Are Processes in Acceptance & Commitment Therapy (ACT) Related to Chronic Pain Outcomes Within Individuals Over Time? An Exploratory Study Using *n*-of-1 Designs

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Abstract: *Introduction*. Acceptance & Commitment Therapy (ACT) explicitly postulates experiential avoidance (EA) and values-based living (VBL) as essential treatment processes. As outcomes from between-subject studies cannot readily be generalized to within-subject processes in individuals, we explored the unfolding of, and relationship between, EA and VBL and levels of pain interference in daily life and emotional well-being within individuals experiencing chronic pain. *Methods*. Using *n*-of-1 designs, three participants following a multidisciplinary treatment program filled out a 12-item daily questionnaire (87–110 days). After multiple imputation of missing data, McKnight Time-series analysis procedures were performed for each participant separately. The interrelationships of EA, VBL and pain intensity, and the relationship of EA and VBL beyond pain intensity with both chronic pain outcomes were assessed both concurrently (same day) and prospectively (consecutive days). *Results*. Both EA and VBL were associated with at least one of five outcome variables (four domains of pain interference and emotional well-being) beyond pain intensity in two participants, but not in the third participant. These associations primarily existed for concurrent, but not consecutive, days. In contrast to VBL, EA was not associated with emotional well-being for any of the three participants. *Conclusions*. Although the finding that ACT-processes were associated with pain outcomes on concurrent days is consistent with ACT theory, the absence of such associations on consecutive days means that alternative explanations cannot be rule out. One possibility is that pain interference fluctuates within days at a higher variability rate than was currently assessed. Future research should consider using a higher measurement frequency to be able to grasp time-lagged effects.

Keywords: Acceptance & Commitment Therapy, Experiential avoidance, Chronic pain, Within-subject, n-of-1 design, Single case

Introduction

Efforts are made in different disciplines of psychology to improve the evidence-based nature of theory and interventions (e.g. Chambless & Hollon, 1998; Davidson et al., 2003; Michie & Prestwich, 2010). In addition to generating knowledge on general effectiveness of interventions, it is important to derive how, why, for whom and to what extent changes in behaviour occur (Elliott, 2010; Kazdin, 2009; Kraemer, Wilson, Fairburn, & Agras, 2002). Such research questions can focus on the identification of relevant treatment processes by assessing the relationship of these processes with individual functioning, and subsequently the ability of these processes to serve as causal working mechanisms of change. Especially in the area of chronic pain it is important to adopt research questions beyond mere average effectiveness on the group level, as treatment effects of psychological interventions are generally modest and treatment is not effective for everyone (McCracken & Turk, 2002; Turk, Wilson, & Cahana, 2011; Williams, Eccleston, & Morley, 2013).

A form of cognitive behaviour therapy that is very suitable to the treatment of chronic pain is Acceptance & Comment Therapy (ACT) (Hayes, Strosahl, & Wilson, 2011). Contrary to many other forms of cognitive behaviour therapy (Williams et al., 2013), ACT is built on a clearly outlined theoretical framework that explicitly postulates hypothesized treatment processes. The overarching goal in ACT is to promote psychological flexibility, which can be understood as an umbrella term for six sub-processes.

Psychological flexibility is the ability to perform values-based behaviour in the presence of unwanted private experiences like pain or pain-related cognitions and emotions (e.g., pain catastrophizing, pain-related fear; Hayes et al., 2004, 2006, 2011). To provide an alternative strategy to experiential avoidance – on-going, fruitless attempts of an individual to avoid, control or change these unwanted experiences – ACT fosters acceptance of these private experiences (Hayes, Luoma, Bond, Masuda, & Lillis, 2006). This creates the necessary space for (re-)evaluation and commitment towards valued life activities. The processes of experiential avoidance and values-based living are elaborated upon and strengthened by the other, related treatment processes (cognitive defusion, present-moment awareness, self-as-context and committed action).

Many studies have shown that ACT is effective in the treatment of multiple conditions, including chronic pain (e.g., Fledderus, Bohlmeijer, Pieterse, & Schreurs, 2012; Ost, 2008; Powers, Zum Vorde Sive Vording, & Emmelkamp, 2009; Thorsell et al., 2011; Veehof, Trompetter, Bohlmeijer & Schreurs, 2016; Wetherell et al., 2011). Overall, randomized controlled trials (RCT) report small to moderate effect sizes of ACT for chronic pain on outcomes including anxiety, depression, pain interference in daily life, pain intensity and physical functioning (Hann & McCracken, 2014; Veehof et al., 2016). These effect sizes are equal to those reported of Cognitive Behavioral Therapy for chronic pain (Williams et al., 2013).

Considerable efforts have been made in the area of chronic pain to study the relationship of ACT-processes to patient functioning, and the ability of these processes to function as working mechanisms of treatment change (e.g., McCracken & Eccleston, 2005; McCracken & Gutiérrez-Martínez, 2011; McCracken, Vowles, & Eccleston, 2005; Vowles & McCracken, 2008; Vowles, McCracken, & Eccleston, 2008; Wicksell, Olsson, & Hayes, 2010). Unfortunately, these studies all employed between-subject designs, thereby assessing between-subject variance. In other words, these studies – even when performing sequential measurements in a group of individuals over time – assessed if differences between people in treatment processes are able to predict outcomes (Johnston & Johnston, 2013). However, like many other psychological theories, ACT proposes that an individual's behaviour varies depending on one's personal variance in, for example, experiential avoidance. As outcomes from between-subject studies in psychology are almost never stationary (stable over time) and homogeneous (apply to the same extent across all people) (Molenaar, 2004; Molenaar & Campbell, 2009), conclusions based on group level aggregates cannot be transferred to the individual level, something that is often implicitly assumed (Borsboom, Mellenbergh, & van Heerden, 2003; Curran & Bauer, 2012).

Reflecting the above, both clinical and statistical considerations lead one to consider the necessity to step down from the level of aggregate group studies and additionally focus on the individual. Nevertheless, only a few studies in the area of ACT have applied research designs and/or statistical techniques suitable for the analysis of within-subject variance, such as multilevel (hierarchical) modelling or n-of-1 designs (Arch, Wolitzky-Taylor, Eifert, & Craske, 2012; Forman et al., 2012; Twohig, Hayes, & Masuda, 2006a, 2006b). Also, these existing within-subject studies often focus on questions regarding the effectiveness of ACT-interventions, rather than mechanisms. The fields of health and clinical psychology in general have seen an increase in studies exploring the functioning of processes and the relationship with outcomes within individuals over time (e.g. Peters, Sorbi, Kruise, Kerssens, Verhaak, & Bensing, 2000; Snippe, Nyklíček, Schroevers, & Bos, 2015). Yet, few have asked research questions that make it possible to draw conclusions for separate individuals (for a systematic review on n-of-1 designs in the field of health psychology, see McDonald, Quinn, Vieira, O'Brien, White, Johnston & Sniehotta, 2017).

We applied a series of n-of-1 studies in three people suffering from chronic pain in the weeks before, during and after enrolment in an eight-week, ACT-based multidisciplinary chronic pain rehabilitation program. The n-of-1 design is applied by taking multiple measurements within an individual for a prolonged period of time, with equal time intervals between the successive measures (e.g., daily) (Bar-

low, Nock, & Hersen, 2009; Borckardt et al., 2008; Hadert & Quinn, 2008; Morgan & Morgan, 2001). Power is in the number of measurements taken within individuals, not in the number of study participants. The *n*-of-1 design has been recognized as a useful tool for the evaluation of complex interventions in the area of health care (Craig et al., 2008), and has been advocated as a possible alternative to the performance of new, expensive RCTs in the area of chronic pain to refine knowledge on what aspects of treatment works for whom, and to what extent (Williams et al., 2013). Although often used to study the effectiveness of interventions, the design can be used to study the natural history of relationships between processes and outcomes and thereby establish how well these relationships are described by theory for single cases (e.g. Hobbs, Dixon, Johnston, & Howie, 2013; 2013, McDonald et al., 2017).

As this is the first study performed in this area, we employed a basic and exploratory research question: Are experiential avoidance and values-based living – hypothesized to be central treatment processes from the theoretical framework of Acceptance & Commitment Therapy (ACT) – significantly related to chronic pain outcomes over time within individuals? We assessed our research question by undertaking the following steps sequentially for each of the participants separately:

(1) Description of the natural unfolding over time of experiential avoidance and values-based living, and of pain interference in daily life in multiple life domains (household, social activities, family and recreation) and emotional well-being as important chronic pain outcomes. In addition to these process- and outcome variables, pain intensity is assessed as an important context-variable.

(2) Assessment of the interrelationship of experiential avoidance and values-based living with pain interference in daily life and emotional well-being over time, beyond the effects of pain intensity. Here we assessed both concurrent relationships at the same day and prospective relationships on consecutive days.

We hypothesized that experiential avoidance and values-based living would be simultaneously associated with at least one of five outcome variables (one of four pain interference domains, or emotional well-being) within each individual, beyond pain intensity. Confirmation of this hypothesis would corroborate ACT-theory, and imply that an ACT-based intervention that has an effect on experiential avoidance and values-based living would thereby also be able to influence an individual's pain interference, or emotional well-being.

We examined the unfolding, natural history and relationship of treatment processes and outcomes over time in individuals who simultaneously received an ACT-based treatment. As the ACT-based treatment was a crucial context in which we assessed the process-outcome relationship, we also explored if there were intervention effects present for each individual. Finally, we assessed pain intensity as a highly relevant factor in the context of chronic pain that influences and interacts with cognitive, emotional and social pain-related factors (Gatchel, Peng, Peters, Fuchs, & Turk, 2007). Both of the included psychological factors of interest were expected, however, to be more important predictors of chronic pain outcomes than levels of pain intensity. The way one responds to pain has been found to be more predictive of chronic pain-related disability and well-being than the pain itself (e.g., Gatchel et al., 2007; McCracken and Gutiérrez-Martínez, 2011; Quinn, Johnston & Johnston, 2013; Viane, Crombez, Eccleston, Poppe, Devulder, Van Houdenhove, & De Corte, 2003; Vowles, McCracken & Eccleston, 2007).

Method

This study was approved of by the Dutch Medical-Ethical Review Board (METC Twente, trial number NL33188.044.10), which operates under the Dutch Central Committee for Research involving human participants (CCMO).

Participants

Study participants followed an eight-week, inpatient, multidisciplinary group rehabilitation program in a local pain rehabilitation centre in the Netherlands. Assignment to the inpatient treatment program occurred approximately two to eight weeks before the start of the program. Once assigned, participants from two parallel, six-member treatment groups who were interested in the study received an information letter and consent form.

The aim was to invite participants until four study participants would be obtained. Six people were contacted by telephone one to two weeks after receiving the information letter to meet the required number of four study participants. After five weeks of measurement, one of four participants dropped out of the study as the burden of simultaneous participation in both the study and treatment program was too high. Data from this participant are not analysed. All three of the remaining participants were female and between 22 and 32 years old. A description of participant characteristics can be found in the Results section.

Procedure

At the start and end of the study, the participants were visited at their homes by a member of the research team. Both home-visits took approximately one hour. During the first visit, participants received instructions on using the PDA (smartphone) that was used to gather daily questionnaire data, and discussed with the researcher the best time and place to fill out the daily questionnaire. Furthermore, they had the opportunity to ask for clarification of the diary items. Participants were instructed to answer 17 questions on a PDA at the end of each day, in the weeks before (one to four weeks), during, and after (three to four weeks) the treatment program. Baseline measurements were made as long as possible depending on the moment of assignment to

the in-patient treatment program. During the final visit, a short exit-interview was performed with each of the participants. During the interview, participants were asked to reflect on the measurement period and the multidisciplinary treatment received.

The PDA was programmed specifically for this study. A time window for filling out the questionnaire was installed on the PDA, extending from 6 PM to 10 AM the following morning. Although the ordering of the variables within the questionnaire was kept constant, the ordering of the separate questions within each variable was randomised. One to two weeks after the start of the study, and in the first week of treatment, the researcher contacted the participants to discuss and solve any eventual problems. SMS text message reminders were sent if the daily questionnaire was not filled out for two or more consecutive days.

Measures

The daily questionnaire consisted of 17 items, 12 of which were used for this report. All items were taken from validated questionnaires. As suggested by IMMPACT recommendations with regard to core outcome measures in chronic pain research (Dworkin et al., 2005), all items were measured on a 10-point Numeric Rating Scale (NRS). Slight adjustments to the items or answering categories were made to make these suitable for daily assessment. A description of each of the concepts and items is given below.

Process variables

Experiential avoidance, The Psychological Inflexibility in Pain Scale (PIPS) assesses psychological inflexibility (Trompetter et al., 2014; Wicksell, Lekander, Sorjonen, & Olsson, 2010). Two items of the subscale experiential avoidance were used in this study, formulated as 'Today I... (1) ..avoided doing things when there was a risk it would hurt or make things worse, (2) ..postponed things because of my pain complaints.' Response alternatives ranged from (0) 'not true' to (10) 'very much true', with higher scores indicating more experiential avoidance.

Values-based living. No process-oriented questionnaires were available to assess the process values from the framework of ACT. Therefore, ten chronic pain patients following the multidisciplinary rehabilitation program participated in a short pilot study. During this pilot study, different items formulated by the researchers were answered by the participants and evaluated with a member of the research-team. Based on outcomes of the pilot study, two items were selected. These items were 'Today I feel I... (1) ..was able to do things that make life worthwhile, (2) ..did things that are important to me.' Response alternatives ranged from (0) 'not agree' to (10) 'totally agree', with higher scores indicating more values-based living.

Outcome variables

Pain interference in daily life. The Multidimensional Pain Inventory (MPI) - Interference subscale assesses interference in daily life due to pain (Kerns, Turk, & Rudy, 1985; Lousberg et al., 1999). Items assessing interference or changes in the life domains household chores, recreational activities, social activities, and enjoyment from family -related activities were relevant for the participants and used in the study. The items were 'Today my pain complaints interfered with/influenced... (1) ..my ability to do household chores, (2) ..undertaking recreational activities, (3) ..undertaking social activities, (4) ..the enjoyment I get from family-related activities.' The response alternatives were adjusted to fit the daily item format and ranged from (0) 'not true/not influenced' to (10) 'very much true/very much influenced', with higher scores indicating more interference in daily life.

Emotional well-being. The Mental Health Continuum (MHC) (Lamers, Westerhof, Bohlmeijer, ten Klooster, & Keyes, 2011) measures positive mental health. This study used the subscale emotional well-being (three items) that assesses feelings of happiness and satisfaction with life. Items were formulated as 'Today I felt... (1) ..happy, (2) ..interested in life, (3) ..satisfied.' As the original item format of the MHC is on the frequency of feelings experienced over the last month, the answering scale was adjusted. Response alternatives ranged from (0) 'not true' to (10) 'very much true', with higher scores indicating more emotional well-being.

Pain intensity

Pain intensity was assessed in this study as a crucial context-variable in chronic pain rehabilitation. Pain intensity was assessed with one question, 'How much pain did you experience over the last 24 hours?' Response alternatives ranged from (0) 'no pain' to (10) 'pain as bad as I can imagine'.

Analysis

The *n*-of-1 daily measures data represent a time series for which specific analyses are applicable. All data were analysed separately for each of the participants.

Missing data

Missing data were 14% for participant 1 (PP1; 15 of 110 observations), 25% for participant 2 (PP2; 23 of 89 observations) and 29% for participant 3 (PP3; 25 of 87 observations). As both PP1 and PP2 felt they were unable to adequately rate their pain interference in the domains 'family' and 'household' during the days staying overnight at the rehabilitation centre (two consecutive nights during eight weeks of total measurement period), data for these two questions on these specific days were also treated as missing values. All missing data was imputed with the AMELIA II software package using bootstrapping procedures within R (Honaker & King, 2010; Honaker, King, & Blackwell,

2009). The AMELIA-II software programme applies multiple imputation of missing values taking into account the time-series nature of the data. As quite a large proportion of missing data had to be imputed for each participant, boundaries (0–10; range of response alternatives) were included in AMELIA-II to ensure more stable imputation. Multiple imputation produced five different datasets for each of the participants. Each of these datasets was used separately to perform all analyses. After performing the analyses, the results for each of the five datasets were combined – for example, for the cross-correlation between EA and emotional well-being – based on the point estimates' averages and standard errors (Hobbs et al., 2013; Rubin, 1987). The variance of the point estimate was calculated as the average of the estimated variances from within each completed data set, plus the sample variance in the point estimates across the data sets. This was multiplied by a factor that corrects for bias.

Descriptives and autocorrelation

SPSS 20.0 statistics was used to calculate descriptive statistics for the data. The different interference domains were analysed separately. This resulted in 40 data series per participant (four separate MPI-interference variables, emotional well-being, experiential avoidance, values-based living and pain intensity x five imputed datasets for each variable). For each participant, average means and standard deviations (over the five imputed datasets) for all variables can be found in Table 1. After graphically displaying the data series for visual inspection of variability over time, the SPSS Forecasting analysis tool was applied to assess serial dependency/autocorrelation in each of the data series. Intra-individual variability was present in all constructs in each of the participants. Outcomes of forecasting procedures were assessed to detect any significant time lags exceeding 95% confidence intervals. A maximum time lag of seven days was assessed.

Relationships between processes and outcomes

Further analysis was performed using the open source McKnight time series software package (McKnight, Mckean, & Huitema, 2000). This software package applies double bootstrapping procedures and is especially useful in analysing small sample time-series interventions in the behavioural sciences. The package is also very useful when assessing small numbers of data points in the total measurement period or one of the phases (baseline, intervention or follow-up) in the design and can account for deviations from normality often encountered in small samples.

The general model used to test the process-outcome relationships was $Y = X * b + error$, with the error following an autoregressive time series of order p. Full models were tested in which pain intensity, experiential avoidance and values were included simultaneously. This was done to assess the relationship of both ACT treatment processes beyond pain intensity. Also, three variables representing the value of these predictor variables the day before (-1) were included in the full model together with the first three predictors. This was done to assess if there were any carry-over effects of pain intensity, experiential avoidance or values during consecutive days beyond the same day in predicting outcome variables. This resulted in 25 data series for each participant (one model for each of the five dependent variables x five imputed datasets).

A first-order autoregressive model was applied, taking into account lag 1 autocorrelation for each of the models assessed. Nevertheless, outcomes of SPSS Forecasting procedures indicated that a lag 2 relationship fitted the data better for two variables in two participants and a second-order autoregressive model was applied in these instances. Taking into account a lag 1 or lag 2 autocorrelation correctly applied adjustments for autocorrelation in 80% - 90% of the data series for each participant.

Check on intervention effects

Before assessing the process-outcome relationship, we tested if there were intervention effects present on both processes and outcomes for each individual. Again, we used McKnight Time Series analyses procedures. The model applied was $Y = X1 * b1 + X2 * b2 + X3 * b3 + X4 * b4 + error$. As recommended by McKnight, predictors included in the model were a constant (X1), a time-variable (X2: measurement number, starting at 1, 2, 3 etc), a phase-variable (X3: 0 during baseline phase, 1 from start of intervention) and a slope-variable (X4: 0 during baseline, measurement number 1, 2, 3 etc during the intervention phase). Outcomes of this check revealed that there were no significant changes in any of the processes or outcomes over time or during the intervention for any of the individuals, indicating ineffective treatment.[1]

In addition to a check on intervention effects on the individual level, we checked if there were any aggregate interventions effects for the twelve attendees of the two six-member groups which our participants attended. Available data from standard test batteries at start and end of treatment during the intervention program were assessed. Paired sample t-tests (IBM SPSS Statistics 20) for the total group showed significant aggregate reductions in both pain interference in daily life as measured with the MPI, subscale pain interference in daily life, $t(11) = 2.73$, $p = .02$, and psychological inflexibility as measured with the PIPS, $t(11) = 4.26$, $p < .001$.

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[1] Outcomes regarding the check on intervention effects for individuals are not included in the article. Tables containing this information for each of the participants can be requested from the corresponding author.

Table 1. *Means and standard deviations within individuals over time for all three participants.*

	PP1	PP2	PP3
N measurements	110	89	87
Outcome variables			
Pain interference domains (MPI)			
Household	6.19 (1.33)	3.81 (3.39)	3.98 (2.12)
Social activities	2.02 (2.13)	3.49 (2.96)	4.59 (2.13)
Family	3.55 (1.81)	2.75 (2.62)	4.94 (2.21)
Recreation	6.10 (1.44)	4.54 (3.77)	4.69 (1.89)
Emotional Well-being (MHC)	6.29 (1.01)	6.88 (1.17)	6.97 (0.99)
Process/context variables			
Pain avoidance	4.49 (1.65)	3.82 (3.25)	3.83 (2.05)
Values-based living	4.90 (1.51)	6.35 (1.80)	6.09 (1.51)
Pain intensity	6.81 (1.16)	6.34 (1.97)	7.20 (0.90)

Note: All variables were measured on a numeric rating scale ranging from 0 to 10.
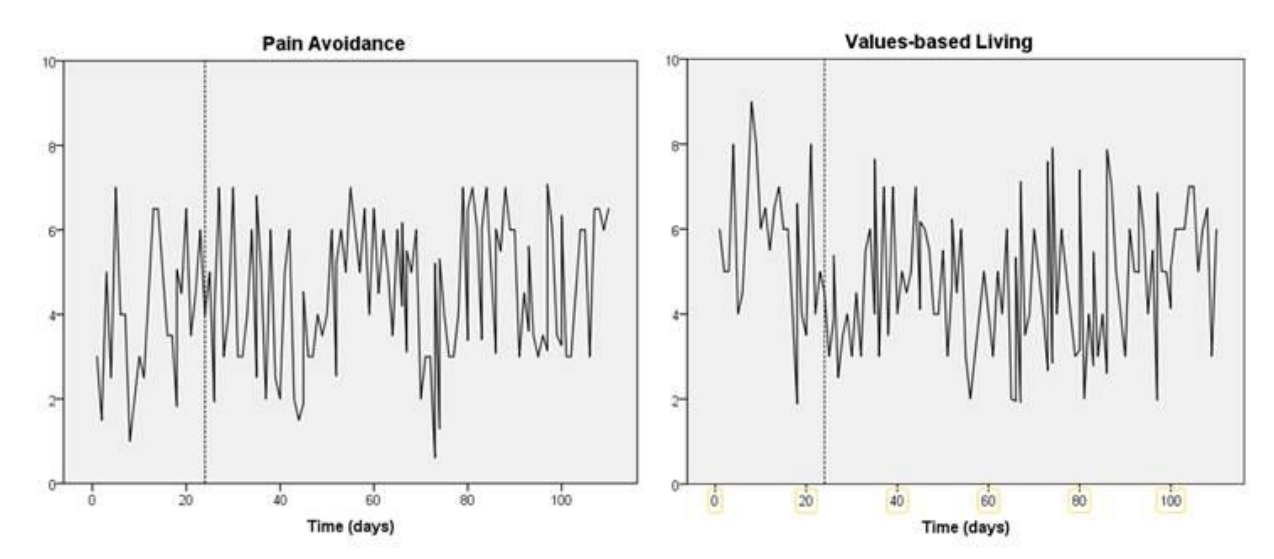
Table 2. *Relationships (unstandardized Beta estimates) between treatment processes and outcomes beyond pain intensity on concurrent and consecutive days for PP1.*

	Pain Interference in daily life				Emotional well-being
	Household	Social activities	Family	Recreation	
Constant	3.730*	-2.794	-3.568	4.833*	6.466*
Pain intensity	.330*	.148	.501*	.384*	-.190*
Pain intensity (-1)	-.168	-.110	-.131	-.178	-.051
Avoidance	.306*	.402*	.550*	.215*	-.026
Avoidance (-1)	.030	.201	.120	-.013	-.024
Values	-.127	.223	.075	-.197*	.344*
Values (-1)	.095	.146	.249*	-.015	-.008

* Significant effects based on 95% CIs

Note: Outcomes shown are combined results from five multiple imputed datasets;

(-1) = value for specific construct one day earlier (lag 1)

Note: Vertical dotted line marks start of treatment phase

Figure 2: Variability over time for PP2 in pain avoidance and values-based living
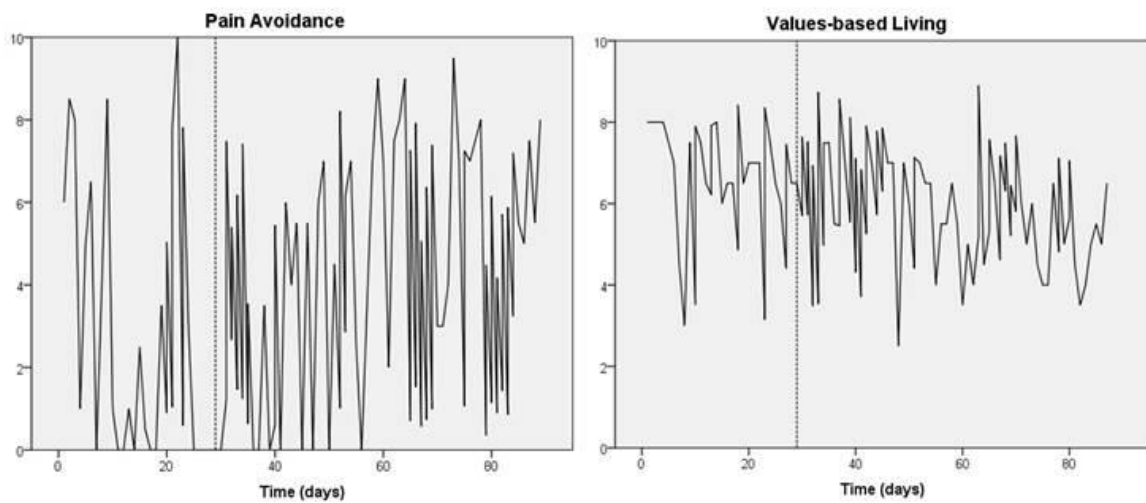
Table 3. *Relationships (unstandardized Beta estimates) between treatment processes and outcomes beyond pain intensity on concurrent and consecutive days for PP2.*

	Pain Interference in daily life				Emotional well-being
	Household	Social activities	Family	Recreation	
Constant	8.54*	5.549*	.687	1.230	7.184*
Pain intensity	-.005	.214	214	.369*	-.033
Pain intensity (-1)	-.037	.010	.180	.076	-.078
Avoidance	.158	.115	-.136	.237*	-.054
Avoidance (-1)	-.049	.000	-.134	-.037	-.026
Values	-.794*	-.364	.203	-.048	.133
Values (-1)	.025	-.116	-.131	.003	-.023

* Significant effects based on 95% CIs

Note: Outcomes shown are combined results from five multiple imputed datasets;

(-1) = value for specific construct one day earlier (lag 1)

Note: Vertical dotted line marks start of treatment phase

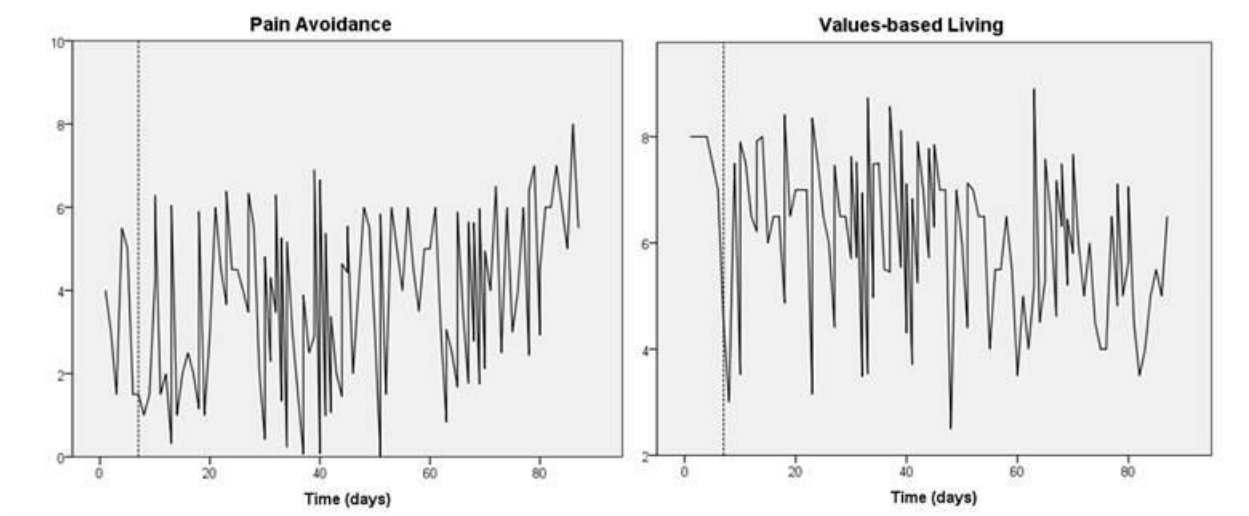*Figure 2:* Variability over time for PP2 in pain avoidance and values-based living

Table 4. *Relationships (unstandardized Beta estimates) between treatment processes and outcomes beyond pain intensity on concurrent and consecutive days for PP3.*

	Pain Interference in daily life				Emotional well-being
	Household	Social activities	Family	Recreation	
Constant	12.004*	7.249*	4.554*	6.297*	5.423*
Pain intensity	-.226	-.056	1.173*	.148	-.040
Pain intensity (-1)	-.262	.207	-.291	.029	-.108
Avoidance	.249*	.032	-.013	.338*	-.025
Avoidance (-1)	-.098	.134	-.075	.011	-.007
Values	-.388*	-.619*	-.722*	-.456*	.379*
Values (-1)	-.462*	-.088	-.202	-.272*	068

* Significant effects based on 95% CIs

Note: Outcomes shown are combined results from five multiple imputed datasets;

(-1) = value for specific construct one day earlier (lag 1)

Note: Vertical dotted line marks start of treatment phase

Figure 3: Variability over time for PP3 in pain avoidance and values-based living

Results

PP1

PP1 was a 22-year old female. She lived together with a partner, had one child and was pregnant with her second child during the study. Her educational level was medium (received 12-16 years of education). PP1 did not work outside home but was responsible for all household and family caretaking activities. She was diagnosed with fibromyalgia. Her current complaints started one to two years ago during pregnancy.

Variability over time in experiential avoidance and values-based living are displayed in Figure 1. Descriptive statistics (Table 1) showed that the scores for both experiential avoidance ($M = 4.49$, $SD = 1.65$) and values-based living ($M = 4.90$, $SD = 1.51$) on average approached the median of the response alternatives. The highest interference in daily life due to pain was experienced in the domains of 'recreation' and 'household activities' ($M = 6.19$, $SD = 1.33$; $M = 6.10$, $SD = 1.44$ respectively). Almost no interference was experienced in 'social activities' ($M = 2.02$, $SD = 2.13$). In addition to pain intensity, emotional well-being scores were relatively high compared to other variables and the most stable over time ($M = 6.29$, $SD = 1.01$).

As seen in Table 2, experiential avoidance and values-based living showed significant relationships over time beyond pain intensity with various pain interference domains and emotional well-being. Pain avoidance was related to all four pain interference outcomes, ranging from b = .215 (domain 'recreation') to b = .550 (domain 'family'), but not to emotional well-being. Values-based living was related to emotional well-being and the domain 'recreation' (b = -.197), but not to the other interference domains. Both process variables were simultaneously related to one outcome variable, the pain interference domain 'recreation'.

Only one significant relationship existed between ACT-processes measured one day earlier and any of the outcome variables. Values-based living one day earlier was positively related – and thus in a different direction than hypothesized - to pain interference in the domain 'family' (b = .249). Overall, however, the presence of same-day correlations between process- and outcome variables confirmed our hypothesis for this participant.

PP2

PP2 was a 23-year old, married female, with one child. Her educational level was medium (12-16 years of education). PP2 in general worked outside home on a part-time basis, but not during the weeks before, during and after following the multidisciplinary treatment program. She was recently retrained by her employer because of her pain complaints. PP2 was primarily responsible for household and family caretaking activities. She was diagnosed with low back complaints after hernia and subsequent failed surgery. Her current complaints started a few years ago with the onset of the hernia.

Variability over time in experiential avoidance and values-based living is displayed in Figure 2. Descriptive statistics (Table 1) showed that the experiential avoidance

scores were on average below the median score on the scale, but quite unstable over time ($M = 3.82$, $SD = 3.25$). Scores on values-based living were more stable than scores on experiential avoidance ($M = 6.35$, $SD = 1.80$). As for experiential avoidance, mean scores for interference in daily life domains were below the median of the response alternatives, with the least interference in the domain 'family' ($M = 2.75$, $SD = 2.62$). Again, variability in the pain interference domains seemed relatively high. In addition to pain intensity, emotional well-being scores were relatively high compared to other variables and the most stable over time ($M = 6.88$, $SD = 1.17$).

As seen in Table 3, experiential avoidance and values-based living showed few significant relationships over time beyond pain intensity with various pain interference domains and emotional well-being. Experiential avoidance was related to the pain interference domain 'recreation' ($b = .237$). Values-based living was also related to one of five pain interference domains, 'household' ($b = -.794$). None of the process variables were related simultaneously to any of the outcome variables. There were no further relationship between any of the predictor variables or pain intensity and each of the five outcome variables. As there was no simultaneous relationship of experiential avoidance and values-based living with any of the outcome variables, our hypothesis was disconfirmed for this participant.

PP3

PP3 was a 32-year old, married female, with two children. Her educational level was high (> 18 years of education). Prior to start of the study she lost her full-time job in which she was very ambitious. She was now responsible for household and family caretaking activities, and explored how to realize her work ambitions more realistically in the future. She was diagnosed with low back complaints that started approximately one to two years ago during pregnancy with her second child.

Variability over time in experiential avoidance and values-based living are displayed in Figure 3. Descriptive statistics (Table 1) showed that the average experiential avoidance scores were below median ($M = 3.83$, $SD = 2.05$), and that average values-based living scores over time were above median ($M = 6.09$, sd = 1.51). The mean scores for the four pain interference domains were relatively similar and all approached the median of the response alternatives. The highest pain interference was experienced in the domain 'family' ($M = 4.94$, $SD = 2.21$). Both pain intensity and emotional well-being scores were relatively high compared to other variables and the most stable over time (pain intensity, $M = 7.20$, $SD = 0.90$, emotional well-being $M = 6.97$, $SD = 0.99$).

As seen in Table 4, experiential avoidance and values-based living showed significant relationships over time beyond pain intensity with various pain interference domains and emotional well-being. Experiential avoidance

was significantly related to both the interference domains 'household' ($b = .429$) and 'recreation' ($b = .338$), but not to emotional well-being. Furthermore, values-based living was related to each of the dependent variables, ranging from $b = .379$ (emotional well-being) to $b = -.722$ (the pain interference domain 'family'). Both process variables were simultaneously related to two pain interference domains ('household' and 'recreation'). Significant relationships were also present between the interference domains 'household' and 'recreation' and values-based living scores one day earlier beyond the values-based living scores on the current day. Overall, these outcomes confirmed our hypothesis for this participant.

Discussion

This study examined the unfolding and natural history of the processes experiential avoidance and values-based living from the framework of Acceptance & Commitment Therapy (ACT) (Hayes et al., 2011), and the relationship between these processes and outcomes over time (pain interference and emotional well-being) within individuals experiencing chronic pain. Intra-individual variability was present in all constructs in each of the participants. This enabled us to explore whether individuals high (or low) in experiential avoidance and values-based living on a certain day were also high (or low) in pain interference in daily life and emotional well-being on these, or consecutive, days. In accordance with our central hypothesis, the results showed that experiential avoidance and values-based living as key components of psychological flexibility were simultaneously associated with at least one out of four pain interference domains or emotional well-being in two out of three participants. This is consistent with predictions from ACT theory. The findings corroborate and elaborate on outcomes from previous between-subject group studies that suggest that ACT processes are related to chronic pain outcomes and that these processes are able to function as working mechanisms of treatment change (e.g. McCracken & Eccleston, 2005; McCracken & Gutiérrez-Martínez, 2011; Wicksell, Olsson, et al., 2010).

Importantly, however, the ACT processes were only related to chronic pain outcomes on concurrent days. Significant temporal, time-shifted relationships in the hypothesized direction between processes measured one day earlier and pain outcome variables were largely non-existent. Such temporal precedence of change in processes before outcomes is a necessary condition to establish mediation and working mechanisms of change (MacKinnon, Fairchild & Fritz, 2007). Despite the fact that the included constructs and their expected causal relationships were derived from theory, the analytic outcomes do not enable us to draw conclusions regarding the causality of the relationship between the measured constructs. One alternative explanation for our findings is that changes in pain interference and emotional well-being, due to some other factors (e.g., positive

or negative life events) were the actual drivers of consequential changes in aspects of psychological flexibility. As an example, it might be that a decrease in pain interference in daily life, due to positive life events, fueled the experience of higher values-based living and less experiential avoidance in PP3.

Another alternative explanation lies in the fact that a certain degree of conceptual and measurement overlap probably existed between the included constructs and their operationalizations. This is reflected, for example, by the operationalized wordings in items to measure experiential avoidance (e.g., "avoided doing things" or "postponed things" because of pain complaints, or fear that it might hurt) and some of the items to measure pain interference in daily life (e.g., "Today my pain complaints interfered with…"). The possibility cannot be excluded that correlations between experiential avoidance and pain interference may have been influenced by conceptual overlaps in the measures used.

Overall, these issues make it difficult to draw definitive conclusions regarding causality. We hypothesize that temporal, more stable relationships can be formed during effective ACT treatment and subsequently represent internalization of ACT principles. Future research should further assess the variation between individuals in temporal relationships and implications thereof. In this context, it might be the case that pain interference and emotional well-being (especially its affective facets) fluctuate within days, at a higher variability rate than currently assessed. Future research should therefore consider to implement a higher measurement frequency than the currently used daily measurements to be able to grasp time-shifted effects between our processes and outcomes of interest.

We build on previous findings in two ways due to the within-person orientation of this study. First of all, the applicability of ACT theory at the level of the individual was disconfirmed for one of the participants. This implies that ACT may not be a suitable treatment modality for everyone. Furthermore, it implies that conclusions on the group level as often made in group studies, such as randomized controlled trials or tests of theory (McDonald et al., 2017), do not apply uniformly to each individual within that group. Researchers have recognized that average effects mask large changes for some patients and little or none for others (Williams et al., 2013). This is especially the case in the area of chronic pain, where aggregate treatment effects are often modest and inconsistent, and treatment is not effective for everyone (McCracken & Turk, 2002; Turk et al., 2011; Williams et al., 2013).

The finding that the multidisciplinary ACT-based treatment program that our participants followed did not bring about any significant changes within each individuals' functioning over time, also indicate that the picture regarding the effectiveness and working mechanisms of chronic pain treatment is perhaps even more difficult to entangle on the individual level than acknowledged previously. The

findings imply that, although theoretically ACT could have brought about changes in two participants by targeting change in experiential avoidance and values-based living, the intervention still failed to improve and stabilize both processes and outcomes. For these participants, factors such as non-compliance with therapeutic recommendations during treatment and deliverance of treatment by inexperienced staff could have interfered with possible treatment effects (Turk & Rudy, 1991; Williams et al., 2013). In this study, deliverance of treatment by ineffective staff does not seem to be a significant intervening factor. This is indicated by the presence of aggregate improvement for the total group of participants with whom our study participants attended treatment. These aggregate improvements resonate with consistently reported positive effects of ACT for chronic pain outcomes (Hann & McCracken, 2014; Veehof et al., 2016). On the other hand, the exit-interviews held with each of the participants revealed possible non-compliance with therapeutic recommendations during treatment. In each of the exit-interviews, participants spontaneously revealed that they had not followed the recommendations made by at least one of the professional disciplines involved in the treatment program.

Additionally, we showed that predictions from ACT theory are testable not only between individuals but also within individuals. Although the transfer from group level conclusions to the individual level is very often implicitly assumed in psychology, the statistical and methodological conditions necessary to justify this assumption are often not met (Molenaar, 2004; Molenaar & Campbell, 2009). As the level of the individual is the level where change is theoretically described and assumed in ACT and many other psychological theories (Hayes et al., 2011), research within individuals is necessary to properly address research questions regarding treatment effectiveness and working mechanisms of treatment. Our study showed that the n-of-1 design is an appropriate, useful and feasible method to test clinical theory and assess the natural history of relationships between treatment processes and outcomes within individuals, as also shown by Hobbs and colleagues (2013; McDonald et al., 2017). The use of n-of-1 designs can have practical relevance for science practitioners. N-of-1 designs can be implemented relatively easy in practice in contrast to other research designs. It enables a therapist to track the (timing of) effectiveness of their interventions within and between individuals. It also enables a therapist to track patients during an observation period or during intervention (components), and can inform decisions to change the intervention content or offer different intervention based on these results. In our experience, outcomes of n-of-1 design can also be used as an intervention itself as the results can function as input for therapy sessions.

Finally, several findings deserve a short discussion. As expected, pain intensity was consistently related to chronic pain outcomes in only one of three participants (PP1). In all three participants, experiential avoidance and values-based

living seem at least equally or even more important in association to chronic pain outcomes. This corroborates findings from existing within- and between-subject studies (e.g. McCracken and Gutiérrez-Martínez, 2011; Quinn et al., 2013; Viane et al., 2003; Vowles et al., 2007). The findings also corroborate ACT theory and other theories acknowledging that the chronic pain experience is not only related to and influenced by pain intensity, but is a complex interplay between physical, emotional and social factors (Gatchel et al., 2007; Hayes et al., 2006). Second, experiential avoidance was not associated with emotional well-being in any of the three participants, while values-based living was. This suggests that each of the ACT-processes might have differential effects on separate chronic pain outcomes. The findings makes sense as – in comparison to CBT - ACT is well aligned with positive mental health outcomes (such as emotional well-being) through its exact focus on the ability to perform behavior in alignment with personal values despite persistent pain (Fledderus et al., 2012; McCracken and Vowles, 2014).

There are some limitations to this study and implications for future research. Although the n-of-1 design has proven to be a useful design to explore the within-subject level of behaviour change in detail, generalization from outcomes of n-of-1 studies to the larger chronic pain population is not possible (Barlow et al., 2009). Furthermore, as applied here the n-of-1 design was an observational design. Although the use of the design heightened the ecological validity of our study, each of our participants experienced a significant life-event during the measurement period (pregnancy and moving house) that probably influenced our measurements. In general, other designs and methodologies should be used together with, or as a follow up on, the n-of-1 design. We propose the use of multilevel models that can account for variance both within and between individuals. Another limitation was the amount of missing data in our study for two out of three participants. The fact that patients received a separate device for data collection may have increased the percentage of missing data. To adequately deal with the relatively high amount of missing data we explicitly chose to use a program for multiple imputation of missing data especially suitable for time series data (Amelia II, Honaker et al., 2009). The inclusion of boundaries was necessary to produce robust data where the large majority of datasets underlying the aggregated datasets resulted in similar, reproducible conclusions regarding (non)significance. An alternative route to robust data imputation for future n-of-1 trials would be to increase the number of imputations to match the percentage of missing data (e.g., 29 imputations for 29% of missing data) (White, Royston & Wood, 2011). We finally suggest that future research focuses on both the aggregate and individual level in larger-N studies when testing the applicability and effectiveness of ACT (Johnston & Johnston, 2013). Such studies could replicate our exploratory findings and further unravel subsequent, related research questions focusing on working mechanisms of

treatment change within individuals for whom ACT was effective, but also on further unraveling differences in within-subject and between-subject variance in chronic pain patients for whom ACT was ineffective.

Overall, this study was the first to test ACT theory by studying within-person processes in individuals experiencing chronic pain. We also showed the feasibility and utility of the n-of-1 design - and probably other within-subject designs - to assess the unfolding, natural history and relationship between important treatment processes and outcomes over time. Assessing research questions related to our study aim on the individual level can help to generate more knowledge on the effectiveness and specific working mechanisms of ACT and other cognitive behavioural therapies. Hopefully, effectiveness, efficiency and fit of chronic pain treatment to the individual can thereby be enhanced in the future.

Author contributions

HT designed the study, organized the data collection, carried out the statistical analyses and drafted the first version of the manuscript. DJ and MJ supervised the statistical analyses and were actively involved in writing and revising the manuscript. MVH and KS designed the study and were actively involved in writing and revising the manuscript. All authors read and approved the final manuscript.

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Declaration of interests

The authors declare that there is no conflict of interest.

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