

How and for whom 'Living with pain online' works

An integrated moderation mediation analysis.

-Master thesis-

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Abstract

The aim of the current research was to assess whether the online intervention ‘Living with pain online’ based on acceptance and commitment therapy (ACT) and mindfulness was effective in reducing interference of pain in daily life. We additionally investigated whether psychological inflexibility and the degree of mindfulness mediated and gender and education moderated the intervention response and how these possible mediators and moderators influenced each other.

A randomized controlled trial with pretest- posttest design and three parallel groups was adopted. A total of 162 chronic pain patients completed the interventions and were included in the study. The experimental group received the web-based intervention ‘Living with pain online’, the active treatment control group received a minimal online intervention based on ‘Expressive Writing’, and the waiting list control group received no treatment. Participants completed measures before and after the interventions to assess pain interference in daily life, psychological inflexibility and the degree of mindfulness.

The experimental group showed significantly higher decrements in pain interference and psychological inflexibility. Psychological inflexibility, but not mindfulness, showed a significant mediating effect of the intervention response. Education and gender showed no significant moderating effects independent of the mediation. Education, but not gender, moderated the mediating effect of psychological inflexibility on pain interference, where no significant mediating effect of psychological inflexibility could be detected for low educated participants.

The web-based ‘Living with pain online’ intervention was shown to be an effective method for the treatment of chronic pain conditions and worked as intended by reducing psychological inflexibility. The intervention response could be improved through tailoring the intervention to the needs of low educated participants.

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Introduction

The Implications of Chronic Pain

Chronic pain is a major health care problem with broad implications ranging from individual impairments to economic consequences. A total of 19% of European adults were shown to be affected by moderate to severe intensities of chronic pain. Those affected individuals were seriously impaired in the quality of their daily activities and social as well as working lives (Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006). The reduced ability to work and the increasing use of medical services have further implications for the economy of society. The total costs of back pain alone in the Netherlands decreased since 2002 but still amounted €3.5 billion in 2007 and the majority of these costs were due to production losses and costs related to society on account of morbidity and mortality (Lambeek et al., 2011). Although the costs of back pain decreased, the economic burden on society is still substantially high.

Moreover chronic pain was shown to be associated with various psychological impairments. An association between chronic pain conditions and alcohol, anxiety and mood disorders was indicated, showing a greater frequency of psychological interferences among persons with chronic back or neck pain (Demyttenaere et al., 2007). Additionally high comorbidity of chronic pain conditions with depression and other psychological disorders were found (Miller & Cano, 2009). These findings additionally stress the impact of chronic pain and indicate that effective and cost efficient treatment is needed to overcome the negative implications of chronic pain for the affected individuals as well as for the economy of society.

Effectiveness of Acceptance and Mindfulness Based Approaches to Chronic Pain

Behavior therapy oriented approaches based on acceptance and mindfulness were shown to be effective in the treatment of chronic pain conditions. Acceptance strategies improved functioning and life satisfaction in people with chronic pain (Wicksell, Ahlqvist, Bring, Melin, & Olsson). Reasonable responses of chronic pain patients to acceptance-based therapies and small to moderate effect sizes for pain intensity, depression, anxiety, physical wellbeing, and quality of life were found by a meta-analysis including 22 controlled as well as non-controlled studies (Veehof, Oskam, Schreurs, & Bohlmeijer 2011). Additionally, significant improvements on depression and pain ratings of chronic pain patients after attending a mindfulness based stress reduction program (MBSR) (Kabat-Zinn, 1982) were indicated (Baer, 2003). Dr. Jon Kabat-Zinn developed MBSR as a group program containing various exercises which were designed to give participants experiences of mindfulness by means of yoga, meditation and relaxation-techniques (Kabat-Zinn, 1982).

The data on the model of psychopathology and treatment underlying acceptance and commitment therapy (ACT) is promising so far, but there are still not enough controlled studies to infer that ACT is more effective than other treatment approaches across a wide range of examined problems (Hayes, Luoma, Bond, Masuda, & Lillis, 2006). The number of randomized controlled trials (RCTs) in the field of ACT and mindfulness approaches for the treatment of chronic pain is limited and little is known about the underlying mechanisms (Veehof et al., 2011; Shapiro, Carlson, Astin, & Freedman, 2006).

The ACT and mindfulness based intervention utilized in the current research is based on the self-help book 'Living with pain' (Veehof, Hulsbergen, Bohlmeijer, & Schreurs, 2010). The 'Living with pain' book is intended for people with chronic pain conditions and is based on the information and exercises from the self-help book 'Living to the full' (Bohlmeijer &

Hulsbergen, 2008). Veehof et al. (2010) created an online intervention for chronic pain conditions based on their self-help book which is deployed in the current research.

A recent research showed an intervention based on the self-help book 'Living to the full' (Bohlmeijer & Hulsbergen, 2008), where participants received this guided ACT self-help intervention by regular mail, to be effective in reducing depressive symptoms, anxiety and fatigue and also to improve positive mental health in people with mild to moderate depressive symptomatology even with minimal email support by a counselor (Fledderus, Bohlmeijer, Pieterse, & Schreurs, 2012). Another guided internet-delivered ACT intervention for chronic pain patients was shown to be effective in increasing activity engagement and pain willingness and decreasing pain-related distress, anxiety and depressive symptoms (Buhrman et al., 2013). Web-based ACT interventions seem to be effective in the treatment of chronic pain conditions on a variety of outcome measures and therefore could be cost effective interventions as a complement or even an alternative for costly chronic pain rehabilitation with the potential to reach more individuals (Andersson, 2009; Hedman et al., 2011). However, little research is done in the field of online ACT and mindfulness self-help interventions for chronic pain conditions. The current study examines the effects of an online intervention based on ACT and mindfulness designed for the treatment of chronic pain with a control group and a comparison group with another active treatment condition.

The utilized active control treatment in this study is also delivered online and is based on 'Expressive Writing' (EW) (Pennebaker, 1997). The presumed mechanism of EW is that writing can help to give a stressful event meaning (Pennebaker, 1997) and can foster the acceptance of stressful events (Pennebaker, 1993). In the area of psychological quality of life and psychological problems, moderate positive effects of EW were found (Pennebaker & Chung, 2007). The aim of the online EW intervention is that participants receive an active but minimal treatment.

Core Principles of Acceptance and Mindfulness Based Approaches

Acceptance and commitment therapy (ACT) is an acceptance-based intervention that uses negative thoughts associated with pain as targets for exposure rather than trying to change their content (Hayes, Strosahl, & Wilson, 1999). ACT focuses on improving psychological flexibility through clarifying values and committing to these values in daily life (Dahl, Wilson, & Nilsson, 2004). Psychological flexibility describes the ability to change or persist in behavior when this behavior profits valued ends and to stay more fully and consciously in contact with the present moment. To reach psychological flexibility one has to create space for appreciated values in daily life despite negative experiences. Therefore acceptance of the pain is encouraged as a method of promoting values-based action (Hayes et al., 1999).

One strategy in ACT is to obtain mindfulness. Attending to the present moment and the inner and/ or outer experiences in a non-judgmental way is a core principal of mindfulness (Kabat-Zinn et al., 1992). The essence of mindfulness is to focus attention on a sensation in a detached manner rather than escaping the unpleasant experience of pain by means of distraction (Kabat-Zinn, 1982). The central idea of mindfulness is learning to orient attention flexibly towards a stimulus and attending to that stimulus in a neutral way. The ability to be mindful has two functions. First, it can function as a reinforcement. By allocating attention to a variety of sensations, one can realize that there are still pleasant experiences in daily life. For example, consciously attending to the sensation of eating could make you realize that your food tastes good and that you actually enjoy it. The second function of mindfulness is the awareness of automatic behavior. Rather than escaping the unpleasant experience of pain by automatically avoiding it, mindfulness fosters focusing attention to this experience. Through that a more conscious decision for values-based behavior can be made instead of automatically avoiding unpleasant sensations.

As suggested by Veehof et al. (2011) the current study uses interference of pain in daily life as outcome measure for the acceptance based intervention in chronic pain patients. These researchers reasoned that, while pain intensity was the most used outcome measure in studies on acceptance based interventions for chronic pain conditions, the reduction of pain intensity not to be the main focus of acceptance based approaches. Instead participants learn to accept the pain as part of their daily lives and to let go of control strategies (Veehof et al., 2011).

Mediators and Moderators

The objective of this study is not only to examine whether the utilized online intervention is effective, but also to investigate how and for whom the web-based ACT intervention works in terms of mediators and moderators. Examining how the ‘Living with pain online’ intervention works in terms of mediators of intervention response, permits to draw conclusions about underlying mechanisms or to make the intervention more cost-effective or efficacious by adding, removing or strengthening certain elements (Kraemer, Wilson, Fairburn, & Agras, 2002). Gathering information about moderators of intervention response allows conclusions about who does and who does not respond to the intervention, therefore facilitating the improvement of treatment outcomes by a possible match of the treatment to patient characteristics and optimally targeting the intervention (Kraemer et al., 2002).

The applied online intervention in this study is based on ACT and mindfulness, therefore the core concepts of these approaches were proposed as possible mediators. If the intervention works as intended, the decrease in pain interference should be due to increases in psychological flexibility and/ or the degree of mindfulness. Psychological flexibility (i.e., acceptance of present experiences and value-based behavior) was shown to mediate the effects of the ‘Living to the Full’ intervention based on ACT and mindfulness on positive

mental health (Bohlmeijer & Hulsbergen, 2008; Fledderus, Bohlmeijer, Smit, & Westerhof 2010). However, to our knowledge, no other research has investigated mediating effects of an online ACT and mindfulness based intervention on chronic pain patients with pain interference as outcome.

Turner, Holtzman, and Mancl (2007) pointed out that patients with chronic pain conditions vary in their responses to treatment, but still little is known about patient characteristics that moderate intervention effects. A correlational study by Miller and Cano (2009) pointed out that certain demographic groups with chronic pain conditions, especially women and less educated individuals, may in particular benefit from early treatments and that access to care should therefore be improved for those individuals. Although these conclusions were based on a correlational study rather than a moderation study, we nevertheless examine how gender and education could moderate intervention responses. We hypothesize that there are differences in intervention responses between men and women and/ or high and low educated participants.

Beyond a Separate Mediation and Moderation Analysis

To fully comprehend the complexity of an intervention we need a more elaborate framework than a sheer moderation or mediation analysis. Moderator and mediator variables can influence each other and thereby give an intricate impression of the complexity of an intervention and its mechanisms that can not be grasped by isolated moderator or mediator analyses (Muller, Judd, & Yzerbyt, 2005).

This paper goes beyond a pure moderation and a pure mediation analysis, and applies a regression-based path-analytic framework suggested by Hayes (2013) to combine moderation and mediation, thereby allowing conclusions about possible influences of moderators and mediators on each other. His framework includes both mediated moderation,

in which a mediator variable transmits a moderating effect (Baron & Kenny, 1986), and moderated mediation, where a mediated effect is moderated by some variable (Baron & Kenny, 1986). However, Hayes (2013) argues that mediated moderation hypotheses should be avoided, because the focus of these analyses is the estimation of the product of the independent variable and a moderator variable, but since this product has no meaning and no substantive interpretation, the analysis of mediated moderation hypotheses would be meaningless and uninteresting. This study therefore focuses on moderated mediation processes and examines how the mediating effects of psychological inflexibility and/ or the degree of mindfulness could be influenced by the moderating effects of gender and/ or education.

Moreover Hayes' (2013) framework overcomes problems with current methods for combining moderation and mediation. Most researchers utilize approaches that use the causal steps procedure to assess mediation when combining mediation and moderation (Baron & Kenny, 1986). However, the causal steps procedure was shown to have several limitations, such as low power, Type I error, not addressing suppression effects and whether the indirect effect is significantly different from zero (Collins, Graham, & Flaherty, 1998; MacKinnon, Lockwood, Hoffman, West & Sheets, 2002; Shrout & Bolger, 2002; Hayes, 2009; Zhao, Lynch, & Chen, 2010), which are inherited by approaches that use this method to combine mediation and moderation (Edwards & Lambert, 2007; Hayes, 2013). The proposed framework overcomes various problems by integrating moderated regression analysis and path analysis and by showing how paths that constitute these effects vary across levels of the moderator variable (Hayes, 2013).

In conclusion the aim of the current study is to assess whether the online intervention 'Living with pain online' based on ACT and mindfulness is effective in reducing interference of pain in daily life and whether psychological inflexibility and/ or the degree of mindfulness

mediate and gender and/ or education moderate the intervention response and whether these possible mediators and moderators in the next place influence each other.

We examine four hypotheses in the current study. The first hypothesis is that the participants who took part in the online ACT intervention would show significantly higher decrements in pain interferences as well as psychological inflexibility and higher increments in mindfulness after the intervention as compared to the participants in the online EW intervention and the waiting list. The second hypothesis is that the intervention response would be mediated by psychological inflexibility and/ or the degree of mindfulness. The third hypothesis states that the intervention response would be moderated by education and/ or gender. The fourth hypothesis states that the mediator and moderator variables would influence each other in terms of a moderated mediation effect. So it could be that the mediating effect of psychological inflexibility and/ or mindfulness could depend on the participants' level of education and/ or gender, and thereby be moderated. This would mean that there are differences in intervention responses through underlying mechanisms between male and female and/ or high and low educated participants.

Methods

Participants

In February and March 2012, participants were recruited through advertisements in Dutch newspapers, magazines and via frequently attended chronic pain websites.

Inclusion criteria were an age of 18 years or older, a self-reported duration of chronic pain for longer than six months and a pain intensity score of 3 or higher on a Pain Intensity Numeric Rating Scale (Pain NRS) (McCaffery & Beebe, 1993) for 3 or more days within a 7 day period, measured during the baseline period at screening.

Exclusion criteria were reading problems due to insufficient Dutch language skills or literacy, having no internet access at home, having no e-mail address, not having enough time to follow the intervention, already receiving psychological treatment, having extremely low scores on psychological inflexibility and severe psychiatric problems. The cut-off score for psychological inflexibility was 26.4 points representing 2 or more standard deviations below the mean of a population of chronic pain patients in a pain rehabilitation center on the Psychological inflexibility in Pain Scale (PIPS) (Wicksell, Lekander, Sorjonen, & Olsson, 2010). People with severe anxiety and/ or depressive symptomatology [more than one standard deviation above the mean of a population of chronic pain patients in a pain rehabilitation center on the Hospital Anxiety and Depression Scale (HADS) (Spinhoven et al., 1997)] were excluded because severe distress would require more intensive treatment.

For further diagnostics the remaining participants were screened with a Web Screening Questionnaire (WSQ) (Donker, van Straten, Marks, & Cuijpers, 2009). Because the WSQ was shown to yield high numbers of false positives (Donker et al., 2009), participants who responded positively to the WSQ were telephoned and additionally underwent the Mini International Neuropsychiatric Interview (MINI) (Sheehan et al. 1998). Participants whom the

MINI diagnosed as having a severe psychological disorder were excluded from the current study and advised to see their general practitioner.

Procedure

Initially 269 people applied to take part in this research, obtained information and signed an informed consent form. After submission of written informed consent, participants filled in the PIPS, HADS and the WSQ online. Based on the inclusion and exclusion criteria as described above 31 people were excluded. On account of their scores on the HADS 15 people were excluded. The other 16 people were excluded because they reported a pain duration of less than 6 months (n=2), had a pain intensity score of 3 or higher for less than 3 days in a 7 day period (n=2), attended another psychological treatment (n=3), had not enough time to follow the intervention (n=1), had reading problems (n=2), or did not fill in the baseline questionnaires (n=6) (see Figure 1).

The remaining 238 participants were randomly assigned to one of the three experimental conditions. Eighty-two participants were assigned to the web-based ACT intervention group and 54 (66%) of them completed the intervention and filled in the post treatment questionnaires. Seventy-nine participants were assigned to the EW active treatment control group and 46 (58%) completed the intervention and filled in the post treatment questionnaires. Seventy-seven participants were assigned to the waiting list (WL) and 62 (81%) responded to the post treatment questionnaires. Therefore the data of 162 (68%) participants was used for the data analysis.

An overview of the participants' characteristics is shown in Table 1. Their mean age was 54 years (ranging from 20 to 84 years) and the majority was female (76.5%). A total of 19.8% had a low education, 69.1% had a middle education and 11.1% of the participants were high educated.

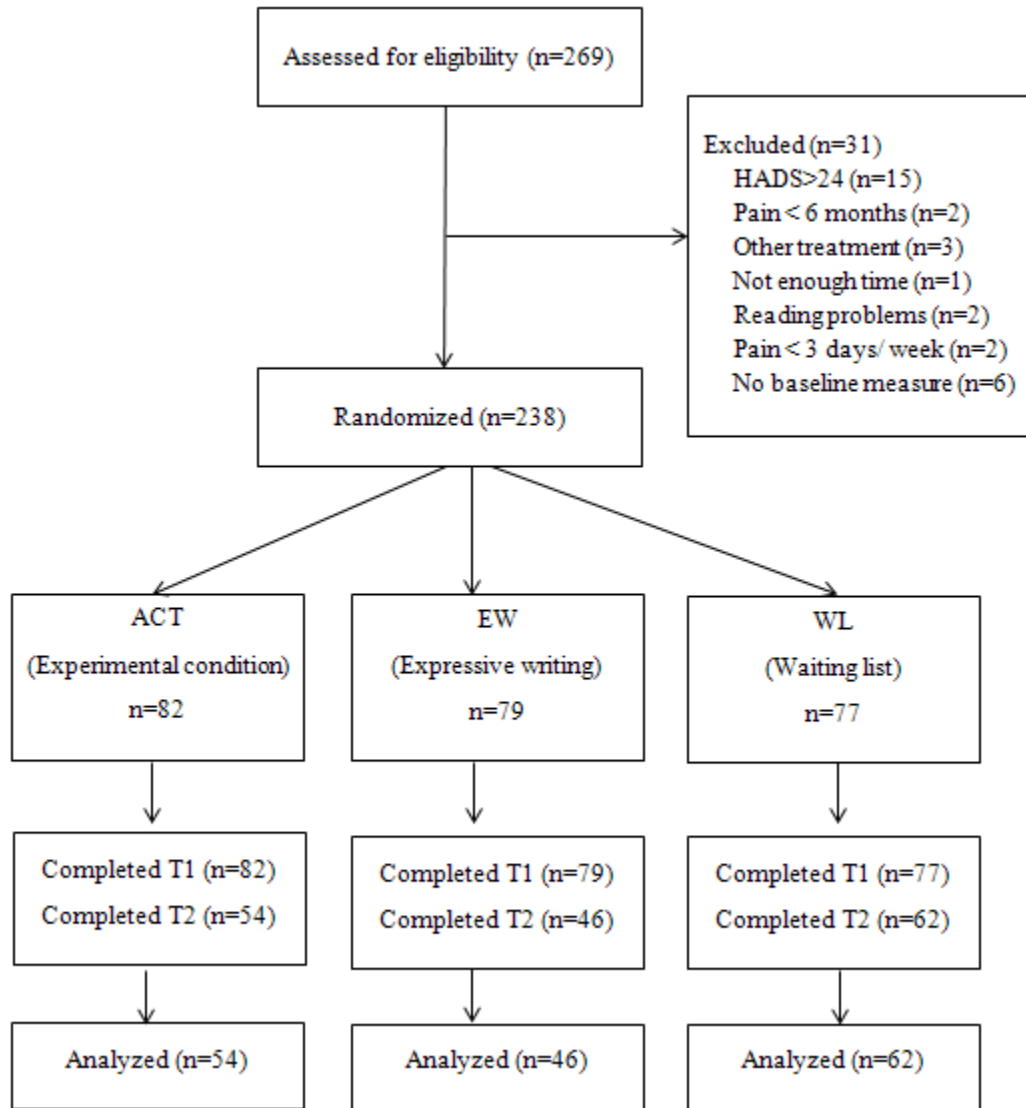


Figure 1. Participant flow. ACT, web-based intervention group who received the intervention ‘Living with pain online’; EW, expressive writing active treatment control group; WL, waiting list control group; T1, baseline measurement; T2, post-intervention.

Characteristic	ACT (n=54)	EW (n=46)	WL (n=62)
Gender, <i>n</i>			
Female	41	37	46
Male	13	9	16
Education, <i>n</i>			
High	7	5	6
Middle	38	33	41
Low	9	8	15
Mean age, years (<i>SD</i>)	55.20 (11.91)	53.33(11.39)	54.0 (11.50)
Duration of complaints, <i>n</i>			
6 months-1 year	4	5	3
1-2 years	8	2	6
2-5 years	10	8	12
<5 years	32	31	41
Diagnosis, <i>n</i>			
No diagnosis	7	6	13
Back pain	8	7	11
Fibro	7	11	9
Joint pain	7	4	6
Rheumatic complaint	3	6	6
Neuropathic pain	6	3	5
Other	16	9	12

Table 1. Characteristics of participants. ACT, web-based intervention group who received the intervention ‘Living with pain online’; EW, expressive writing active treatment control group; WL, waiting list control group.

Experimental Design

A randomized controlled trial with pretest- posttest design and three parallel groups was chosen for the current research. After entry in the current study, participants were screened for inclusion and exclusion criteria and filled in the baseline questionnaires. Thereafter the participants were randomly assigned to one of the three experimental groups. In the experimental condition participants received the web-based intervention ‘Living with pain online’ based on ACT and mindfulness (ACT group). The second group received a minimal online intervention based on ‘Expressive Writing’ (Pennebaker, 1997) and represented the active treatment control condition (EW group). The third group received no treatment throughout the duration of the study and constituted the waiting list control condition (WL group). After the last measurement the waiting list control group received the opportunity to follow the web-based intervention ‘Living with pain online’.

Twelve weeks after the start of the intervention all participants filled in the questionnaires for the second time. All questionnaires were administered online so that both the intervention and the questionnaires could be worked through in the participants’ home environment.

Interventions

Two interventions were included in the current research. ‘Living with pain online’ is in accordance with the self-help book ‘Living with pain’ (Veehof et al., 2010) and the web-based intervention ‘Living to the full’ (Bohlmeijer & Hulsbergen, 2008). The ‘Living with pain online’ intervention is based on ACT and mindfulness and consists of 9 modules, which can be worked through in 9 to 12 weeks.

The first module mainly consists of psycho-education about pain and information about the goals of the intervention. Module 1 also acquaints participants with mindfulness

exercises, which are central to all modules of the intervention. Participants are encouraged to practice mindfulness on a daily basis. In module 2, participants learn about experiential avoidance and its aversive effects. Modules 3 and 4 introduce values and offer exercises to allow participants gaining insight into their personal values and how they could apply these values in their daily life. In module 5, participants align the sights on the possibility of accepting their pain condition. Modules 6 and 7 introduce the concepts cognitive defusion and self-as-context. Here participants practice to recognize unhelpful thoughts about their pain condition and learn the difference between the judging/ subjective and the objective self. Module 8 takes the environment of the affected person into account. Module 9 concentrates on prevention of relapse and on the application of formulated goals and values in the participants' daily life.

During this intervention participants received weekly feedback on exercises and personal problems from a counselor through e-mail. Through this feedback adherence to the intervention was promoted and participants who developed serious problems could be recognized and advised to find help. Counseling has been carried out by master students Psychology of the University of Twente under the supervision of a health psychologist. The role of the counselors was the support and guidance of the intervention process (Cuijpers & Schuurmans, 2007).

Participants in the active treatment control group received the web-based intervention 'Expressive Writing' (EW) (Pennebaker, 1997). This group wrote approximately 15-30 minutes on a daily or regular basis about negative emotions experienced during the day. Participants in this group received weekly feedback by e-mail from a counselor in the same way as did the participants of the web-based ACT intervention.

Measures

The current study used interference of pain in daily life as outcome measure for the acceptance based intervention in chronic pain patients. The subscale pain interference of the Multidimensional Pain Inventory (MPI) (Kerns, Turk, & Rudy, 1985) was used to measure the interference of pain in daily life. This subscale consists of 9 items which can be answered on a 7-point Likert scale where higher scores indicate more pain interference with work, homework chores and social activities in daily life. Lousberg et al. (1999) translated the MPI into Dutch and validated it soundly. In our sample the MPI subscale showed high internal consistency (Cronbach's $\alpha = 0.864$ at baseline).

Process measures included assessments of psychological flexibility and the degree of mindfulness. Psychological flexibility was operationalized by measuring psychological *inflexibility* (Wicksell, Lekander, Sorjonen, & Olsson, 2010). Here psychological *inflexibility* was viewed as opposite of psychological flexibility and conceptualized in terms of avoidance and cognitive fusion related to pain. Psychological inflexibility was measured by means of the Psychological Inflexibility in Pain Scale (PIPS) (Wicksell et al., 2010). The PIPS consists of 12 items with two subscales measuring cognitive fusion (4 items) and avoidance (8 items). Each item had to be scored on a 7-point Likert scale where higher scores indicate greater psychological inflexibility. Trompetter et al. (submitted) showed the Dutch version to have acceptable to good model fit, good internal consistencies as well as good construct validity. The PIPS showed high internal consistency in our sample as well (Cronbach's $\alpha = 0.876$ at baseline).

The Five Facet Mindfulness Questionnaire (FFMQ) (Baer et al., 2008) measures the degree of mindfulness. Bohlmeijer et al. (2011) translated the FFMQ into Dutch and constructed a short form (FFMQ-SF), which we used in the current study. The FFMQ-SF questionnaire measures the five facets of mindfulness observing (8 items), describing (8

items), acting with awareness (8 items), non-judging (8 items) and non-reactivity (7 items) on a 5-point Likert scale where some scores had to be reversed because of negative formulated items. The total score of the FFMQ-SF ranges from 24 to 120 where higher scores indicate higher degrees of mindfulness. Bohlmeijer et al. (2011) showed the Dutch FFMQ-SF to have good model fit and reliability. In our sample the FFMQ-SF showed high internal consistency (Cronbach's $\alpha = 0.789$ at baseline).

Data Analysis

The statistical analysis was performed using SPSS (Version 21.0; 2012, SPSS Inc.). The data was analyzed using the completers only approach, thereby exclusively selecting the data of those who completed the intervention and filled in the post-treatment questionnaires. Chi-square tests and one way analyses of variance (ANOVA) showed no significant differences in gender, education, duration of complaints, diagnosis, pain interference, psychological inflexibility and mindfulness between completers ($n=162$) and non-completers ($n=76$) at baseline. However, there was a significant difference in age ($F(1,237)=6.983$, $p=0.009$), indicating that completers ($M=54.21$, $SD=11.56$) were significantly older than non-completers ($M=49.72$, $SD=13.50$). Additional chi-square tests and one way ANOVAs for the data of completers only showed no significant differences in background variables and outcome as well as process measures between the three experimental groups, indicating that the randomization was successful.

To test the first hypothesis, whether the 'Living with pain online' intervention (ACT) group showed significantly higher decrements in pain interference as well as psychological inflexibility and higher increments in mindfulness as compared to the expressive writing intervention (EW) group and the waiting list (WL) group, we applied three repeated measures ANOVAs with the within subject factor measurement (pre-test/ post-test) and the between

subject factor group (ACT/ EW/ WL) for the outcome measure pain interference (MPI) as well as the two process measures psychological inflexibility (PIPS) and mindfulness (FFMQ-SF).

To test the mediation and moderation related hypotheses we used PROCESS (Version 2.04 for SPSS) created by Hayes (2013). This is a computational tool for path analysis-based moderation and mediation analysis as well as their integration. Using ordinary least squares (OLS) regression, PROCESS estimates various mediation and moderation models, provides direct, indirect and total effects as well as standard regression statistics. Prior to analysis we computed difference scores of all three measures (MPI, PIPS, FFMQ-SF) by subtracting the scores of the first measurement from the scores of the second measurement. These difference scores were used for further analysis of the mediation and moderation related hypotheses (see Table 2 for descriptive statistics of the difference scores).

To test the second hypothesis, that the intervention response would be mediated by psychological inflexibility and/ or the degree of mindfulness, we estimated Hayes' (2013) parallel multiple mediator model, displayed in Figure 2, for the experimental conditions with three comparisons. We compared the mediating effects of psychological inflexibility and the degree of mindfulness between the ACT and EW, the ACT and WL as well as the EW and WL group to see whether these mediators are specific for the ACT group. We tested model 4 in PROCESS (Hayes, 2013) three times with the difference scores of the MPI as outcome variable, the experimental condition (ACT/ EW, ACT/ WL and EW/ WL) as independent variable and the difference scores of the PIPS and FFMQ-SF as mediator variables. Bias corrected bootstrap confidence intervals of 10.000 bootstrap samples were drawn to estimate the direct and indirect effects. On account of the findings of the parallel multiple mediator analyses, we excluded mindfulness as mediating variable and the data of the EW group from further analysis and focused on a simple mediation model with only psychological inflexibility as mediator variable (see Figure 3).

To test the third and fourth hypotheses, whether education and/ or gender serve as moderators and how these moderating effects could influence the mediating effect of psychological inflexibility, we first integrated education and second gender as moderators to the simple mediation model. Here education or gender were included as moderators of each path, therefore representing the total effect moderation model (Edwards & Lambert, 2007), as displayed in Figure 4. We tested this model two times, comparing the ACT and WL group with psychological inflexibility as mediator variable and first with education and second with gender as moderator variable.

The third hypothesis was examined through estimating the moderation of the direct effect of the total effect moderation model. Here we tested the conditional direct effect, where the direct effect was dependent (or conditional) on the levels of first education and second gender. The fourth hypothesis was tested by examining moderation of the mediating effect. Here we estimated the conditional indirect effect, where the indirect effect of psychological inflexibility was dependent (or conditional) on the levels of first education and second gender.

We tested model 59 in PROCESS with the difference scores of the MPI as outcome variable, the experimental condition (ACT/ WL) as independent variable, the difference scores of the PIPS as mediator variable, and first with education as moderator variable and second with gender as moderator variable. Based on 95% bias corrected bootstrap confidence intervals of 10.000 bootstrap samples we estimated the conditional direct and indirect effects of the two total effect moderation models.

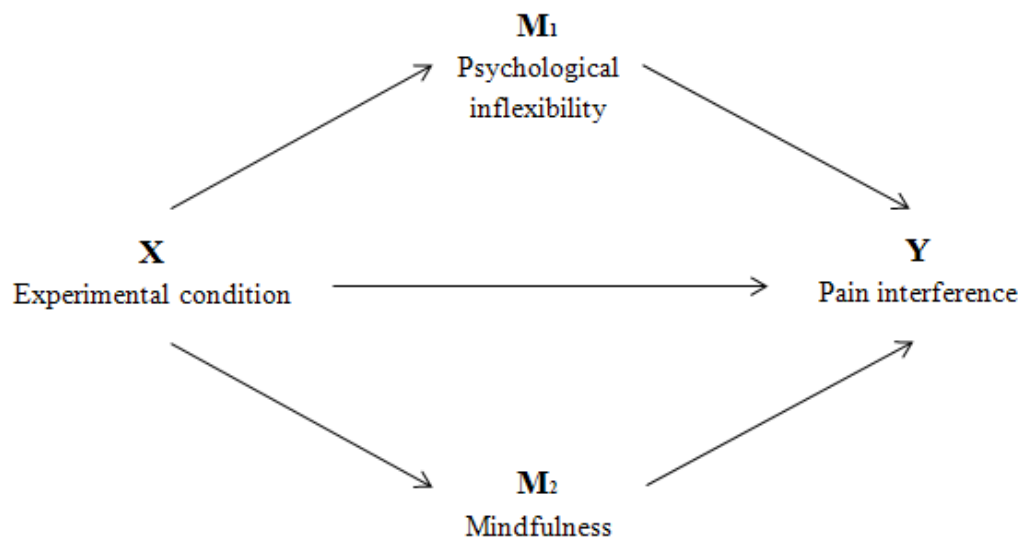


Figure 2. A conceptual diagram of the parallel multiple mediator model. In this diagram X represents the independent variable (here the experimental conditions), Y the dependent variable (here pain interference in daily life), and M₁ and M₂ represent the mediator variables (psychological inflexibility and mindfulness, respectively)

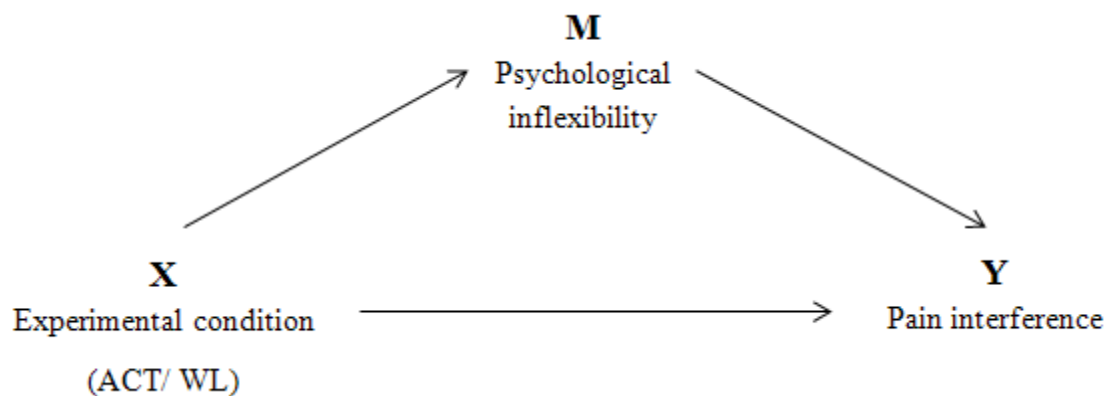


Figure 3. A conceptual diagram of the simple mediation model. In this diagram X represents the independent variable (ACT, web-based intervention group who received the intervention ‘Living with pain online’; WL, waiting list control group), Y the dependent variable (pain interference in daily life), and M represents the mediator variable (psychological inflexibility).

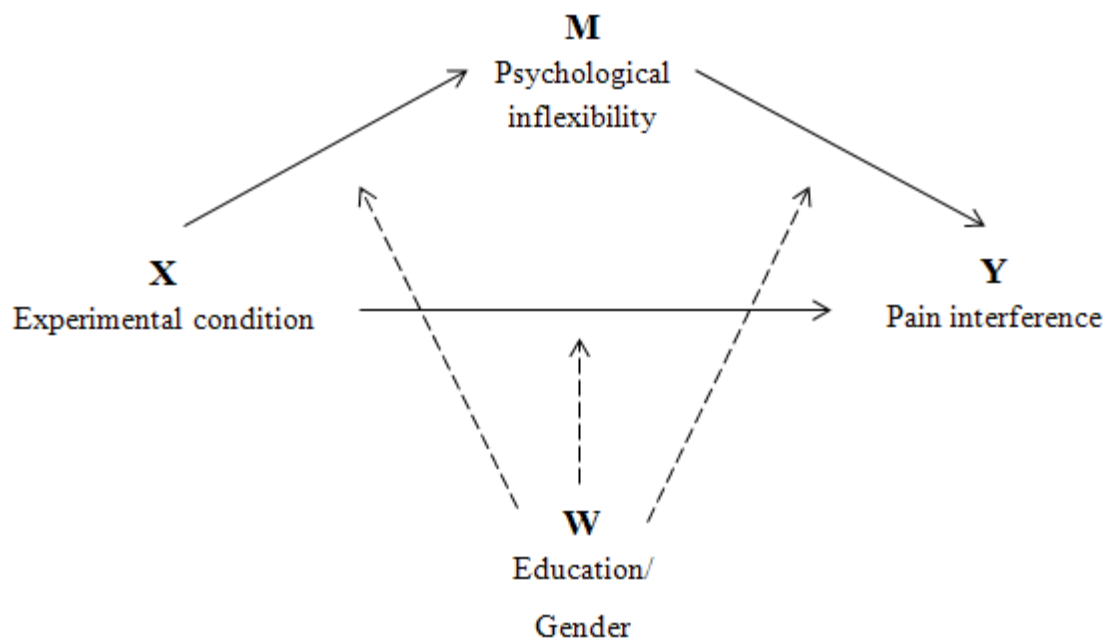


Figure 4. Conceptual diagram of the total effect moderation model with the experimental conditions as independent variable (X), psychological inflexibility as mediator variable (M), pain interference as outcome variable (Y) and education or gender as moderator variables (W).

Results

Effectiveness of the Interventions

Descriptive statistics of the scores between the three groups are shown in Table 2. The repeated measures ANOVA for pain interference scores showed a significant main effect of the factor measurement ($F(1, 159)=6.655, p=0.011$) indicating a significant difference in scores between the two measurements. Additionally a significant interaction effect between the factors measurement and group was detected ($F(2, 159)=5.175, p=0.007$) pointing out that there were significant differences in changes of scores between the three groups. Post hoc comparisons revealed that only the ACT group showed a significant main effect of measurements ($F(1,53)=16.921, p<0.001$) indicating a significant decrement in pain interference scores of 4 points at the second measurement (see Table 2). The EW group as well as the WL group did not show any significant main effects of measurement.

The repeated measures ANOVA for psychological inflexibility scores showed a significant main effect of the factor measurement ($F(1, 159)=130.233, p<0.001$) indicating a significant difference in scores between the two measurements. Additionally a significant interaction effect between the factors measurement and group was detected ($F(2, 159)=10.822, p<0.001$) pointing out that there were significant differences in changes of scores between the three groups. Post hoc comparisons revealed that all three group showed a significant main effect of measurements (ACT: $F(1,53)=72.183, p<0.001$; EW: $F(1,45)=30.782, p<0.001$; WL: $F(1,61)=25.725, p<0.001$) indicating a significant decrement in psychological inflexibility in all groups at the second measurement, where the ACT group showed the highest decrement with approximately 16 points (see Table 2).

The repeated measures ANOVA for mindfulness scores showed a significant main effect of the factor measurement ($F(1, 159)=58.265, p<0.001$) indicating a significant

difference in scores between the two measurements. No significant interaction effect between the factors measurement and group was detected, indicating that there were no significant differences in changes of scores between the three groups. These findings are represented in Figure 5.

		Y			M ₁			M ₂		
		Pain interference			Psychological inflexibility			Mindfulness		
		T ₁	T ₂	T ₂ -T ₁	T ₁	T ₂	T ₂ -T ₁	T ₁	T ₂	T ₂ -T ₁
ACT	Mean	31.648	27.389	-4.259	55.167	39.833	-15.333	81.796	87.593	5.796
	SD	10.040	10.342	7.609	12.665	11.438	13.262	8.638	9.152	6.764
EW	Mean	30.739	31.500	0.761	54.565	45.326	-9.239	82.435	88.609	6.174
	SD	9.427	11.380	8.982	11.002	12.702	11.294	8.612	8.070	9.824
WL	Mean	33.403	32.081	-1.323	54.694	48.984	-5.710	79.968	83.629	3.661
	SD	10.497	11.492	7.186	11.872	12.847	8.864	11.589	11.798	9.106
Total	Mean	32.062	30.352	-1.710	54.815	44.895	-9.920	81.278	86.364	5.086
	SD	10.051	11.221	8.072	11.836	12.875	11.837	9.864	10.166	8.645

Table 2. Descriptive statistics of scores in the three experimental conditions. The means and standard deviations of the three groups are displayed at baseline (T₁), after the interventions (T₂) and as difference scores (T₂-T₁). ACT, web-based intervention group who received the intervention ‘Living with pain online’; EW, expressive writing active treatment control group; WL, waiting list control group.¹

¹ Negative difference scores in pain interference suggest lower pain interference scores at the second measurement and therefore a decrease in pain interference. Negative difference scores in psychological inflexibility suggest lower psychological inflexibility scores at the second measurement, thus a decrement in psychological inflexibility. Positive difference scores in mindfulness suggest higher mindfulness scores at the second measurement, hence an increase in mindfulness.

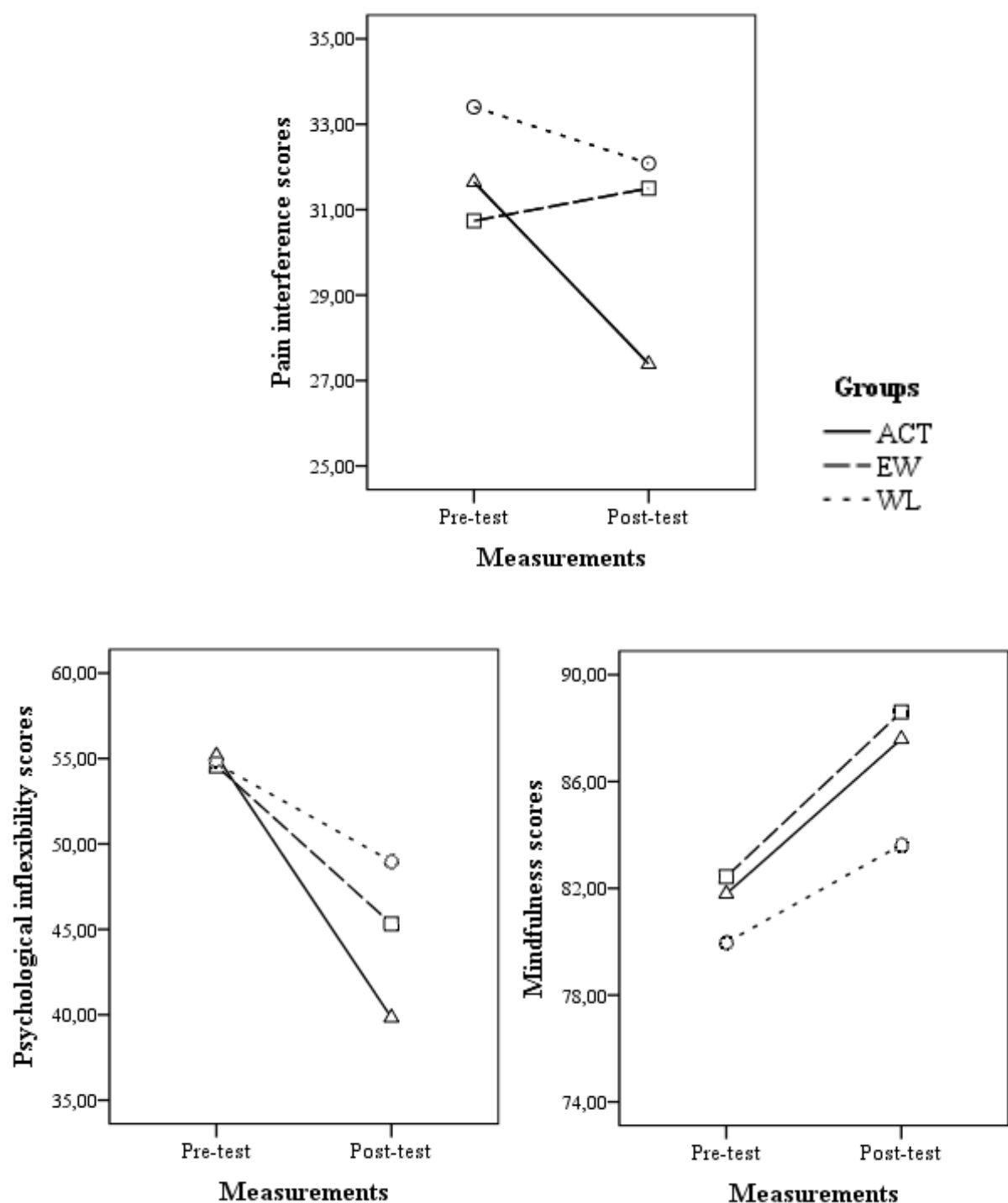


Figure 5. Intervention responses in the three groups. Scores are displayed for the expressive writing active treatment control group (EW), the ‘Living with pain online’ intervention group (ACT) and the waiting list control group (WL) before (pre-test) and after (post-test) the interventions. Pain interference scores are shown in the upper panel, psychological inflexibility scores are shown in the lower left panel and mindfulness scores are shown in the lower right panel.

Mediation of Psychological Inflexibility and Mindfulness

Since the three comparisons of the parallel multiple mediator models showed no significant indirect effects of mindfulness as mediator, this variable was excluded from further analysis because it was no addition to the model. Moreover, the comparison of the EW with the WL group showed no significant indirect effects, suggesting that the mediating effects were specific for the ACT group. The EW group therefore was of no further relevance for our hypotheses and we excluded the data of the EW group from additional analysis and focused on the comparison of the ACT and WL group in favor of a concise report of the findings and interpretation of the results. The complete direct and indirect effects (Table A1) of the parallel multiple mediator model for all three comparison as well as the statistical models (Figure A1) and according tables (Table A2 to A4) can be found in Appendix A of this paper. Consequently we further reported the results of a simple mediation model (displayed in Figure 3) with psychological inflexibility as mediator and the ACT and WL groups as experimental conditions.

The estimation of the simple mediation model comparing the ACT to the WL group showed no significant direct effect (see path coefficient c' in Figure 6 and Table 3), indicating that there was no influence of the experimental condition on pain interference independent of the mediator psychological inflexibility.

Consistent with our prediction, the experimental condition (ACT/ WL) was negatively related to psychological inflexibility (see path coefficient a in Figure 6 and Table 3), suggesting that participants in the ACT group showed lower psychological inflexibility than those assigned to the waiting list. Additionally, psychological inflexibility positively predicted pain interference while controlling for the experimental condition (see path coefficient b in Figure 6 and Table 3), meaning that those participants who showed higher psychological inflexibility also showed higher pain interference.

Most pertinent to the mediation hypothesis was the estimation of the indirect effect ($a \times b$) of psychological inflexibility on pain interference. Accordant with our hypothesis, there was evidence of a significant indirect effect of experimental condition on pain interference through psychological inflexibility ($a \times b = -2.839$, bootstrap confidence interval: -4.642 to -1.455), meaning that psychological inflexibility indeed functioned as a mediator of the intervention response.

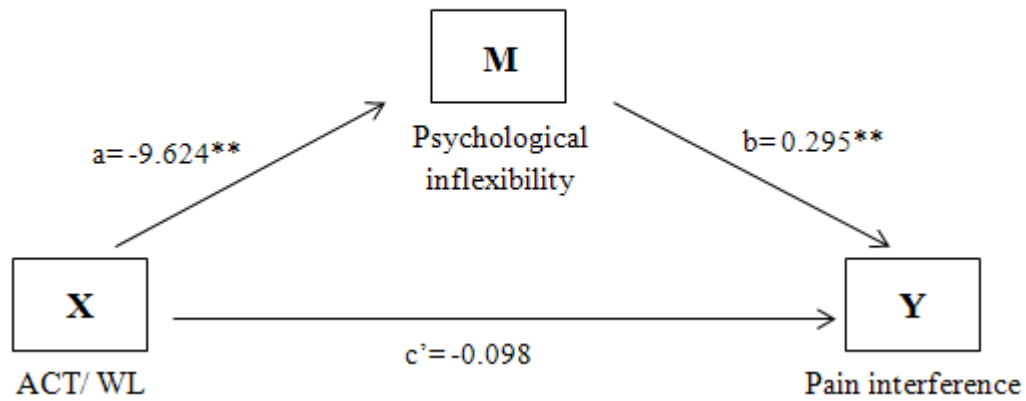


Figure 6. Statistical diagram of the simple mediation model of the comparison between the ACT ('Living with pain online' intervention) and the WL (waiting list) group.

* significant at $\alpha=0.05$

** significant at $\alpha=0.01$

		Consequent								
		M				Y				
		(psychological inflexibility)				(pain interference)				
Antecedent		Coeff.	SE	p	t	Coeff.	SE	p	t	
X (ACT/ WL)	a	-9.624	2.071	<0.001	-4.646	c'	-0.098	1.349	0.943	-0.072
M (psychological inflexibility)		–	–	–	–	b	0.295	0.056	<0.001	5.275
Constant	i _M	-5.710	1.413	<0.001	-4.040	i _Y	0.362	0.902	0.689	0.401
		$R^2=0.159$				$R^2=0.229$				
		$F(1, 114)=21.589, p<0.001$				$F(2, 112)=16.730, p<0.001$				

Table 3. Regression coefficients (Coeff.), standard errors (SE), and model summary information of the simple mediation model depicted in Figure 5 for the comparison between the ACT ('Living with pain online' intervention) and the WL (waiting list) group.

Moderation of Education and Gender

Moderation of Education

The estimation of the total effect moderation model comparing the ACT group to the WL group with education as moderator variable showed the direct effect of the experimental condition on pain interference, when holding psychological inflexibility constant, to be independent of education (see path $XW \rightarrow Y$ with coefficient c'_3 in Figure 7 panel A and Table 4 upper section). Also, the conditional direct effect ($c'_1 + c'_3W$) of the experimental condition on pain interference was not significant at any level of education. These results suggest, that there was no effect of the experimental condition on pain interference independent of the mediator psychological inflexibility at any level of education. Hence, education did not moderate the effect of the intervention on pain interference independent of the mediation of psychological inflexibility.

Moderation of Gender

The estimation of the total effect moderation model comparing the ACT group to the WL group with gender as moderator variable showed the direct effect of experimental condition on pain interference, when holding psychological inflexibility constant, to be independent of gender (see path $XW \rightarrow Y$ with coefficient c'_3 in Figure 7 panel B and Table 4 lower section). Accordingly, the conditional direct effect ($c'_1 + c'_3W$) of the experimental condition on pain interference was not significant for all participants. Hence, there seemed to be no effect of the experimental condition on pain interference independent of psychological inflexibility at any level of gender. Thus, gender did not moderate the effect of the intervention on pain interference independent of the mediation of psychological inflexibility.

Moderation of the Mediation

Moderation of the Mediation by Education

Investigating possible moderation of the mediating effect of psychological inflexibility by education, we detected no significant moderation of the effect of experimental condition on psychological inflexibility (see path $XW \rightarrow M$ with coefficient a_3 in Figure 7 panel A and Table 4 upper section), meaning that the effect of the experimental condition on psychological inflexibility was independent of education. Also, there was no significant moderation effect of education on the effect of psychological inflexibility on pain interference (see path $MW \rightarrow Y$ with coefficient b_2 in Figure 7 panel A and Table 4 upper section), indicating that the effect of psychological inflexibility on pain interference was also independent of the education of participants. Because these paths did not show a significant moderating effect of education (a_3 and b_2), this indicated that the mediation would be independent of the levels of education.

However, taking a closer look at Figure 8 (panel A, left) it seems that there were differences in psychological inflexibility scores between the levels of education. For example it appears that middle and high educated participants in the ACT group showed higher decrements in psychological inflexibility after the intervention than middle and high educated participants in the WL group. Moreover taking the apart psychological inflexibility scores at the two measurement points into consideration, it seems that middle and high educated participants in the ACT group had considerably lower psychological inflexibility after the intervention as compared to middle and high educated participants in the WL group (see Table B1 in Appendix B). That is why we additionally estimated the conditional indirect effect $((a_1 + a_3W) \times (b_1 + b_2W))$ of the experimental condition on pain interference through psychological inflexibility to further investigate whether the mediation of psychological inflexibility was moderated by education. The bias corrected bootstrap confidence intervals indeed showed the conditional indirect effect to be consistently negative for middle

$((a_1+a_3 \times 0)(b_1+b_2 \times 0)=-2.978$, bootstrap confidence interval: -4.924 to -1.535) and high educated participants $((a_1+a_3 \times 1)(b_1+b_2 \times 1)=-5.945$, bootstrap confidence interval: -11.179 to -1.578), but not to be significant for low educated participants. These results suggest, that, except for low educated participants, the ACT group did show statistically significant lower psychological inflexibility difference scores, therefore a significantly higher decrement, than the WL group (see Figure 8, panel A, left and Table B1 in Appendix B).

Thus, the indirect effect of the experimental condition on pain interference through psychological inflexibility was negative, except among low educated participants, where no significant indirect effect could be detected. Consequently, comparing the ACT with the WL group, the mediating effect of psychological inflexibility appeared to be moderated by education.

Moderation of the Mediation by Gender

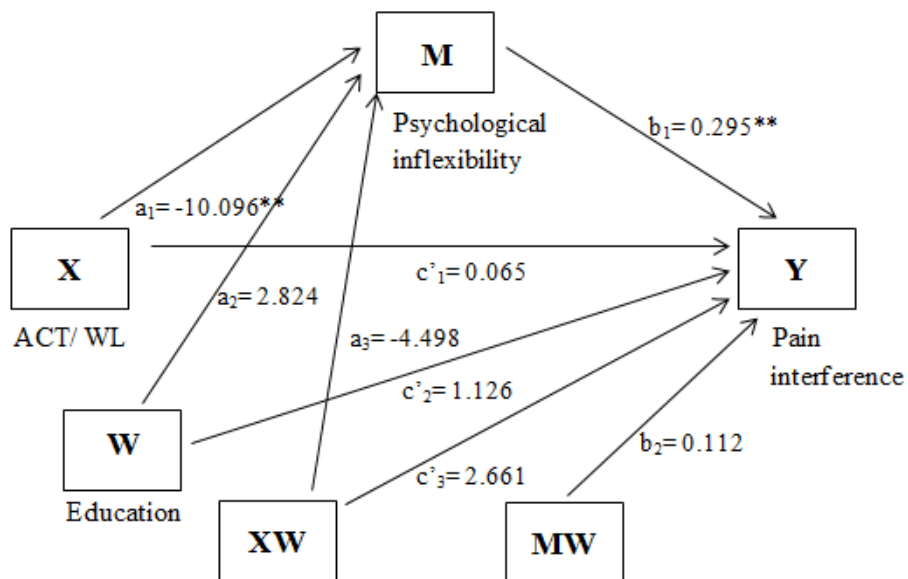
Investigating possible moderation of the mediating effect of psychological inflexibility by gender, we detected no significant moderation of the effect of experimental condition on psychological inflexibility (see path $XW \rightarrow M$ with coefficient a_3 in Figure 7 panel B and Table 4 lower section), meaning that the effect of experimental condition on psychological inflexibility was independent of gender. Also, there was no significant moderation of gender on the effect of psychological inflexibility on pain interference (see path $MW \rightarrow Y$ with coefficient b_2 in Figure 7 panel B and Table 4 lower section), indicating that the effect of psychological inflexibility on pain interference was independent of the gender of participants, thus suggesting that gender did not function as a moderator of the mediating effect of psychological inflexibility.

Accordingly, the conditional indirect effect $((a_1+a_3W) \times (b_1+b_2W))$ of the experimental condition on pain interference through psychological inflexibility was shown to be significant for men as well as women. The bootstrap confidence intervals showed the conditional indirect

effect to be consistently negative for all participants (women: $(a_1+a_3\times 0)(b_1+b_2\times 0)=-3.124$, bootstrap confidence interval: -5.363 to -1.482; men: $(a_1+a_3\times 1)(b_1+b_2\times 1)=-2.303$, bootstrap confidence interval: -56.075 to -0.415), suggesting that the ACT group showed significantly lower psychological inflexibility difference scores, therefore a significantly higher decrement, than the WL group (see Figure 8, panel B, left). Taking the apart psychological inflexibility scores at the two measurement points into consideration, this means that male and female participants in the ACT group had significantly lower psychological inflexibility scores after the intervention as compared to male and female participants in the WL group (see Table B1 in Appendix B).

Hence, the indirect effect of the experimental condition on pain interference through psychological inflexibility was negative among all participants. Consequently, comparing the ACT with the WL group, psychological inflexibility functioned as a mediator for all participants and this mediation did not appear to be moderated by gender.

A: Education



B: Gender

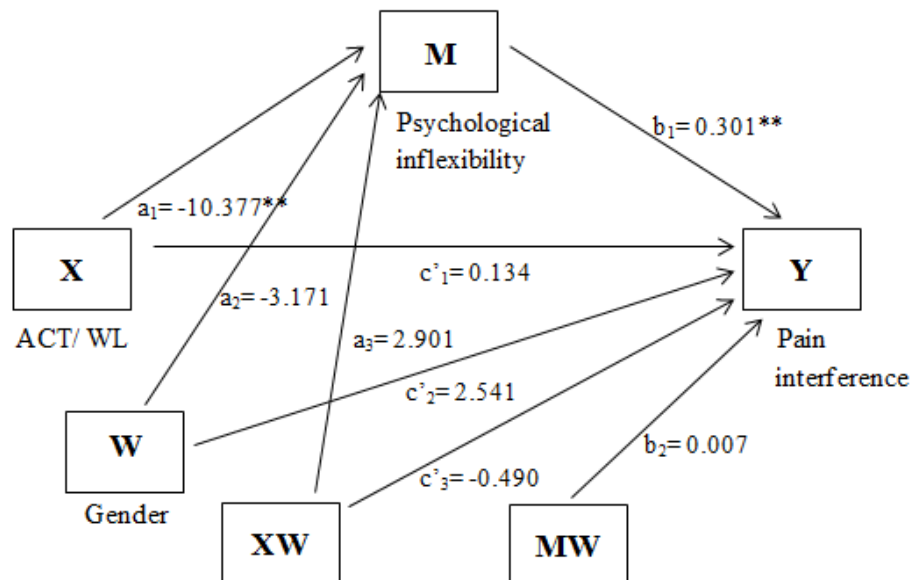


Figure 7. Statistical diagrams of the total effect moderation models comparing the ACT ('Living with pain online' intervention) to the WL (waiting list) group with psychological inflexibility as mediator and education (panel A) and gender (panel B) as moderator variables.

* significant at $\alpha=0.05$

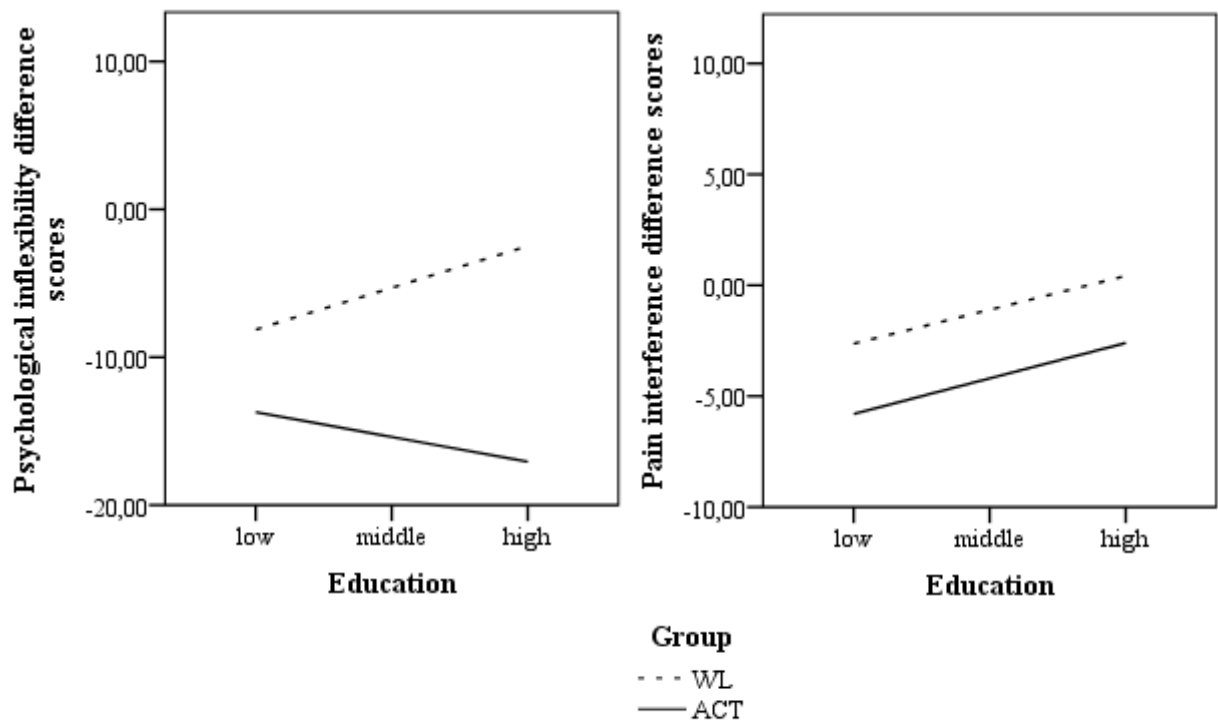
** significant at $\alpha=0.01$

Education										
Antecedent		Consequent								
		M				Y				
		(psychological inflexibility)				(pain interference)				
		Coeff.	SE	p	t		Coeff.	SE	p	t
X (ACT/ WL)	a ₁	-10.096	2.109	<0.001	-4.787	c' ₁	0.065	1.387	0.963	0.047
M		—	—	—	—	b ₁	0.295	0.056	<0.001	5.241
(psychological inflexibility)										
M×W		—	—	—	—	b ₂	0.112	0.095	0.241	1.180
W (education)	a ₂	2.824	2.512	0.263	1.124	c' ₂	1.126	1.549	0.469	0.727
X×W	a ₃	-4.498	3.756	0.234	-1.198	c' ₃	2.661	2.491	0.288	1.068
Constant	i ₁	-5.300	1.462	<0.001	-3.626	i ₂	0.331	0.928	0.722	0.357
R ² =0.171						R ² =0.250				
F(3, 112)=7.714, p<0.001						F(5, 110)=7.342, p<0.001				

Gender										
Antecedent		Consequent								
		M				Y				
		(psychological inflexibility)				(pain interference)				
		Coeff.	SE	p	t		Coeff.	SE	p	t
X (ACT/ WL)	a ₁	-10.377	2.401	<0.001	-4.322	c' ₁	0.134	1.563	0.932	0.086
M		—	—	—	—	b ₁	0.301	0.061	<0.001	4.960
(psychological inflexibility)										
M×W		—	—	—	—	b ₂	0.007	0.162	0.966	0.043
W (gender)	a ₂	-3.171	3.244	0.331	-0.977	c' ₂	2.541	2.302	0.272	1.104
X×W	a ₃	2.901	4.815	0.548	0.603	c' ₃	-0.490	3.146	0.877	-0.156
Constant	i ₁	-4.891	1.648	0.004	-2.968	i ₂	-0.245	1.026	0.812	-0.239
R ² =0.166						R ² =0.246				
F(3, 112)=7.451, p<0.001						F(5, 110)=7.158, p<0.001				

Table 4. Regression coefficients (*Coeff.*), standard errors (*SE*), and model summary information of the total effect moderation model depicted in Figure 7 for the comparison between the ACT ('Living with pain online' intervention) and the WL (waiting list) group with first education (upper section of this table) and second with gender (lower section of this table) as moderator variables.

A: Education as moderator



B: Gender as moderator

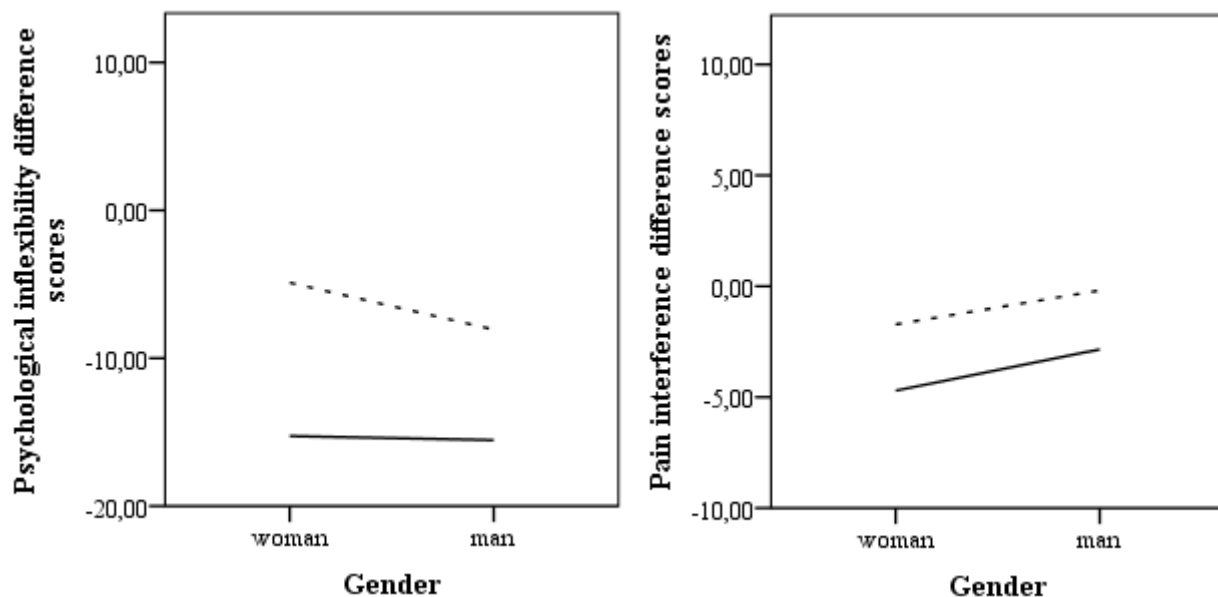


Figure 8. A visual representation of the moderating effects of education (panel A) and gender (panel B) when comparing the ACT ('Living with pain online' intervention) with the WL (waiting list) group. On the left side the moderation effects of the experimental condition (ACT/ WL) on psychological inflexibility difference scores are displayed as a function of education (low (W=-1)/ middle (W=0)/ high (W=1)) in panel A and gender (woman (W=0)/ man (W=1)) in panel B. On the right side the moderation of the effect of experimental condition (ACT/ WL) on pain interference difference scores by education (low/ middle/ high) in panel A and by gender (woman/ man) in panel B are displayed while controlling for psychological inflexibility.

Discussion

The results of this study show that pain interference levels were significantly decreased after the ‘Living with pain online’ intervention, based on acceptance and commitment therapy (ACT) and mindfulness. Furthermore, levels of psychological interference were significantly reduced after the intervention. The decrease in pain interference is attributable to reductions in psychological inflexibility. Independent of this underlying mechanism of psychological inflexibility, there were no differences between intervention responses in high or low educated as well as male or female participants. However, when estimating the influence of demographic factors on the effect of psychological inflexibility, our results showed a significant influence of education. This influence indicated that the intervention response in low educated participants was not attributable to decrements in psychological inflexibility.

Consistent with our first hypothesis, the participants who took part in the online ACT and mindfulness based intervention showed significantly higher decrements in pain interference after the intervention than the other participants. Therefore showing that the web-based ACT intervention was successful in the reduction of pain interference in daily life and additionally supporting previous findings of effective ACT and mindfulness based interventions (e.g. Fledderus et al., 2012; Veehof et al., 2011; Hayes et al., 2006; Buhrman et al., 2013). Although other researchers showed their ACT and mindfulness based approaches to be effective in the treatment of chronic pain complaints, the present research was the first to show an online intervention based on ACT and mindfulness to be effective in reducing pain interference in daily life.

Moreover, we found the online ACT intervention to be more effective in the reduction of pain interference than another online treatment approach based on expressive writing (EW) (Pennebaker, 1997). Our findings therefore provide evidence for Hayes’ et al. (2006) indication that ACT could be more effective in the treatment of chronic pain conditions than

other treatment approaches like EW. We can therefore conclude that the utilized ‘Living with pain online’ intervention is indeed an effective treatment approach for people suffering from chronic pain complaints.

Analysis of our process measures showed the ‘Living with pain online’ intervention to be also effective in reducing psychological inflexibility and accordant with our second hypothesis, the intervention response was mediated by psychological inflexibility. This mediating effect indicates that the reduction in pain interference was due to decreases in psychological inflexibility. This finding corresponds to another research where psychological flexibility was found to mediate the effect of an acceptance and mindfulness based intervention on positive mental health (Fledderus et al., 2010). These researchers conceptualized psychological flexibility as acceptance of present experiences and value-based behavior. We handled psychological *inflexibility* as opposite of psychological flexibility and conceptualized it in terms of avoidance and cognitive fusion related to pain. Despite these two different conceptualizations, our research seemed to yield similar results in assessing mediating effects of acceptance and mindfulness based intervention responses.

The mediating effect of psychological inflexibility was specific for the ACT group and no mediating effects could be detected when comparing the EW group with the waiting list, showing that only the web-based ACT intervention effectively reduced pain interference in daily life through the decrement in psychological inflexibility. This mediating effect of psychological inflexibility gives us information about the underlying mechanism of the web-based ACT intervention and therefore more details on how the ‘Living with pain online’ intervention works. The mediating effect indicated that the effectiveness of this intervention lies in changes of psychological inflexibility and that the intervention therefore worked as intended.

The lack of a mediating effect of mindfulness was rather unexpected. Analysis of our process measures showed that there were increases in mindfulness scores among all three

groups. The increments in mindfulness were thus not specific for the ACT group. A possible explanation could be that the general increase in the degree of mindfulness was initiated by the measurements. It could be that participants in the EW group and waiting list showed an increment in mindfulness purely through filling in the questionnaires. Because of the first contact with a mindfulness questionnaire those participants could have adopted a more mindful way of thinking and thereby achieved an increment in mindfulness.

Another explanation could be that the 'Living with pain online' intervention targeted mindfulness effectively after all and the ACT group showed higher increments in mindfulness than the other participants, but we were not able to detect such higher increments in mindfulness through exclusively using a questionnaire. Even though we could not detect any increments in the degree of mindfulness using the FFMQ-SF, participants in the ACT group still might be more mindful after the intervention than the other participants. Here it could be that participants in the ACT group maintain mindfulness exercises and experience positive effects on pain interference in daily life through these exercises, but that the utilized questionnaire does not assess these practical implementations of mindfulness thoroughly enough and rather measures the understanding of the concepts of mindfulness. Additional research is needed to investigate whether there are indeed no effects on mindfulness through the web-based ACT intervention. One possibility would be to conduct interviews with the participants of the ACT group and assess how they experienced the mindfulness elements in the web-based intervention and filling in the FFMQ-SF. Through interviews we could additionally determine whether they had some experiences on mindfulness beyond the questionnaire or whether they integrated regular mindfulness exercises in their daily life and how those exercises possibly influenced the interference of pain.

With regard to our third hypothesis, we did not detect any significant conditional direct effects, therefore indicating that no moderating effects of education and gender on the intervention response occurred independent of the mediation. This is in accordance with

several studies were also no relationship between treatment responses and demographic variables like age, gender, education, race, or pain duration could be detected (McCracken & Turk, 2002).

Concerning our moderated mediation hypotheses we detected no significant moderating effects of gender on the mediating effect of psychological inflexibility. The estimated conditional indirect effect was significant for both genders, thus suggesting that the ‘Living with pain online’ intervention was equally effective for men as well as women through the reduction of psychological inflexibility. This web-based intervention therefore seems to be applicable for men and women alike.

However, when adding the moderator education to the mediation model, we indeed detected a moderated mediation effect in accordance with our fourth hypothesis, where education moderated the mediating effect of psychological inflexibility. In middle to high educated participants, the ‘Living with pain online’ intervention seemed to reduce psychological inflexibility, which translated into lower pain interference in daily life. For participants with low education, the effect of the web-based ACT intervention on pain interference did not operate through psychological inflexibility, but still reduced pain interference effectively.

One possible explanation could be that low educated participants experienced difficulties to comprehend the core principles of the intervention and rather profited from more generic elements of the web-based ACT intervention, like the feedback from a counselor. Another possible explanation would be that the decrease in pain interference for low educated participants was due to increments in mindfulness, but we could not detect such effects on mindfulness successfully. Additional interviews after the web-based ACT intervention could give more information about which elements helped low educated participants in the decrement of pain interference and whether they experienced positive effects because of mindfulness, for example through regular mindfulness exercises.

The moderated mediation finding allows the ‘Living with pain online’ intervention to aim at low educated individuals suffering from chronic pain more effectively by tailoring the web-based ACT intervention to the needs of this particular group. This consideration of the needs of low educated individuals could be applied by using simpler language or, like suggested by Fledderus et al. (2012), by using comics to illustrate the main concepts of the web-based ACT intervention and thereby facilitating understandability of the intervention. The conclusions based on the moderated mediation effect of education could facilitate a more effective targeting of the utilized intervention for low educated participants, therefore possibly improving the treatment outcomes through a match between treatment and patient characteristics (Kraemer et al., 2002). Further research is needed to see how using simpler language and comics for illustrating the concepts could facilitate the interventions effect on psychological inflexibility or which particular elements of the web-based intervention supported the decrement in pain interference in low educated participants independent of psychological inflexibility.

Although the detected moderated mediation effect of education could have important implications for the improvement of the ‘Living with pain online’ intervention, these results should be considered with caution. Our sample size was reasonably high, but by assorting our sample into high, middle and low educated participants, the comparison of the ACT group with the waiting list contained small samples of high and low educated participants (see Table 1) with high standard deviations (see Table B1 in Appendix B). Additional research with higher samples of high and low educated participants is therefore needed to support our findings.

Another limitation of the current study was that our sample mainly consisted of female and middle educated participants, so the results should be generalized with prudence. However, reaching a primarily female and higher educated group is not uncommon for web-based self-help (e-health) interventions (e.g. Carlbring et al. 2007).

An additional limitation of this study could be the completers only approach in our data analysis. Only selecting those participants who adhered to the intervention and filled in the post-treatment questionnaires could introduce bias to the sample. Although we found a significant difference in age between completers and non-completers (drop-out), indicating that completers were significantly older, this difference was rather small (5 years). Further examination of other background variables (i.e. gender, education, duration of complaints, and diagnosis) and outcome as well as process measures between completers and non-completers showed no significant differences, indicating that there was no variance between participants who adhered to the treatment and those who dropped out. Therefore, we have reason to assume that the completers only approach did not introduce bias to our sample, but rather provided an accurate estimation of the effect of the ‘Living with pain online’ intervention to the treatment of chronic pain conditions.

This research did not include a follow up measurement to investigate whether the detected changes in psychological inflexibility and pain interference remain after the web-based intervention. It would have strengthened the design if a follow-up assessment of the intervention response would have been included, so that stronger conclusions could be drawn about whether the detected effects remain stable over a longer period of time. Buhrman et al. (2013) showed their guided internet-delivered ACT intervention for chronic pain patients to maintain improvements in various outcome measures at a 6-months follow-up. The effects of a web-based ACT intervention therefore potentially produce long term effects.

All in all, the current study represents a high quality research showing the web-based ‘Living with pain online’ intervention to be an effective method for the treatment of chronic pain conditions through reducing pain interference in daily life. The utilized online ACT intervention was even more effective than an active treatment approach based on expressive writing. Furthermore the mediating effect of psychological inflexibility gave more insight in underlying mechanisms of the intervention and showed that the intervention worked as

intended. The lack of a mediating effect of mindfulness and the moderated mediation effect of education suggest that there are possibilities for improvement of the online ACT intervention through adding mindfulness elements and improving comprehensiveness through simpler language or the use of comics to illustrate the main concepts of the 'Living with pain online' intervention. In that way the intervention could be tailored to the needs of low educated participants and effectiveness could be improved. The web-based ACT intervention has the potential to reach more individuals and represents a cost effective intervention as a complement or even an alternative for costly chronic pain rehabilitation.

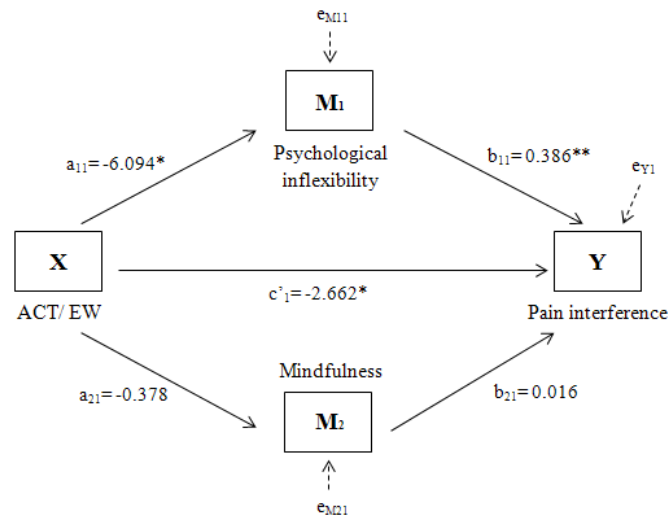
Appendix

A: Results of the Parallel Multiple Mediator Models

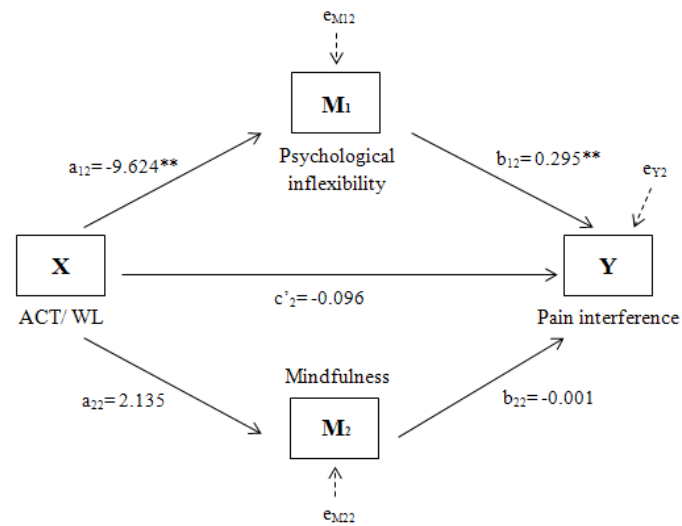
	Direct effect			Indirect effects					
	Point estimate	p	t	M ₁		M ₂		Total	
				Psychological inflexibility		Mindfulness			
				Point estimate	CI	Point estimate	CI	Point estimate	CI
ACT/ EW	-2.662	0.038	-2.109	-2.353	-4.789 to -0.521	-0.006	-0.415 to 0.282	-2.359	-4.800 to -0.504
ACT/ WL	-0.096	0.9406	-0.076	-2.838	-4.745 to -1.466	-0.003	-0.482 to 0.364	-2.841	-4.692 to -1.473
EW/ WL	3.403	0.035	2.136	-1.435	-3.088 to 0.071	0.115	-0.208 to 0.884	-1.320	-3.044 to 0.224

Table A1. Direct and indirect effects of the three parallel multiple mediator models. The indirect effects were estimated using bias corrected bootstrap confidence intervals (CI) of 10.000 bootstrap samples. ACT, web-based intervention group who received the intervention ‘Living with pain online’; EW, expressive writing active treatment control group; WL, waiting list control group.

A: ACT compared to EW



B: ACT compared to WL



C: EW compared to WL

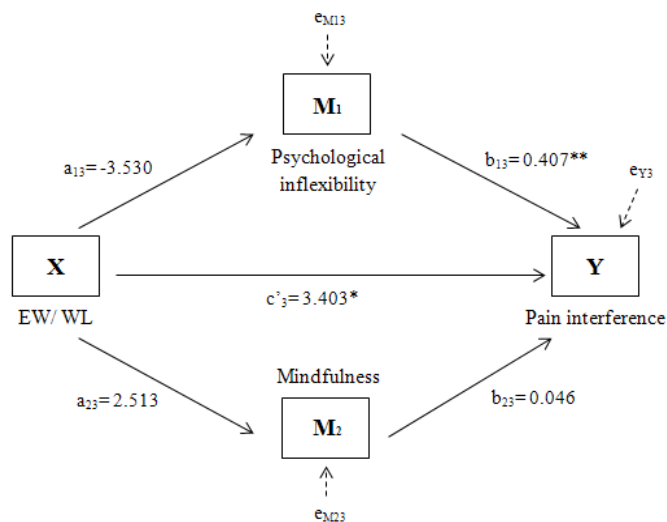


Figure A1. Statistical diagrams of the parallel multiple mediator models. The comparison of the mediating effects of psychological inflexibility and the degree of mindfulness are shown between the ACT and EW (panel A), the ACT and WL (panel B) and the EW and WL group (panel C). Errors in the estimation of the mediator variables M₁ and M₂ (e_{M1} , e_{M2}) as well as the outcome variable Y (e_Y) are displayed. * significant at $\alpha=0.05$; ** significant at $\alpha=0.01$

		Consequent															
		M ₁						M ₂						Y			
		(psychological inflexibility)						(mindfulness)						(pain interference)			
Antecedent		Coeff.	SE	p	t			Coeff.	SE	p	t			Coeff.	SE	p	t
X (ACT/EW)	a ₁₁	-6.094	2.481	0.016	-2.457	a ₂₁		-0.378	1.734	0.828	-0.218	c' ₁		-2.662	1.262	0.038	-2.109
M1 (psychological inflexibility)		-	-	-	-			-	-	-	-	b ₁₁		0.386	0.089	<0.001	4.351
M2 (mindfulness)		-	-	-	-			-	-	-	-	b ₂₁		0.016	0.097	0.872	0.162
Constant	iM ₁	-9.239	1.684	<0.001	-5.488	iM ₂		6.174	1.464	<0.001	4.216	I _{y1}		4.231	1.843	0.024	2.296
		R ² =0.058						R ² =0.001						R ² =0.391			
		F(1, 98)=6.036, p=0.016						F(1, 98)=0.047, p=0.828						F(3, 96)=7.502, p<0.001			

Table A2. Regression coefficients (*Coeff.*), standard errors (*SE*), and model summary information of the parallel multiple mediator model depicted in Figure A1 (panel A) for the comparison between the ACT and EW group.

Antecedent	Consequent														
	M ₁						M ₂						Y		
	(psychological inflexibility)						(mindfulness)						(pain interference)		
	Coeff.	SE	p	t			Coeff.	SE	p	t		Coeff.	SE	p	t
X (ACT/ WL)	a ₁₂	-9.624	2.146	<0.001	-4.484	a ₂₂	2.135	1.491	0.155	1.423	c' ₂	-0.096	1.266	0.940	-0.076
M1 (psychological inflexibility)	-	-	-	-	-	-	-	-	-	-	b ₁₂	0.295	0.075	<0.001	3.947
M2 (mindfulness)	-	-	-	-	-	-	-	-	-	-	b ₂₂	-0.001	0.077	0.987	-0.016
Constant	iM ₁₂	-5.710	1.135	<0.001	-5.031	iM ₂₂	3.661	1.166	0.002	3.140	I ₂₂	0.366	0.954	0.702	0.383
R ² =0.159						R ² =0.017						R ² =0.229			
F(1, 114)=20.105, p<0.001						F(1, 114)=2.051, p=0.155						F(3, 112)=6.329, p<0.001			

Table A3. Regression coefficients (*Coeff.*), standard errors (*SE*), and model summary information of the parallel multiple mediator model depicted in Figure A1 (panel B) for the comparison between the ACT and WL group.

Antecedent	Consequent														
	M ₁					M ₂					Y				
	(psychological inflexibility)					(mindfulness)					(pain interference)				
	Coeff.	SE	p	t		Coeff.	SE	p	t		Coeff.	SE	p	t	
X (EW/ WL)	a ₁₃	-3.530	2.031	0.085	-1.738	a ₂₃	2.513	1.872	0.182	1.342	c' ₃	3.403	1.593	0.035	2.136
M1 (psychological inflexibility)	-	-	-	-	-	-	-	-	-	-	b ₁₃	0.407	0.083	<0.001	4.888
M2 (mindfulness)	-	-	-	-	-	-	-	-	-	-	b ₂₃	0.046	0.077	0.554	0.594
Constant	iM ₁₃	-5.710	1.135	<0.001	-5.031	iM ₂₃	3.661	1.166	0.002	3.140	I _{y3}	0.831	1.050	0.431	0.791
R ² =0.030					R ² =0.017					R ² =0.263					
F(1, 106)=3.022, p=0.085					F(1, 106)=1.802, p=0.182					F(3, 104)=8.387, p<0.001					

Table A4. Regression coefficients (*Coeff.*), standard errors (*SE*), and model summary information of the parallel multiple mediator model depicted in Figure A1 (panel C) for the comparison between the EW and WL group.

B: Descriptive Statistics of Scores Organized by Education and Gender

Mean (SD)	M (psychological inflexibility)						Y (pain interference)					
	t ₁			t ₂			t ₁			t ₂		
	ACT	WL		ACT	WL		ACT	WL		ACT	WL	
Education												
low	61.333 (13.105)	56.000 (7.020)	47.778 (14.687)	49.400 (10.868)	-13.556 (12.381)	-6.600 (8.895)	37.111 (5.988)	35.533 (9.410)	30.778 (10.895)	33.733 (9.714)	-6.333 (6.910)	-1.800 (6.394)
middle	53.553 (12.636)	54.756 (13.490)	38.079 (9.307)	48.342 (14.136)	-15.474 (12.649)	-6.415 (8.911)	30.684 (10.601)	33.244 (10.871)	26.737 (9.563)	31.537 (12.186)	-3.947 (7.580)	-1.707 (7.574)
high	56.000 (11.358)	51.000 (10.198)	39.143 (14.803)	52.333 (8.165)	-16.857 (18.845)	1.333 (5.989)	29.857 (9.754)	29.167 (10.741)	26.571 (14.212)	31.667 (12.176)	-3.286 (9.232)	2.500 (6.091)
Gender												
women	53.951 (12.114)	54.848 (11.841)	38.683 (10.694)	49.957 (12.824)	-15.268 (14.505)	-4.891 (8.975)	31.732 (9.930)	35.370 (9.586)	27.024 (9.797)	33.652 (10.955)	-4.707 (7.727)	-1.717 (7.808)
man	59.000 (14.083)	54.250 (12.337)	43.462 (13.333)	46.188 (12.910)	-15.539 (8.685)	-8.063 (8.363)	31.385 (10.790)	27.750 (11.246)	28.539 (12.272)	27.563 (12.154)	-2.846 (7.335)	-0.188 (5.023)
Total	55.167 (12.665)	54.694 (11.872)	39.833 (11.438)	48.984 (12.847)	-15.333 (13.262)	-5.710 (8.864)	31.648 (10.040)	33.403 (10.497)	27.389 (10.342)	32.081 (11.492)	-4.259 (7.609)	-1.323 (7.186)

Table B1. Descriptive statistics of scores in the ACT and WL group organized by education and gender. The means and standard deviations of the two groups are displayed at baseline (t₁), after the interventions (t₂) and as difference scores (t₂-t₁) for the mediator variable psychological inflexibility and the outcome variable pain interference.

References

- Andersson, G. (2009). Using the internet to provide cognitive behavior therapy. *Behavior Research and Therapy*, 47, 175-180.
- Baer, R.A. (2003). Mindfulness training as a clinical intervention: A conceptual and empirical review. *Clinical Psychology*, 10, 125–143.
- Baer, R.A., Smith, G.T., Lykins, E., Button, D., Krietemeyer, J., Sauer, S., Walsh, E., Duggan, D., & Williams, J.M.G. (2008). Construct validity of the five facet mindfulness questionnaire in meditating and non-meditating samples. *Assessment*, 15(3), 329-342.
- Baron, R.M., & Kenny, D.A. (1986). The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology*, 5, 1173–1182.
- Bohlmeijer, E.T., & Hulsbergen, M. (2008). *Voluit leven. Mindfulness of de kunst van het aanvaarden, nu als praktisch hulpboek [Living to the Full. Mindfulness or the Art of Acceptance, now as a Practical Help Book]*. Boom: Amsterdam.
- Bohlmeijer, E.T., ten Klooster, P.M., Fledderus, M., Veehof, M.M., & Baer, R. (2011). Psychometric properties of the Five Facet Mindfulness Questionnaire in depressed adults and development of a short form. *Assessment*, 8, 308-320.

- Breivik, H., Collett, B., Ventafridda, V., Cohen, R., & Gallacher, D. (2006). Survey of chronic pain in Europe: Prevalence, impact on daily life, and treatment. *European Journal of Pain*, 10, 287-333.
- Buhrman, M., Skoglund, A., Husell, J., Bergström, K., Gordh, T., Hursti, T., et al. (2013). Guided internet-delivered acceptance and commitment therapy for chronic pain patients: A randomized controlled trial. *Behaviour Research and Therapy*, 51(6), 307–315.
- Carlbring, P., Gunnarsdottir, M., Hedensjö, L., Andersson, G., Ekselius, L., & Furmark, T. (2007). Treatment of social phobia, randomized trial of Internet-delivered cognitive behavioral therapy with telephone support. *British Journal of Psychiatry*, 90, 123–128.
- Collins, L.M., Graham, J.W., & Flaherty, B.P. (1998). An alternative framework for defining mediation. *Multivariate Behavioral Research*, 33, 295–312.
- Cuijpers, P., & Schuurmans, J. (2007). Self-help interventions for anxiety disorders: An overview. *Current Psychiatry Reports*, 9(4), 284-290.
- Dahl, J., Wilson, K.G., & Nilsson, A. (2004). Acceptance and commitment therapy and the treatment of persons at risk for long-term disability resulting from stress and pain symptoms: A preliminary randomized trial. *Behavior Therapy*, 35, 785–801.
- Demyttenaere, K., Bruffaerts, R., Lee, S., Posada-Villa, J., Kovess, V., Angermeyer, M.C., et al. (2007). Mental disorders among persons with chronic back pain or neck pain: Results from the world mental health surveys. *Pain*, 129, 332-342.

- Donker, T., van Straten, A., Marks, I., & Cuijpers, P. (2009). A brief Web-based screening questionnaire for common mental disorders: Development and validation. *Journal of Medical Internet Research*, 11(3), e19.
- Edwards, J.R., & Lambert, L.S. (2007). Methods for integrating moderation and mediation: A general analytical framework using moderated path analysis. *Psychological Methods*, 12, 1-22.
- Fledderus, M., Bohlmeijer, E.T., Pieterse, M. E., & Schreurs, K.M.G (2012). Acceptance and commitment therapy as guided self-help for psychological distress and positive mental health: A randomized controlled trial. *Psychological Medicine*, 42(3), 485 495.
- Fledderus, M., Bohlmeijer, E.T., Smit, F., & Westerhof, G.J. (2010). Mental Health Promotion as a New Goal in Public Mental Health Care: A Randomized Controlled Trial of an Intervention Enhancing Psychological Flexibility. *American Journal of Public Health*, 100(12), 2372- 2378.
- Hayes, A.F. (2009). Beyond Baron and Kenny: Statistical mediation analysis in the new millennium. *Communication Monographs*, 76(4), 408-420.
- Hayes, A.F. (2013). *Introduction to mediation, moderation, and conditional process analysis: A regression-based approach*. New York: Guilford Press.
- Hayes, S.C., Luoma, J.B., Bond, F.W., Masuda, A., & Lillis, J. (2006). Acceptance and Commitment Therapy: Model, processes and outcomes. *Behaviour Research and Therapy*, 44, 1–25.

- Hayes, S.C., Strosahl, K., & Wilson, K.G. (1999). *Acceptance and commitment therapy: An experiential approach to behavior change*. New York: Guilford Press.
- Hedman, E., Andersson, E., Ljótsson, B., Andersson, G., Rück, C., & Lindefors, N. (2011). Cost-effectiveness of Internet-based cognitive behavior therapy vs. cognitive behavioral group therapy for social anxiety disorder: Results from a randomized controlled trial. *Behavior Research and Therapy*, 49, 729-736.
- Kabat-Zinn, J. (1982). An outpatients program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: Theoretical considerations and preliminary results. *General Hospital Psychiatry*, 4, 33–47.
- Kabat-Zinn, J., Massion, A.O., Kristeller, J., Peterson, L.G., Fletcher, K.E., Pbert, L., Lenderking, W.R., & Santorelli, S.F. (1992). Effectiveness of a meditation-based stress reduction program in the treatment of anxiety disorders. *American Journal of Psychiatry*, 149, 936–943.
- Kerns, R.D., Turk, D.C., & Rudy, T.E. (1985). The West Haven-Yale Multidimensional Pain Inventory (WHYMPI). *Pain*, 23(4), 345-356.
- Kraemer, H.C., Wilson, G.T., Fairburn, C.G., & Agras, W.S. (2002). Mediators and moderators of treatment effects in randomized clinical trials. *Archives of General Psychiatry*, 59, 877– 883.

- Lambeek, L.C., van Tulder, M.W., Swinkels, I.C., Koppes, L.L., Anema, J.R., & van Mechelen, W. (2011). The trend in total cost of back pain in The Netherlands in the period 2002 to 2007. *Spine*, 36(13), 1050-1058.
- Lousberg, R., Van Breukelen, G.J.P., Groenman, N.H., Schmidt, A.J.M., Arntz, A., & Winter, F.A.M. (1999). Psychometric properties of the Multidimensional Pain Inventory, Dutch language version (MPI-DLV). *Behavior Research and Therapy*, 37, 167-182.
- MacKinnon, D.P., Lockwood, C.M., Hoffman, J.M., West, S.G., & Sheets, V. (2002). A comparison of methods to test mediation and other intervening variable effects. *Psychological Methods*, 7, 83–104.
- McCaffery, M., & Beebe, A. (1993). *Pain: Clinical Manual for Nursing Practice*. Baltimore: V.V. Mosby Company.
- McCracken, L.M., & Turk, D.C. (2002). Behavioral and cognitive-behavioral treatment for chronic pain: Outcome, predictors of outcome, and treatment process. *Spine*, 27(22), 2564-2573.
- Miller L.R., & Cano, A. (2009). Comorbid chronic pain and depression: Who is at risk? *The Journal of Pain*, 10, 619–27.
- Muller, D., Judd, C.M., & Yzerbyt, V.Y. (2005). When moderation is mediated and mediation is moderated. *Journal of Personality and Social Psychology*, 89(6), 852.

- Pennebaker, J.W. (1993). Putting stress into words: Health, linguistic, and therapeutic implications. *Behavior Research and Therapy*, 31(6), 539-548.
- Pennebaker, J.W. (1997). Writing About Emotional Experiences as a Therapeutic Process. *Psychological Science*, 8(3), 162-166.
- Pennebaker, J.W., & Chung, C.K. (2007). *Expressive writing, emotional upheavals, and health*. In H. Friedman and R. Silver (Eds.), *Handbook of health psychology*. New York: Oxford University Press.
- Shapiro, S.L., Carlson, L.E., Astin, J.A., & Freedman, B. (2006). Mechanisms of mindfulness. *Journal of Clinical Psychology*, 62, 373-86.
- Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., et al. (1998). The Mini-International Neuropsychiatric Interview (MINI): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry*, 59, 22-33.
- Shrout, P.E., & Bolger, N. (2002). Mediation in experimental and non-experimental studies: New procedures and recommendations. *Psychological Methods*, 7, 422–445.
- Spinhoven, P.H., Ormel, J., Sloekers, P.P.A., Kempen, G.I.J.M., Speckens, A.E.M., & Hemert, A.V. (1997). A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychological Medicine*, 27(2), 363-370.

- Trompetter, H.R., Bohlmeijer, E.T., van Baalen, B., Kleen, M., Köke, A., Reneman, M., & Schreurs, K.M.G. (submitted). Is the Psychological Inflexibility in Pain Scale (PIPS) a valid measure of processes in Acceptance & Commitment Therapy (ACT)? Extending validity and exploring its relationship with mindfulness. *Submitted*.
- Turner, J.A., Holtzman, S., & Mancl, L. (2007). Mediators, moderators, and predictors of therapeutic change in cognitive-behavioral therapy for chronic pain. *Pain*, 127, 276–286.
- Veehof, M.M., Hulsbergen, M., Bohlmeijer, E.T., & Schreurs, K.M.G. (2010). *Leven met pijn. De kunst van het aanvaarden. [Living with pain. The Art of Acceptance]*. Boom: Amsterdam.
- Veehof, M.M., Oskam, M.J., Schreurs, K.M.G., & Bohlmeijer, E.T. (2011). Acceptance-based interventions for the treatment of chronic pain: A systematic review and meta-analysis. *Pain*, 152, 533–542.
- Wicksell, R.K., Ahlqvist, J., Bring, A., Melin, L., & Olsson, G.L. (2008). Can exposure and acceptance strategies improve functioning and life satisfaction in people with chronic pain and whiplash-associated disorders (wad)? A randomized controlled trial. *Cognitive Behavioral Therapy*, 37, 183-191.
- Wicksell, R.K., Lekander, M., Sorjonen, K., & Olsson, G.L. (2010). The Psychological Inflexibility in Pain Scale (PIPS): Statistical properties and model fit of an instrument to assess change processes in pain related disability. *European Journal of Pain*, 14(7),771-785.

Zhao, X., Lynch, J.G., & Chen, Q. (2010). Reconsidering Baron and Kenny: Myths and truths about mediation analysis. *Journal of Consumer Research*, 37(2), 197-206.