on core outcome measures in chronic pain research (Dworkin et al., 2005).

Pain disability

The Pain Disability Index (PDI) (Pollard, 1984) consists of seven items and assesses the degree to which chronic pain disables a

person from performing daily activities, such as work, household responsibilities and recreational activities. Total scores range from 7 to 70, with higher scores indicating more pain disability. Internal consistency in the current study at baseline was $\alpha = 0.82$.

Psychological distress

The HADS (Zigmond and Snaith, 1983) consists of 14 items. The scale measures the presence and severity of symptoms regarding anxiety (seven items) and depression (seven items). In this study the both subscales were used, with sum scores for each scale ranging from 0–21. Higher scores indicate more anxiety or depression. Internal consistency in the present study at baseline was at $\alpha = 0.73$ (anxiety) and $\alpha = 0.79$ (depression).

Positive mental health

The Mental Health Continuum-Short Form (MHC-SF) (Keyes, 2002) consists of 14 items that measure three dimensions of positive mental health. Participants rate their frequency of feelings over the past month. Dimensions are *emotional wellbeing*, pertaining to positive feelings, happiness and satisfaction with life (three items) (score range 3–18); *psychological wellbeing*, pertaining to aspects of positive psychological functioning, such as autonomy, environmental mastery and personal growth (six items) (score range 6–36); and *social wellbeing*, pertaining to feelings of positive functioning in community life (five items) (score range 5–30). The MHC items did not show differential item functioning in a sample of individuals suffering from physical diseases compared to a healthy subsample (Lamers et al., 2012b). The total scale and all subscales are analyzed separately in this study. In general, higher scores indicate more wellbeing. Internal consistency in the current study at baseline was $\alpha = 0.91$ (total MHC), $\alpha = 0.85$ (emotional wellbeing), $\alpha = 0.82$ (psychological wellbeing) and $\alpha = 0.73$ (social wellbeing).

Statistical Analyses

There were no missing data at T0. Missing data at T1 (29.8%) were imputed using the Expectation Maximization (EM) Algorithm (Dempster et al., 1977). Prior to main analyses, independent sample *t*-tests and χ^2-tests were applied to determine if there were significant differences in all potential moderator/predictor variables at T0 between ACT and both control conditions.

In performing exploratory analyses, we followed steps taken by Turner et al. (2007) in a well-regarded study on moderators and predictors of change during CBT for chronic pain (Morley and Keefe, 2007). Pain interference in daily life at 3-month follow-up, as measured with the MPI interference subscale, was used as indicator of treatment effect. To determine if selected moderator/predictor variables functioned as moderators or predictors of change in MPI interference, linear regression models were applied using the PROCESS macro for SPSS (Hayes, 2013). All tests were two-tailed. Thirteen moderator/predictor variables were assessed, including age, gender, educational level, employment status, pain duration, pain intensity (NRS), pain disability (PDI), pain interference (MPI subscale), depression (HADS), anxiety (HADS), and emotional, psychological and social well-being (MHC). For demographic moderators/predictors, dummy variables were created for gender (male = 1, female = 0), employment status (working full/parttime = 1, other = 0), and duration of pain complaints (>5 years = 1, <5 years = 0). Educational level was divided into three groups (low, medium and high). During the analyses, each potential moderator/predictor was grand mean centered to reduce possible scaling problems and multicollinearity (Aiken and West, 1991). In the regression models, the MPI-interference score at T1 was entered as the dependent variable. The dummy variable representing Treatment (web-based ACT = 1, WL = 0 or EW = 0), the centered potential moderator/predictor, and the Treatment by centered moderator/predictor interaction variable were entered as independent variables. To control for baseline variation in outcome scores, the MPI interference score at T0 was added as independent variable to the model in the same step as all other independent variables. Analyses were performed separately for ACT compared to EW, and ACT compared to WL.

In the presence of a significant interaction effect the variable in concern was interpreted as being a moderator of change. In case the interaction effect was not significant but the main effect for the variable was, a variable was interpreted as being a predictor of change. Moderators are baseline characteristics that interact with treatment to affect outcome, meaning that patient improvement depends on the value on the moderator variable. When a variable is not a moderator, it is possibly a non-specific predictor of change. Non-specific predictors do not interact with treatment but predict later scores on outcomes for all participants. Both moderators and predictors of change should be measured prior to treatment randomization (Turner et al., 2007; Pincus et al., 2011). Overall, significance of the moderators and predictors was interpreted at $p < 0.05$. Although the number of tests performed could call for a restriction on the borderline *p*-value, the *p*-value was not adjusted as such given the exploratory nature of this study. In case of significant interactions, simple slopes for mean, −1 and +1 standard deviation moderator values as calculated in PROCESS were interpreted, as were outcomes of the Johnson-Neyman technique (Johnson and Fay, 1950; Hayes, 2013). This latter method derives a zone of significance, thereby identifying exact cut-off values of the moderator for which web-based ACT was (not) more effective compared to control conditions.

RESULTS

Outcomes of independent sample *t*-tests and χ^2-tests revealed there were no significant differences at T0 between ACT and both control conditions on all included potential moderator/predictor variables, although the difference between ACT and WL in the percentage of people working full/part-time reached marginal significance, with ACT participants working full/part-time more often than WL participants [$\chi^2(1) = 3.439$, $p = 0.064$].

A large proportion of participants were highly educated (44.1%), female (76.0%) pain sufferers with an average age of 52.80 years ($SD = 12.37$). More than half of the participants suffered from pain complaints for more than 5 years (63.0%), and almost all participants (93%) reported pain on a daily basis. Most prevalent diagnoses were fibromyalgia (20.2%), back complaints

TABLE 1 | Baseline characteristics of participants in ACT and both control conditions.

	ACT ($n = 82$)	EW ($n = 79$)	WL ($n = 77$)
Demographic characteristics			
Mean age, years (SD)	52.9 (13.3)	52.3 (11.8)	53.2 (12.0)
Female gender (%)	76.8	75.9	75.3
Education (%)			
Low	19.5	19.0	22.1
Intermediate	35.4	36.7	35.0
High	45.1	44.3	42.9
Working full-/part-time (%)	42.7	48.1	28.6
Pain duration >5 years (%)	58.5	69.6	61.0
Diagnosis			
None	14.6	17.7	19.5
Back complaints	9.8	13.9	14.3
Fibromyalgia	15.9	29.1	15.6
Joint complaints	8.5	7.6	9.1
Rheumatic disease	9.8	7.6	11.7
Neuropathic complaints	11.0	6.3	9.1
Other	30.5	20.8	20.7
Physical domain measures			
Mean MPI Interference (SD)	32.3 (9.8)	32.2 (9.8)	33.3 (9.8)
Mean Pain intensity (SD)	6.3 (1.8)	6.1 (1.6)	6.2 (1.6)
Mean Pain Disability (SD)	36.0 (12.7)	36.4 (12.0)	36.1 (12.7)
Psychosocial domain measures			
Mean HADS depression (SD)	6.1 (3.5)	6.5 (3.5)	6.1 (3.2)
Mean HADS anxiety (SD)	7.2 (3.1)	7.5 (3.2)	6.9 (3.4)
Mean MHC emotional (SD)	12.4 (3.1)	12.1 (2.9)	11.1 (3.2)
Mean MHC psychological (SD)	23.9 (5.7)	23.9 (5.8)	22.8 (6.4)
Mean MHC social (SD)	16.2 (4.9)	16.2 (5.1)	16.0 (4.6)

ACT, Acceptance and Commitment Therapy; EW, Expressive Writing; WL, Waiting List; MPI, Multidimensional Pain Inventory; HADS, Hospital Anxiety and Depression Scale; PDI, Pain Disability Index; MHC, Mental Health Continuum.

(12.7%), rheumatic diseases (9.7%), neuropathic complaints (8.8%), and other joint complaints (8.4%). An overview of demographic characteristics and baseline scores on all measures can be found in **Table 1**.

Moderators of Changes in MPI Interference

Outcomes of interaction tests for all 13 potential moderators can be found in **Table 2**. No significant interaction effects on MPI interference at 3-month follow-up were present for any of the demographic variables. Of the remaining measures, the only interaction effect that reached significance compared to both control conditions was MHC Psychological wellbeing (vs. EW: $b = -0.424$, $p = 0.035$; vs. WL: $b = -0.419$, $p = 0.022$). A visual representation of the outcomes of simple slope analyses for mean scores, and scores one standard deviation below and above the mean value, are displayed in **Figure 1**. Web-based ACT was no more effective than WL in changing MPI interference for those scoring one standard deviation below mean (effect MPI interference T1 ACT vs. WL = 0.323, $p = 0.837$). More specifically, an interpretation of the output of the Johnson-Neyman technique showed that the MHC Psychological wellbeing cut-off score for reaching significant effects of ACT compared to WL was 23.57. ACT was more effective in changing the primary outcome MPI interference than WL for those in the highest 51% of MHC scores. Compared to control condition EW, the MHC Psychological Wellbeing cut-off score for reaching significant effects of ACT was 16.97. ACT was more effective in changing MPI interference than EW for those in the highest 88.2% of MHC scores.

None of the measures representing the physical domain, being pain intensity, PDI and MPI interference, showed significant interaction effects compared to WL. However, a significant moderation effect existed for ACT compared to EW alone on pain intensity (NRS) ($b = -2.018$, $p = 0.003$). An inspection of the output of the Johnson-Neyman technique indicated that ACT was more effective than EW for those individuals having the highest 85.1% scores on pain intensity (NRS) at baseline. The corresponding cut-off score was 4.61.

Predictors of Change in MPI Interference

Outcomes regarding non-specific predictor analyses can be found in **Table 3**. As was the case for moderator analyses, none of the demographic characteristics were significantly associated with MPI interference at 3-month follow-up, and neither were baseline PDI and pain intensity. T0 measures that were significantly associated with MPI interference 6 months later were similar for both sets of analyses (ACT compared to EW and ACT compared to WL). Significant predictors were MPI interference (vs. EW: $b = 0.732$, $p < 0.001$, vs. WL: $b = 0.760$, $p < 0.001$), HADS depression (vs. EW: $b = 0.632$, $p < 0.001$, vs. WL: $b = 0.628$, $p < 0.001$), HADS anxiety (vs. EW: $b = 0.806$, $p < 0.001$, vs. WL: $b = 0.529$, $p = 0.013$) and MHC Emotional wellbeing (vs. EW: $b = -0.554$, $p = 0.007$, vs. WL: $b = -0.627$, $p = 0.001$).

DISCUSSION

The present study explored moderators and predictors of treatment change during a previously evaluated RCT on the efficacy of a guided, self-help web-based program based on ACT in chronic pain patients (Trompetter et al., 2014). Compared to both control conditions neither demographic nor physical domain factors prospectively predicted or moderated pain interference in daily life after 6 months. Despite variable findings in individual studies, this is in line with knowledge on predictors of face-to-face CBT treatment effects (McCracken and Turk, 2002). Importantly, the only existing moderator compared to both control conditions was psychological wellbeing as a central aspect of positive mental health and optimal human functioning (Keyes, 2002).

Emotional and psychological wellbeing are highly relevant factors that function independent from vulnerabilities and distress in predicting mental and physical illness (Ruini et al., 2003; Steptoe et al., 2009; Boehm and Kubzansky, 2012; Lamers et al., 2012a). This study suggests that psychological wellbeing is also relevant for allocation of treatment. Self-managing a challenging intervention that requires the transformation

TABLE 2 | Interaction effect outcomes of linear regression models to assess possible moderators of change in MPI interference.

	ACT vs. EW			ACT vs. WL		
	b	95% CI	*p*-value	*b*	95% CI	*p*-value
Demographic characteristics						
Age	−0.152	−0.37; 0.07	0.172	0.804	−4.56; 6.18	0.768
Gender	−2.422	−9.10; 4.25	0.475	−0.003	−0.18; 0.18	0.978
Educational level	2.19	−1.39; 5.77	0.228	−0.110	−3.07; 2.85	0.941
Employment status	3.018	−2.00; 8.04	0.237	−2.788	−7.59; 2.02	0.253
Pain duration	0.878	−3.85; 6.61	0.763	2.289	−2.35; 6.93	0.332
Physical domain measures						
Pain intensity	−2.018	−3.36; −0.68	0.003	−0.371	−1.74; 1.00	0.594
Pain disability (PDI)	−0.179	−0.37; 0.02	0.073	−0.161	−0.34; 0.01	0.071
Pain interference (MPI)	−0.077	−0.37; 0.22	0.606	−0.135	−0.37; 0.10	0.251
Psychosocial domain measures						
Depression (HADS)	0.263	−0.40; 0.92	0.431	0.169	−0.46; 0.80	0.599
Anxiety (HADS)	0.254	−0.51; 1.01	0.510	0.732	−0.04; 1.50	0.063
Emotional wellbeing (MHC)	−0.712	−1.50; 0.07	0.074	−0.525	−1.22; 0.17	0.138
Psychological wellbeing (MHC)	−0.424	−0.82;-0.03	0.035	−0.419	−0.78; −0.06	0.022
Social wellbeing (MHC)	−0.460	−0.99; 0.07	0.128	−0.451	−0.95; 0.05	0.078

95% CI, 95% confidence interval.

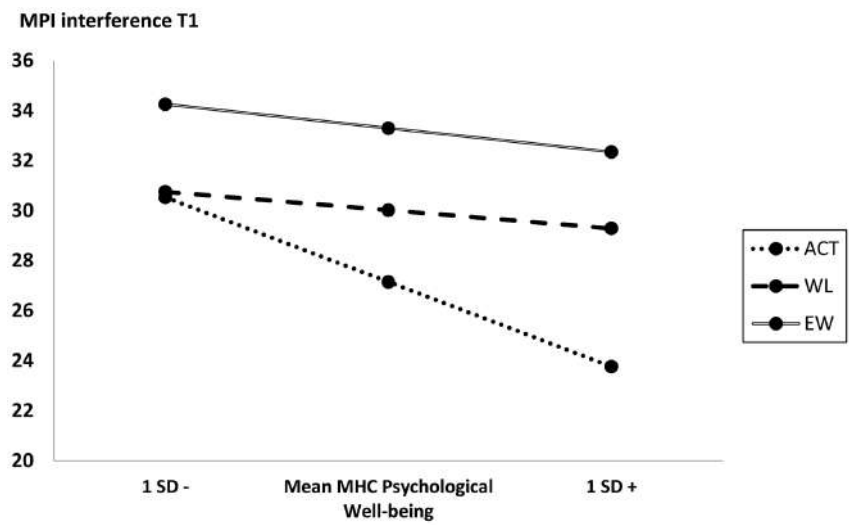

FIGURE 1 | Pain interference outcome scores at different baseline values of moderator MHC Psychological Wellbeing for ACT compared to both control conditions.

of cognitive-behavioral patterns that narrowed effective living for a prolonged period of time, could simply be too much for individuals lacking psychological resources. This process could evolve, for example, through a lack of feelings of environmental mastery, personal growth and positive social relations. Among other things, these processes relate to the feeling that oneself is able to develop new attitudes and behaviors, a sense of control over the external world, and the feeling that one is supported by significant others (Ryff, 1989, 2014; Fava and Tomba, 2009). Practically, these results indicate that web-based ACT should perhaps not be allocated to those experiencing low positive psychological functioning at baseline. A primary task for future web-based trials is to examine if aspects of resilience and psychological wellbeing recurrently function as moderators of treatment change for pain and other physical and mental health problems.

The design of psychosocial interventions that aim at enhancing resilience and psychological wellbeing provides interesting and perhaps necessary treatment opportunities for chronic pain and illness. Wellbeing Therapy (WBT) is a primary example of an effective, positive intervention designed explicitly to complement CBT that improves psychological wellbeing and prevents relapse for depression and anxiety

TABLE 3 | Main effect outcomes of linear regression models to assess possible predictors of change in MPI interference.

	ACT vs. EW			ACT vs. WL		
	b	95% CI	*p*-value	*b*	95% CI	*p*-value
Demographic characteristics						
Age	0.012	−0.10; 0.12	0.830	−0.061	−0.15; 0.03	0.183
Gender	2.997	−0.34; 6.33	0.078	1.412	−1.27; 4.11	0.299
Educational level	−1.054	−2.85; 0.74	0.247	0.084	−1.40; 1.56	0.911
Employment status	−0.928	−3.53; 1.67	0.482	2.006	−0.383; 4.39	0.099
Pain duration	0.369	−2.45; 3.19	0.796	−0.332	−2.65; 1.99	0.778
Physical domain measures						
Pain intensity	0.344	−0.44; 1.13	0.388	−0.570	−1.30; 0.15	0.118
Pain disability (PDI)	0.009	−0.20; 0.22	0.931	−0.054	−0.18; 0.08	0.420
Pain interference (MPI)	0.732	0.59; 0.88	< 0.001	0.760	0.64; 0.88	< 0.001
Psychosocial domain measures						
Depression (HADS)	0.632	0.22; 1.04	0.003	0.628	0.27; 0.99	0.001
Anxiety (HADS)	0.806	0.37; 1.25	< 0.001	0.529	0.11; 0.95	0.013
Emotional wellbeing (MHC)	−0.554	−0.96; 0.15	0.007	−0.627	−0.99; −0.26	0.001
Psychological wellbeing (MHC)	−0.384	−0.59; −0.18	< 0.001	−0.377	−0.57; −0.19	< 0.001
Social wellbeing (MHC)	−0.205	−0.47; 0.06	0.128	−0.197	−0.44; 0.05	0.117

95% CI, 95% confidence interval.

disorders (Fava et al., 1998, 2004, 2005). Such an increase of psychological wellbeing to be able to bounce back from highly frequent and intense moments of distress can be highly relevant for those suffering from chronic pain and illness. We suggest future study explores the efficacy of the parallel application of resilience-based treatments such as WBT in addition to standard psychosocial treatments aimed at reducing pain-related complaints. The increase of effective adaptation and normal functioning in the face of chronic pain might help to overcome the modest effects of current chronic pain treatment (Turk et al., 2011; Eccleston et al., 2013).

Two other findings deserve exploration. First, a further interpretation of moderator findings indicates that EW might not work so well when high in pain intensity. This explains outcomes from a range of studies indicating that EW has mixed and at best, modest, benefits for people suffering from chronic pain (e.g., Lumley et al., 2013), while it seems more effective for mild and major depression (e.g., Gortner et al., 2006). Emotional disclosure can be an unsettling experience that can instigate more pain and negative mood in those suffering from chronic pain. Although not the primary target of our study, these findings can possible fuel further study on EW in chronic pain. Additionally, several non-specific predictor of change were identified. Higher baseline levels of depression, anxiety and pain interference in daily life, and lower levels of emotional wellbeing, were prospectively and generically related to higher levels of pain interference. Practically, this knowledge can be used to further explore if specific tailoring of web-based ACT and other web-based interventions toward these characteristics is helpful. Applying more intensive therapist guidance and monitoring for specific individuals are examples of tailoring opportunities. Also, the application of persuasive technology in developing web-based interventions offers interesting future venues for the future (Kelders et al., 2012).

An important limitation to this study is that the RCT protocol of this study was not powered *a priori* for the application of moderator analyses. Therefore, analyses were *post-hoc* and exploratory, and should be interpreted accordingly. It might be that the number of participants available to perform moderator analyses was not sufficient to indicate other potential relevant moderators of change in addition the moderators we identified. Nevertheless, our study pertains to methodological requirements of exploratory moderators studies (Turner et al., 2007; Pincus et al., 2011), and highlighted several interesting outcomes. Another limitation is that we produced specific cut-off scores to exemplify for whom self-help ACT seems specifically (in)effective. This is the first efficacy trial to produce cut-off scores, which are therefore not readily transferable to clinical practice. However, we believe that the production of our cut-off scores is one step forward to translating scientific output into useful applications for practice.

Overall, this study was the first to assess moderators and predictors of change during web-based psychosocial treatment for chronic pain. This resulted in relevant insights on the future allocation to pain sufferers of the 'Living with Pain' program in specific, and other web-based psychosocial interventions for pain and the broader range of physical and mental health disorders in general. Illuminating theoretical insights were gathered regarding ACT theory (Hayes et al., 2012) and findings revealed that, broadly, moderators of change for web-based ACT treatment seem to follow similar patterns as in face-to-face CBT. We hope that future studies use these

outcomes as a springboard for further study. Of all topics discussed, a focus on psychological wellbeing and resilience seem most promising to further increase effective and efficient intervention for chronic pain and illness in the future.

AUTHOR CONTRIBUTIONS

HT designed the study, performed acquisition, analysis and interpretation of the data, and drafted the manuscript. EB was involved in the conception of the study, data interpretation and writing. SL contributed to data interpretation and writing of the manuscript. KS was responsible for conception of the study, supervised acquisition and analysis of data, and contributed to data interpretation and writing of the manuscript. All authors contributed to critical revisions of the manuscript and approved the final version of the manuscript.

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REVIEW
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Psychological Treatments and Psychotherapies in the Neurorehabilitation of Pain: Evidences and Recommendations from the Italian Consensus Conference on Pain in Neurorehabilitation

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Background: It is increasingly recognized that treating pain is crucial for effective care within neurological rehabilitation in the setting of the neurological rehabilitation. The Italian Consensus Conference on Pain in Neurorehabilitation was constituted with the purpose identifying best practices for us in this context. Along with drug therapies and physical interventions, psychological treatments have been proven to be some of the most valuable tools that can be used within a multidisciplinary approach for fostering a reduction in pain intensity. However, there is a need to elucidate what forms of psychotherapy could be effectively matched with the specific pathologies that are typically addressed by neurorehabilitation teams.

Objectives: To extensively assess the available evidence which supports the use of psychological therapies for pain reduction in neurological diseases.

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Methods: A systematic review of the studies evaluating the effect of psychotherapies on pain intensity in neurological disorders was performed through an electronic search using PUBMED, EMBASE, and the Cochrane Database of Systematic Reviews. Based on the level of evidence of the included studies, recommendations were outlined separately for the different conditions.

Results: The literature search yielded 2352 results and the final database included 400 articles. The overall strength of the recommendations was medium/low. The different forms of psychological interventions, including Cognitive—Behavioral Therapy, cognitive or behavioral techniques, Mindfulness, hypnosis, Acceptance and Commitment Therapy (ACT), Brief Interpersonal Therapy, virtual reality interventions, various forms of biofeedback and mirror therapy were found to be effective for pain reduction in pathologies such as musculoskeletal pain, fibromyalgia, Complex Regional Pain Syndrome, Central Post—Stroke pain, Phantom Limb Pain, pain secondary to Spinal Cord Injury, multiple sclerosis and other debilitating syndromes, diabetic neuropathy, Medically Unexplained Symptoms, migraine and headache.

Conclusions: Psychological interventions and psychotherapies are safe and effective treatments that can be used within an integrated approach for patients undergoing neurological rehabilitation for pain. The different interventions can be specifically selected depending on the disease being treated. A table of evidence and recommendations from the Italian Consensus Conference on Pain in Neurorehabilitation is also provided in the final part of the paper.

Keywords: psychological treatments, psychotherapy, neurological rehabilitation, chronic pain, pain, clinical psychology, health psychology

INTRODUCTION

Pain is frequent in the setting of neurorehabilitation. Most patients undergoing rehabilitation for neurological diseases complain of pain. Both pain and side effects of the drugs used to provide relief from pain from pain may interfere or have a negative effect within the rehabilitation process (Gallagher, 2005; Pongparadee et al., 2012; Singh et al., 2013; Desai et al., 2015). Moreover, pharmacological therapies are effective only in a minority of patients with neuropathic pain (NP) or pain associated with neurological conditions. To date, there are no specific guidelines on the treatment of pain in neurorehabilitation. The Italian Consensus Conference on Pain in Neurorehabilitation (ICCPN) was established in October 2012 and aims to collect and review the evidence and to offer updated conclusions on the treatment of pain in this setting. The ICCPN is composed of a multidisciplinary board involving physicians, psychologists, physiotherapists and other medical and clinical experts. An effective pain treatment in the neurorehabilitation setting requires the contribution of all these specialists as it is now clear that biological and psychological aspects influence each other in a complex way to generate, maintain and modify the patient's experience of pain (Castelnuovo, 2010a,b, 2013; Chang et al., 2014; Gallien et al., 2014; Hussain and Erdek, 2014; Simons et al., 2014; Zheng et al., 2014; Cragg et al., 2015; Durand et al., 2015; Allegri et al., 2016). Psychological therapies play an important role in the multidisciplinary treatment of pain in the neurorehabilitation setting because of their efficacy and the general absence of side effects. The experience of pain, in particular when chronic, is often associated with a general discomfort that can foster conditions of anxiety, depression and insomnia, consistently affecting the quality of life of the patient. Psychotherapies, through different mechanisms, act on three levels:

- treatment of comorbid conditions (e.g., depression and anxiety);
- improvement in psychological issues that, if not treated, can contribute by maintaining the painful condition;
- reduction in perceived pain through activation of descending inhibitory control systems.

These three aspects are strongly interrelated. The painful experience is often worsened by maladaptive changes in physiological systems, such as the sleep—wake processes and the stress reaction systems, and in psychological processes, such as cognition, mood, and motivation, consequently affecting the behavior of the patient (Wiech and Tracey, 2013; Simons et al., 2014; Tamburin et al., 2014). Conversely, the different forms of psychological interventions may have positive effects on these domains, both triggering a readjustment of the physiological processes (e.g., biofeedback and virtual reality interventions) and\or tackling maladaptive thoughts and attitudes about pain,

and\or leading to new pain coping strategies (Turk et al., 2010; Sturgeon, 2014).

It should be noted that psychological treatments in general can lead to a mild or moderate reduction in pain intensity. That is a significant result, as different pain diseases are difficult to treat with drugs and because neuropathic pain responds to the current pharmacological therapies at most in 30–40% of cases (Magrinelli et al., 2013). Nevertheless, drug therapies and non-drug therapies should not be considered as mutually exclusive: different treatments might be integrated with each other and the simultaneous action on different aspects of the disease, conducted by professionals belonging to different disciplines, ensures greater effectiveness of care (Guzman et al., 2006; Turk et al., 2010).

The ICCPN systematically reviewed the evidence regarding the role of psychotherapy in the neurorehabilitation setting. A search of all the research reports, systematic reviews or meta-analyses which evaluated psychological therapies, addressed neurological conditions and considered pain as an outcome was performed in PUBMED, EMBASE, and the Cochrane Database of Systematic Reviews. Accordingly, keywords included "pain," "neurological diseases" the names of specific neurological conditions, "psychological therapies" the names of specific psychotherapies (see **Box 1** for search strings and **Box 2** for the main psychotherapies considered). The presence of an evaluation of at least one psychological treatment for pain intensity in at least one neurological condition was also used as the inclusion criterion in the subsequent steps. The search was conducted on October 2013 and yielded 2038 articles, two updates were then performed on July 2014 and January 2015 restricting the results to the 2013–2014 period, yielding respectively 225 and 89 additional articles. The selected research reports were then assessed on whether they met the inclusion criterion examining their abstract or, if needed, their full text. During this phase their bibliographies were scanned and other relevant articles were included. The final database was composed of 400 articles. The studies were rated good, fair, or poor quality following a checklist specifically built to assess the number of subjects included, the dropout rate, the risk of bias (i.e., assessment of potential confounders) and the presence of blinding procedures. Reviews and meta-analyses were rated according to the comprehensiveness of the literature search and the assessment of the risk of bias. The level of evidence was then assigned to each article following an adaptation of the SIGN grading system (Harbour and Miller, 2001; **Table 1**) and the recommendations were formulated accordingly (**Table 2**), considering pain intensity reduction as the only outcome.

EVIDENCES AND DISCUSSION

The analysis of collected data suggests that psychological therapies are highly indicated both for the treatment of painful conditions and for the treatment of pain related to several neurological diseases (**Table 3**). The reviews and meta-analyses conducted to evaluate the effectiveness of different forms of psychotherapy across several disorders, albeit with different levels of experimental evidence, confirmed that psychological interventions can improve the experience of patients, both in adults (Raine et al., 2002; Astin et al., 2003; Williams et al., 2012) and in children and adolescents (Eccleston et al., 2014; Fisher et al., 2014). Similar results were reported by the reviews and meta-analyses that evaluated the effect of psychotherapy as addressed to the treatment of specific pain disorders such as low back pain (Nielson and Weir, 2001; Chou and Huffman, 2007; Hoffman et al., 2007), fibromyalgia (Lami et al., 2013), tension-type Headache (TTH) and migraine (Andrasik, 2007), pain associated with rheumatoid arthritis (Astin et al., 2002; Knittle et al., 2010), chronic abdominal pain in adolescents (Sprenger et al., 2011), and chronic orofacial pain (Aggarwal et al., 2011), although in the latter instance the authors indicate a high risk of biases in their conclusions. The study on the impact of the different forms of psychotherapy on phantom limb pain is also promising (Moura et al., 2012; Niraj and Niraj, 2014) although, in this case, more research is needed to validate the effects.

A number of studies evaluated the effects of psychological therapies for chronic pain, grouping together under this category various forms of persistent pain with heterogeneous pathophysiology, including musculoskeletal nociceptive pain, pain secondary to osteoarthritis or rheumatoid arthritis, fibromyalgia, chronic headache, and migraine.

For these conditions the following approaches are recommended:

- *Mindfulness* interventions (Grade of recommendation: A) (Grossman et al., 2004; Gardner-Nix et al., 2008; Teixeira, 2008; Rosenzweig et al., 2010; Chiesa and Serretti, 2011; Veehof et al., 2011; Wong et al., 2011; Lakhan and Schofield, 2013)
- Cognitive Behavioral Therapy (CBT), both in individual setting (Grade of recommendation: B) (McCarberg and Wolf, 1999; Morley et al., 1999; Lunde et al., 2009), group setting (Grade of recommendation: B) (Moore and Chaney, 1985; Ersek et al., 2003; Elomaa et al., 2009; Thorn et al., 2011), and internet—based, both for adults (Grade of recommendation: B) (Macea et al., 2010; Ruehlman et al., 2012; Nevedal et al., 2013), and for pediatric patients (Grade of recommendation: B) (Hicks et al., 2006; Palermo et al., 2009).
- Hypnotic therapies: systematic reviews (Hawkins, 2001; Elkins et al., 2007), while stressing that there are many methodologically weak studies in literature, support their analgesic power, and this effect has been confirmed by a meta-analysis (Montgomery et al., 2000) (Grade of recommendation: B).
- Virtual reality: VR-based distraction interventions have been used in acute pain management for over a decade and a systematic review suggests its use for clinicians who work with a variety of pain problems (Malloy and Milling, 2010). While sense of presence influences the effectiveness of VR as a distraction tool, anxiety as well as positive emotions directly affect the experience of pain (Triberti et al., 2014). However the use of VR with chronic pain is still in its infancy and only a few controlled trials are available (Hua et al., 2015; Roosink et al., 2015) (Grade of recommendation: D).
- The techniques of self-management for chronic have been evaluated by a single randomized controlled trial

(Kroenke et al., 2009) and, therefore, they are still to be assessed extensively. Also Acceptance and Commitment Therapy (ACT), an extension of CBT (Vowles et al., 2014), cannot be recommended for the treatment of chronic pain. Indeed, not all of the studies published so far have found empirical evidence to support the effectiveness of specific psychological therapies on pain intensity, when conducted in individual setting, group setting, or administered via computer (Vowles and McCracken, 2008; Wicksell et al., 2009; Thorsell et al., 2011; Wetherell et al., 2011; Buhrman et al., 2013; McCracken et al., 2013).

BOX 1 | Search strings.

Pubmed:	Embase:	Cochrane database of systematic reviews:
(PDN OR "neuropathy" OR "brain injury" OR "multiple sclerosis" OR stroke OR "cerebral palsy" OR "post-polio syndrome" OR parkinson OR guillain-barre OR "nervous system diseases"[MeSH]) AND (rehabilitation* OR neurorehabilitation OR therapy) AND pain[Title/abstract] AND (psychotherapy[title/abstract] OR "cognitive therapy"[title/abstract] OR "group therapy"[Title/abstract] OR "family therapy"[Title/abstract] OR mindfulness[Title/abstract] OR biofeedback[Title/abstract] OR hypnosis[title/abstract] OR "cognitive-behavioral"[title/abstract] OR "psychodynamic"[title/abstract] OR "brief therapy"[title/abstract] OR "autogenic training"[title/abstract] OR "psychological treatment*"[title/abstract] OR "virtual reality"[title/abstract]) AND (trial OR review OR RCT OR "case reports"[publication type] OR "clinical trial"[publication type] OR "comparative study"[publication type] OR "meta-analysis"[publication type] OR "cohort study*" OR "case-control" OR "efficacy" OR "pain reduction" OR "pain management" OR "panel study")	neurologic disease'/exp OR 'neurologic disease' AND pain:ab,ti AND (psychotherapy:ab,ti OR 'cognitive therapy':ab,ti OR 'behavioral therapy':ab,ti OR 'cognitive-behavioral':ab,ti OR mindfulness:ab,ti OR hypnosis:ab,ti OR 'brief therapy':ab,ti OR 'psychodynamic therapy':ab,ti OR 'acceptance therapy':ab,ti OR 'autogenic training':ab,ti OR biofeedback:ab,ti OR 'virtual reality':ab,ti OR 'psychological treatment':ab,ti)	#1: MeSH descriptor: [Nervous System Diseases]; #2: pain and (psychotherapy or "cognitive therapy" or "behavioral therapy" or "cognitive-behavioral therapy" or "hypnosis" or biofeedback or "psychodinamic" or "brief therapy" or "acceptance therapy" or "family therapy" or "virtual reality") #3: #1 and #2

BOX 2 | Definitions of the main psychotherapeutic approaches reported in the article (using common and popular sources such as wikipedia and other informative websites - january 2016).

Psychological interventions: actions performed to bring about change in people. A wide range of intervention strategies exist and they are directed toward various types of issues. Most generally, it means any activities used to modify behavior, emotional state, or feelings. Psychological interventions have many different applications and the most common use is for the treatment of mental disorders, most commonly using psychotherapy.

Psychotherapy: psychotherapy is the use of psychological methods, particularly when based on regular personal interaction, to help a person change and overcome problems in desired ways. Psychotherapy aims to increase each individual's well-being and mental health, to resolve or mitigate troublesome behaviors, beliefs, compulsions, thoughts, or emotions, and to improve relationships and social functioning.

Acceptance and Commitment Therapy (ACT): a type of psychological intervention that focuses on the development of psychological flexibility, or the ability to contact the present moment and accept negative thoughts without judgment.

Biofeedback intervention: a treatment technique in which people are trained to improve their health by using signals from their own bodies.

Cognitive Behavioral Therapy (CBT): a broad range of psychotherapies that aim to help clients overcome dysfunctional thought patterns and behavioral patterns.

Eye Movement Desensitization and Reprocessing therapy (EMDR): a psychotherapy developed by Francine Shapiro that reduces the long-lasting effects of distressing memories by developing more adaptive coping mechanisms.

Hypnosis-Hypnotic therapies: a form of psychotherapy used to create subconscious change in a patient in the form of new responses, thoughts, attitudes, behaviors or feelings.

Mindfulness based interventions: programs developed by Jon Kabat-Zinn that include mindfulness meditation and yoga. They are based on the concept of mindfulness, or being fully engaged in the present moment rather than worrying about past or future events, an ancient concept in Buddhist psychology.

Mirror therapy: an approach originally developed for the relief of Phantom Limb Pain that uses a mirror box (which is a box with two mirrors in the center - one facing each way) and draws on the principle of visual feedback.

Psychodynamic therapy: a psychotherapy that focuses on unconscious processes as they are manifested in a person's present behavior. The goals are to develop the client's self-awareness and understanding of the influence of the past on present behavior.

Relaxation training-tecnique: any method, process, procedure, or activity that helps a person to relax; to attain a state of increased calmness; or otherwise reduce levels of pain, anxiety, stress or anger.

TABLE 1 | Levels of evidence (Harbour and Miller, 2001).

Levels of evidence	Type of evidence
1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1−	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort or studies; high quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2−	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g., case reports, case series
4	Expert opinion

TABLE 2 | Grades of recommendations (Harbour and Miller, 2001).

Grades of recommendations	Evidence
A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or extrapolated evidence from studies rated as 2+
GPP	Recommended best practice based on the clinical experience of the guideline development group

According to the biopsychosocial approach (Engel, 1977), all these treatments have a higher effectiveness when included into multidimensional and multidisciplinary interventions, and their efficacy is even greater than the pharmacological therapies or physical therapies alone (Grade of recommendation: B) (Lipchik et al., 1993; Mattenklodt et al., 2008; Samwel et al., 2009; Pieh et al., 2012; Gagnon et al., 2013).

Taking into consideration specific pain conditions, psychological therapies have the potential to play a major role in the treatment of acute and chronic musculoskeletal pain. The majority of international guidelines agree about the importance of psychological approaches for treating a single episode of back pain (Koes et al., 2001, 2010) and, although there is strong evidence that preventing acute pain from becoming chronic is cost-effective (Waddell and Burton, 2001), this condition is seldom treated with psychotherapies, mostly for waiting-list reasons. Therefore, few psychological interventions have been evaluated for back pain in its early stages. However, research supports that CBT or treatments that feature cognitive techniques are able to prevent its evolution to chronicity, the increase in use of health care resources and days of absence from work, as well as modestly reducing the intensity of the perceived pain (Grade of recommendation: C) (Hasenbring et al., 1999; Linton and Andersson, 2000; Sullivan et al., 2006; Slater et al., 2009). For chronic musculoskeletal pain, interventions that appear to be more effective are the multidisciplinary and multidimensional ones (Grade of recommendation: A) (Guzman et al., 2006; Kääpä et al., 2006; Mangels et al., 2009; Mannion et al., 2013; Monticone et al., 2013; Kamper et al., 2014). CBT, both conducted in individual settings (Grade of recommendation: B, these studies are not always methodologically perfect and the impact on pain is still quite low) (Turner and Jensen, 1993; Turner, 1996; Rose et al., 1997; Smeets et al., 2006; Trapp et al., 2009; Glombiewski et al., 2010a; Taloyan et al., 2013) and group settings (Grade of recommendation: A) (Turner et al., 1990; Turner and Jensen, 1993; Newton-John et al., 1995; Basler et al., 1997; Rose et al., 1997; Haldorsen et al., 1998; Linton and Ryberg, 2001; Linton and Nordin, 2006; Lamb et al., 2010a,b), and educational and behavioral interventions (Grade of recommendation: B) (Tavafian et al., 2007; Brox et al., 2008; Henschke et al., 2010; van Middelkoop et al., 2011) are also highly recommended. It must be noted that the efficacy of cognitive-behavioral therapies are consistent across both individual and group settings (Rose et al., 1997) and that all of the interventions previously listed are also effective are also effective in the context of patients planning early retirement as a result of pain or a highly disabling condition, both of which are frequently perceived as obstacles to improvement (Trapp et al., 2009).

It is not possible to conclusively determine the effectiveness of electromyographic, postural and respiratory biofeedback interventions for chronic musculoskeletal pain. In fact, the methodological quality of the studies addressing this issue is often insufficient and the two best conducted trials (Ehrenborg and Archenholtz, 2010; Kapitza et al., 2010) do not support a specific effect of these therapies; however, there are some data in support of its analgesic potential (Flor and Birbaumer, 1993; Magnusson et al., 2008; Glombiewski et al., 2010a; Hallman et al., 2011; Ma et al., 2011). The heterogeneity of the results may be due to differences in the methodological quality of the studies and in the interventions examined. It is also possible that the short-term effect of biofeedback is similar to the early outcome of cognitive behavioral therapies, while the long-term benefits of the former could be greater (Flor and Birbaumer, 1993; Glombiewski et al., 2010a). Further studies will shed light on the subject (Grade of recommendation: GPP).

Psychological therapies can be a valuable resource in the treatment of Chronic Widespread Pain (CWP) and fibromyalgia

TABLE 3 | Summary table of evidence and recommendations from the Italian Consensus Conference on Pain in Neurorehabilitation.

Psychological therapies are highly recommended for the treatment of painful conditions and for the treatment of pain associated with various neurological diseases. Psychological therapies act on three levels: treatment of psychopathological comorbidities, reduction in perceived pain, improvement in the psychological aspects that contribute to maintain the pain. Most interventions are more effective and may enhance the outcomes of pharmacological and physical therapies if they are included in multidisciplinary treatments (GPP).
Recommended interventions for the whole of the chronic pain syndromes with heterogeneous physiopathology are: Mindfulness (A), Cognitive Behavioral Therapy (CBT), either conducted in individual, group setting or administered via computer (B), multidisciplinary interventions (B) and hypnosis (B).
Acute musculoskeletal pain is rarely treated with psychological treatments due to its favorable prognosis and waiting-list issues. However, CBT is considered effective for this condition (C). For chronic musculoskeletal pain multidisciplinary interventions (A), CBT in individual setting (B) or in group setting (A) and educational and behavioral interventions (B) are recommended. Also biofeedback may be used (GPP).
Telephone – delivered CBT can be used for the treatment of Chronic Widespread Pain (GPP). With regards to fibromyalgia, CBT (A), educational and behavioral interventions for the management of the disease in daily life (B), multidisciplinary interventions (B), mindfulness (C), electromyographic biofeedback and neurofeedback (GPP), and Acceptance and Commitment Therapy conducted in group setting (GPP) have been proven effective. CBT is recommended for the treatment of juvenile fibromyalgia (C). It is not possible to give recommendations for the treatment of pain associated with Chronic Fatigue Syndrome.
Complex Regional Pain Syndrome type I due to stroke or injury can be treated with motor imagery interventions (GPP) or with mirror therapy (if the pathology is due to stroke) (GPP). Early evidence may support the use of cognitive interventions or CBT associated with physical therapies (e.g. TENS, massages) (GPP). An interdisciplinary approach that includes physical, occupational and cognitive-behavioral interventions can be used for the treatment of CRPS-I in pediatric patients (GPP). No recommendation can be made with regards to CRPS-II.
For Central Post-Stroke Pain, mirror therapy and immersive virtual reality interventions are recommended (GPP).
For the treatment of Phantom Limb Pain, hypnosis, mirror therapy, immersive virtual reality interventions and EMDR are recommended (D).
Neuropathic pain secondary to spinal cord injury is difficult to treat; therefore, it is necessary to use multidisciplinary interventions on its different symptoms (GPP). The most effective approach can be the use of hypnosis (D) or virtual reality protocols in particular if associated with hypnosis or transcranial Direct Current Stimulation (D).
For chronic pain associated with multiple sclerosis, hypnosis (D) and virtual reality interventions (D) are recommended.
Hypnosis is recommended for patients suffering from pain associated with Amyotrophic Lateral Sclerosis, Parkinson's Disease, Guillain-Barré syndrome, HIV and Post – Polio Syndrome (GPP).
For the treatment of diabetic neuropathy and neuropathic pain associated with cancer or HIV, CBT may be used (GPP).
Electromyographic biofeedback interventions or protocols that combine relaxation techniques and biofeedback are effective in the treatment of pain associated with cervical dystonia (D), cerebral palsy, focal hand dystonia and postherpetic neuralgia (GPP).
It is possible to give only a weak recommendation for the treatment of chronic pain associated with Rheumatoid Arthritis. Early evidences support the use of hypnosis (GPP), interventions based on patient's education or on relaxation (GPP) and interventions based on meditation (GPP). CBT is effective on various psychological aspects associated with pain in Rheumatoid Arthritis but not on pain intensity. A multidisciplinary intervention is recommended for the treatment of Ehlers-Danlos Syndrome (GPP) and biofeedback may be used for the care of people affected by systemic lupus erythematosus (GPP).
For the treatment of chronic Tension-type Headache and migraine, electromyographic, thermal and electrogalvanic biofeedback interventions (A) in addition to autogenic training, relaxation training (B), hypnosis (C), and biofeedback intervention combined with virtual reality (GPP) are recommended. A very low recommendation can be given for hypnosis for the treatment of pain due to post-concussion syndrome (GPP) and to mindfulness therapies for the treatment of post-traumatic headache (GPP).
Burning Mouth Syndrome and facial pain can be treated with CBT or psychodynamic therapy combined with pharmacological interventions (GPP).
For temporomandibular disorders, Brief CBT or CBT conducted in group settings integrated with pharmacological interventions or hypnosis (B), and hypnosis (C) are recommended.
Medically Unexplained Symptoms and somatoform disorders can be treated with CBT conducted in group setting or as a part of a multidimensional approach that combines medication and psychotherapy, as well as Brief Dynamic Interpersonal Therapy (GPP).
There is preliminary evidence supporting the effectiveness of cognitive – behavioral therapies on chronic abdominal pain in children (C).

(FM), syndromes that are notoriously difficult to manage with a pharmacological approach. Telephone-delivered CBT has been proven to be an effective intervention for CWP, although there is a need for further research to support this conclusion (Grade of recommendation: GPP) (McBeth et al., 2012). There is general agreement on the fact that most psychological therapies can lead to clinically significant improvements in the experience of patients suffering from FM as these can prevent and treat depressive symptoms often associated with the condition, promote the management of insomnia and fatigue and reduce the impact of psychological factors related to the pain. If the criterion is the reduction of perceived pain, there are differences between the various interventions. CBT is effective both in the treatment of related symptoms and for the reduction in the intensity of perceived pain (Grade of recommendation: A) (Rossy et al., 1999; Bernardy et al., 2010; Glombiewski et al., 2010b; Gritzner et al., 2012; Clauw, 2014). Psycho-educational and behavioral interventions, aimed at helping the patient to improve the management of the disease in his daily life, appear also to be effective in reducing perceived pain (Grade of recommendation: B) (Burckhardt et al., 1994; Nicassio et al., 1997; Thieme et al., 2003, 2006; Hammond and Freeman, 2006) as well as multidisciplinary treatments (Grade of recommendation: B) (Lemstra and Olszynski, 2005; Lera et al., 2009; Lange et al., 2011; Vincent et al., 2013).

Studies on the effectiveness of mindfulness-based interventions, that seem to be a very promising resource in the treatment of FM (Grade of recommendation: C) (Grossman et al., 2007; Schmidt et al., 2011; Lauche et al., 2013; Shaheen, 2014), and ACT in a group setting (Grade of recommendation: GPP) (Luciano et al., 2014) are still conflicting. Electromyographic biofeedback and neurofeedback

interventions may also be used, even if further studies are needed to support the effectiveness of these therapies, since the best study conducted so far did not identify any significant effect (Santen et al., 2002). The class of recommendation for these interventions is low, although there are two randomized controlled trials and two case series that support their role in pain management (Grade of recommendation: GPP) (Mur et al., 1999; Babu et al., 2007; Hassett et al., 2007; Kayiran et al., 2010). Finally, CBT is effective for juvenile fibromyalgia (Grade of recommendation: C) (Kashikar-Zuck et al., 2005, 2012; Degotardi et al., 2006).

Conversely, it is not possible to make a recommendation for the treatment of pain associated with Chronic Fatigue Syndrome. Research on the topic, mainly focused on CBT conducted in individual or group settings, gave mixed results (Stulemeijer et al., 2004; Núñez et al., 2011; Bloot et al., 2015) and the underlying rationale has been questioned (Twisk and Maes, 2009). Therefore, further studies are needed.

Several imagery or visual feedback interventions can be used in the care of patients with a diagnosis of Complex Regional Pain Syndrome type 1 (CRPS-I), although further studies are needed to confirm their effectiveness. In particular, motor imagery interventions are recommended for CRPS-I due to injury or stroke (Grade of recommendation: GPP) (Moseley, 2004, 2005, 2006; O'Connell et al., 2013) and mirror therapy is recommended for CRPS-I due to stroke (Grade of recommendation: GPP) (Cacchio et al., 2009; Sato et al., 2010; O'Connell et al., 2013). It is to be noted that the first reported attempts to use graded motor imagery in clinical practice for this condition did not yield significant result, perhaps due to the lower control of the therapeutic procedures (Johnson et al., 2012).

Preliminary data indicate that cognitive interventions based on graded exposure and CBT associated with physical therapies (TENS, massages, etc.) could also be used (Grade of recommendation: GPP): (Lee et al., 2002; De Jong and Vlaeyen, 2005). In the treatment of CRPS-I an interdisciplinary approach that combines physical, occupational, and cognitive-behavioral interventions may lead to clinically significant results with pediatric patients (Grade of recommendation: GPP) (Patterson, 2011; Logan et al., 2012). There is insufficient evidence to draw conclusions about the efficacy of psychological interventions for CRPS-II (O'Connell et al., 2013).

Among the other conditions associated with neuropathic pain, there is early evidence that Central Post-stroke Pain may be effectively treated with mirror therapy and with immersive virtual reality interventions (Grade of recommendation: GPP) (Rodriguez et al., 2011; Thieme et al., 2012).

Phantom limb pain can be addressed with different psychological treatments. Early findings, mainly based on case reports, support the use of hypnosis (Grade of recommendation: D) (Rosén et al., 2001; Oakley et al., 2002; Bamford, 2006; Niraj and Niraj, 2014), biofeedback interventions (Grade of recommendation: D) (Belleggia and Birbaumer, 2001; Flor et al., 2001; Harden et al., 2005), Eye Movement Desensitization and Reprocessing therapy (EMDR) (Grade of recommendation: D) (Schneider et al., 2008; de Roos et al., 2010), and mirror therapy (Grade of recommendation: D) (Brodie et al., 2007; Chan et al., 2007; Murray et al., 2007; Mercier and Sirigu, 2009; Seidel et al., 2011) in the treatment of this condition, although there is no general agreement on the effectiveness of the latter.

Neuropathic pain is one of the most debilitating complications of spinal cord injury and since the underlying mechanisms are only partly understood, it is difficult to treat (Wrigley et al., 2009; Defrates and Cook, 2011). Therefore, multidisciplinary neurorehabilitation interventions acting simultaneously on different symptoms are needed (Grade of recommendation: GPP) (Heutink et al., 2014). So far, hypnotic treatments (Grade of recommendation: D) (Jensen and Barber, 2000; Jensen et al., 2009c, 2013; the recommendation is limited as all three studies were conducted by the same author) and virtual reality protocols (that are more effective when associated with hypnosis or transcranial Direct Current Stimulation (tDCS)), (grade of recommendation: D) (Moseley, 2007; Oneal et al., 2008; Soler et al., 2010; Villiger et al., 2012, 2013; Boldt et al., 2014) have been evaluated.

Hypnosis might be an effective intervention in the case of chronic pain associated with Multiple Sclerosis (Grade of recommendation: D) (Dane, 1996; Jensen et al., 2009a,b, 2011; Tierno et al., 2014). Preliminary evidence supports the use of hypnosis in the treatment of pain in various neurological conditions, including Amyotrophic Lateral Sclerosis (Palmieri et al., 2012; Kleinbub et al., 2015), Parkinson's Disease (Elkins et al., 2013), Guillain-Barré Syndrome (Fowler and Falkner, 1992), neuropathic pain due to HIV (Dorfman et al., 2013), and Post-Polio Syndrome (Hammond, 1991) (Grade of recommendation: GPP). The role of CBT in the treatment of pain due to diabetic neuropathy (Otis et al., 2013), neuropathic cancer pain (Steggles, 2009), and neuropathic HIV pain (Evans et al., 2003) is under evaluation (Grade of recommendation: GPP).

Electromyographic biofeedback interventions and the use of relaxation techniques that feature biofeedback appear to be promising for the treatment of chronic pain associated with Cervical Dystonia (Grade of recommendation: D) (Smania et al., 2003; Mueller and Wissel, 2010; De Pauw et al., 2014), Cerebral Palsy (Engel et al., 2004), Focal Hand Dystonia (Deepak and Behari, 1999), and Postherpetic Neuralgia (Ing, 2007) (Grade of recommendation: GPP).

It is possible to make only weak recommendations regarding the treatment of chronic pain associated with Rheumatoid Arthritis. Although it is established that different psychological therapies can have a short-term effect on the intensity of pain, related studies are very heterogeneous and the statistical power of analysis conducted is often low (Astin et al., 2002). Early evidence supports the use of hypnosis (Horton-Hausknecht et al., 2000), interventions based on relaxation or arthritis education (Barsky et al., 2010), and an Internal Family Systems—based intervention similar to mindfulness therapy (Shadick et al., 2013) (Grade of recommendation: GPP). The trials that evaluated CBT agree about its positive effects on different physical and psychological aspects but reported non—significant effects on pain intensity (Leibing et al., 1999; Sharpe et al., 2001; Evers et al., 2002; Zautra et al., 2008; Sharpe and Schrieber, 2012). With regards to other forms of rheumatic diseases, multidisciplinary treatments may be recommended for Ehlers-Danlos Syndrome (Bathen et al., 2013) (Grade of recommendation: GPP) and biofeedback therapy may

be indicated for the treatment of systemic lupus erythematosus (Greco et al., 2004).

Various biofeedback modalities might be used for the treatment of TTH and migraine patients. In particular electromyographic, thermal, and electrogalvanic biofeedback interventions have been proven effective both with adults and pediatric patients when included in multidimensional programs, in addition to cognitive-behavioral therapies, or administered as single treatments (Grade of recommendation: A) (Falkenstein et al., 1985; Fentress et al., 1986; Grazzi et al., 1990; Allen and McKeen, 1991; Allen and Shriver, 1998; Gatti et al., 2002; Scharff et al., 2002; Vasudeva et al., 2003; Nestoriuc and Martin, 2007; Nestoriuc et al., 2008; Mullally et al., 2009; Bembalgi and Naik, 2012, 2013; Magnoux et al., 2012; Gomez et al., 2013; Sanchez et al., 2013). The meta-analysis conducted by Nestoriuc et al. (2008), stated that biofeedback interventions can be effective for the treatment of TTH and migraine. Autogenic training, relaxation training (Grade of recommendation: B) (Janssen and Neutgens, 1986; Vandyck et al., 1991; Spinhoven et al., 1992; Ter Kuile et al., 1994; Stetter and Kupper, 2002; Pickering et al., 2012) and hypnosis (Grade of recommendation: C) (Berlin et al., 1985; Zitman et al., 1992; Hammond, 2007) may be used on adult patients. In addition, preliminary data support the effectiveness of treatments that involve a combination of biofeedback and virtual reality (Grade of recommendation: GPP) (Shiri et al., 2013). Research to support the effect mindfulness-based interventions on post-traumatic headache is still ongoing (Grade of recommendation: GPP) (Bédard et al., 2012). Finally, one study supports the use of hypnosis for the treatment of pain in post—concussion syndrome (GPP) (Dilks and Bourassa, 2012).

Psychotherapies have proven effective in the treatment of Burning Mouth Syndrome, facial pain, and temporomandibular disorders. Regarding the first, CBT, conducted in individual and group settings, appears to be promising (Grade of recommendation: GPP) (Bergdahl et al., 1995; Miziara et al., 2009) as well as psychodynamic interventions combined with pharmacological interventions (Grade of recommendation: GPP) (Femiano et al., 2004). Brief CBT, CBT conducted in group setting, or CBT integrated with pharmacological interventions or hypnosis are recommended for the treatment of temporomandibular disorders (Grade of recommendation: B) (Dworkin et al., 2002; Turner et al., 2006; Ferrando et al., 2012; Wang et al., 2012). Finally, hypnosis may be used in the treatment of these disorders as well as in the care of people with Persistent Idiopathic Facial Pain (Grade of recommendation: C) (Simon and Lewis, 2000; Abrahamsen et al., 2008, 2011).

Psychotherapy interventions are recommended in the treatment of patients with Medically Unexplained Symptoms and Somatoform Disorders to reduce the pain component. So far, CBT, conducted in group settings or included in a personalized multidimensional approach that combines pharmacotherapy and psychotherapy (Grade of recommendation: GPP) (Smith et al., 2006; Schroder et al., 2012), and Brief Dynamic Interpersonal Therapy (Grade of recommendation: GPP) (Sattel et al., 2012) have been evaluated.

Finally, studies that have evaluated the impact of cognitive-behavioral therapies on the reduction of chronic abdominal pain in children and adolescents, provide preliminary evidence of its effectiveness (Grade of recommendation: C) (Weydert et al., 2003; Youssef et al., 2004; Groß and Warschburger, 2013).

THE ITALIAN CONSENSUS CONFERENCE ON PAIN IN NEUROREHABILITATION

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