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Psychological flexibility as a mediator of improvement in Acceptance and Commitment Therapy for patients with chronic pain following whiplash

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ABSTRACT

Cognitive behavior therapy (CBT) has made important contributions to chronic pain management, but the process by which it is effective is not clear. Recently, strong arguments have been raised concerning the need for theory driven research to e.g. identify mechanisms of change in CBT and enhance the effectiveness of this type of treatment. However, the number of studies addressing these issues is still relatively scarce. Furthermore, the arrival of varieties of CBT with seemingly different process targets increases the need for such information. The present study explored the processes of change in a previously reported successful randomized controlled trial evaluating the effectiveness of an exposure-based form of behavioral and cognitive therapy, Acceptance and Commitment Therapy (ACT), on improvement in pain-related disability and life satisfaction for patients suffering from whiplash-associated disorder (WAD). Several process variables relevant to theories underlying traditional CBT were included: pain, distress, kinesiophobia, self-efficacy, and the process primarily targeted by ACT: psychological inflexibility. Mediation analyses were performed using a non-parametric cross-product of the coefficients approach. Results illustrated that pain intensity, anxiety, depression, kinesiophobia, and self-efficacy did not have significant mediating effects on the dependent variables. In contrast, significant indirect effects were seen for psychological inflexibility on pain-related disability (pre- to post-change scores) and life satisfaction (pre- to post; pre- to 4-month follow-up change scores). Although tentative, these results support the mediating role of psychological inflexibility in ACT-oriented interventions aimed at improving functioning and life satisfaction in people with chronic pain.

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1. Background

For chronic pain, cognitive behavior therapy (CBT) has received strong empirical support (Hoffman et al., 2007; Morley et al., 1999), but the change processes through which CBT operates is still rather unclear (Morley, 2004; Vlaeyen and Morley, 2005). This may be due to the wide variety of interventions and targets used in CBT, e.g. reduction in pain and distress (Turner et al., 2006), correction of inaccurate predictions and reduction of fear (de Jong et al., 2005), and improved self-efficacy (Bunketorp et al., 2006a). Infor-

mation regarding change processes is considered central to further develop theories and enhance treatment effectiveness by e.g. improve methods for matching treatments to specific patient needs (Keefe et al., 2002; Vlaeyen and Morley, 2005). However, change processes have previously been explored in relatively few studies (Lackner et al., 2007; Söderlund and Lindberg, 2002; Turner et al., 2007). Also, the need for such research has further increased with the arrival of acceptance-oriented forms of CBT, such as Acceptance and Commitment Therapy (ACT) (Hayes et al., 1999). From an ACT perspective, peoples' difficulties to persist with, or change, behaviors in order to serve long term values (i.e. *psychological inflexibility*) strongly contribute to disability. In short, ACT seeks to improve functioning and quality of life by increasing psychological flexibility, defined as the ability to act effectively in accordance with personal values in the presence of interfering thoughts,

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emotions, and bodily sensations (Hayes et al., 2006). As a form of exposure-based behavior therapy, ACT shares several important features with other CBT interventions, but differences with regards to targeted processes exist. ACT is explicitly not aimed at reducing pain or distress, or at changing the frequency or content of thoughts. Instead, it promotes greater acceptance of negative private experiences in order to increase psychological flexibility. Several treatment evaluations have suggested the utility of an ACT-oriented approach for chronic pain (McCracken et al., 2005; Wicksell et al., 2009a). Also, studies have illustrated the importance of variables related to psychological flexibility in chronic pain, such as acceptance (McCracken, 1998; Wicksell et al., 2009b), cognitive defusion (Wicksell et al., 2008b) and valued actions (McCracken and Vowles, 2008; Vowles and McCracken, 2008). Furthermore, recent studies have indicated the specific contribution of psychological flexibility in predicting outcome and explaining other relevant processes such as catastrophizing (Kratz et al., 2007; Wicksell et al., in press; Vowles et al., 2007, 2008). However, there is yet no study investigating possible mediators in randomized controlled trials (RCTs) of acceptance-oriented interventions for chronic pain.

The purpose of the present study was to explore theoretically relevant mechanisms of change in a recently reported a RCT (Wicksell et al., 2008a), in which ACT delivered in addition to treatment as usual (TAU) was shown to improve pain-related disability and life satisfaction as compared to a waiting list control condition receiving TAU only, in people with chronic debilitating pain following whiplash injuries.

2. Method

2.1. Setting and participants

Although the sample was described in detail in the previously presented RCT (Wicksell et al., 2008a), a brief outline of the setting and participants will be presented here. Participants were recruited through a patient organization for WAD and included people older than 20 years, with pain duration of more than 3 months, and reporting being diagnosed with WAD. In short, patients were excluded if: (a) pain resulted from a pathological process other than whiplash, (b) psychiatric issues were considered more relevant than pain (including risk for suicide), (c) having severe difficulties in understanding and/or speaking Swedish, (d) suffering from major cognitive dysfunctions, or (e) currently participating in another CBT-oriented treatment.

Twenty-one participants enrolled in the study. One in the control condition dropped out, and 20 completed the study (including 11 in the treatment condition). The mean pain duration was 83.0 months (SD 41.8) for both groups. No participant worked full time, and 71% of all participants were on full sick leave. Previous treatments consisted of pharmacological treatment (i.e. strong opioids, anti-epileptics, amitriptyline, and SSRI), physiotherapy, rehabilitation medicine, and in some cases alternative medicine. The two groups did not differ significantly on any of the demographic variables or symptoms, except more frequent symptoms of numbness ($p = 0.025$) in the treatment group. Also, the treatment and control groups were comparable on all outcome and process measures at pre-treatment assessments (all variables $p > .46$, except for pain intensity: $p = .08$).

2.2. Intervention

In the RCT, participants received treatment as usual (TAU; e.g. medication, acupuncture, physiotherapy, naprapathy, osteopathy) or TAU + ACT. The ACT-intervention consisted of 10 individual ses-

sions (60 min each) during 8 weeks. Eight sessions were conducted by psychologists trained in CBT, and two by a physician. All involved had previous experience of using ACT. Treatment content and patient progress were discussed continuously to maintain treatment fidelity.

The protocol for this exposure and acceptance intervention resembled in all important aspects the treatment content described in detail in previous papers (Wicksell et al., 2005, 2007, 2008a, 2009a). In short, exposure to previously avoided situations and private experiences was considered the core intervention, emphasizing acceptance as an alternative to avoidance in coping with negative reactions (such as pain and distress) that cannot be directly changed. The dysfunctional character of longstanding pain syndromes was discussed, in order to alter the context in which pain was experienced and to facilitate a shift in perspective from symptom reduction to valued living (i.e. setting the stage for exposure and acceptance). An assessment of individual values in important life domains was performed, followed by an exercise in which the workability of previous strategies to reduce pain and improve functioning was thoroughly evaluated. In essence, the discussion of values and workability of previous strategies functioned to illustrate the possibility of increasing functionality and life quality by accepting a certain amount of pain and distress. Based on identified values, behavioral goals were defined, followed by a discussion of gradual increase of previously avoided activities. Throughout the treatment, the participant was encouraged to notice and accept unpleasant private experiences, thus facilitating acceptance and defusion (being aware of a thought without acting on its content) processes. Behavioral activation involving exposure to possible pain-eliciting situations other than emotional reactions was not performed in session but by the patients between sessions. Illustrations and metaphors were sometimes used to clarify concepts such as acceptance and defusion.

2.3. Summary of previously reported results from the RCT

Statistically significant improvements in the treatment group, as compared with the control condition, were seen in the primary outcome variables (pain disability and life satisfaction) as well as the secondary outcome and process variables (e.g. fear of movement, psychological inflexibility). Large effects, as measured by partial eta squared ($\eta_p^2 > 0.25$) were obtained in several measures, such as disability, life satisfaction, kinesiophobia, and psychological inflexibility. In contrast, no differences were seen in any of the groups with regards to pain intensity.

2.4. Overview of mediation analysis

Several different characteristics or processes may be involved in therapeutic changes (Vlaeyen and Morley, 2005). In short, mediators refer to processes through which changes are considered to occur (Kazdin and Nock, 2003). In general, mediation analyses explore the impact of a mediating variable (M) on a relationship between an independent (X) and a dependent (Y) variable. This reflects the treatment effect on the outcome measure through a third variable (mediator), and mediation effects are therefore referred to as indirect effects. For example, improvements in functioning and quality of life may occur as a result of changes in pain-related distress but may also be due to increases in psychological flexibility. Importantly, mediation does not show causation. Instead, it illustrates the functional importance of the treatment's impact on a process (referred to as the a path), and that process' effect on outcome while controlling for treatment (i.e. the b path). Mediation is the combination of these two relations, which elevate it above e.g. mere correlation by requiring that a variable that is

altered by treatment must continue to be functionally relevant over and above that effect.

Analyses of mediators should be based on theoretically relevant *a priori* hypotheses (Vlaeyen and Morley, 2005). Also, in order to provide more precise theoretical tests it is useful, although relatively uncommon, to explore several plausible mediator variables, including some not emphasized in the theory underlying the intervention (Kazdin and Nock, 2003). Thus, by considering several different but related theoretical constructs it can be investigated if the hypothesized mediator is more functionally important than other parallel processes. An established hypothesis in chronic pain management is that psychological treatments work by reducing pain intensity in itself (Lackner et al., 2007) and/or the psychological distress associated with it (Turk and Okifuji, 2002) by methods such as relaxation, stress management, and cognitive restructuring (Marhold et al., 2001; Turner et al., 2006). Also, based on the fear-avoidance model of pain and disability, behavioral and cognitive interventions (e.g. decatastrophizing) may be used to correct inaccurate predictions about avoided situations and reduce pain-related fear and anxiety (de Jong et al., 2005).

In the present study, reductions in *pain* and two forms of psychological distress (*anxiety* and *depression*) were examined as possible mediators in this exposure based treatment. In addition, fear of movement and/or reinjury (i.e. *kinesiophobia*) represents a central link between pain and disability and was therefore evaluated as a potential mediator. Furthermore, it has been argued that *self-efficacy* (perceived confidence in performing behaviors and overcoming barriers related to e.g. pain) represents an important mediator in pain-related disability (Bandura, 1977; Denison et al., 2004). Self-efficacy has repeatedly shown to be important in explaining coping styles as well as linking pain to decreased functioning and psychological comorbidity (Bunketorp-Kall et al., 2007; Bunketorp et al., 2006b; Denison et al., 2004; Jensen et al., 1991; Soderlund et al., 2000). Self-efficacy and psychological flexibility appear to be somewhat related, in that both constructs involve the perceived ability to perform relevant activities in the presence of interfering private experiences such as pain or distress. Thus, self-efficacy represents a potentially relevant mediator variable in an ACT-oriented intervention and was, consequently, included in the analyses. The ACT-intervention was not aimed at reducing pain or distress but at increasing the patients' *psychological flexibility* (Wicksell et al., 2008a), which was, thus, used as the primary and theoretically specified mediating process. Psychological flexibility, as an ACT-related construct, consists of several different components including experiential avoidance and cognitive fusion. The measure of psychological flexibility used in the previous study (Wicksell et al., 2008b) includes a total scale score as well as subscales for *avoidance* and *fusion*, allowing for both the broader concept (i.e. psychological flexibility) and these specific aspects to be examined for their functional importance in the creation of positive changes in disability and life satisfaction.

2.5. Measures of outcome variables and hypothesized mediators

As dependent variables in the present set of analyses we used the primary outcome variables from the RCT (disability and life satisfaction) (Wicksell et al., 2008a). Mediating variables consisted of pain intensity, anxiety, depression, kinesiophobia, self-efficacy, and psychological flexibility (including the subscales on avoidance and cognitive fusion).

2.5.1. Pain disability

Pain Disability Index (PDI) assesses the degree to which chronic pain interfere(s) with daily activities (Tait et al., 1987). Seven items are rated by the patients on a 0–10 scale from “no trouble” to “total disability”. Several studies support the reliability and validity of

the PDI (Tait et al., 1987, 1990), including a Swedish study with WAD-patients (Soderlund et al., 2000).

2.5.2. Life satisfaction

Satisfaction With Life Scale (SWLS) measures global life satisfaction based on five items (Diener et al., 1985) that are rated on a 7-point scale from “strongly disagree” to “strongly agree” (higher scores indicating higher life satisfaction). SWLS has repeatedly shown to have good psychometric properties (Pavot et al., 1991; Wicksell et al., 2009b).

2.5.3. Pain intensity

Daily self-ratings of experienced pain intensity were performed during one week using a 10 cm visual analogue scale (VAS).

2.5.4. Anxiety and depression

The Hospital Anxiety and Depression Scale (HAD) is a reliable instrument for detecting anxiety and depression among patients in medical settings (Andersson et al., 2003; Zigmond and Snaith, 1983). The 14 items are rated on a 4-point Likert scale and form two subscales, i.e. for anxiety and depression.

2.5.5. Self-efficacy

The Self-efficacy Scale (SES) assesses the perceived ability to perform various activities (e.g. going shopping, visiting friends) in the presence of e.g. chronic back pain (Altmaier et al., 1992). The instrument consists of 20 items that are rated on an 11-point scale with 0 indicating “not at all confident” and 10 indicating “very confident”. The reliability of a Swedish version was supported in a cross-sectional study with subacute, chronic, or recurrent musculoskeletal pain (Denison et al., 2004).

2.5.6. Kinesiophobia

The Tampa Scale of Kinesiophobia (TSK) assesses the participants' fear of (re)injury by physical movement or activity (Swinkels-Meewisse et al., 2003; Vlaeyen et al., 1995b) on a 4-point scale from “strongly disagree” to “strongly agree” (higher scores indicating stronger fear). The TSK is widely used in people with chronic pain (Crombez et al., 1999; Vlaeyen et al., 1995a) and the statistical properties appear stable across pain diagnoses and nationalities (Roelofs et al., 2007). Although recent studies have supported a 2-factor solution (Roelofs et al., 2004), the total scale was used in the present study to enable analyses of kinesiophobia as a single construct.

2.5.7. Psychological inflexibility

The Psychological Inflexibility in Pain Scale (PIPS) assesses psychological inflexibility in relation to chronic pain. Two studies have supported a 2-factor solution (avoidance of pain, cognitive fusion related to pain), with satisfactory statistical properties (Wicksell et al., in press, 2008b). In specific, the avoidance subscale measures the self-reported tendency to engage in certain behaviors that function to avoid pain and related distress (e.g. “I avoid scheduling activities because of my pain”), while the fusion subscale assesses the frequency of thoughts that, if they are acted on, are likely to lead to avoidance behaviors (e.g. “I need to understand what is wrong in order to move on”). Items are rated on a 7-point Likert-type scale from “never true” (1) to “always true” (7), with higher scores indicating greater psychological inflexibility. Results from the previously reported RCT indicated that the measure is sensitive to change following an intervention based on exposure and acceptance (Wicksell et al., 2008a). Also, a lack of change in the control condition suggested, tentatively, a test–retest stability of the questionnaire. Furthermore, cross-sectional analyses have indicated the instrument's ability to assess indirect effects (Wicksell et al., in press).

2.6. Statistical analyses

Analyses of socio-demographic data and pre-treatment assessments (*t*-tests for independent samples or χ^2) were performed to ascertain comparability of the two groups. The small amount of missing data (in three different questionnaires, one participant each) was replaced by values estimated by the expectation–maximization-likelihood method (EM).

Hypotheses regarding possible mediators have traditionally been tested using the causal steps approach, as outlined by Baron and Kenny (Baron and Kenny, 1986). Today, the cross-product of the coefficients approach is widely viewed as the best overall test of mediation (MacKinnon et al., 2007). In a cross-product test the coefficient for the relation between *X* and *M* (the *a* path) is multiplied times the coefficient for the relation between *M* and *Y* controlling for *X* (the *b* path) and the significance for the overall *a* * *b* cross-product is tested. Because in finite data sets $c - c' = a * b$ this method directly assess the significance of the indirect, or mediating, effect and thereby effectively handle analytic difficulties provided by the mutual relation of the *a* and *b* paths.

Furthermore, a non-parametric bootstrap approach to the cross-product of the coefficients test has been recommended to test indirect effects, because it deals with the common problem of *a* * *b* distribution deviating from normality (meaning that the assumption of normality is not justified) (Baron and Kenny, 1986; MacKinnon et al., 2002; Preacher and Hayes, 2004). In addition, the described approach has the advantage of being more applicable to smaller data sets because of increased power as compared to traditional methods (Preacher and Hayes, 2004).

A bias-corrected confidence interval is provided for the tested mediators (Preacher and Hayes, 2004, 2008) by calculating the *a* * *b* cross-product in *n* bootstrap samples of the original size, drawn from the original data with replacement after each value is drawn. The mean value for the *a* * *b* product across the bootstrapped samples provides a point estimate of the indirect effect. Confidence intervals are derived from the obtained distribution of *a* * *b* scores, with *z*-score based corrections for bias due to the underlying distribution. If lower and upper bounds do not contain zero, the indirect effect is significant at the level specified in the analysis. In the present study, each analysis was based on 3000 bootstrapped samples.

Mainly, simple mediation model analyses were conducted to evaluate the importance of each of the hypothesized mediators. However, supplementary multiple mediator models were also used to investigate the mediating effects of PIPS when controlling for related variables (TSK and SES).

In this set of mediation analyses, post-assessment scores were used for the hypothesized mediators. For the outcome measures, two different change scores were calculated; pre- to post-assessment scores and pre- to 4-month follow-up assessment scores (i.e. 6 months following pre-treatment assessments). Statistical significance was interpreted conventionally ($p < .05$ = “significant”; $p < .10$ = “marginally significant”) but *p*-values were reported to facilitate a critical interpretation of the data (Greenwald et al., 1996). The analyses were performed using SPSS version 16.0.

3. Results

3.1. Initial analyses

Most outcome and process data from the RCT have been presented previously (Wicksell et al., 2008a) and are not reported here. For the present analyses, change scores (pre- to post; pre- to follow-up) were calculated for the two groups on the primary outcome measures (PDI and SWLS). Notably, although change

scores are sometimes used also for the process variables, particularly when pre-scores differ among groups, the present study utilized post scores as mediators. The theoretical argument for choosing post instead of change scores for the mediators is that psychological flexibility, rather than change per se, was expected to predict positive outcomes. To illustrate, a person that changes markedly from a very low baseline may remain psychologically inflexible and improve less (in e.g. functioning) than a person with higher post score levels of psychological flexibility but a relatively smaller change. In addition, lack of pre-treatment differences further reduced the need to use change scores and the use of post instead of change scores also improves the clarity and statistical simplicity of the results. Furthermore supplementary analyses were conducted to ascertain that mediator analyses based on change scores did not provide a different pattern of results.

Table 1 provides an overview of the change scores (dependent variables) and post-assessments (mediators), including *t*-tests and effect sizes to analyze differences between the ACT and the control condition on the variables used in the analyses. The ACT group improved significantly more than the control condition with large effect sizes on both dependent variables (PDI, SWLS). With the exception of pain intensity and SES, there were also significant differences between the groups on the mediators (HAD-anxiety, TSK, PIPS total, PIPS-avoidance, and PIPS-fusion), with large effects in PIPS, TSK, and HAD-depression.

Simple Pearson correlation coefficients between mediators and dependent variables were calculated to characterize broadly the relationship between the dependent variables (change scores) and the hypothesized mediators (post-assessment scores). There was a strong relationship between PIPS (total and subscales) and both of the SWLS change scores (*r* ranging from $-.595$ to $-.777$), as well as with the PDI pre- to post-change score (*r* ranging from $.502$ to $.637$). TSK was correlated with SWLS, pre- to post-change ($r = -.457$) and SES was mainly related to PDI changes from pre- to post ($r = -.506$). HAD-anxiety correlated with SWLS (pre-post:

Table 1

Means, standard deviations and between group comparisons for the variables used in the mediator analyses.

	Condition	<i>m</i> (<i>sd</i>)	<i>t</i>	<i>p</i>	<i>d</i> ^a
<i>Outcome variables (change scores)</i>					
<i>PDI: pre to post</i>	Treatment	−12.8 (14.3)	−3.41	.004	−1.54
	Control	4.4 (8.0)			
<i>PDI: pre to follow-up</i>	Treatment	−5.3 (10.2)	−2.59	.018	−1.17
	Control	7.0 (10.9)			
<i>SWLS: pre to post</i>	Treatment	6.7 (4.0)	4.74	<.001	2.13
	Control	−1.3 (3.5)			
<i>SWLS: pre to follow-up</i>	Treatment	6.3 (6.4)	2.74	.013	1.24
	Control	−1.0 (5.4)			
<i>Mediator variables (post-assessments)</i>					
<i>Pain intensity</i>	Treatment	4.8 (2.1)	−1.10	.286	−0.49
	Control	5.7 (1.6)			
<i>HAD-anxiety</i>	Treatment	5.2 (3.6)	−1.58	.131	−0.70
	Control	8.4 (5.6)			
<i>HAD-depression</i>	Treatment	4.2 (3.5)	−2.75	.013	−1.20
	Control	8.7 (4.0)			
<i>SES</i>	Treatment	135.6 (36.6)	1.17	.256	0.52
	Control	115.1 (41.8)			
<i>TSK</i>	Treatment	29.0 (6.1)	−3.10	.008	−1.45
	Control	40.1 (9.2)			
<i>PIPS-avoidance</i>	Treatment	25.6 (7.4)	−2.98	.008	−1.35
	Control	39.1 (12.6)			
<i>PIPS-fusion</i>	Treatment	22.3 (8.5)	−2.83	.011	−1.32
	Control	31.7 (5.7)			
<i>PIPS-total scale</i>	Treatment	47.9 (12.8)	−3.64	.002	−1.63
	Control	70.8 (15.3)			

^a *d* = 0.2 (small effect), *d* = 0.5 (medium effect), *d* = 0.8 (large effect) (Cohen, 1988).

Table 2

Results from mediator analyses with pain disability (PDI, change scores: pre to post) as outcome measure.

Mediator		Path	Normal theory tests				Bootstrap results for indirect effects (BCa; 95% CI)		
			Coefficient	SE	<i>t</i> ^a	<i>p</i>	Point estimate (SE)	Lower	Upper
PIPS	Total	<i>a</i>	22.87	6.29	3.64	.0019			
		<i>b</i>	.34	.19	1.81	.0876			
		Total (<i>c</i>)	17.24	5.34	3.23	.0047			
		Direct (<i>c'</i>)	9.43	6.62	1.42	.1728			
	Avoidance	<i>a * b</i>	7.81	4.58	1.71	.0882	7.69 (4.27)**	.24	17.19
		<i>a</i>	13.47	4.52	2.98	.0080			
		<i>b</i>	.28	.28	1.00	.3312			
		Total (<i>c</i>)	17.24	5.34	3.23	.0047			
	Fusion	Direct (<i>c'</i>)	13.49	6.53	2.07	.0544			
		<i>a * b</i>	3.76	3.76	1.00	.3175	3.57 (3.64)	–3.78	10.64
		<i>a</i>	9.43	3.14	3.00	.0073			
		<i>b</i>	.71	.34	2.07	.0528			
TSK	Kinesiophobia	Total (<i>c</i>)	17.24	5.34	3.23	.0047			
		Direct (<i>c'</i>)	10.12	5.68	1.78	.0917			
		<i>a * b</i>	6.68	3.74	1.78	.0747	6.63 (3.89)*	.69	13.26
		<i>a</i>	11.06	3.43	3.23	.0047			
	Self-efficacy	<i>b</i>	.15	.38	.39	.7027			
		Total (<i>c</i>)	17.24	5.34	3.23	.0047			
		Direct (<i>c'</i>)	15.63	6.87	2.27	.0362			
		<i>a * b</i>	1.62	3.97	.41	.6838	2.11 (4.24)	–7.30	9.45
	Anxiety	<i>a</i>	–20.55	17.54	–1.17	.2565			
		<i>b</i>	–.14	.07	–2.07	.0535			
		Total (<i>c</i>)	17.24	5.34	3.23	.0047			
		Direct (<i>c'</i>)	14.43	5.09	2.83	.0115			
HAD-a	Anxiety	<i>a * b</i>	2.81	2.66	1.06	.2912	3.10 (3.13)	–.95	12.26
		<i>a</i>	3.26	2.06	1.58	.1305			
		<i>b</i>	.77	.60	1.29	.2141			
		Total (<i>c</i>)	17.24	5.34	3.23	.0047			
	Depression	Direct (<i>c'</i>)	14.71	5.60	2.63	.0176			
		<i>a * b</i>	2.53	2.42	1.05	.2957	2.70 (2.42)	–.78	8.19
		<i>a</i>	4.56	1.66	2.75	.0132			
		<i>b</i>	1.03	.74	1.40	.1806			
	Pain intensity	Total (<i>c</i>)	17.24	5.34	3.23	.0047			
		Direct (<i>c'</i>)	12.53	6.20	2.02	.0592			
		<i>a * b</i>	4.71	3.60	1.31	.1908	5.26 (4.18)	–1.14	14.04
		<i>a</i>	.92	.84	1.10	.2863			
Pain-VAS	Pain intensity	<i>b</i>	.59	1.53	.39	.7030			
		Total (<i>c</i>)	17.24	5.34	3.23	.0047			
		Direct (<i>c'</i>)	16.69	5.65	2.95	.0089			
		<i>a * b</i>	.55	1.43	.38	.7008	.87 (2.05)	–1.77	6.60

Note: Number of bootstrap resamples = 3000. The indirect effect is statistically significant at the chosen level when the confidence interval does not include zero (95% equals $p < .05$ level significance).

^a For the $a * b$ paths, *z*-values are presented.

* The bootstrapped point estimate is marginally significant at $p < .10$.

** The bootstrapped point estimate is significant at $p < .05$.

$r = -.481$), and HAD-depression correlated significantly with both of the PDI change scores ($r = .544$ and $.475$) as well as SWLS, pre-post ($r = -.492$).

3.2. Tests of indirect effects

All possible mediators were analyzed in relation to the four different dependent variables: PDI and SWLS, pre- to post and pre- to follow-up change scores. Tables 2 and 3, as well as Tables S1 and S2 see the online version at 10.1016/j.ejpain.2010.05.001, illustrate the indirect effects of treatment (ACT + TAU and TAU) on the outcome measures through the possible mediators: pain, HAD-anxiety, HAD-depression, TSK, SES, and PIPS.

3.2.1. Pain disability at post

There were no significant mediation effects for measures neither of pain, anxiety, or depression, nor for kinesiophobia or self-efficacy (see Table 2) on pre- to post-changes in pain-related disability as measured by the PDI. In contrast, psychological flexibility as assessed by the PIPS-total scale score, significantly ($p < .05$) mediated the treatment effects obtained (bootstrapped

point estimate = 7.69; 95% CI lower and upper = .24, 17.19). Normal theory tests showed that the significant total effect ($t = 3.23$, $p = .0047$) was no longer significant when controlling for the effect of psychological flexibility ($t = 1.42$, $p = .1728$; proportion of effect mediated = .45). When subscales of the PIPS were examined the PIPS-fusion was a marginally significant mediator ($p < .10$; see Table 2), but PIPS-avoidance did not evidence a significant indirect effect.

3.2.2. Pain disability at follow-up

None of the process variables significantly mediated treatment effects on pre- to follow-up change scores in pain disability as measured by the PDI (see Table S1 see the online version at 10.1016/j.ejpain.2010.05.001). In examining the scores, it seemed possible that the lack of significance was related to restricted variability in pre- to follow-up change scores, which in turn may have limited the variability in regression. As an indication of this, pre- to follow-up PDI change scores in the TAU condition did not correlate ($p > .25$) with either the pre- or the follow-up PDI scores (i.e. the two values from which change scores were mathematically composed). Therefore, to further explore the indirect effects post hoc

Table 3

Results from mediator analyses with life satisfaction (SWLS, change scores: pre to four months follow-up) as outcome measure.

Mediator	Path	Normal theory tests					Bootstrap results for indirect effects (BCa; 95% CI)		
		Coefficient	SE	t^a	p		Point Estimate (SE)	Lower	Upper
PIPS	Total	a	22.87	6.29	3.64	.0019			
		b	-.23	.09	-2.62	.0180			
		Total (c)	-7.35	2.68	-2.74	.0134			
		Direct (c')	-2.12	3.07	-.69	.4982			
	Avoidance	$a * b$	-5.23	2.35	-2.22	.0261	-5.23 (3.20)**	-14.30	-.37
		a	13.25	4.50	2.94	.0087			
		b	.22	.13	-1.62	.1241			
		Total (c)	-7.35	2.68	-2.74	.0134			
	Fusion	Direct (c')	-4.76	3.11	-1.53	.1445			
		$a * b$	-2.87	1.93	-1.49	.1365	-2.98 (2.34)*	-8.61	-.18
		a	9.39	3.32	2.83	.0111			
		b	-.44	.16	-2.67	.0163			
TSK	Kinesiophobia	Total (c)	-7.35	2.68	-2.74	.0134			
		Direct (c')	-7.49	3.47	-2.16	.0452			
		$a * b$	-.14	1.99	.07	.9436	.09 (2.20)	-5.40	3.72
		a	11.06	3.43	3.23	.0047			
	Self-efficacy	b	.01	.19	.07	.9474			
		Total (c)	-7.35	2.68	-2.74	.0134			
		Direct (c')	-7.10	2.85	-2.49	.0235			
		$a * b$	-.25	.75	-.34	.7365	-.42 (1.03)	-3.12	1.09
HAD-a	Anxiety	a	3.26	2.06	1.58	.1305			
		b	-.22	.31	-.69	.4969			
		Total (c)	-7.35	2.68	-2.74	.0134			
		Direct (c')	-6.65	2.90	-2.29	.0352			
	Depression	$a * b$	-.71	1.05	-.67	.5034	-.99 (1.55)	-4.94	1.20
		a	4.56	1.66	2.75	.0132			
		b	-.02	.39	-.06	.9558			
		Total (c)	-7.35	2.68	-2.74	.0134			
Pain-VAS	Pain intensity	Direct (c')	-7.25	3.29	-2.21	.0414			
		$a * b$	-.10	1.69	-.06	.9525	-.53 (2.05)	-4.40	4.11
		a	.92	.84	1.10	.2863			
		b	.03	.77	.03	.9727			
	Pain intensity	Total (c)	-7.35	2.68	-2.74	.0134			
		Direct (c')	-7.38	2.85	-2.59	.0191			
		$a * b$.02	.68	.04	.9707	.02 (.91)	-1.44	2.81
		a							

Note: Number of bootstrap resamples = 3000. The indirect effect is statistically significant at the chosen level when the confidence interval does not include zero (95% equals $p < .05$ level significance).

^a For the $a * b$ paths, z -values are presented.

* The bootstrapped point estimate is marginally significant at $p < .10$.

** The bootstrapped point estimate is significant at $p < .05$.

mediation analyses were calculated using post PIPS scores as mediators and the PDI follow-up scores (not change scores) as the outcome, both with and without the pre-scores on PDI as a covariate. In short, both the post PIPS-total score (bootstrapped point estimate = 10.49, 95% CI lower and upper: .61, 24.91) and PIPS-avoidance score (bootstrapped point estimate = 9.42, 95% CI lower and upper: 2.43, 22.00) significantly ($p < .05$) mediated PDI follow-up scores. When the pre-PDI score was entered as a covariate, the PIPS-avoidance score did so at marginal levels of significance (bootstrapped point estimate = 4.51, 90% CI lower and upper: .32, 11.90).

3.2.3. Life satisfaction at post

There were no significant mediation effects for measures of pain, anxiety, or depression, or for kinesiophobia or self-efficacy (see Table S2 see the online version at [10.1016/j.ejpain.2010.05.001](https://doi.org/10.1016/j.ejpain.2010.05.001)) on pre- to post-changes in life satisfaction as measured by the SWLS. In contrast, psychological flexibility as assessed by the PIPS-total scale score, significantly ($p < .05$) mediated the treatment effects obtained (bootstrapped point estimate = -3.47; 95% CI lower and upper = -8.00, -.96). Normal theory tests showed that the significant total effect ($t = -4.74$,

$p = .0002$) was still significant but considerably reduced when controlling for the effect of psychological flexibility ($t = -2.39$, $p = .0288$; proportion of effect mediated = .44). When subscales of the PIPS were examined, both the fusion and avoidance subscales significantly ($p < .05$) mediated life satisfaction outcomes at post and at nearly equal strength (PIPS-avoidance: bootstrapped point estimate = -2.40; 95% CI lower and upper = -6.04, -.32; PIPS-fusion: bootstrapped point estimate = -2.34; 95% CI lower and upper = -6.12, -.13; see Table S2 see the online version at [10.1016/j.ejpain.2010.05.001](https://doi.org/10.1016/j.ejpain.2010.05.001)).

3.2.4. Life satisfaction at follow-up

There were no significant mediation effects for measures of pain, anxiety, or depression, or for kinesiophobia or self-efficacy (see Table 3) on pre- to follow-up changes in life satisfaction as measured by the SWLS. In contrast, psychological flexibility as assessed by the PIPS-total scale score post, significantly ($p < .05$) mediated the treatment effects obtained at the 4-month follow-up (bootstrapped point estimate = -5.23; 95% CI lower and upper = -14.30, -.37). Normal theory tests showed that the significant total effect of treatment ($t = -2.74$, $p = .0134$) was no longer significant when controlling for the effect of psychological flexibility.

ity ($t = -.69$, $p = .4982$; proportion of effect mediated = .71). When subscales of the PIPS were examined, the post PIPS-fusion subscale significantly ($p < .05$) mediated life satisfaction outcomes at the 4-month follow-up and the post PIPS-avoidance subscale did so at a marginal ($p < .10$) level of statistical significance (PIPS-fusion: bootstrapped point estimate = -4.18 ; 95% CI lower and upper = -11.14 , $-.34$; PIPS-avoidance: bootstrapped point estimate = -2.98 ; 90% CI lower and upper = -8.61 , $-.18$; see Table 3).

3.2.5. Supplementary analyses: multiple mediators and mediators as outcomes

The relatively robust mediating effects of PIPS on SWLS pre- to follow-up change score provide the strongest indication that psychological flexibility should be considered a functionally important process in the original study. Therefore, additional analyses were conducted in order to explore this key finding. In order to directly compare the PIPS with other possible mediators, multiple mediator analyses were conducted with the PIPS and the other available process measures. In separate analyses, the PIPS-total score was entered together with (1) pain, anxiety, and depression, and (2) TSK and SES, to investigate if the mediating effects of psychological inflexibility on the outcome variables were retained when controlling for these other possible mediators. The mediating effect of PIPS on life satisfaction (pre- to follow-up change) remained when controlling for pain, anxiety, and depression (point estimate = -8.21 , 95% CI lower and upper = -26.49 , -1.91) as well as when controlling for TSK and SES (point estimate = -5.89 , 95% CI lower and upper = -20.36 , $-.75$).

A second set of analyses examined the issue of directionality. The PIPS was only collected at pre, post, and follow-up, and SWLS outcome changes were already evident at post-treatment. Thus, it is possible that life satisfaction outcomes were functionally related to psychological flexibility mediators as much as vice versa. In order to explore further the possible directionality of the strongest mediational result, supplementary analyses were conducted as suggested by Baron and Kenny, in which post SWLS outcomes were entered as the mediator and PIPS pre- to follow-up change scores were entered as an outcome, essentially inverting the original analysis (Baron and Kenny, 1986). Post SWLS scores did not have a significant indirect effect on follow-up changes in neither PIPS-total score nor in the avoidance or fusion subscale scores ($p > .20$; proportion of effect mediated $< .05$) providing incremental support for the directionality of the mediational effect in the original analyses.

4. Discussion

The focus of the present study was to explore hypothesized mechanisms of change for an ACT-based intervention with people suffering from chronic pain following whiplash. According to ACT theory, psychological flexibility should function as a primary mediator for this type of intervention. Conversely, although reductions in pain, anxiety, or depression may well occur they are not primary targets and, thus, would not be theoretically specified a priori as likely mediators at the same level of expected strength as psychological flexibility. Similarly, because the ACT-intervention did not directly target change in the content of thought or emotion, kinesiophobia and self-efficacy should be less powerful and/or less consistent mediators than psychological flexibility.

In general, results fit with these expectations. Pain or distress did not bear a significant functional relation to disability and life satisfaction outcomes in this data set, indicating that the improvements seen were not mainly accomplished through such symptom alleviation. Similarly, neither reduced kinesiophobia nor improved self-efficacy appeared to be relevant mediating variables. In con-

trast, results showed significant indirect effects for psychological inflexibility as measured by the PIPS on life satisfaction (pre- to post; pre- to follow-up change scores) as well as some support for a functional role for psychological flexibility on disability, particularly when considering pre- to post-change scores. Thus, the pattern of the data strengthens the view that the improvements in outcome seen in this RCT were obtained through theoretically targeted changes in psychological inflexibility.

Despite the strong empirical support for CBT for chronic pain (Eccleston et al., 2002; Morley et al., 1999), a substantial number of patients do not benefit from these treatments and the effect sizes are often relatively modest (Ostelo et al., 2005; Turk and Rudy, 1990; Vlaeyen and Morley, 2005). Indeed, many of the studies providing the empirical base for CBT in pain management have utilized extensive multimodal treatment programs (Flor et al., 1992). Although previous research has suggested that these are generally more effective than less intensive interventions (Guzman et al., 2001) many, if not most, patients do not have access to such programs. All of these factors imply a need to develop interventions that are effective even though less extensive, and that target patient needs in an efficient, precise and coherent way. A better understanding for processes of change appear helpful in that regard by giving treatment developers proximal functional targets, by providing suggestions that might be explored regarding treatment matching, and by indicating which theories or aspects of theories that deserve further exploration. Refining process knowledge in CBT for chronic pain is not easy however, in part because most programs are not strictly derived from a given theory, such as learning theory, and processes of change are normally neither clearly stated a priori nor properly measured. Furthermore, CBT itself is difficult to define and characterize precisely, and has come to include a wide variety of techniques based on several different theoretical assumptions (Turk and Okifuji, 2002) further complicating the search for processes of change. The development of comprehensive multimodal treatments reflects this trend. In addition to their cost and complexity, such broad and extensive programs may include unnecessary components (Turk and Okifuji, 2002). To identify such components will require either expensive and difficult component analyses, or better process information.

This reasoning leads to the view that both efficacy and process knowledge are key to the continuous development of more effective and efficient treatments (Kazdin, 2007). Nevertheless, empirical clinical approaches have greatly emphasized efficacy information over the development of theories from which processes and components of known importance can be derived (Vlaeyen and Morley, 2005). The importance of mediation effects have been noted for decades, both generally (Baron and Kenny, 1986) and specifically with regard to CBT (DeRubeis et al., 1990; Vlaeyen and Morley, 2005), but mediation analyses have only recently begun to appear with regularity (Turner et al., 2007).

It is evident that a variety of functional paths may exist in successful treatments of chronic pain. A well conducted study on CBT for temporomandibular disorder (Turner et al., 2006) found that the effects of treatment were mediated through self-efficacy, catastrophizing, and perceived control (Turner et al., 2007). Another study found that the working mechanisms of CBT for with irritable bowel syndrome (Lackner et al., 2007) were its direct effects on gastrointestinal symptoms rather than a consequence of reduced distress.

The present study contributes to the growing body of evidence for exposure and acceptance-based treatments in chronic pain (Dahl et al., 2004; McCracken et al., 2005, 2007; Wicksell et al., 2007, 2008b, 2009a). Process evidence from open trials have indicated the importance of variables related to psychological flexibility (e.g. acceptance/willingness, activities engagement, avoidance, and fusion) in chronic pain (Wicksell et al., in press, 2009b; Vowles

et al., 2008) as well as other areas of behavioral medicine, e.g. tinnitus (Westin et al., 2008). Recently, mediation analyses have been utilized to explore the change processes in ACT (Hayes et al., 2006), and aspects of psychological flexibility have been shown to mediate the impact of ACT on weight (Lillis et al., 2009), epilepsy (Lundgren et al., 2008), and diabetes (Gregg et al., 2007). The present study is the first to apply formal mediation analysis to examining the effects of an ACT RCT for chronic pain and, although tentative, the findings support the mediating role of psychological flexibility also with this group.

A small number of studies have directly compared the processes of change, or mediators, for ACT as compared to traditional CBT methods, and all have detected distinct processes of change (Hayes et al., in press). The present set of results deviates somewhat from previous evaluations of CBT interventions (Lackner et al., 2007; Turner et al., 2007) by suggesting the possibility of functionally distinct sub-groupings of CBT treatments (i.e. working through different processes), and this needs to be further explored. If the evidence for functionally distinct groupings of CBT interventions continues to grow, it will be important not just to compare them but also to look for differential moderators of treatment that might lead to evidence-based forms of treatment matching across these wings of CBT (Holroyd et al., 2009; Vlaeyen and Morley, 2005). Thus, the establishment of theoretically relevant moderators and predictors could also lead to further theoretical development, accelerating the process of treatment development in CBT.

In order to further refine these issues it is important that interventions, hypothesized change mechanisms, and measures of processes of change are precisely based on specific theories (Kazdin, 2007). In the present study, the PIPS measured avoidance and cognitive fusion, two variables which are central to both ACT and its theoretical base Relational Frame Theory (Hayes et al., 2001, 2006). It will be continuously useful to test mediators drawn from related perspectives to determine their mediational role as well as the specificity of these processes, which was a notable incremental contribution of the present study. Both kinesiophobia and self-efficacy bear similarities of psychological flexibility or its inverse, and it will not be surprising if these function as mediators in studies on ACT, although expected to be weaker or less consistent in that role than measures of psychological flexibility. In the original RCT on which the present study is based, kinesiophobia was significantly reduced by ACT ($d = 1.45$), self-efficacy was not ($d = .52$), but neither were shown here to be a significant mediator of any of the primary outcomes.

There are some methodological weaknesses in the present study that should be noted. First, this study was carried out as an attempt to explore possible mediators in acceptance-based treatment, and the findings should be considered tentative both given the relatively small sample size and the particular patient group included. Consequently, replication of these findings is important and larger scale studies would help ascertain the stability and generalizability of these results. Second, the present study was not specifically designed to address the concern with temporal precedence. The fact that both outcomes and processes had already changed at post-treatment assessment indicates the need to more properly address this concern, for example by assessing mediators more frequently and earlier in treatment. Third, mediation analyses of this kind provide no protection against a third variable that accounts for the process, outcome, and the relation between them. Thus, ideally, a study evaluating possible mediators should as much as possible control for parallel processes although balancing the risk for types I and II errors. Future studies with more participants will be better suited to identify possible predictors and add these to the analyses as covariates. In addition, future studies on ACT and pain may benefit from also including measures of additional aspects of the model, such as willingness and values. Simi-

larly, other processes of known importance might usefully be tested, such as catastrophizing, perceived control, or general cognitive styles.

In conclusion, the challenge of developing the theoretical framework underlying CB-treatment (Vlaeyen and Morley, 2005) implies a shift from mere treatment effectiveness to change processes. In the present study, the strongest finding may be the mediating effects of PIPS post scores on the change between pre- and follow-up life satisfaction, since this relationship extended over 4 months time and the reversal of mediators and outcomes resulted in non-significant effects, tentatively supporting the directionality of PIPS' mediating effects. Given the exploratory character of these analyses, more studies are needed to replicate these findings and to further explore possible change processes in acceptance-oriented treatments as well as other forms of CBT. However, results from the present study provide incremental support for the functional importance of psychological inflexibility in ACT-interventions for chronic pain.

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Table S1

Results from mediator analyses with pain disability (PDI, change scores: pre to four months follow-up) as outcome measure.

Mediator		Path	Normal theory tests				Bootstrap results for indirect effects (BCa; 95% CI)		
			Coefficient	SE	<i>t</i> ^a	<i>p</i>	Point estimate (SE)	Lower	Upper
PIPS	Total	<i>a</i>	22.87	6.29	3.64	.0019			
		<i>b</i>	.08	.18	.42	.6806			
		Total (<i>c</i>)	12.25	4.73	2.59	.0185			
		Direct (<i>c'</i>)	10.51	6.38	1.65	.1177			
	Avoidance	<i>a * b</i>	1.74	3.95	.44	.6602	1.61 (4.07)	−5.94	10.82
		<i>a</i>	13.47	4.52	2.98	.0080			
		<i>b</i>	.08	.25	.30	.7669			
		Total (<i>c</i>)	12.25	4.73	2.59	.0185			
	Fusion	Direct (<i>c'</i>)	11.22	5.94	1.89	.0758			
		<i>a * b</i>	1.03	3.25	.32	.7514	1.01 (3.33)	−6.80	7.31
		<i>a</i>	9.40	3.32	2.83	.0111			
		<i>b</i>	.13	.34	.38	.7072			
TSK	Kinesiophobia	Total (<i>c</i>)	12.25	4.73	2.59	.0185			
		Direct (<i>c'</i>)	11.02	5.83	1.89	.0758			
		<i>a * b</i>	1.23	3.09	.40	.6892	1.17 (3.68)	−4.53	11.28
		<i>a</i>	11.06	3.43	3.23	.0047			
	Self-efficacy	<i>b</i>	.06	.33	.18	.8557			
		Total (<i>c</i>)	12.25	4.73	2.59	.0185			
		Direct (<i>c'</i>)	11.57	6.11	1.89	.0755			
		<i>a * b</i>	.68	3.51	.19	.8455	.67 (3.62)	−5.31	9.79
SES	Anxiety	<i>a</i>	−20.55	17.54	−1.17	.2565			
		<i>b</i>	−.08	.06	−1.27	.2218			
		Total (<i>c</i>)	12.25	4.73	2.59	.0185			
		Direct (<i>c'</i>)	10.62	4.83	2.20	.0419			
HAD-a	Depression	<i>a * b</i>	1.63	1.82	.90	.3703	1.93 (2.44)	−.90	9.32
		<i>a</i>	3.26	2.06	1.58	.1305			
		<i>b</i>	.24	.55	.44	.6667			
		Total (<i>c</i>)	12.25	4.73	2.59	.0185			
HAD-d	Pain intensity	Direct (<i>c'</i>)	11.46	5.17	2.22	.0405			
		<i>a * b</i>	.79	1.78	.45	.6559	.77 (2.23)	−2.73	6.31
		<i>a</i>	4.56	1.66	2.75	.0132			
		<i>b</i>	.76	.67	1.15	.2677			
Pain-VAS	Pain intensity	Total (<i>c</i>)	12.25	4.73	2.59	.0185			
		Direct (<i>c'</i>)	8.77	5.59	1.60	.1350			
		<i>a * b</i>	3.48	3.13	1.11	.2656	4.44 (4.55)	−3.14	14.01
		<i>a</i>	.92	.84	1.10	.2863			
		<i>b</i>	1.01	1.34	.75	.4628			
		Total (<i>c</i>)	12.25	4.73	2.59	.0185			
		Direct (<i>c'</i>)	11.32	4.95	2.29	.0352			
		<i>a * b</i>	.93	1.43	.65	.5160	.86 (1.73)	−1.09	6.69

Note: Number of bootstrap resamples = 3000. The indirect effect is statistically significant at the chosen level when the confidence interval does not include zero (95% equals $p < .05$ level significance).

^a For the $a * b$ paths, z -values are presented.

* The bootstrapped point estimate is significant at $p < .10$.

** The bootstrapped point estimate is significant at $p < .05$.

Table S2

Results from mediator analyses with life satisfaction (SWLS, change scores: pre to post) as outcome measure.

Mediator		Path	Normal theory tests				Bootstrap results for indirect effects (BCa; 95% CI)		
			Coefficient	SE	<i>t</i> ^a	<i>p</i>	Point estimate (SE)	Lower	Upper
PIPS	Total	<i>a</i>	22.87	6.29	3.64	.0019			
		<i>b</i>	−.16	.05	−2.90	.0099			
		Total (<i>c</i>)	−8.07	1.70	−4.74	.0002			
		Direct (<i>c'</i>)	−4.51	1.89	−2.39	.0288			
	Avoidance	<i>a * b</i>	−3.57	1.50	−2.37	.0177	−3.47 (1.64)**	−8.00	−.96
		<i>a</i>	13.47	4.52	2.98	.0080			
		<i>b</i>	−.17	.08	−2.03	.0578			
		Total (<i>c</i>)	−8.07	1.70	−4.74	.0002			
	Fusion	Direct (<i>c'</i>)	−5.83	1.92	−3.03	.0075			
		<i>a * b</i>	−2.25	1.28	−1.76	.0783	−2.40 (1.45)**	−6.04	−.32
		<i>a</i>	9.39	3.32	2.83	.0111			
		<i>b</i>	−.25	.11	−2.31	.0338			
TSK	Kinesiophobia	Total (<i>c</i>)	−8.07	1.70	−4.74	.0002			
		Direct (<i>c'</i>)	−5.72	1.84	−3.11	.0063			
		<i>a * b</i>	−2.35	1.26	−1.87	.0616	−2.34 (1.47)**	−6.12	−.13
		<i>a</i>	11.06	3.43	3.23	.0047			
	Self-efficacy	<i>b</i>	−.01	.12	−.05	.9368			
		Total (<i>c</i>)	−8.07	1.70	−4.74	.0002			
		Direct (<i>c'</i>)	−8.01	2.20	−3.64	.0020			
		<i>a * b</i>	−.06	1.26	−.05	.9612	−.13 (1.55)	−3.85	2.57
	SES	<i>a</i>	−20.55	17.54	−1.17	.2565			
		<i>b</i>	.03	.02	1.24	.2305			
		Total (<i>c</i>)	−8.07	1.70	−4.74	.0002			
		Direct (<i>c'</i>)	−7.50	1.74	−4.31	.0005			
HAD-a	Anxiety	<i>a * b</i>	−.58	.65	−.89	.3746	−.54 (.70)	−2.32	.43
		<i>a</i>	3.26	2.06	1.58	.1305			
		<i>b</i>	−.29	.19	1.56	.1378			
		Total (<i>c</i>)	−8.07	1.70	−4.74	.0002			
HAD-d	Depression	Direct (<i>c'</i>)	−.712	1.75	−4.07	.0008			
		<i>a * b</i>	−.95	.82	−1.16	.2470	−1.01 (1.01)	−4.37	.10
		<i>a</i>	4.56	1.66	2.75	.0132			
		<i>b</i>	−.16	.25	−.65	.5267			
Pain-VAS	Pain intensity	Total (<i>c</i>)	−8.07	1.70	−4.74	.0002			
		Direct (<i>c'</i>)	−7.35	2.06	−3.56	.0024			
		<i>a * b</i>	−.72	1.09	−.66	.5066	−.82 (1.16)	−3.46	1.27
		<i>a</i>	.92	.84	1.10	.2863			
		<i>b</i>	−.09	.49	−.18	.86			
		Total (<i>c</i>)	−8.07	1.70	−4.74	.0002			
		Direct (<i>c'</i>)	−7.99	1.81	−4.42	.0004			
		<i>a * b</i>	−.08	.44	−.19	.8495	−.09 (.59)	−1.97	.77

Note: Number of bootstrap resamples = 3000. The indirect effect is statistically significant at the chosen level when the confidence interval does not include zero (95% equals $p < .05$ level significance).

^a For the $a * b$ paths, z-values are presented.

* The bootstrapped point estimate is significant at $p < .10$.

** The bootstrapped point estimate is significant at $p < .05$.