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How does change unfold? an evaluation of the process of change in four people with chronic low back pain and high pain-related fear managed with Cognitive Functional Therapy: A replicated single-case experimental design study

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ABSTRACT

Purpose: To understand the process of change at an individual level, this study used a single-case experimental design to evaluate how change in potential mediators related to change in disability over time, during an exposure-based behavioural intervention in four people with chronic low back pain and high pain-related fear. A second aim was to evaluate whether the change (sequential or simultaneous) in mediators and disability occurred at the same timepoint for all individuals.

Results: For all participants, visual and statistical analyses indicated that changes in disability and proposed mediators were clearly related to the commencement of Cognitive Functional Therapy. This was supported by standard outcome assessments at pre-post timepoints. Cross-lag correlation analysis determined that, for all participants, most of the proposed mediators (pain intensity, pain controllability, and fear) were most strongly associated with disability at *lag zero*, suggesting that mediators changed concomitantly and not before disability. Importantly, these changes occurred at different rates and patterns for different individuals, highlighting the individual temporal variability of change.

Conclusion: This study demonstrated the interplay of factors associated with treatment response, highlighting '*how change unfolded*' uniquely for each individual. The findings that factors underpinning treatment response and the outcome changed simultaneously, challenge the traditional understanding of therapeutic change.

1. Introduction

Chronic low back pain (LBP) that is associated with high pain-related fear is disabling (Vlaeyen, Crombez, & Linton, 2016), as indexed by its impacts on work (Coggon et al., 2013), physical activity (Martel, Thibault, & Sullivan, 2010) and social participation (Hoogendoorn, van Poppel, Bongers, Koes, & Bouter, 2000). This high fear group often presents with changes across multiple interacting factors, including cognitive (Bunzli, Smith, Schutze, & O'Sullivan, 2015), emotional (Glombiewski et al., 2015), behavioural (Geisser, Haig, Wallbom, & Wiggert, 2004; Karayannis, Smeets, van den Hoorn, & Hodges, 2013; Thomas & France, 2007), lifestyle, social (Bunzli, Watkins, Smith, Schutze, & O'Sullivan, 2013), and pain processing factors (O'Sullivan et al., 2014; Rabey, Slater, O'Sullivan, Beales, & Smith, 2015). The interplay of these factors is likely to vary for each person, and fluctuate over time (Kongsted, Kent, Axen, Downie, & Dunn, 2016; O'Sullivan, Caneiro, O'Keeffe, & O'Sullivan, 2016).

Therefore, understanding how changes in these factors relate to fear and disability reduction over the course of an intervention may provide important insight into processes involved in behavioural change in people with high levels of pain-related fear. The traditional biomedical understanding of therapeutic change is that improvement occurs in a sequential and gradual manner over the treatment period (Brodal, 2017; George, 2017; Vlaeyen, de Jong, Geilen, Heuts, & van Breukelen, 2001). Mediation analysis provides a useful method to investigate how multiple factors relate to the outcome over time. Mediators are defined

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statistically as factors that change because of an intervention, and that correlate with changes in the selected outcome (Lee et al., 2017). This can provide information regarding factors that contributed the most to the treatment effect. In clinically based research, randomised controlled trials (RCTs) are the most common framework for analysis of mediators of the tested treatment effect (Mansell, Kamper, & Kent, 2013). However, they require large samples and expenditure which is often a limiting factor in the number of variables and timepoints that can be captured. Although this is not an inherent rule, with many studies often assessing a single mediator at a single timepoint during the intervention (Mansell, Hill, Main, Vowles, & van der Windt, 2016). This is an obvious limitation when investigating complex problems such as chronic LBP because the time course of the mediator-outcome relationship is likely to vary between individuals. Considering that RCTs often only capture a limited number of timepoints, their design may therefore be insensitive to the timing of mediator and outcome change in relation to the intervention (Riley & Gaynor, 2014), an important limitation in establishing mediation (Kazdin, 2007).

In contrast to mediation analysis conducted in RCTs, single-case experimental design studies (SCEDs) facilitate detailed assessment at frequent timepoints, capturing multiple potential factors related to an individual's response to treatment (Borckardt et al., 2008; Gaynor & Harris, 2008; Morley, 2018; Morley, Vlaeyen, & Linton, 2015). An SCED is an intensive, prospective and controlled study of the individual, using each person as his/her own control to enhance reliability (Morley, 2018; Morley et al., 2015). SCEDs enable the adoption of a complex system perspective, which accommodates interaction of multiple factors and within-person temporal variations, thereby reflecting individuality in the evaluation of the therapeutic change process. Well-designed SCEDs, that include repeated measures and a stable baseline, can answer questions about improvement and the change process, to unravel the anatomy of therapeutic change (Borckardt et al., 2008).

Considering the need to understand how change unfolds at an individual level, we employed a SCED. The primary aim was to evaluate how measures of potential mediators related to outcome (disability) over time during a behavioural intervention for people with chronic LBP and high fear. A second aim was to evaluate whether the change (sequential or simultaneous) in mediators and disability occurred at the same timepoint during the intervention period for all individuals. A prerequisite for evaluating the process of change was that the intervention changed both the outcome and proposed mediators. The intervention was an individualised, exposure-based, behavioural approach for the management of people with chronic LBP, called Cognitive Functional Therapy (CFT) (O'Sullivan et al., 2018). The efficacy of CFT has been tested in an RCT (Bunzli, McEvoy, Dankaerts, O'Sullivan, & O'Sullivan, 2016; Caneiro, Smith, Rabey, Moseley, & O'Sullivan, 2017; O'Sullivan, Dankaerts, O'Sullivan, & O'Sullivan, 2015; Vibe Fersum, O'Sullivan, Skouen, Smith, & Kvale, 2013), which showed it to be superior to standard physiotherapy, demonstrating large effect sizes for reductions in pain-related fear, pain intensity and disability in people with chronic LBP and moderate disability. In a recent case series (Bunzli et al., 2016; Caneiro, Smith, et al., 2017; O'Sullivan et al., 2015; Vibe Fersum et al., 2013), CFT was also shown to be effective in decreasing disability, pain and fear, and increasing pain-related self-efficacy in people with chronic LBP waitlisted at a pain clinic. However, CFT had not been specifically tested in people with chronic LBP and high pain-related fear, and the process by which reduction in disability is mediated had not been quantitatively investigated (Bunzli et al., 2016). CFT is informed by the fear-avoidance model (Vlaeyen & Linton, 2000) which is the prevailing model of the development of pain-related disability. It proposes that pain-related cognitive and emotional responses can drive unhelpful behavioural responses that in turn lead to disability. Based on (i) the fear-avoidance model (Vlaeyen & Linton, 2000); (ii) prior research on mediators of treatment effect in people with back pain (Lee et al., 2015; Leeuw et al., 2008; Mansell, Hill, Main, Von Korff, & van der Windt, 2017), and (iii) the hypothesised mechanisms of action of CFT (Bunzli et al., 2016; Caneiro, Smith, et al., 2017; O'Sullivan et al., 2015; Vibe Fersum et al., 2013), it was hypothesised that pain intensity, pain controllability, fear, emotional distress and sleep would mediate reduction in disability.

2. Methods

This study complies with the Single-Case Reporting guideline In BEhavioural interventions (SCRIBE) 2016 (Tate et al., 2017).

2.1. Design

An SCED with replication across four participants was employed. There were three-phases (A-B-A'/B') with a criterion-based phase-changing (A'/B') sequence. **Phase A** consisted of an eight-week baseline period with no intervention. **Phase B** was a twelve-week period of CFT. Behavioural interventions are non-withdrawable, meaning their effect is expected to carry over after the intervention is terminated. Therefore, a subsequent **Phase A'** was used as a follow-up period of 12 weeks, with an embedded criterion-based phase-changing (A'/B') sequence. A **criterion** was set *a priori* to trigger **Phase B'**, which consisted of a second treatment phase of up to five 'booster' sessions. The criterion was defined as: disability scores during follow up (Phase A') that were equal to, or greater than, the average disability scores during baseline (Phase A) plus one point, for 2 consecutive weeks.

2.2. Participants

Participants were recruited from the cohort of a recently completed laboratory study involving people with chronic LBP and pain-related fear (Caneiro, O'Sullivan, Smith, Moseley, & Lipp, 2017). **Inclusion criteria were:** adults aged 18 years or older with dominant axial LBP (between T12 and gluteal fold), greater than 6 months' duration; pain intensity $\geq$4/10 on a numerical rating scale (0–10) for average pain in the past week; and high pain-related fear (scoring $\geq$40 on the Tampa Scale of Kinesiophobia - TSK) (Kori, Miller, & Todd, 1990) and specific fear of bending and lifting with a flexed lumbar spine (Caneiro, O'Sullivan, et al., 2017). This was operationalised as a score of $\geq$7/10 on a pictorial numerical rating scale displaying a side view picture of a person bending and lifting a box with a flexed lumbar spine followed by the question: "How fearful are you of performing this task?" - anchored by "0: No fear", and "10: Maximum fear") (Caneiro, O'Sullivan, et al., 2017). **Exclusion criteria were:** report of dominant leg pain, diagnosis of serious pathology (infection, cancer, inflammatory disorders, fracture), radicular pain with neurological deficit, grade 3 or 4 spondylolisthesis, pregnancy or inability to speak English. Fifteen people responded and completed the inclusion criteria questionnaires. Nine met the criteria, and four of those, consented to participate in this study.

This study was approved by the Health Research Ethics Committee at Curtin University – approval number HRE157/2015. Written informed consent was obtained from each participant prior to the start of the study.

2.3. Assessment timepoints

Following SCED guidelines (Kratochwill et al., 2010; Tate et al., 2017), weekly assessments of the outcome and proposed mediators were taken for each participant during the baseline phase (8 data points, allowing for assessment of stability of data during this period) (Morley et al., 2015), the treatment phase (12 data points) and follow-up phase (12 data points); with a total of 32 data points collected. Establishment of stability over the baseline phase enhances the internal validity of the design by controlling for time and thus maturation and regression to the mean, thereby serving a similar function to a no-treatment control group (Auld, Johnston, Russo, & Moseley, 2017; Kratochwill et al., 2013; Morley et al., 2015; Moseley, Zalucki, & Wiech,

2008; Polli et al., 2017). The follow-up period provides information about the short-term maintenance of the intervention effect. Direct inter-subject (original plus three cases) and inter-clinician (two physiotherapists) replication enhances the strength and generalisability of the findings (Morley et al., 2015).

2.3.1. Weekly assessment

A 23-item online questionnaire (Appendix) was developed to assess the primary outcome (disability) and proposed mediators of change on a *weekly* basis. Each of the items was rated on an 11-point numerical rating scale (0–10 anchored accordingly) (Dworkin et al., 2005). The questionnaires were completed weekly, before the treatment session. The items are described below.

2.3.1.1. Primary outcome. **Disability** was assessed with the *Patient-Specific Functional Scale* (PSFS) (Beurskens et al., 1999). At the initial assessment, participants listed three activities of daily living, each item was rated on an 11-point numerical rating scale in response to the question "*How difficult is it for you to perform this activity because of your back pain?*", anchored by '0 = able' and '10 = unable'. The activity with the highest rating was selected and used as the personalised disability item for the remaining weekly measures (Beurskens, de Vet, & Koke, 1996).

2.3.1.2. Proposed mediators. Potential mediators were hypothesised from theory (Bunzli et al., 2016; Caneiro, Smith, et al., 2017; Lee et al., 2015; Leeuw et al., 2008; Mansell et al., 2017; O'Sullivan et al., 2015; Vibe Fersum et al., 2013). A total of ten potential mediators were assessed and allocated into five 'mediator groupings': Pain (pain intensity, pain interference); Pain controllability (pain control, pain self-efficacy); Fear (fear of damage/pain, pain anxiety, pain catastrophizing, avoidance beliefs); Distress (depression, anxiety and pain bothersomeness), and Sleep (sleep difficulty).

The rationale for the selection of these items was as follows: pain (intensity and interference) was considered based on recommendations from a consensus paper on standardisation of outcomes in LBP (Dionne et al., 2008); specific items from well-established questionnaires assessing pain-related fear, anxiety, catastrophising and avoidance were selected on the basis that they have been used as a measure of fear in previous foundational studies in this area (de Jong et al., 2005; Vlaeyen et al., 2001), holding acceptability and clinical utility in single-case studies. Pain controllability (self-efficacy and pain control) and distress (depression, tension and anxiety) have been identified as key mediators in chronic LBP trials (Lee et al., 2017). Sleep was considered a potential mediator because there is evidence that it modulates pain threshold and tolerance (Sivertsen et al., 2015), even though the mechanisms by which that relationship occurs remain to be elucidated (Camfferman, Moseley, Gertz, Pettet, & Jensen, 2017). This short instrument can be seen in the Appendix.

2.3.2. Pre-post assessment

The use of **standardised outcome measures** with established psychometric properties provides information about whether participants have made a reliable change (Kazdin, 1982; Morley, 2018; Morley & Adams, 1989; Onghena & Van Damme, 1994). The following were assessed online at *four timepoints*: twice during baseline (Weeks 1 and 8), at the end of the intervention (Week 12 of Phase A) and at the end of the follow up (Week 12 of Phase A').

Disability was assessed with the *Roland Morris Disability Questionnaire* (RMDQ) (Roland & Morris, 1983). The RMDQ measures the effects of LBP on physical activities and activities of daily living. It is valid, reliable, and responsive to change. Scores range from o to 24, with higher scores indicating higher levels of disability (Roland & Morris, 1983).

Pain-related fear beliefs (fear of damage and/or pain) were assessed with the *Tampa Scale of Kinesiophobia* (TSK) (Kori et al., 1990). The TSK is a widely-used to assess fear of damage and/or pain (Bunzli, Smith, Watkins, Schutze, & O'Sullivan, 2015). Scores range from 17 to 68, with higher scores indicating higher levels of fear of movement and a cut off of 40 is typically used to define a high degree of pain-related fear (Vlaeyen, Morley, Linton, Boersma, & De Jong, 2012).

Pain-related anxiety symptoms were assessed with the *Pain Anxiety Symptoms Scale* (PASS-20) (McCracken & Dhingra, 2002). The PASS-20 was used to assess cognitive anxiety symptoms, escape and avoidance responses, fearful appraisals of pain and physiological anxiety symptoms associated with pain. The participant makes a frequency rating for each item (where 0 = never and 5 = always). The PASS-20 has acceptable psychometric properties (McCracken & Dhingra, 2002). Scores range from 0 to 100, with higher score indicating higher levels of pain-related-anxiety.

Pain catastrophising was assessed with the *Pain Catastrophising Scale* (PCS) (Sullivan, Bishop, & Pivik, 1995). The PCS has good psychometric properties, assessing catastrophic thinking with 13 statements that are rated on 0–4 Likert scales. Scores range from 0 to 52, with scores over 20 typically used as a cut off to define a high degree of catastrophising (Sullivan et al., 1995).

Back beliefs were assessed with the *Back Pain Attitudes Questionnaire (*BackPAQ*)* (Darlow et al., 2014). The BackPAQ10 consists of 10 items using a five-point Likert scale rating that ranges from 'false' to 'true', assessing five key components: relationship between back pain and injury, vulnerability of the back, activity participation during back pain, psychological influences on pain and recovery, and prognosis of back pain. The responses are scored from −2 ('true') to +2 ('false'), with scores ranging from −20 to +20. Negative scores reflect beliefs that are unhelpful for recovery from back pain (Darlow et al., 2014).

Illness perceptions were assessed with the *Brief Illness Perception Questionnaire* (B-IPQ) (Broadbent, Petrie, Main, & Weinman, 2006). The B-IPQ covers the five dimensions and has nine items, of which eight are rated on an 11-point numerical rating scale. Five items assess cognitive illness perceptions: consequences (Item 1), timeline (Item 2), control (Item 3), curability (Item 4), and identity or diagnostic label (Item 5). Two items assess emotional perceptions: concern (Item 6) and emotional response (Item 8) and one item assesses understanding of the condition or coherence (Item 7). Scores range from 0 to 80, with higher scores indicating more negative illness perceptions. Item 9 assesses causal beliefs, where participants are requested to list the three most important causal factors in their illness; this is treated as an open-ended response (Item 9) (de Raaij, Pool, Maissan, & Wittink, 2014).

Back Awareness was assessed with the *Fremantle Back Awareness Questionnaire* (FreBAQ) (Wand et al., 2014). The FreBAQ contains nine items on a five-point Likert scale (0 = never feels like that; 4 = always, or most of the time, feels like that). Based on a Rasch analysis of the FreBAQ (Wand et al., 2016), two of the best performing items with the highest item-test correlations were selected: "*When I am performing everyday tasks, I am not sure exactly what position my back is in*" and "*I can't perceive the exact outline of my back*". The scores were transformed to an 11-point numerical rating scale and summed (max = 20), with higher scores indicating poorer back awareness.

2.4. Intervention

2.4.1. Cognitive Functional Therapy (CFT)

CFT is an integrated behavioural approach for individualising the management of people with chronic LBP once serious and specific pathology has been excluded. CFT has evolved from an integration of physiotherapy rehabilitation with foundational cognitive and behavioural interventions (Fordyce, 1976; Keefe, 1982; Vlaeyen et al., 2001), and has shown promising results in the reduction of fear, pain and disability (Bunzli et al., 2016; Caneiro, Smith, et al., 2017; Lee et al., 2015; Leeuw et al., 2008; Mansell et al., 2017; O'Sullivan et al., 2015; Vibe Fersum et al., 2013). CFT differs from other behavioural

approaches, as it uses a multidimensional clinical-reasoning framework to identify and target modifiable contributors to pain and disability in a person-centred manner. A key point of difference from traditional behavioural approaches is that CFT explicitly targets pain control during exposure to feared and/or provocative movements by challenging negative and inaccurate cognitions and modifying how the person physically performs the task (via body relaxation, body control, and extinction of safety-seeking behaviours). Personalised reconceptualisation of pain is achieved via self-reflection, behavioural learning and personalised education. This process violates expectations that pain equals harm, disconfirming previously held unhelpful beliefs, allowing the person to reconceptualise and make sense of their pain experience. Based on an interview and examination, the clinician identifies and targets modifiable contributors to pain, distress and disability in a person-centred manner. This enables the physiotherapist to design a management plan that is tailored to the person's unique clinical presentation and context (P. O'Sullivan et al., 2018). There are three broad components to the intervention:

Making sense of pain: a reflective process that combines the person's own narrative (via interview) and experience (during guided behavioural experiments) to disconfirm unhelpful beliefs and responses to pain, developing a personally-relevant multidimensional understanding of pain that is consistent with contemporary pain science.

Exposure with 'control': a process of behavioural change through experiential learning following a 'graded exposure' model, designed to violate expectations of pain and damage consequences via guided behavioural experiments. Specifically, sympathetic nervous system responses (rapid upper chest breathing and body tension) and safety-seeking behaviours (protective muscle guarding, breath holding, movement avoidance and propping of the hand) that manifested during exposure to painful, feared or avoided functional tasks are explicitly targeted and controlled. This provides patients with strategies to relax, control respiration, and normalise postural and movement behaviours that they nominated as painful, feared or avoided. The new strategies are immediately integrated into daily activities to build self-efficacy (P. O'Sullivan et al., 2018).

Lifestyle change: behavioural modification addressing unhelpful lifestyle factors aimed at increasing physical activity levels based on preference, social participation, and regulation of tension and sleep where relevant.

CFT is underpinned by a strong therapeutic alliance and motivational interviewing style (open, non-judgmental, reflective) (O'Sullivan et al., 2018) providing validation and facilitating disclosure (Edmond & Keefe, 2015; Linton, 2015). The initial session was 1 h and the follow-ups were 30–45 min. Participants were seen on a weekly basis for the first two to three sessions and then progressed to one session every 2–3 weeks during the twelve-week intervention period. The frequency of treatment however was left to the physiotherapist's discretion based on his/her perception of the patient's needs and goals. An individualised self-management program was provided that included progressive functional exercises and lifestyle changes, tailored to personal goals. Further information about the intervention is published in detail elsewhere (O'Sullivan et al., 2018).

Treatment compliance was operationalised as the self-reported proportion of days in a week on which the management routine was practised. Treatment compliance was measured weekly during the treatment phase, with the question: "*Over the past week, how many days have you practised your management routine?*

2.5. Treating clinicians and setting

The two experienced physiotherapists who delivered the intervention were trained in CFT. The clinicians were trained over 100 h by two specialist physiotherapists (POS and JPC) during a program purposefully developed for this study. The training consisted of: theoretical and clinical sessions, including direct clinical mentoring by observation and practice with real patients with disabling back pain and high fear. The treatment was delivered in a primary care musculoskeletal physiotherapy practice in Perth, Western Australia.

2.6. Treatment fidelity

To ensure treatment fidelity, the developer of CFT (POS) was present as an observer in the first session, as well as at two follow ups (Week 6 and Week 12), using as assessment form previously used in another CFT study (Vibe Fersum et al., 2013). *Therapeutic alliance* was also assessed as a measure of treatment fidelity using the *Working Alliance Theory of Change Inventory* (WATOCI). The WATOCI has well-accepted clinical measurement properties, and measures a one-dimensional construct when used with LBP. Scores vary from 16 to 112, with higher scores indicating higher therapeutic alliance (Ferreira et al., 2013).

2.7. Internal validity

SCEDs are particularly vulnerable to plausible rival hypotheses that may explain the outcomes such as, maturation, regression to the mean and external factors. Internal validity refers to whether the outcomes observed in the study are due to the manipulation of the independent variable (intervention) and not to other factors. In other words, if the observed changes can be validly attributed to the intervention. In this study, internal validity for attribution of any systematic change to the intervention was assessed by: **a)** a short interview with the participant (in the last week of the baseline phase), **b)** a short interview with the participant's partner (at the end of the treatment phase), and **c)** a therapist log to identify explanations for change other than the intervention. Qualitative reports from the patient and/or his/her partner that demonstrated clear behavioural change during the intervention were identified (e.g. "I returned to work"). See the Table in the Appendix for a detailed schedule of the short interviews used for internal validity. During the treatment and follow-up phases, participants were also encouraged to communicate any relevant events by email or by completing a comments box in the weekly online questionnaire. Together, these reports provided additional validity of attribution of change to the intervention.

2.8. Data analysis

Although there is no consensus regarding methods for analysis of SCEDs (Kratochwill et al., 2013; Maggin & Odom, 2014), this study followed the recommendation that a combination of visual and statistical analyses that consider design requirements and data assumptions be conducted (Manolov, Gast, Perdices, & Evans, 2014).

2.8.1. Assessment of treatment effect

This study used three analysis methods to determine if changes had occurred once the intervention was introduced: visual analysis, *Conservative Dual-Criterion* (CDC) (Fisher, Kelley, & Lomas, 2003; Swoboda, Kratochwill, & Levin, 2010), and non-overlap analysis (Tau-U) (Parker, Vannest, Davis, & Sauber, 2011). All three methods were used for analysis of the primary outcome and all proposed mediators.

2.8.1.1. Visual analysis. This process involved a systematic analysis of the visual display of the data. Following well-established guidelines in the field (Kratochwill et al., 2010) data were visually examined for *level* (stability of data within a phase); *trend* (slope of the best fitting straight line for the data), and *immediacy of the effects* (comparison of the last three data points from the baseline, Phase A with the first three data points from the treatment phase, Phase B).

2.8.1.2. Statistical analysis

2.8.1.2.1. Conservative Dual- Criterion (CDC). CDC uses *a priori*

criteria to determine the occurrence of systematic change (treatment effect) between baseline and treatment phases (Fisher et al., 2003; Swoboda et al., 2010). This method was developed to refine visual inspection and interpretation of graphed data, and it was used in this study for the analysis of the primary outcome and all potential mediators. This was done by: **1)** plotting two lines (linear trend and mean of the baseline data points); **2)** subtracting 0.25 of the standard deviation of the baseline mean from both lines, and superimposing them on the treatment phase (these lines determined the predicted direction the data would take should no intervention have taken place, or the treatment had no effect); **3)** comparing the number of data points (observations) in the treatment phase that were below the criteria lines, to the minimum number of points required by the guidelines (Fisher et al., 2003) to determine that change occurred (effect). The CDC method allows multiple assessors to review a graph and achieve the same conclusion about the pattern of the data, increasing interrater reliability of the visual decision-making process (Swoboda et al., 2010).

2.8.1.2.2. Non-overlap - Tau-U. Tau-U is the most robust non-overlap method for analysis of single-case research data (Parker et al., 2011). Tau-U uses pairwise comparison of individual data points across phases A and B to determine a dominance index of the score of one data set over the other. This index provides the percentage of non-overlap after controlling for the baseline trend (Parker et al., 2011).

2.8.2. Determining potential mediators of treatment response

2.8.2.1. Cross-lag correlation analysis. To assess the temporal association between proposed mediators and disability, a series of cross-lag correlation analyses adjusted for autocorrelation was performed using Simulation Modelling Analysis (program downloadable at no cost from http://clinicalresearcher.org) (Borckardt et al., 2008). This analysis estimates temporality (*lag*) of associations between two variables over the course of an SCED after adjusting for autocorrelation. Correlations between mediators and disability were estimated and compared at *lags* −2 to +2, to assess the degree the data supported that a proposed mediator changes prior to (negative lag), after (positive lag) or contemporaneously (zero lag) with the outcome. As recommended (Borckardt et al., 2008), this analysis used the last data point of the baseline phase (before introduction of the intervention) and all points of the treatment phase.

3. Results

3.1. Participant characteristics

Four people (one male) with chronic LBP and high pain-related fear participated– see Table 1 for detailed characteristics of the participants, and Table 2 for details at baseline (Weeks 1 and 8).

All participants showed a stable baseline for the measures of outcome and proposed mediators. All participants completed the treatment and all assessments across the three phases of the study. There were no adverse events, and treatment compliance was high across all participants (see Table 2 for details). None of the participants reached the criterion for booster sessions. Therefore, **Phase A'** served as a three-month follow-up period. The mean number of sessions was 10.2 (range 7–12). One participant (P1) had a break from treatment for 2 weeks because of illness. Nonetheless, the weekly online assessments continued and this participant had two extra data points during Phase B (i.e. 14 weeks). The clinicians reported in the therapist log that for all participants, their functional movement behaviours were modifiable

Table 2
Standardised outcome measures across the three phases of the study.

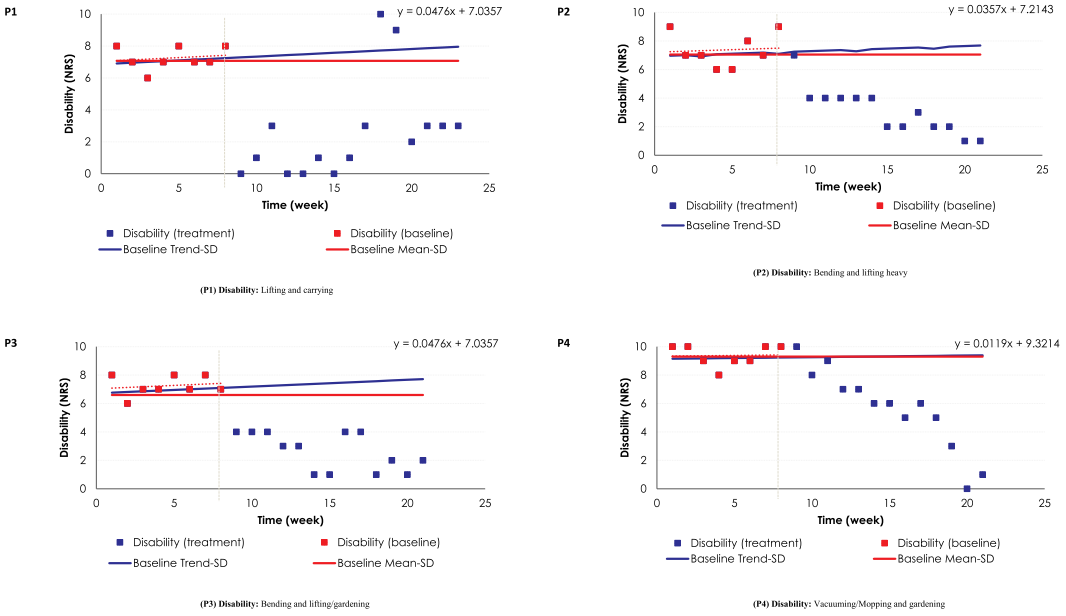
Measures	Timeline	P1	P2	P3	P4
Disability (RMDQ)	Baseline 1 (BAS-W1)	11	10	16	10
	Baseline 2 (BAS-W8)	11	10	17	11
	End-CFT	1	2	6	0
	Follow up (3mo)	2	3	8	0
Pain-related fear (TSK)	Baseline 1 (BAS-W1)	48	45	55	50
	Baseline 2 (BAS-W8)	49	47	56	51
	End-CFT	19	26	34	18
	Follow up (3mo)	19	25	35	18
Pain catastrophising (PCS)	Baseline 1 (BAS-W1)	40	25	42	21
	Baseline 2 (BAS-W8)	40	26	44	22
	End-CFT	7	8	28	0
	Follow up (3mo)	3	9	26	3
Pain-related anxiety (PASS-20)	Baseline 1 (BAS-W1)	51	42	67	32
	Baseline 2 (BAS-W8)	53	46	66	35
	End-CFT	14	14	49	6
	Follow up (3mo)	3	15	44	4
Back beliefs (BackPAQ)	Baseline 1 (BAS-W1)	−11	−7	−11	−10
	Baseline 2 (BAS-W8)	−11	−6	−12	−9
	End-CFT	4	6	1	5
	Follow up (3mo)	8	4	0	4
Illness perceptions (B-IPQ)	Baseline 1 (BAS-W1)	61	58	63	55
	Baseline 2 (BAS-W8)	63	56	62	59
	End-CFT	29	15	41	5
	Follow up (3mo)	15	19	42	3
Back awareness (FreBAQ)	Baseline 1 (BAS-W1)	18	13	15	3
	Baseline 2 (BAS-W8)	15	12	15	3
	End-CFT	2	2	10	0
	Follow up (3mo)	0	3	9	0
Treatment compliance		84%	92%	90%	92%

RMDQ (score range 0–24. High scores indicate higher disability); TSK (score range 17–68. High scores indicate higher fear of damage/pain); PASS-20 (score range 0–100. High scores indicate higher pain anxiety); PCS (score range 0–52. High scores indicate higher pain-related catastrophic thoughts); Disability (score range 0–24. High scores indicate higher disability); $BackPAQ_{10}$ (score range -20-20. Negative scores indicate negative beliefs); B-IPQ (score range 0–80): higher scores indicate more negative illness perceptions; FreBAQ (2 items; score range 0–20. High scores indicate poor back awareness); Treatment compliance (proportion of days which the management routine was practised in a week, measured weekly over the treatment and follow-up periods); BAS-W1: assessment at first week of baseline (Week 1); BAS-W2: assessment at last week of baseline (Week 8).

Table 1
Detailed characteristics of the participants at baseline.

Participants	P1	P2	P3	P4
Age (years)	66	40	52	67
LBP duration (years)	6	22	13	45
Person-specific disability (PSFS)	Lifting and carrying heavy	Bending and lifting heavy	Bending and lifting/gardening	Vacuuming/Mopping and gardening
Action (Past management – B-IPQ)	Manual therapy, stabilization exercises, Pilates, spine injections	Chiropractic, Physiotherapy, massage, Pilates, spine injections, Opioids (over 20 years)	Rest, manual therapy, inversion table, electrotherapy, spine injections	Massage, exercise, pain medication, spine injections
Appraisal (Was the action effective?)	ineffective	ineffective	ineffective	ineffective

P (Participants 1 to 4); LBP (Low Back Pain); PSFS (Patient Specific Functional Scale – most disabling activity for each participant is presented here); B-IPQ (score range 0–80): higher scores indicate more negative illness perceptions.



CAPTIONS: Disability (baseline): baseline datapoints (8 weeks); Dotted line (baseline linear trend): least squares regression line of the baseline datapoints; Baseline Trend-SD: linear trend minus 0.25 SD of the baseline mean plotted across the treatment phase using linear equation; Baseline Mean-SD: mean of the baseline datapoints minus 0.25 SD of its mean plotted across the treatment phase – both Trend-SD and Mean-SD determine the predicted direction which the data would follow should no intervention take place, or if the treatment had no effect. Disability (treatment): treatment phase datapoints (15 weeks for P1; 13 weeks for P2-P4).

Fig. 1. Graphical display of disability data across baseline and treatment phases, for visual and CDC analysis of treatment effect.

and pain was controllable via guided behavioural experiments used in the first consultation. Therapeutic alliance, measured after the first session, was high across participants (P1: 80; P2: 100; P3: 97; P4: 102 – available scale range 16–112) (Ferreira et al., 2013).

3.2. Treatment effect

3.2.1. Effect of CFT on disability

For all participants, visual and CDC analysis indicated reduction in disability after the start of the intervention (Fig. 1 - see footnotes for detailed explanation). The Tau-U index indicated that after controlling for the baseline trend, a large proportion of the data from baseline and treatment phases were non-overlapping and phase-dependent (Table 3), meaning that disability improved significantly for all participants in the treatment phase. Together, these results suggest the presence of a treatment effect (i.e. reduction in disability) for all participants. Attribution of change to the intervention was further supported by therapist log and interview content (participant and partner), which did not identify other explanations for change other than the intervention. Table 4 displays key pre-post qualitative reports from the patient and/or his/her partner that provide support for behavioural change.

3.2.2. Effect of CFT on potential mediators of treatment response

Visual and statistical analysis (CDC and Tau-U) indicated a treatment effect for proposed mediators in the *pain* and *fear* groupings for all participants (see Table 3 for details). For *pain controllability*, pain control was enhanced in all participants, and pain self-efficacy improved in three participants (P1, P3, P4). *Distress* was reduced in three participants (P2, P3, 4), and *Sleep* was improved in two participants (P3 and P4). See the Figure in the Appendix that illustrates the CDC analysis process in one of the proposed mediators, indicating treatment was effective in reducing pain intensity in all cases.

Cross-lag correlation analysis suggested that most of the proposed mediators changed concomitantly with disability, with the strongest correlations observed at *lag zero*. Table 5 reports correlations between each of the proposed mediators and disability at lag zero, and respective p-values; and Fig. 2 displays all lag zero correlations between the proposed mediators and disability for each participant.

The three mediators with the highest correlation at lag zero for each participant were from the *pain*, *pain controllability*, and *fear* groupings. For summary visualisation of the change process across the three phases of the study and for discussion purposes, these results are graphically displayed by mediator groupings in Fig. 3. They illustrate that for all participants, *pain*, *pain controllability*, and *fear* were most strongly associated with disability at lag zero after the first treatment session. In addition, Fig. 3 illustrates that large changes occurred immediately for P1 and P2, whereas changes occurred more gradually for P3 and P4.

3.3. Standardised outcome measures

Changes in standardised outcome measures at pre-post assessment timepoints supported results of assessments at weekly timepoints. Reductions in standardised measures of disability (RMDQ), pain-related fear (TSK), pain anxiety (PASS-20), pain catastrophising (PCS), illness perceptions (B-IPQ), and improvements in back beliefs (BackPAQ), and back awareness (FreBAQ) were observed over the treatment phase for all participants. Specifically, scores at the end of follow up are representative of low disability levels, with changes beyond the minimal clinically important change of 2.5 points in the RMDQ (Roland & Morris, 1983) for all four participants. Three participants (P1, P2, P4) had changes that were more than double the minimal clinically important change of 8 points for pain-related fear (TSK) (Lundberg, Grimby-Ekman, Verbunt, & Simmonds, 2011), and had scores below cut off (14) for pain catastrophising (PCS), indicating clinically meaningful changes (Scott, Wideman, & Sullivan, 2014). All participants had substantial changes in standardised measures of illness perceptions, back beliefs, back awareness and pain anxiety. At follow up, all but one participant (P3) had scores below cut-off levels of fear, catastrophising and pain anxiety (see Table 2 for details).

4. Discussion

The primary aim of this study was to evaluate how potential mediators relate to disability over time, during a behavioural intervention (CFT) in four people with chronic LBP and high pain-related fear of bending and lifting. A second aim was to evaluate whether the change

Table 3
Statistical analysis of treatment effect on disability and proposed mediators employing CDC and Tau-U methods.

	P-1				P-2				P-3				P-4			
	CDC		TAU-U		CDC		TAU-U		CDC		TAU-U		CDC		TAU-U	
	n criterion (criterion = 12)	Effect (Y/N)	Non-overlap (%)	p -value	n criterion (criterion = 10)	Effect (Y/N)	Non-overlap (%)	p -value	n criterion (criterion = 10)	Effect (Y/N)	Non-overlap (%)	*p* -value	n criterion (criterion = 10)	Effect (Y/N)	**Non-overlap (%)**	*p* -value
Disability	13	Y	76	0.0045	12	Y	94	0.0004	13	Y	100	0.0002	12	Y	84	0.0018
Pain intensity	12	Y	63	0.0136	13	Y	99	0.0004	13	Y	100	0.0001	12	Y	92	0.0010
Pain Interference	13	Y	93	0.0002	12	Y	87	0.0012	13	Y	93	0.0002	13	Y	100	0.0003
Pain Control	13	Y	88	0.0018	13	Y	97	0.0002	13	Y	94	0.0002	13	Y	100	0.0002
Pain Self-Efficacy	12	Y	73	0.0097	7	N	49	0.0277	11	Y	76	0.0036	13	Y	100	0.0003
Fear of damage/pain	15	Y	100	0.0001	13	Y	100	0.0002	13	Y	100	0.0002	13	Y	100	0.0002
Pain Anxiety	13	Y	92	0.0004	13	Y	100	0.0002	13	Y	99	0.0002	13	Y	100	0.0002
Catastrophising	14	Y	89	0.0007	13	Y	100	0.0002	12	Y	94	0.0002	13	Y	100	0.0002
Avoidance beliefs	12	Y	83	0.0023	13	Y	100	0.0002	13	Y	100	0.0002	13	Y	99	0.0002
Distress	10	N	55	0.0442	12	Y	99	0.0003	11	Y	91	0.0002	12	Y	95	0.0002
Sleep	8	N	37	0.3393	7	N	40	0.1733	13	Y	99	0.0002	12	Y	70	0.0160

P-1-4: participants 1 to 4; criterion: minimum number of data points required to reach a systematic change; n criterion: identified number of data points below the criterion lines; Effect: presence (Y) or absence (N) of a systematic change; Non-overlap (%): Tau-U index.

(sequential or simultaneous) in mediators and disability occurred at the same timepoint during the intervention period for all individuals.

First, the results verified that reductions in disability and proposed mediators (pain, pain controllability and fear in all participants, distress in three participants and sleep in two participants) were clearly related to the commencement of the CFT intervention. This was identified via visual and statistical analyses, and supported by standard outcome assessments at pre-post timepoints, which demonstrated changes beyond the minimal clinically important change for disability (for all), and fear (for most). The therapist log and interview content (participant and partner), did not reveal any other explanations for change during the study period other than the intervention.

Second, the statistical analyses determined that, for all participants, most of the proposed mediators (*pain*, *pain controllability*, and *fear*) were most strongly associated with disability at *lag zero*, suggesting that the changes occurred concomitantly and not before changes in disability. Furthermore, visual analysis indicated how these changes occurred at different rates and in different patterns, demonstrating the individual variability of the temporal process of change. Specifically, two participants (P1, P2) had a fast response, displaying large changes immediately after the first treatment session, whereas the other two participants had a more gradual response, with moderate changes soon after the start of treatment. While all participants showed changes in pain, pain controllability and fear, the specific factors within these groupings that were associated with the treatment response varied between individuals. For pain, three participants (P1, P2, P3) had improvement in pain interference, and one (P4) in pain intensity. For pain controllability, two participants (P1, P4) improved in self-efficacy, and two (P2, P3) in pain control. For fear, two participants (P1, P3) displayed a reduction in avoidance beliefs, one (P2) in fear of damage/pain, and one (P4) in catastrophising. In terms of factors underpinning treatment response, our findings are somewhat in line with results from RCTs using psychological interventions for people with chronic LBP that identified fear (Leeuw et al., 2008; Mansell et al., 2016), self-efficacy (Lee et al., 2015), pain and distress (Mansell et al., 2016) as factors that underpin reduction in disability. This study adds to this knowledge by providing evidence that several of these factors improved at the same time as disability. The findings that potential 'mediators' and the outcome changed simultaneously, challenge the traditional understanding of therapeutic change, that improvement occurs in a sequential manner and gradually over the treatment period. This was an important and novel finding of this study.

The rapid changes observed in this study are unlikely to be solely explained by a biomedical perspective, which would require changes in tissue, muscle strength, flexibility and/or physical conditioning for improvement to occur (George, 2017; Vlaeyen et al., 2001). Rather, these changes are more likely to be explained according to contemporary pain science, which emphasises learning and perceptual processes being critical in pain (Brodal, 2017). Changes in expectation and the meaning of a stimulus can rapidly modulate a person's pain experience (Buchel, Geuter, Sprenger, & Eippert, 2014; Bushnell, Ceko, & Low, 2013; Hedderson, Dover, George, Crow, & Borsa, 2018; Moseley & Arntz, 2007; Tracey & Mantyh, 2007; Wiech, 2016; Wiech & Tracey, 2013). It is plausible that the experiential learning encouraged by an exposure-based behavioural intervention such as CFT, may lead to a rapid disruption of a person's schema. That is, CFT shifts the person's pre-existing pattern of beliefs, memories, emotions, and cognitions that together represent the construct of their LBP, and that guides their behaviour (Banaji & Greenwald, 2013), thus facilitating behavioural change.

The process described in this study provides insight into how four people 'trapped' in a chronic state of pain, fear and disability could change considerably over the course of a twelve-week intervention, and subsequently be led on a pathway of self-management and independence. **Follow-up** data from this study support this. At 3 months post-intervention, all participants experienced reduction in pain and

Table 4
Qualitative reports from the patient and/or his/her partner that provide support for behavioural change.

	Baseline	End-treatment	End-treatment
		Participant	Partner
P1	"Stopped dancing … took time off work …. stopped teaching …. I was delivering workshops … facilitating multicultural groups at the university … I cannot set it up by myself"	"I'm back teaching workshops again" "On Sunday, I was Morris-dancing at a small farm field day in the countryside …. I was leaping in the air and doing silly things."	"For last few years she had stagnated – seen lots of different clinicians with different ideas, but no real improvement …. until now" "Going for bike rides, being more active, dancing and teaching again … These changes were despite some illnesses we both went through over the last couple of months …" "…she now insists in picking up things, weights, heavier objects … she doesn't talk about her back anymore …"
P2	"I care for the kids … so, I work from home baking cakes … I stopped that for a while due to pain …. " "I'm limited in how much can do with the kids … like cycling … I miss out on things with them"	… "a few weeks ago, I had taken on as many cakes in 1 day as I would for three days solid, and afterwards I came out of it okay …" "After 20 years on it, I reduced my medication to about a third"	"No changes in our lives in the last 3 months … same old same old" "She is happier, talking about the positive side of things … about long term management of her back … baking again … more involved with fun things we do (bike riding, running around with kids … before she would just stay out of it … she wouldn't go near a bike for years … that's a big change for us)" "…she cut down on her meds by a third"
P3	"I have been off work …. I fear of not being able to work and having to retire early" "…reduced activities around the house …. there is a clear link between activities and pain" "I changed the way I do basic things … feels that I aged a lot … I have trouble putting my socks and jocks … it isn't just a one off pain, you know, it's more like can I get by today without putting shoes and socks on?"	"I'm back a t work" "It's been fantastic … I was mucking around outside in the shed for six or 7 h yesterday (working on son's car). Still pulled up a little bit sore but after doing that I think anyone would pull up a little bit sore." "we are going away on long holidays for the first time … to America"	"Total 180 to what he was doing before. Absolutely" …. "Well, put it this way. We haven't been on big, large plane rides or anything like that, because he can't sit for extended periods of time. We've only just now, are having a holiday where we're going to be doing travelling because he seems to be a lot better." "No other significant changes in our lives" "He's actually involving himself more with things around the house. And that's a lot more than he has done, which has been good …. he's been out there helping with that (fixing son's car), and all that sort of stuff. I don't think that he would have done that six months ago. He would have been out for about an hour or so, and he would have said, 'No. That's it.' Whereas now, he's been out there for a few hours"
P4	"Pain impacts on my ability to do my chores around the house … I can't do gardening, I can't vacuum, I can't lift …. my husband is doing more …. " "My pain has been the same up to ten days ago when for no clear reason it got worse … although, your body gets worse with time"	"What used to trigger my pain is what I use to relieve it – bending, lifting, gardening, sowing, vacuuming – the more I do the better I feel. If I have pain, I move and do more and I feel better" "I haven't had a significant flare up for the last few months"	""No major changes … apart from the fact we are doing a lot more things together …. We've been away for a weekend, which we hadn't done before because of pain" "We're working out in the garden and doing all … She's picking up all the pavers and doing all the paving, shifting these things around, carrying them and lifting them, I say, "That's looking great. Do you want a hand? "Do you want me to lift them?" "No, I'm fine." That's like, whoa!" "Her goal was to get 50% better …. She's now boasting it's up around the 95% of the pain gone, and only every now and then she gets a twinge"

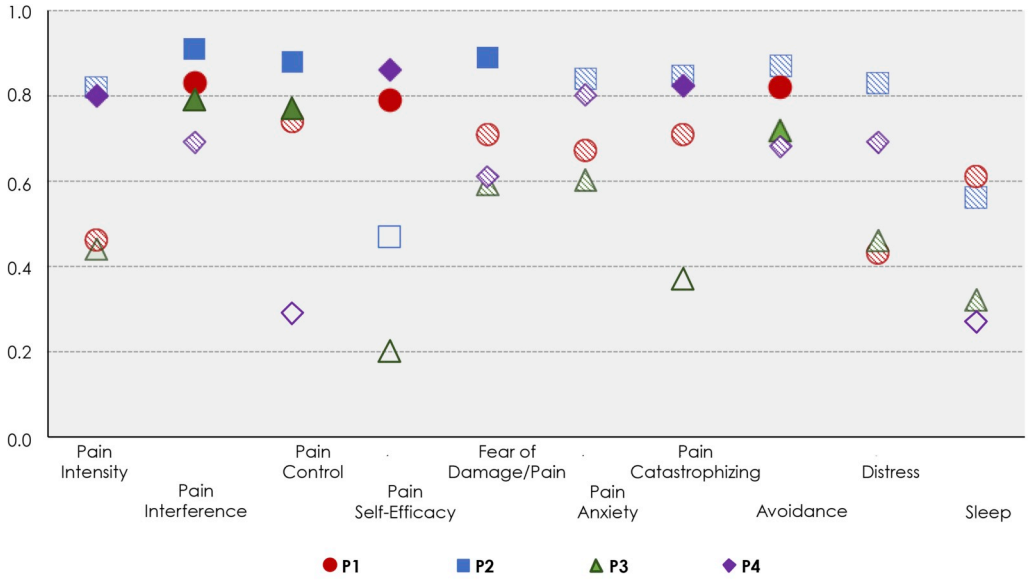
Temporal association between proposed mediators and disability.

development of more positive perceptions and back beliefs, which are important predictors of the long-term trajectory of people with LBP (Chen et al., 2017). In this process, all participants experienced a transitory increase in symptoms ('flare-ups') of variable intensities and duration. Interestingly, these were triggered by non-physical factors (P1: viral illness and fatigue, P2: opioids withdrawal, P4: feeling of fatigue) and changes in geographical context (P3). This may reflect the close link between immune, endocrine and nervous systems in the

Table 5
Cross-correlations at *lag zero* indicating the level of association between each proposed mediator and disability, and respective p-values.

		P1		P2		P3		P4	
		r	p	r	p	r	p	r	p
Pain	Pain intensity	0.46	0.053	0.82	0.001	0.44	0.051	0.80[a]	0.002
	Pain Interference	0.83[a]	0.001	0.91[a]	0.000	0.79[a]	0.001	0.69	0.003
Pain controllability	Pain control	0.75	0.000	0.88[a]	0.000	0.76[a]	0.000	0.29	0.111
	Pain Self-Efficacy	0.79[a]	0.000	0.47	0.089	0.2	0.433	0.86[a]	0.001
Fear	Fear damage/pain	0.71	0.003	0.89[a]	0.000	0.59	0.016	0.61	0.024
	Pain Anxiety	0.67	0.004	0.84	0.001	0.60	0.007	0.80	0.002
	Pain Catastrophising	0.71	0.002	0.84	0.001	0.37	0.087	0.83[a]	0.003
	Avoidance beliefs	0.82[a]	0.000	0.87	0.000	0.71[a]	0.007	0.69	0.008
Distress	Depression/Anxiety/Pain bothersomeness	0.44	0.032	0.83	0.000	0.45	0.041	0.69	0.016
Sleep	Capacity	0.61	0.012	0.56	0.066	0.32	0.117	0.27	0.147

[a] Indicates the three correlation coefficients (r) with the highest association at lag zero for each participant.



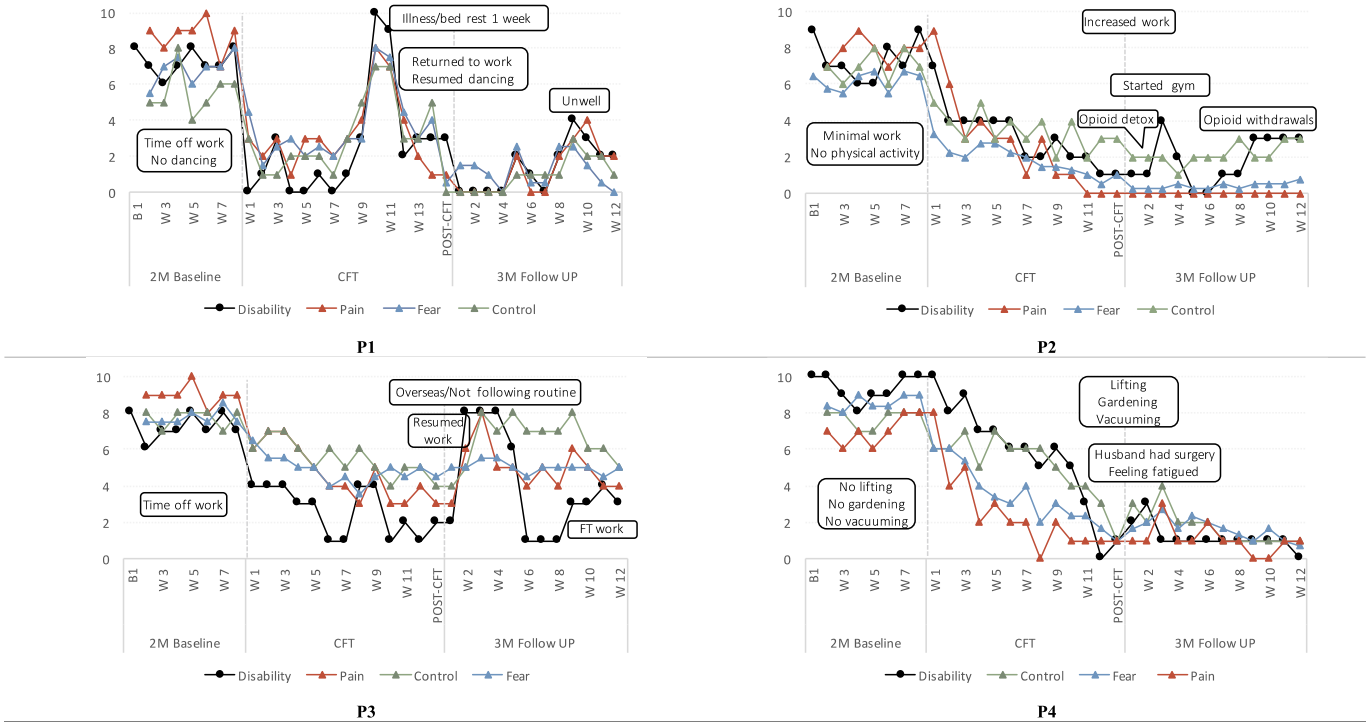
Color gradient of each data point indicates strength of correlation at lag zero. **Colour-filled markers:** indicate highest correlations (top 3) that reached statistical significance; **Pattern-filled markers:** indicate other correlations that reached statistical significance; **Unfilled markers:** indicate correlations that did not reach statistical significance.

Fig. 2. Cross-correlations of all proposed mediators and disability at lag zero, illustrating factors associated with change in each participant.

context of learning and adaptation in response to a threat (Davies, 2016; Lenaert, Boddez, Vlaeyen, & van Heugten, 2018; Rubinow & Rubinow, 2017).

This study highlights the value of using SCEDs to understand the process of change. Larger group-level analysis often conducted in RCTs typically examine group effects informing on a summary or a common pathway to change. In contrast, SCEDs examine within-person changes, and thus are able to demonstrate that change processes may vary among individuals. Understanding the process of change at an individual level is valuable to inform evaluation of mediators in future RCTs.

Data from this study raise some interesting questions in relation to promoting clinical change in persistent disorders such as chronic LBP: *What is necessary for change to occur? Is it important to target specific 'mediators'? Do several factors need targeting at once?* The individualised experience illustrated by the four participants in this study suggests the



Pain control and self-efficacy: for visualisation purposes, original scores were reversed, so that reduction in scores indicate improvement. **FT:** full time work.

Fig. 3. Illustration of the change process - 'How change unfolds' for each person across the phases of the study. This figure displays the top three 'mediator groupings' of factors associated with treatment response with the highest association at lag zero.

idea of a 'pain schema disruption' promoting change in several factors at the same time. Furthermore, it suggests that how the schema is disrupted, and which factors change vary between and within individuals over time. Although speculative, we propose that experiential learning which de-threatens pain and enhances pain control may be a potential underpinning mechanism of change in disability in people with chronic LBP and high pain-related fear. This however, warrants further testing.

4.1. Limitations

To our knowledge, this is the first study to use an SCED to analyse temporal associations of change in outcome and proposed mediators in people with chronic LBP and high pain-related fear. Although, this provided novel information about the relationship of change in outcome and factors associated with treatment response, some limitations should be noted.

First, SCEDs can be burdensome to a person living with chronic pain because they require a long baseline and extensive data collection. However, there are aspects of this design that make it useful for patients, clinicians and researchers: i) before the start of the intervention, determining a stable baseline enhances the clinician's ability to attribute subsequent change to the intervention, and to draw valid conclusions about the effects of the intervention; ii) during the intervention, this design allows for immediate feedback about the targeted outcome to both patient and clinician, which can facilitate treatment modification and progress. These aspects highlight an important overlap between this design and clinical practice. In fact, SCEDs have been suggested as an important design to bridge the gap between science and practice (Borckardt et al., 2008; Morley, 2018; Vlaeyen, Morley, & Crombez, 2016). *Second,* SCEDs are vulnerable to plausible rival hypotheses that may explain the outcomes such as, maturation, regression to the mean and external factors. We strategized to limit this problem, for example using a stable baseline with eight data points (above the recommended five) (Kratochwill et al., 2010; Tate et al., 2017), a therapist log and interview content (with the participant and his/her partner), but can't exclude it. *Third,* as is the case for most studies investigating behavioural interventions, data were collected via self-report which can be vulnerable to self-preservation bias. *Fourth,* most SCEDs in this field used daily measures of the outcome, whereas this study used weekly measures. It has been suggested that the use of daily measures in previous SCEDs, could be a mechanism for behavioural change in itself (J. Vlaeyen et al., 2012), although the more frequent the assessment, the higher the risk of perseveration, suggesting an advantage of weekly over daily assessments. Weekly assessments are considered sufficient to detect measure change (Kratochwill et al., 2013), but they obviously cannot detect changes that occurred within the week. The frequency of assessments in SCEDs therefore represents a three-way burden-perseveration risk-sensitivity trade off. Future studies evaluating mediator-outcome relationship could include more frequent assessments (every third day, for example) that would provide good temporal resolution, while minimising self-report bias. *Fifth,* some of the assessed constructs may overlap conceptually, which would increase correlation between them, and that they were all rated at the same time may also have increased their correlation. We mitigated the latter by using Simulation Modelling Analysis, which accounts for the autocorrelation in each measure before estimating the cross correlations (Borckardt et al., 2008).

4.2. Future directions

Future RCTs aiming to evaluate mediators of treatment effect may need to include frequent and early measures (at each treatment session, for instance) of the outcome and proposed mediators to allow adequate temporal evaluation of change in the mediators-outcome relationships. New technologies including online registries, smartphone apps, and wearable sensors may provide avenues to enhance the frequency of measurement in larger trials. To minimise participant burden, the decision as to which factors to measure can be informed by well-designed SCEDs.

5. Conclusion

This single-case experimental design study demonstrated the interplay of factors associated with treatment response, highlighting '*how change unfolded*' uniquely for each individual. Changes in *pain*, *pain controllability*, and *fear* occurred concomitantly to changes in disability, suggesting a disruption in the person's entire pain schema. The findings that factors underpinning treatment response and the outcome changed simultaneously, challenge the traditional understanding of therapeutic change.

Data statement

Data for the four participants of this study is embedded in the manuscript and individually presented either in a graphic or table format.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brat.2019.02.007.

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