Philipps Universität Marburg

THERAPIEPROZESSE UND WIRKMECHANISMEN PSYCHOLOGISCHER SCHMERZTHERAPIE

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Inhaltsverzeichnis

Abbildungsverzeichnis

1. Zusammenfassung und Abstract

1.1 Zusammenfassung

Das übergeordnete Ziel dieses Dissertationsprojektes war es Therapieprozesse und Wirkmechanismen von Expositionstherapie bzw. kognitiver Verhaltenstherapie zur Behandlung chronischer Rückenschmerzen zu untersuchen. Im Rahmen einer randomisiert kontrollierten Therapiestudie mit hochängstlichen chronischen Rückenschmerzpatientinnen und Rückenschmerzpatienten (n=61) wurden therapiespezifische und gemeinsame Therapieprozesse auf Grundlage wöchentlicher Prozessmessungen untersucht. Hierbei wurden Veränderungen in Angstvermeidungsüberzeugungen als gemeinsamer Therapieprozess identifiziert. Weiterhin beeinflussten Entspannung, Ablenkung, Konfrontation, Aktivitätsniveau und Selbstwirksamkeit sowohl den Therapieerfolg der Expositionstherapie als auch der kognitiven Verhaltenstherapie.

Im Rahmen einer anschließenden Einzelfallstudie mit hochängstlichen chronischen Rückenschmerzpatientinnen und Rückenschmerzpatienten (n=12) wurden einzelne Therapieelemente auf Grundlage täglicher Prozessmessungen evaluiert. Zudem wurden Effekte auf biologische Stressmarker exploriert. Während individuelle Expositionserfahrungen eine Reihe von unmittelbaren Veränderungsprozessen bewirkten, führte die kognitive Verhaltenstherapie eher zu zeitverzögerten Veränderungsprozessen. Weiterhin zeigten sich in der Expositionsgruppe vergleichsweise niedrigere Kortisolwerte während eines Verhaltenstests unmittelbar nach Therapieende. Die Erforschung von Therapieeffekten auf biologische Stressmarker scheint also ein vielversprechender Untersuchungsgegenstand für zukünftige Forschung.

Im Rahmen eines Experiments mit gesunden Studentinnen (n=112) wurden zwei therapeutische Instruktionen während der Durchführung von Expositionen evaluiert. Diese Instruktionen beruhten auf konkurrierenden Theorien über zugrundeliegende Wirkmechanismen. Die Annahmen des Habituationsmodells und des Inhibitionsmodells wurden einander gegenübergestellt. Beide Instruktionen verbesserten die kognitive Schmerzbewältigung. Allerdings verbesserte nur die Instruktion gemäß des Inhibitionsmodells die Schmerztoleranz. Zudem führte nur die Instruktion gemäß des Inhibitionsmodells zu einem spezifischen psychophysiologischen Aktivierungsmuster, welches sich besser durch Annahmen des Inhibitionsmodells als durch Annahmen des Habituationsmodells erklären lässt.

Insgesamt trägt die vorliegende Arbeit unter Einsatz unterschiedlicher Forschungsmethoden zu einem besseren Verständnis von Therapieprozessen und Wirkmechanismen psychologischer Schmerztherapie bei. Gleichzeitig wurden isolierte Therapieelemente sowie therapeutische Instruktionen evaluiert. Methodische Überlegungen bei der Auswahl der jeweiligen Forschungsdesigns werden im Hinblick auf zukünftige Psychotherapieforschung diskutiert.

1.2 Abstract

This dissertation project investigated treatment processes and mechanisms of graded in vivo exposure and cognitive-behavioral therapy during the treatment of individuals suffering from chronic low back pain and high levels of fear-avoidance. A randomized controlled trial design with individuals suffering from chronic low back pain and high levels of fear-avoidance (n=61) was applied to investigate unique and common treatment processes based on weekly session-by-session measures. We identified changes in fear-avoidance belief as a common treatment process. In addition, changes in relaxation, distraction, confrontation, activity and self-efficacy influenced the treatment success of exposure and cognitive-behavioral therapy.

A subsequent single-case design with individuals suffering from chronic low back pain and high levels of fear-avoidance (n=12) was used to evaluate isolated treatment elements based on daily processes measurements. Moreover, effects on biological stress markers were explored. While exposure experience initiated several immediate changes, cognitive-behavioral interventions seemed to build their effect later in time. Furthermore, the exposure group showed relatively lower cortisol levels during a behavioral test immediately after treatment. Thus, treatment effects on biological stress markers appear to be a promising object of future investigation.

An experimental design with healthy female students (n=112) was applied to evaluate therapist instructions during the conduction of exposure sessions. These instructions were justified by competing theories on mechanisms of change. Assumptions of the habituation model and the inhibitory learning model were compared. Both instructions improved cognitive pain coping. Only the instruction according to the inhibitory learning model increased pain tolerance. Similarly, only the instruction according to the inhibitory learning model lead to specific psychophysiological changes. These psychophysiological changes can be better explained by assumptions of the inhibitory learning model compared to assumptions of the habituation model.

Overall, this dissertation project contributes to an improved understanding of treatment processes and mechanisms within psychological pain treatments. At the same time, isolated treatment elements and therapist instructions were evaluated. Methodological considerations concerning respective research designs are discussed regarding future psychotherapy research.

2. Theoretischer Hintergrund

2.1 Chronische Rückenschmerzen

Rückenschmerzen kennt heutzutage fast jeder Mensch. Die somatischen Bedingungen für Rückenschmerzen sind vielseitig (Pfingsten & Hildebrandt, 2011). Hierbei wird zwischen akuten und chronischen Schmerzen unterschieden (Krismer & van Tulder, 2007). Akute Schmerzen dauern über einen begrenzten Zeitraum an. Körpereigene Heilungsprozesse können ggf. durch medizinische Maßnahmen unterstützt werden (Loeser & Melzack, 1999). Anders als bei anderen Verletzungen oder Erkrankungen wird allerdings bei Rückenschmerzen eine frühe Wiederaufnahme von Aktivitäten ausdrücklich empfohlen (Pfingsten & Hildebrandt, 2011). Chronische Schmerzen hingegen persistieren über einen Zeitraum länger als drei bis sechs Monate. Im Laufe der Zeit entwickeln die Schmerzen eine Eigendynamik, bei der sie ihre ursprüngliche Warnfunktion verlieren (Gatchel, Peng, Peters, Fuchs, & Turk, 2007). Laut einer repräsentativen Telefonerhebung leidet jeder fünfte Europäer unter chronischen Schmerzen (Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006). Unspezifische Rückenschmerzen machen mit 24% den größten Anteil chronischer Schmerzerkrankungen aus. Beschwerden in der Lendenwirbelsäule sind mit zusätzlich 18% angegeben. Insbesondere chronische Schmerzen stellen somit sowohl für die Betroffenen (Breivik et al., 2006; Schmidt et al., 2011) als auch für das Gesundheitssystem (Wenig, Schmidt, Kohlmann, & Schweikert, 2009) ein relevantes Problem dar. Beim Übergang von akuten zu chronischen Schmerzen erweisen sich, zusätzlich zu möglichen physiologischen Ursachen, psychologische Risikofaktoren als bedeutende Prädiktoren (Chou & Paul Shekelle, 2010; Lee et al., 2015; Linton, 2000). Zur Erklärung von Chronifizierungsprozessen bedarf es also multifaktorieller Modelle, welche über eine rein traditionell medizinische Perspektive hinausgehen.

2.2 Fear-Avoidance (FA) Modell

Das FA Modell gilt als ein etabliertes biopsychologisches Modell zur Erklärung der Entstehung und Aufrechterhaltung chronischer Rückenschmerzen (Vlaeyen & Linton, 2000, 2012). Als Ausgangspunkt des Modells steht ein Schmerzreiz nach irgendeiner Art von Verletzung *(injury)*. Diesem Schmerzreiz messen Personen eine subjektive Bedeutung bei (*pain experience*). Abhängig von dem subjektiven Urteil nimmt das Modell zwei gegenläufige Prozesse an. Entweder es folgt ein von schrittweiser Konfrontation geprägter Weg in die Erholung. Oder es beginnt ein Teufelskreis exzessiver Schonung und Vermeidung. Die Mehrheit der Menschen nimmt Schmerzen zwar als unangenehm wahr, sie legt ihnen allerdings keine katastrophisierende Bedeutung bei *(no fear).* Nach einer angemessenen Schonphase werden Aktivitäten langsam aufgenommen

und der Körper wird allmählich wieder belastet *(confrontation).* Es folgt eine vollständige Heilung der ursprünglichen Verletzung und die Rückkehr in das alte Leben *(recovery).* Eine spezifische Subgruppe allerdings betrachtet Schmerzreize als etwas Bedrohliches. Sie wertet diese Reize als Hinweis auf einen schweren Körperschaden *(pain catastrophizing).* Diese Befürchtungen werden durch eine grundlegende negative Bewertung körperlicher Symptome *(negative affectivity)*, sowie eine zusätzliche Verstärkung durch negative Krankheitsinformationen *(threatening illness infromation)* erklärt. Zusätzlich bewerten diese Personen körperliche Symptome primär negativ. Diese Personen entwickeln eine ausgeprägte Angst *(pain-related fear)* ihrem Körper, beispielsweise durch „falsche" Bewegungen, zu schaden. Folglich vermeiden sie bestimmte Bewegungen entweder vollständig oder führen sie nur unter bestimmten Vorsichtsmaßnahmen aus *(avoidance)*. Gleichzeitig achten sie besonders aufmerksam darauf, inwieweit sich Schmerzen ändern bzw. unter welchen Bedingungen sie auftreten *(hypervigilance).* Kurzfristig erscheint dieses Verhalten, insbesondere vor dem Hintergrund erhöhter schmerzbezogener Ängste, verständlich und nachvollziehbar. Dieses teilweise exzessive Vermeidungsverhalten hat allerdings eine Reihe von langfristigen negativen Folgen. Zum Beispiel geht Vermeidungsverhalten mit einem Abbau der Muskulatur einher *(disuse)*. Der Verlust früherer angenehmer Aktivitäten führt meist zu einer Verschlechterung der Stimmung *(depression)*. Weiterhin weiten sich schmerzbedingte Einschränkungen aus *(disability)*. Die Kernannahmen des Modells sind in der Abbildung 1 graphisch dargestellt.

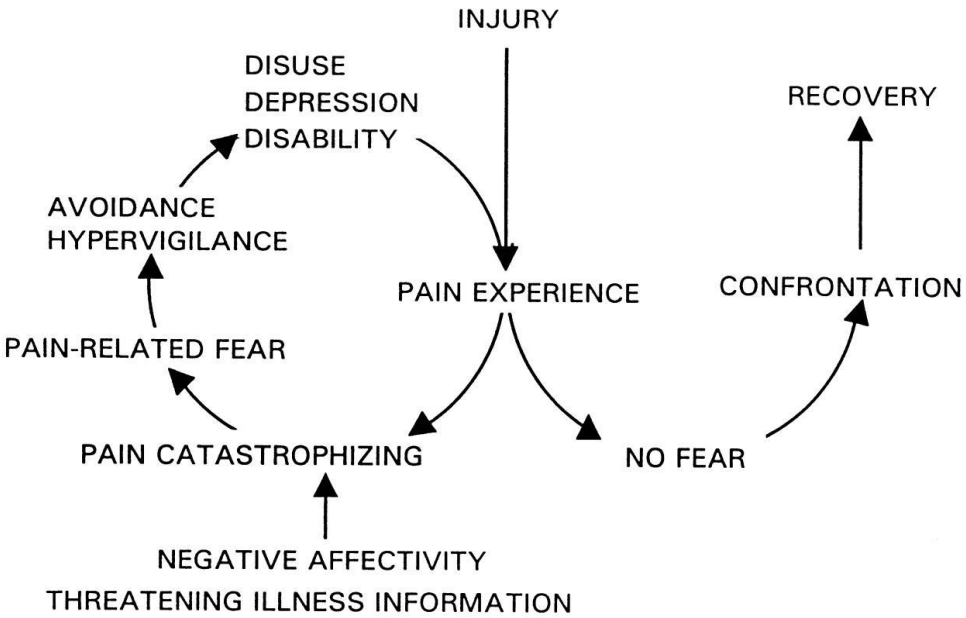

Abbildung 1 Fear-Avoidance Modell (nach Vlaeyen & Linton, 2000)

Als Grundlage für die Entstehung dieses Teufelskreises werden hauptsächlich klassische und operante Lernmechanismen angenommen. Ein Schmerzreiz wird als ein unkonditionierter Stimulus (US, Schmerz) betrachtet, welcher eine automatische Reaktion (UR, schmerzbezogene Angst) hervorruft. Wird dieser US zeitlich mit einem neutralen Stimulus gepaart, kommt es zu einem klassischen Konditionierungseffekt. Der ursprünglich neutrale Stimulus wird zu einem konditionierten Stimulus (CS), welcher dieselbe Reaktion (CR, schmerzbezogene Angst) wie der US hervorruft und welcher zukünftiges Verhalten über operante Mechanismen steuert. Sowohl exterozeptive, interozeptive als auch propriozeptive Stimuli können zu Prädiktoren des US werden (Vlaeyen, Morley, Linton, Boersma, & de Jong, 2012). Allerdings werden vor allem propriozeptive Stimuli (z.B. bestimmte Körperhaltungen oder Bewegungen) als bedeutsam für Rückenbeschwerden betrachtet.

Zusammenfassend erlangte das FA-Modell seit der ersten Formulierung sowohl unter Forschern als auch unter Praktikern eine rasche Popularität (Crombez, Eccleston, Damme, Vlaeyen, & Karoly, 2012). Für die Forschung erlaubten Vorhersagen des Modells die Formulierung spezifischer Hypothesen, welche in anschließenden empirischen Untersuchungen getestet werden konnten. Beispielsweise inspirierte das Modell eine Reihe von experimentellen Studien (Goubert, Francken, Crombez, Vansteenwegen, & Lysens, 2002; Meulders, Vansteenwegen, & Vlaeyen, 2011) sowie Untersuchungen über dessen klinische Relevanz (Hasenbring et al., 2012; Pincus, Smeets, Simmonds, & Sullivan, 2010). Gleichzeitig konnten aus dem FA-Modell neue Behandlungsmöglichkeiten für diese spezifische Patientengruppe abgeleitet werden (Vlaeyen et al., 2012). In der vorliegenden Arbeit diente das FA-Modell als theoretische Grundlage. Darauf aufbauend erfolgte die Auswahl der untersuchten Stichproben sowie der psychotherapeutischen Behandlungsansätze. Weiterhin wurden aus dem Modell Hypothesen über relevante Therapieprozesse und Wirkmechanismen abgeleitet.

2.2.1 Komponenten der schmerzbezogenen Angst

Als Weiterführung des ursprünglichen Modells wurde der zentral angenommene aufrechterhaltende Mechanismus der schmerzbezogenen Angst (*pain-related fear*) in die drei Komponenten der kognitiven Bewertung, der physiologischen Reaktion und einer Verhaltenstendenz differenziert (Norton & Asmundson, 2003). Hierbei wird eine unterschiedliche Gewichtung einzelner Komponenten angenommen. In einer gegenwärtigen, angstauslösenden Situation sollen vor allem eine physiologische Angstreaktion sowie Fluchttendenzen aktiviert werden. Im Hinblick auf erwartete, angstauslösende Situationen sollen hauptsächlich maladaptive Kognitionen sowie Vermeidungs- und Sicherheitsverhalten aktiviert werden (Norton & Asmundson, 2003).

Kognitive Bewertung

Im Unterschied zu Angsterkrankungen werden dysfunktionale Kognitionen (z.B. „Falsche Bewegungen sind schädlich für meinen Rücken.“) im Kontext von schmerzbezogenen Ängsten meistens nicht als irrational angesehen (Vlaeyen, de Jong, Leeuw & Crombez, 2007). Bei der Vermeidung angstbesetzter Situationen können maladaptive Bewertungen zukünftig nicht mehr korrigiert werden. So fanden Studien, dass Patientinnen und Patienten mit chronischen Rückenschmerzen die Schädlichkeit bzw. Zunahme an Schmerzen vor der Ausführung bestimmter Bewegungen zunächst überschätzen. Erst nach der Ausführung derselben Bewegungen konnten sie ihre Erwartungen korrigieren (Crombez et al., 2002; Goubert et al., 2002). Die subjektive Angemessenheit irrationaler schmerzbezogener Bewertungen scheint ein relevantes Hindernis für die Korrektur maladaptiver Erwartungen darzustellen. Beispielsweise sind Angstvermeidungsüberzeugungen sogar in der Allgemeinbevölkerung (Houben, Leeuw, Vlaeyen, Goubert, & Picavet, 2005) und unter Behandelnden (Coudeyre et al., 2006; Lakke et al., 2015) zu finden. Möglicherweise muss deshalb bei der Behandlung schmerzbezogener Ängste ein besonderes Augenmerk auf kognitive Prozesse gelegt werden.

Verhaltensreaktion

Im Bereich des Verhaltens wurden verschiedene Vermeidungsreaktionen zudem genauer differenziert (Volders, Boddez, Peuter, Meulders, & Vlaeyen, 2015). Hierzu wurde zwischen Fluchtverhalten (z.B. sofortige Beendigung einer Aktivität beim Auftreten von Schmerzen), Vermeidungsverhalten (z.B. Heben eines Wasserkastens mit gebeugten Knien) und Sicherheitsverhalten (z.B. Ausführen von Aktivitäten unter Schmerzmedikation) unterschieden. Dadurch erscheint die Messung solch komplexer Verhaltensweisen durch ausschließlich Selbstbeurteilungsinstrumente unzureichend. Deswegen wurde zuletzt ein innovatives Messinstrument für Vermeidungsreaktionen von Bewegungen im Rahmen eines Verhaltenstests entwickelt (Holzapfel, Riecke, Rief, Schneider, & Glombiewski, 2016). Gleichzeitig wirkt es sich beim Umgang mit schmerzbezogenen Ängsten ggf. günstig aus, möglichst spezifisch auf einzelne Vermeidungsreaktionen einzugehen.

Physiologische Reaktion

Weiterführend wird eine zusätzliche Verstärkung von Schmerzen über eine physiologische Angstreaktion angenommen. Gleichzeitig sollen negative Erwartungen durch eine fälschliche Interpretation dieser physiologischen Symptome vermeintlich bestätigt werden (Norton & Asmundson, 2003). Bisherige Studien setzten verschiedene neuropsychologische Kennwerte

(z.B. elektrodermale Aktivität, Startle Response) und Messmethoden (z.B. Elektromyographie, funktionelle Bildgebung) ein, um die physiologischen Angstreaktion bei chronischen Schmerzen zu untersuchen. Die Studienergebnisse sind hierbei teilweise widersprüchlich. Einige Studien finden keine Belege für differentielle psychophysiologische Aktivierungsmuster (Barke, Baudewig, Schmidt-Samoa, Dechent, & Kröner-Herwig, 2012; Kronshage, Kroener-Herwig, & Pfingsten, 2001; Vlaeyen, Kole-Snijders, Boeren, & van Eek, 1995). Andere Studien finden widersprüchliche Befunde (Barke et al., 2016; Vlaeyen et al., 1999). Wieder andere Studienergebnisse belegen die Existenz einer differentiellen physiologischen Angstreaktion (Glombiewski et al., 2015; Meier et al., 2016). Insgesamt scheint die physiologische Reaktion bei schmerzbezogenen Ängsten zwar eine Rolle zu spielen. Allerdings ist es bisher noch schwer diese umfassend zu interpretieren. Erschwerend kommt hinzu, dass sich beispielsweise Effekte auf biologische Stressmarker während einzelner Stadien einer Schmerzchronifizierung teilweise unterschiedlich zu entwickeln scheinen (Sudhaus et al., 2009).

Zusammenfassend trägt die Differenzierung einzelner Komponenten zu einem umfassenderen Verständnis des aufrechterhaltenden Mechanismus schmerzbezogener Ängste bei chronischen Schmerzen bei. Dadurch scheint der Einsatz unterschiedlicher Messmethoden notwendig, um alle Facetten schmerzbezogener Ängste abzudecken. Gleichzeitig wirft diese Differenzierung eine Reihe von Fragen im Hinblick auf den Umgang mit schmerzbezogenen Ängsten auf. Durch welche therapeutischen Strategien kann man beispielsweise den ungünstigen Einfluss schmerzbezogener Ängste wirkungsvoll beeinflussen? Auf welche Angstkomponenten sollte hierbei besondere Aufmerksamkeit gelegt werden, um maximale Veränderungen zu erzielen?

2.3 Psychologische Schmerztherapie

Für die Behandlung von chronischen Rückenschmerzen stehen eine Reihe Behandlungskonzepte unterschiedlicher Fachdisziplinen zur Verfügung. Neben einer traditionell medizinischen Behandlung werden psychologische Schmerztherapien ausdrücklich empfohlen (Airaksinen et al., 2006). Beginnend mit dem Ansatz der Modifikation des Schmerzverhaltens nach operanten Lernprinzipien in den 1960er Jahren, wurden mittlerweile eine Reihe psychologischer Behandlungsansätze entwickelt (Morley, 2011). Diese Behandlungsansätze beruhen auf teilweise verschiedenen Annahmen zur Störungsentwicklung und setzen somit an unterschiedlichen auslösenden und aufrechterhaltenen Mechanismen an (Kröner-Herwig, 2014). Im Folgenden werden zwei psychotherapeutische Behandlungsansätze detailliert beschrieben und der jeweilige Stand der Evidenz dargelegt: Die kognitive Verhaltenstherapie, als allgemeines psychologisches Stan-

dardverfahren, und die graduierte Expositionstherapie in vivo, als spezifischer Therapieansatz für hochängstliche Rückenschmerzpatientinnen und Rückenschmerzpatienten.

2.3.1 Kognitive Verhaltenstherapie

Im Rahmen der kognitiven Verhaltenstherapie durchlaufen Patientinnen und Patienten einige störungsspezifische Behandlungsmodule. Diese umfassen typischerweise ein breites Spektrum an therapeutischen Interventionen (Kröner-Herwig, 2014). Dieser Behandlungsansatz wurde nicht für eine spezifische Patientengruppe entwickelt (beispielsweise im Sinne des FA-Modells). Die kognitive Verhaltenstherapie stellt somit einen allgemeinen Therapieansatz dar. Ziel dieses Vorgehens ist eine Verbesserung des Funktionsniveaus, indem den Patientinnen und Patienten eine Reihe von zusätzlichen Schmerzbewältigungsstrategien aufgezeigt werden (Turk, 2003).

Interventionen innerhalb der kognitiven Verhaltenstherapie

Zu Anfang einer Behandlung hat die Vermittlung eines biopsychosozialen Krankheitsmodells der chronischen Rückenleiden einen besonderen Stellenwert. Dadurch soll das oftmals einseitig somatisch ausgerichtete Erklärungsmodell um eine psychosoziale Perspektive erweitert werden (Kröner-Herwig, 2014). Idealerweise dient dieses anfangs erarbeitete Modell als Traggerüst für den weiteren Behandlungsverlauf. Nachfolgende Interventionen können beispielsweise daraus abgeleitet werden. Dieses Vorgehen soll eine aktive Mitarbeit der Patientinnen und Patienten stärken und die Übertragung der gelernten Strategien in den Alltag erleichtern. Darauf folgende Interventionen lassen sich in operante (= welche die Rolle von externalen Verstärkern für das Schmerzerleben und Verhalten aufgreifen), respondente (= welche Muskelanspannungen über Entspannungstechniken oder Biofeedback reduzieren) und kognitive Interventionen (= welche mit dem Schmerz eingehende automatische Gedanken, Überzeugungen und Gefühle bearbeiten) einteilen (Henschke et al., 2011). Zum Beispiel ist es das Ziel des graduierten Aktivitätenaufbaus übermäßiges Schonungs- und Vermeidungsverhalten über operante Verstärkerprozesse abzubauen (Turk, 2003). Entspannungstrainings haben das Ziel tonische Aktivierung zu reduzieren und einen positiven Umgang mit schmerzbezogenem Stress zu fördern (Kröner-Herwig, 2014). Im Rahmen von Aufmerksamkeitstrainings lernen Patientinnen und Patienten sich trotz ihrer Schmerzen auf positives Erleben zu fokussieren (Kröner-Herwig, 2014). Durch kognitive Techniken sollen zudem ungünstige Überzeugungen und Erwartungen infrage gestellt werden (Kröner-Herwig, 2014). Insgesamt existiert im Rahmen der kognitiven Verhaltenstherapie also nicht ein standardisiertes therapeutisches Vorgehen, sondern dieser Ansatz bedient sich einer Reihe verschiedenartiger Interventionen (Sveinsdottir, Eriksen, & Reme, 2012). Dadurch sollen

maladaptive Gedanken, Gefühle und Verhaltensweisen systematisch in einen funktionaleren Umgang mit Schmerzen verwandelt werden (Turk, 2003).

Wirksamkeit der kognitiven Verhaltenstherapie

Mittlerweile existieren eine Reihe von Übersichtsarbeiten und Metaanalysen zur Wirksamkeit der kognitiven Verhaltenstherapie bei chronischen Schmerzen (Eccleston, Williams, & Morley, 2009; Hoffman, Papas, Chatkoff, & Kerns, 2007; Morley, 2011; Morley, Eccleston, & Williams, 1999; Sturgeon, 2014). Eine neuere Metaanalyse der Cochrane Collaboration untersuchte die Wirksamkeit der kognitiven Verhaltenstherapie zur Behandlung chronischer Schmerzen (Williams, Eccleston, & Morley, 2012). Es wurden 35 Studien mit insgesamt 4788 Patientinnen und Patienten berücksichtigt. Kognitive Verhaltenstherapie erwies sich im Vergleich zur medizinischen Standardbehandlung oder Wartekontrollgruppen mit niedrigen bis mittelgroßen Effekten als wirksam in Bezug auf Schmerzintensität, Funktionseinschränkung, Stimmung und Katastrophisieren. Diese Effekte erwiesen sich allerdings nicht als zeitlich stabil. Im Vergleich zu aktiven Kontrollgruppen konnten niedrige Effekte in Bezug auf die Funktionseinschränkung und das Katastrophisieren, nicht allerdings in Bezug auf die Schmerzintensität oder die Stimmung festgestellt werden. Eine weitere Metaanalyse der Cochrane Collaboration untersuchte die Wirksamkeit von kognitiver Verhaltenstherapie ausschließlich für die Behandlung von chronischen Rückenschmerzen (Henschke et al., 2011). Hierbei wurden Therapieelemente in operante, resondente und kognitive Interventionen eingeteilt. Insgesamt wurden 30 Studien mit 3438 Patientinnen und Patienten in die Analyse eingeschlossen. Operante Interventionen zeigten sich im Vergleich zu Wartekontrollgruppen mit niedrigen bis mittelgroßen Effekten als wirksamer in Bezug auf eine Reduktion der Schmerzen. Es konnten keine Unterschiede zwischen operanten, respondenten und kognitiven Interventionen festgestellt werden. Die Kombination einzelner Interventionen war kurzfristig effektiver als eine Standardbehandlung. Diese Effekte waren allerdings ebenfalls zeitlich nicht stabil. In einer weiteren Überblicksstudie wurde die Wirksamkeit von kognitiver Verhaltenstherapie entweder als alleinstehender oder multimodaler Therapieansatz untersucht (Sveinsdottir et al., 2012). Es wurden insgesamt 46 Studien berücksichtigt. Die Autoren schätzten die kognitive Verhaltenstherapie im Vergleich zur Standardbehandlung oder Wartekontrollgruppen als wirksamer in Bezug auf eine Reihe schmerzbezogener Outcomes ein. Beispielsweise konnten positive Effekte in Bezug auf die Schmerzintensität, schmerzbezogene Angst und Sorgen, Vermeidungsverhalten, Katastrophisieren, Depression, Funktionseinschränkungen, Stress, schmerzbezogene Selbstwirksamkeit, Rückkehr zum Arbeitsplatz, usw. festgestellt werden. Diese Überlegenheit war teilweise ebenfalls im Vergleich zu physiologischen, edukativen und chirurgischen Behandlungen nachweisbar. Im Vergleich zu Biofeedback,

operanten Trainingsprogrammen oder Entspannungsverfahren als isolierte Therapiebausteine war eine Überlegenheit allerdings nicht festzustellen.

Zusammenfassend kann die kognitive Verhaltenstherapie zur Behandlung chronischer Schmerzen als wirksam eingeschätzt werden. Allerdings liegen die Effektstärken in einem unbefriedigenden niedrigen bis mittelgroßen Bereich. Zusätzlich erscheinen diese Effekte zeitlich nicht stabil. Dringende Aufgabe zukünftiger Forschung ist es folglich, Ansatzpunkte für Verbesserungsmöglichkeiten zu finden. Hierbei scheint der Wissenszuwachs durch randomisierte Therapiestudien mit gruppenbasierten Mittelwertvergleichen weitestgehend ausgeschöpft (Williams et al., 2012). Vielmehr sollten verschiedenartige Forschungsdesigns genutzt werden, um die Wirksamkeit isolierter Interventionen zu evaluieren (Morley, Williams, & Eccleston, 2013). Die Evaluation spezifischer Therapieansätze (*tailored treatment*) könnte hierbei der Heterogenität unterschiedlicher Patientengruppen gerecht werden (Vlaeyen & Morley, 2005).

Befunde über relevante Therapieprozesse

Die Untersuchung relevanter Therapieprozesse und Mediatoren (= Variable, welche den statistischen Zusammenhang zwischen einer unabhängigen und abhängigen Variable erklärt) ist ein wichtiger weiterführender Schritt in der Psychotherapieforschung (Kazdin, 2009). Dadurch können relevante Therapieprozesse gezielt gefördert und somit Therapieeffekte verbessert werden. Zudem kann dieses Wissen langfristig zu einem umfassenderen Verständnis über die zugrundeliegenden Wirkmechanismen (= Grundlage, weshalb und wodurch eine Veränderung zustande gekommen ist) beitragen. Bisher existieren nur wenige Arbeiten über relevante Therapieprozesse kognitiver Verhaltenstherapie im Bereich chronischer Rückenschmerzen. Bruns und Kollegen untersuchten Therapieprozesse kognitiver Verhaltenstherapie im Rahmen einer 4-wöchigen multidisziplinären Behandlung (Burns, Glenn, Bruehl, Harden, & Lofland, 2003). Prozess- und Outcomemaße wurden zu drei Messzeitpunkten (1x Therapieanfang, 1x Verlaufsmessung, 1x Therapieende) erhoben. Eine Reduktion in schmerzbedingter Hilflosigkeit, Katatrophisieren und schmerzbezogener Angst waren signifikante Prädiktoren für den Therapieerfolg. Spinhoven und Kollegen verglichen Therapieprozesse eines operanten Trainingprogramms mit oder ohne kognitive Elemente im Rahmen einer multidisziplinären Behandlung mit einer Wartekontrollgruppe (Spinhoven et al., 2004). Prozess- und Outcomemaße wurden zu vier Messzeitpunkten (2x Therapieanfang, 2x Therapieende) erhoben. Veränderungen im Katastrophisieren und in schmerzbedingter Selbstwirksamkeit mediierten den Therapieerfolg beider aktiven Therapiebedingungen. Smeets und Kollegen untersuchten Therapieprozesse kognitiver Verhaltenstherapie, eines aktiven Rückentrainings oder deren Kombination im Vergleich zu einer War-

tekontrollgruppe (Smeets, Vlaeyen, Kester, & Knottnerus, 2006). Prozess- und Outcomemaße wurden zu zwei Messzeitpunkten (1x Therapieanfang, 1x Therapieende) erhoben. Interessanterweise mediierten Veränderungen im Katastrophisieren nicht nur den Therapieerfolg der kognitiven Verhaltenstherapie, sondern auch den des reinen aktiven Rückentrainings. Eine neuere Studie von Akerblom und Kollegen untersuchte Therapieprozesse von kognitiver Verhaltenstherapie im Rahmen einer 5-wöchigen multidisziplinären Behandlung (Akerblom, Perrin, Fischer, & McCracken, 2015). Prozess- und Outcomemaße wurden zu drei Messzeitpunkten (1x Therapieanfang, 2x Therapieende) erhoben. Veränderungen in dem affektiven Stresserleben, in dem Kontrollgefühl über das eigene Leben und teilweise in der sozialen Unterstützung mediierten den Therapieerfolg des Behandlungsprogramms. Darüber hinaus gab es erste Hinweise auf den mediierenden Effekt von Veränderungen in der Schmerzakzeptanz auf den Therapieerfolg. Dieses Ergebnis ist deswegen beachtlich, da Schmerzakzeptanz im Rahmen der Therapie nicht intendiert verändert wurde.

Zusammenfassend wurden Therapieprozesse kognitiver Verhaltenstherapie bisher in nur wenigen Arbeiten systematisch untersucht. Bisherige Untersuchungen weisen darauf hin, dass relevante Therapieprozesse teilweise über den intendierten Effekt der jeweiligen Therapieform hinausgehen (Akerblom et al., 2015; Smeets et al., 2006). Obwohl eine mehrfache Erhebung potentieller Therapieprozesse im Therapieverlauf ausdrücklich empfohlen wird (Laurenceau, Hayes, & Feldman, 2007), fehlt es in bisherigen Studien allerdings meist an Verlaufsmessungen. Deswegen wurde die Notwendigkeit für weitere empirische Arbeiten zuletzt immer häufiger betont (Ehde, Dillworth, & Turner, 2014; Kazdin, 2009; Williams et al., 2012). Ein besseres Verständnis über relevante Therapieprozesse bietet die Chance sowohl gemeinsame als auch therapiespezifische Prozesse unterschiedlicher Therapieformen zu identifizieren. Dadurch kann einerseits der Einfluss einer Therapie verbessert und andererseits die Translation von Forschung in die Praxis erleichtert werden (Kazdin, 2009).

2.3.2 Graduierte Expositionstherapie in vivo

Der Behandlungsansatz der graduierten Expositionstherapie in vivo (Vlaeyen, de Jong, Leeuw, & Crombez, 2004; Vlaeyen et al., 2012) beruht auf theoretischen Grundlagen des FA-Modells. Er wurde ausdrücklich für die Behandlung hochängstlicher Rückenschmerzpatientinnen und Rückenschmerzpatienten entwickelt. Expositionstherapie stellt somit einen spezifischen Therapieansatz dar. Analog zur Behandlung bei phobischen Ängsten werden Patientinnen und Patienten im Rahmen von Expositionsübungen mit angstbesetzten Bewegungen konfrontiert. Ziel dieses

Vorgehens ist eine Verbesserung des Funktionsniveaus, indem schmerzbezogene Ängste und damit einhergehendes Vermeidungsverhalten gezielt abgebaut werden.

Ablauf einer graduierten Expositionstherapie in vivo

Zum Therapieanfang steht ebenfalls die Sensibilisierung für ein biopsychologisches Krankheitsverständnis in Anlehnung des FA-Modells im Vordergrund. Idealerweise soll dies in Zusammenarbeit mit ärztlichen Kolleginnen und Kollegen geschehen. Hierfür wird die individuelle Situation der Patientin bzw. des Patienten in einem Teufelskreismodell dargestellt. Bei dieser Besprechung wird vor allem zwischen kurzfristigen (z.B. Reduktion von Angst) und langfristigen Konsequenzen (z.B. Verlust von positiven Aktivitäten, Muskelabbau) von Vermeidungsverhalten unterschieden. Dadurch soll die Motivation für alternative Verhaltensweisen aufgebaut, sowie konkrete Therapieziele aus dem gemeinsam erarbeiteten Modell abgeleitet werden. In Vorbereitung auf die folgenden Expositionsübungen wird für jede Patientin bzw. jeden Patienten eine individualisierte Angsthierarchie erstellt. Hierfür werden spezifische Bewegungen mithilfe der „Photograph Series of Daily Activties“ (Phoda) Skala in Bezug auf ihre Schädlichkeit eingestuft. Auf dieser Angsthierarchie aufbauend werden im weiteren Therapieverlauf Expositionsübungen durchgeführt. Das Behandlungsmanual schlägt hierfür zwei unterschiedliche therapeutische Instruktionen vor. Diese sollen möglichst ergänzend verwendet werden. Bei der ersten Strategie soll der Fokus während Expositionsübungen insbesondere auf aufkommende Angstgefühle gelegt werden. Hierzu wird die emotionale Reaktion kontinuierlich abfragt, bis es zu einem bedeutsamen Abfall dieser Reaktion kommt. Dieses Vorgehen kann auf theoretische Annahmen des Habituationsmodells (Foa & Kozak, 1986) zurückgeführt werden. Bei der zweiten Strategie sollen spezifische Befürchtungen getestet werden, indem diese konkret ausformuliert („Wenn P, dann Q.“) und die Wahrscheinlichkeit für ihr Auftreten im Rahmen von Expositionsübungen getestet werden. Dieses Vorgehen kann auf therapeutische Annahmen des Inhibitionsmodells (Craske, Treanor, Conway, Zbozinek, & Vervliet, 2014) zurückgeführt werden.

Wirksamkeit der graduierten Expositionstherapie in vivo

Die Wirksamkeit der graduierten Expositionstherapie in vivo (EXP) wurde zunächst in Einzelfalldesigns, später in randomisiert kontrollierten Therapiestudien untersucht. Unabhängig von dem verwendeten Forschungsdesign wurde die Expositionstherapie meist mit dem Ansatz des graduierten Aktivitätenaufbaus (GA) verglichen. Dieser Ansatz galt als bisheriges Standardverfahren, um übermäßiges Schonverhalten abzubauen. Im Gegensatz zu EXP erfolgt hierbei die Reduktion von Schonverhalten nicht über Expositionen, sondern über eine Veränderung der

Kontingenz von Schmerzverhalten und der einhergehenden direkten Konsequenzen. In den ersten Einzelfallstudien veränderten sich die Kernkomponenten des FA-Modells vor allem während der Expositionssitzungen (Boersma et al., 2004; de Jong et al., 2005; Vlaeyen, de Jong, Geilen, Heuts, & van Breukelen, 2001; Vlaeyen, de Jong, Onghena, Kerckhoffs-Hanssen, & Kole-Snijders, 2002). Hierzu gehörten Veränderungen in Bezug auf Katastrophisieren, Angst vor Schmerzen, Angstvermeidungsüberzeugungen und funktionelle Einschränkung. Interessanterweise konnte eine Studie kognitive Veränderungen bereits während der anfänglichen psychoedukativen Sitzungen feststellen, welche allerdings erst während der Expositionssitzungen in konkreten Verhaltensänderungen resultierten (de Jong et al., 2005). Während der GA Phase zeigten sich hingegen keine spezifischen Veränderungsmuster. Die Ergebnisse dieser ersten Einzelfallstudien lassen also vermuten, dass eigene Erfahrungen während Expositionsübungen wirkungsvollere Veränderungen anstoßen, als die ledigliche Besprechung und Planung von alternativen Verhaltensweisen.

Im Gegensatz dazu erbrachten darauffolgende randomisiert kontrollierte Therapiestudien weniger eindeutige Ergebnisse. Woods und Asmundson verglichen EXP mit GA und einer Wartekontrollgruppe (Woods & Asmundson, 2008). Im Vergleich zum GA führte EXP zwar zu signifikant besseren Effekten in Bezug auf Bewegungsangst, Angst vor Schmerzen, Angstvermeidungsüberzeugungen und Selbstwirksamkeit. Allerdings zeigten sich nur tendenziell bessere Ergebnisse von EXP in Bezug auf Katastrophisieren und funktionelle Einschränkung. Leeuw und Kollegen verglichen EXP ebenfalls mit GA (Leeuw et al., 2008). Effekte von EXP waren zwar in Bezug auf Katastrophisieren und Schädlichkeitseinschätzungen bestimmter Bewegungen überlegen, allerdings nicht in Bezug auf funktionelle Einschränkung, Hauptbeschwerden, Schmerzintensität und Aktivitätsniveau. Weiterhin wurde der Effekt von EXP auf die funktionelle Einschränkung und Hauptbeschwerden durch eine Reduktion von Katastrophisieren und Schädlichkeitseinschätzungen mediiert. Dieses Ergebnis lieferte somit erste Hinweise auf für den Therapieerfolg relevante Therapieprozesse. Linton und Kollegen verglichen EXP mit einer Standardschmerzbehandlung (Linton et al., 2008). Ergebnisse dieser Studie weisen auf positive Effekte von EXP in Bezug die funktionelle Einschränkung, nicht allerdings in Bezug auf Angst vor Schmerzen und Schmerzintensität hin. Bliokas und Kollegen untersuchten, inwieweit eine Anreicherung eines multidisziplinären Behandlungsprogramms mit Expositionssitzungen zu besseren Therapieeffekten führt (Bliokas, Cartmill, & Nagy, 2007). Es konnten jedoch keine verbesserten Therapieeffekte im Vergleich zu der Standardbehandlung nachgewiesen werden. Allerdings wurden anders als in bisherigen Untersuchungen keine besonderen Einschlusskriterien in Bezug auf die Patientenpassung nach dem FA-Modell getroffen.

Zusammenfassend scheinen Studien mit unterschiedlichen Forschungsdesigns die Wirksamkeit von EXP im Vergleich zu andern Therapieverfahren unterschiedlich zu bewerten. Während Ergebnisse aus Einzelfalldesigns auf eine Überlegenheit von EXP im Vergleich zu GA hinweisen, lassen Ergebnisse aus randomisiert kontrollierten Therapiestudien auf vergleichbare Effekte der beiden Therapieverfahren schließen. Es konnte lediglich eine Überlegenheit von EXP in Bezug auf einzelne Outcomes festgestellt werden. Entsprechend kommen Macedo und Kollegen im Rahmen einer Übersichtsarbeit zu dem Schluss, dass die Wirksamkeit von EXP vergleichbar zu herkömmlichen psychologischen Behandlungsverfahren zu bewerten ist (Macedo, Smeets, Maher, Latimer, & McAuley, 2010). Bailey und Kollegen schlussfolgern im Rahmen einer weiteren Übersichtsarbeit, dass EXP zwar einen vielversprechenden neuen Therapieansatz darstellt (Bailey, Carleton, Vlaeyen, & Asmundson, 2010). Ihrer Meinung bedarf es allerdings weiterer Forschung, um fundierte Aussagen über eine mögliche Überlegenheit dieses spezifischen Verfahrens treffen zu können.

Annahmen über zugrundeliegende Wirkmechanismen

Aktuell konkurrieren verschiedene Theorien über zugrundeliegende Wirkmechanismen von Expositionstherapie. Nach dem Habituationsmodell (Foa & Kozak, 1986; Rauch & Foa, 2006) führt EXP zu einer Entkopplung der ursprünglichen Angstreaktion vom angstauslösenden Stimulus. Erfolgreiches Lernen zeichnet sich hierbei durch ein spezifisches Veränderungsmuster der psychophysiologischen Angstreaktion aus. Zu Beginn einer Expositionssitzung wird zunächst eine Aktivierung der psychophysiologischen Angstreaktion angenommen (Initial Fear Activation, IFA). Diese Aktivierung erlaubt die Einspeisung inkompatibler Informationen und somit die Veränderung des assoziierten Furchtnetzwerkes. Anschließend führen Habituationsprozesse bei andauernder Konfrontation zu einer bedeutsamen Abnahme der psychophysiologischen Angstreaktion (Within-Session-Habituation, WSH). Die spätere langfristige Veränderung des Furchtnetzwerkes führt zu einer Reduktion der ursprünglichen maximalen Angstreaktion in einer erneuten Konfrontationssituation (Between-Session-Habituation).

Nach dem Inhibitionsmodell (Craske, Liao, Brown, & Vervliet, 2012; Craske et al., 2014) hingegen führen Expositionserfahrungen lediglich zu einer neuen US-noCS Assoziation, welche fortan mit der ursprünglichen US-CS Assoziation konkurriert. Unter Rückbezug auf lerntheoretische Grundlagenforschung wird argumentiert, dass sich erfolgreiches Lernen durch eine maximale Erwartungsverletzung auszeichnet. Hierbei wird von einer neuronalen Hemmung des Furchtnetzwerkes durch den präfrontalen Kortex ausgegangen (Milad et al., 2007). Weiterhin wird im Unterschied zu dem Habituationsmodell angenommen, dass eine anhaltende psychophysiologische Aktivierung zu einer Verbesserung von Lerneffekten beitragen kann. Dement-

sprechend erscheint es für den Lernerfolg entscheidend, aufkommende Angstgefühle tolerieren und aushalten zu lernen.

Entsprechend der jeweiligen Theorie über zugrundeliegende Wirkmechanismen lassen sich unterschiedliche therapeutische Instruktionen während der Expositionssitzungen ableiten. Nach Annahmen des Habituationsmodells sollte sich während Expositionssitzungen auf einen Angstabfall fokussiert werden. Nach Annahmen des Inhibitionsmodells hingegen sollten während der Expositionssitzungen konkrete Befürchtungen getestet werden. Wird durch die entsprechende therapeutische Instruktion der tatsächliche Wirkmechanismus der Expositionstherapie direkt angesprochen, so kann von einer Steigerung der Therapieeffekte ausgegangen werden (Kazdin, 2009).

Mittlerweile existieren einige Arbeiten, welche spezifische Vorhersagen beider Modelle im Kontext von agoraphobischen, sozialphobischen und spezifischen Ängsten überprüft haben. Beispielsweise untersuchte eine Studie die Vorhersagekraft der psychophysiologischen Veränderungsmuster auf den Therapieerfolg im Rahmen einer zweistündigen Expositionsbehandlung von Studierenden mit agoraphobischen Ängsten (Baker et al., 2010). Entgegen den Vorhersagen des Habituationsmodells hatte weder die initiale psychophysiologische Aktivierung (IFA), noch die Habituation während einer Expositionssitzung (WSH) einen prädiktiven Einfluss auf den Therapieerfolg. Während die Habituation zwischen den beiden Expositionssitzungen (BSH) zwar den unmittelbaren Therapieeffekt vorhersagte, verschwand dieser Einfluss zum 2-Wochen-Follow-up wieder. Eine andere Studie untersuchte die Vorhersagekraft von anhaltender psychophysiologischer Aktivierung auf den Therapieerfolg im Rahmen einer dreistündigen Expositionsbehandlung von Studierenden mit Angst in der Öffentlichkeit zu sprechen (Culver, Stoyanova, & Craske, 2012). Eine Gruppe der Probanden führte die Expositionssitzungen ohne den Einsatz zusätzlicher exzitatorische Reizen durch. Zwei andere Gruppen erhielten während der Expositionssitzung entweder zeitgleich oder aufeinanderfolgend zusätzliche exzitatorische Reize bestehend aus einem engen Gürtel und einer Videoaufnahme. In Übereinstimmung mit Vorhersagen des Inhibitionsmodells hatte eine anhaltende psychophysiologische Aktivierung sowie eine erhöhte Variabilität des subjektiven Angstniveaus einen signifikanten Einfluss auf den Therapieerfolg. Dieser Einfluss war allerdings unabhängig von der experimentellen Manipulation. In einer weiteren Studie wurden Studierende mit einer spezifischen Spinnenphobie im Rahmen einer zweistündigen Expositionsbehandlung dazu instruiert ihre emotionale Reaktion zusammen mit einer konkreten Befürchtung zu formulieren (z.B. „Ich habe Angst, dass mich diese eklige Vogelspinne anspringen wird.“) (Kircanski, Lieberman, & Craske, 2012). In Übereinstimmung mit Vorhersagen des Inhibitionsmodells führte diese Instruktion zu einer größeren Reduktion der inneren Anspannung, gemessen durch den Hautleitwert eine Woche später, im

Vergleich zu keiner Instruktion oder der Instruktion zur Ablenkung bzw. kognitiven Umbewertung.

Zusammenfassend scheinen bisherige Studien die Annahmen des Inhibitionsmodells eher zu stützen als die Annahmen des Habituationsmodells. Im Kontext von schmerzbezogenen Ängsten fehlt bisher allerdings eine Gegenüberstellung beider Modelle sowie der daraus abgeleiteten therapeutischen Instruktionen. Eine solche Gegenüberstellung könnte Empfehlungen bezüglich optimaler therapeutischer Instruktionen für die klinische Praxis generieren und möglicherweise indirekt Rückschlüsse über zugrundeliegende Wirkmechanismen ziehen lassen.

3. Darstellung des Dissertationsvorhabens

3.1 Relevanz und Herleitung der Fragestellung

Das Fear-Avoidance Modell liefert ein umfassendes theoretisches Modell über die Rolle von schmerzbezogener Angst und damit einhergehendem Vermeidungsverhalten als zentraler Wirkmechanismus bei der Entstehung und Aufrechterhaltung chronischer Rückenschmerzen (Vlaeyen & Linton, 2000; Vlaeyen & Linton, 2012). Mittlerweile existieren mehrere psychotherapeutische Ansätze zur Behandlung dieser spezifischen Patientengruppe. Graduierte Expositionstherapie in vivo setzt direkt an dem beschriebenen aufrechterhaltenden Mechanismus an (Vlaeyen et al., 2012). Diese Therapieform stellt somit einen spezifischen Therapieansatz dar. Im Rahmen von kognitiver Verhaltenstherapie durchlaufen Patientinnen und Patienten hingegen mehrere störungsspezifische Behandlungsmodule zur Verbesserung allgemeiner Bewältigungsstrategien im Umgang mit chronischen Schmerzen (Kröner-Herwig, 2014; Turk, 2003). Diese Therapieform stellt somit einen allgemeinen Therapieansatz dar. Bisherige Studien konnten die Wirksamkeit beider Therapieformen belegen. Zusammenfassende Metaanalysen und Übersichtsarbeiten stufen Therapieeffekte der kognitiven Verhaltenstherapie als niedrig bis mittelgroß ein (Henschke et al., 2011; Williams et al., 2012). Bezüglich der Wirksamkeit von graduierter Expositionstherapie in vivo weisen Ergebnisse aus Einzelfalldesigns auf eine Überlegenheit der Expositionstherapie im Vergleich zu graduiertem Aktivitätenaufbau, als Standardverfahren vieler kognitiv-verhaltenstherapeutischer Manuale, hin (de Jong et al., 2005; Vlaeyen, et al., 2002). Ergebnisse aus randomisiert kontrollierten Therapiestudien lassen hingegen auf vergleichbare Effekte schließen (Leeuw et al., 2008; Linton et al., 2008). Im Rahmen randomisiert kontrollierter Therapiestudien konnte lediglich eine Überlegenheit auf einzelnen Outcomes festgestellt werden. Insgesamt existiert für beide Therapieformen bisher nur ein rudimentäres Wissen über relevante Therapieprozesse sowie zugrundeliegende Wirkmechanismen (Ehde et al., 2014).

Verschiedene Forschungsdesigns nehmen unterschiedliche Perspektiven auf den zu untersuchenden Gegenstand ein.

Gruppendesigns

Die Idee von Gruppendesigns ist es in der Regel den fehlerbereinigten Gesamteffekt eines Therapieansatzes darzustellen (Barlow, Nock, & Hersen, 2009). Hierbei werden Probanden auf die jeweilige Therapiebedingung randomisiert. In der statistischen Auswertung werden anschlie-

ßend Fragebogenwerte der jeweiligen Bedingungen zum Therapieende unter Berücksichtigung der Fragebogenwerte zum Therapieanfang miteinander verglichen. Um den Fehlereinfluss zu minimieren und somit generalisierbare Aussagen treffen zu können, werden Informationen (z.B. Probanden, Therapieverläufe) zusammengefasst. Gleichzeitig macht es dieses Vorgehen später unmöglich den Einfluss einzelner Therapieelemente zu differenzieren.

Einzelfalldesigns

Im Unterschied zu Gruppendesigns wird bei Einzelfalldesigns das Antwortverhalten einer Patientin bzw. eines Patienten während des Therapieverlaufs kontinuierlich erfasst und mit dem individuellen Antwortverhalten vor Beginn der Therapie verglichen (Onghena & Edgington, 2005). Dies ermöglicht den direkten Einfluss einzelner Therapiebausteine auf die Symptomatik zu evaluieren. Später kann das Antwortverhalten mehrerer Patientinnen und Patienten anhand metaanalytischer Verfahren zusammengefasst werden, um übergreifende Änderungsmuster über Probanden hinweg zu erkennen. Dieses Vorgehen lässt in der Regel eine nur eingeschränkte Generalisierbarkeit der Ergebnisse zu, erlaubt es allerdings empiriegeleitete Hypothesen für zukünftige Forschung zu generieren.

Experimentelle Designs

Der experimentelle Ansatz untersucht eine Fragestellung in der Regel unter maximal kontrollierten Bedingungen (Nestoriuc, Berking, & Rief, 2012). Hierfür werden eine oder mehrere unabhängige Variablen (z.B. Therapeutenverhalten) systematisch manipuliert und deren Auswirkung auf die abhängige Variable (z.B. Veränderungen bei Patientinnen und Patienten) erfasst. Gleichzeitig wird der Einfluss von möglichen Störvariablen minimiert und somit Alternativerklärungen für den Zusammenhang zwischen unabhängiger und abhängiger Variablen ausgeschlossen. Dies ermöglicht Aussagen über kausale Zusammenhänge zu treffen. Experimentelle Designs eignen sich also, um Effekte isolierter therapeutische Instruktionen zu evaluieren. Offen bleibt allerdings, inwieweit diese Effekte auf einen natürlichen Therapieverlauf übertragen werden können.

Das übergeordnete Ziel der vorliegenden Dissertation bestand darin, die drei beschriebenen Forschungsansätze zu nutzen, um Therapieprozesse und Wirkmechanismen der Expositionstherapie bzw. der kognitiven Verhaltenstherapie bei der Behandlung von hochängstlichen chronischen Rückenschmerzpatientinnen und Rückenschmerzpatienten zu untersuchen. Als Ergänzung zu bereits bestehender Forschung soll ein besonderes Augenmerk auf Therapieprozesse

und Wirkmechanismen während des Therapieverlaufs liegen. Dieses Vorgehen ermöglicht gleichzeitig die Evaluation einzelner Therapiebausteine und therapeutischer Instruktionen. Dieses Wissen kann langfristig zu einer Maximierung von Psychotherapieeffekten im Bereich chronischer Schmerzen beitragen und somit zu einer Verbesserung der Versorgungssituation führen.

3.2 Fragestellung des Dissertationsvorhabens

Studie I: Welche Therapieprozesse sind während der Expositionstherapie bzw. der kognitiven Verhaltenstherapie bei der Behandlung von hochängstlichen chronischen Rückenschmerzpatientinnen und Rückenschmerzpatienten relevant? Lassen sich therapiespezifische bzw. gemeinsame Therapieprozesse der jeweiligen Therapieform identifizierten? Sagen diese Therapieprozesse den Therapieerfolg vorher?

Studie II: Welchen Einfluss haben einzelne Therapiebausteine der Expositionstherapie bzw. kognitiven Verhaltenstherapie auf Veränderungsprozesse während des jeweiligen Therapieverlaufs? Wie entwickeln sich solche Veränderungsprozesse langfristig? Welche Effekte hat Psychotherapie auf biologische Stressmarker?

Studie III: Lassen sich Therapieeffekte von Expositionstherapie durch therapeutische Instruktionen maximieren? Welche Rückschlüsse lassen psychophysiologische Veränderungen möglicherweise auf theoretisch angenommene Wirkmechanismen zu?

4. Zusammenfassung der Studien

4.1 Zusammenfassung Studie I:

Schemer, L., Schröder, A., Ørnbøl, E., & Glombiewski, J.A. (submitted). Exposure and cognitive-behavioral therapy for chronic lower back pain: treatment processes. Manuscript submitted for publication in *Journal of Consulting and Clinical Psychology*.

Herleitung und Relevanz der Fragestellung: Das Wissen um relevante Therapieprozesse kann die Effektivität von Psychotherapie erhöhen (Kazdin, 2009). Bisher existieren allerdings nur wenige Arbeiten zu Therapieprozessen während der psychologischen Behandlung chronischer Rückenschmerzen. In einer Studie mediierte die Reduktion in Katastrophisieren und in Schädlichkeitseinschätzungen den Therapieerfolg der Expositionstherapie (Leeuw et al., 2008). In weiteren Studien beeinflussten Veränderungen in Katastrophisieren, Selbstwirksamkeit, schmerzbezogener Angst, affektivem Stresserleben, sozialer Unterstützung und Schmerzakzeptanz den Therapieerfolg von kognitiver Verhaltenstherapie (Akerblom et al., 2015; Burns, Glenn, Bruehl, Harden, & Lofland, 2003; Smeets et al., 2006; Spinhoven et al., 2004). Obwohl eine Erhebung potentieller Therapieprozesse zu mehreren Messzeitpunkten ausdrücklich empfohlen wird (Laurenceau et al., 2007), fehlen bisher Studien mit mehrfachen Verlaufsmessungen. Der Bedarf weiterer empirischer Arbeiten zu relevanten Therapieprozessen wurde zuletzt immer häufiger betont (Ehde et al., 2014; Kazdin, 2009; Williams et al., 2012).

Ziel der Studie: Ziel dieser Studie war es daher, therapiespezifische und gemeinsame Therapieprozesse während der Expositionstherapie bzw. der kognitiver Verhaltenstherapie auf Grundlage wöchentlicher Prozessmessungen zu untersuchen und deren Einfluss auf den jeweiligen Therapieerfolg einzuschätzen.

Methode: Therapieprozesse während der Expositionstherapie bzw. der kognitiver Verhaltenstherapie wurden im Rahmen einer randomisiert kontrollierten Therapiestudie untersucht. Es wurden n=61 hochängstliche chronische Rückenschmerzpatientinnen und Rückenschmerzpatienten in der Analyse berücksichtigt. Die Therapiebedingungen wurden randomisiert zugeteilt. Sie erhielten insgesamt entweder 10 bzw. 15 wöchentliche Therapiesitzungen reine Expositionstherapie oder 15 wöchentliche Therapiesitzungen kognitive Verhaltenstherapie. Die Behandlungstreue wurde anhand von Videomaterial von zwei unabhängigen Beobachtern eingeschätzt. Zwischen den einzelnen Therapiesitzungen wurden wöchentliche Prozessmessungen durchgeführt. Diese beinhalteten je einen Fragebogen zu Angstvermeidungsüberzeugungen (= zur Erhebung eines für Expositionstherapie spezifisch angenommenen Therapieprozesses) und einen Fragebogen zur körperlichen Aktivität (= zur Erhebung eines für beide Therapiebedingungen gemeinsam angenommenen Therapieprozesses). Zur weiteren Exploration wurde ein zusätzli-

cher Itempool an Aussagen zu potentiellen therapiespezifischen bzw. gemeinsamen Therapieprozessen generiert. Zusätzlich gab es drei intensive Hauptmessungen (Therapieanfang, Therapieende, 6-Monats-Follow-up). Als primäres Outcomemaß für den Therapieerfolg wurden nach internationalen Empfehlungen zwei Fragebögen zur schmerzbedingten Einschränkung erhoben. Bei der statistischen Auswertung dienten Mehrebenenmodelle zur Identifikation von therapiespezifischen bzw. gemeinsamen Therapieprozessen. Anschließend wurden individuelle Steigungskoeffizienten gebildet, welche den Gesamtverlauf der wöchentlich erhobenen Prozessvariablen repräsentierten. Diese Steigungskoeffizienten wurden als Prädiktoren für den Therapieerfolg überprüft.

Wichtige Ergebnisse: Entgegen der Hypothesen konnten keine therapiespezifischen Therapieprozesse festgestellt werden. Stattdessen weisen die Ergebnisse auf gemeinsame Therapieprozesse von Expositionstherapie und kognitiver Verhaltenstherapie hin. Im Laufe beider Therapieformen nahmen Angstvermeidungsüberzeugungen signifikant ab. Weitere Therapieprozesse beinhalteten signifikante Anstiege in Bezug auf Entspannung, Ablenkung, schmerzbezogener Selbstwirksamkeit, Konfrontation mit angstbesetzten Bewegungen, Aktivitätsniveau und Genussfähigkeit. Allerdings erschienen nicht alle Therapieprozesse für den Therapieerfolg relevant. Einzig Therapieprozesse in Bezug auf Angstvermeidungsüberzeugungen, Entspannung, Ablenkung, Konfrontation mit angstbesetzten Bewegungen, Aktivitätsniveau und schmerzbezogener Selbstwirksamkeit waren signifikante Prädiktoren für eine Reduktion in Bezug auf die schmerzbedingte Einschränkung.

Diskussion: Unsere Ergebnisse weisen auf gemeinsame Therapieprozesse der Expositionstherapie und der kognitiven Verhaltenstherapie hin. Diese Therapieprozesse sollten folglich in der Behandlung hochängstlicher chronischer Rückenschmerzpatientinnen und Rückenschmerzpatienten gezielt gefördert werden. Hierbei stellt eine besondere Herausforderung dar, dass unterschiedliche Behandlungsansätze nicht in einer therapiespezifischen Weise zu wirken scheinen. In der vorliegenden Studie wurden Prozess- und Outcomemaße anhand von theoretischen Überlegungen sowie anhand des Zeitpunktes der Erhebung eingeteilt. Allerdings weisen Verlaufskurven eher auf parallele Veränderungsprozesse in Prozess- und Outcomevariablen hin. Diese Beobachtung spricht gegen üblicherweise definierte Zeitkriterien über angenommene sequentielle Veränderungsverläufe. Gleichzeitig ist eine reziproke Beeinflussung von Therapieprozessen auf den Therapieerfolg denkbar. Zukünftige Forschung sollte den Einfluss einzelner Therapieprozesse auf den Therapieerfolg durch eine isolierte experimentelle Manipulation untersuchen, um unsere Ergebnisse weiterhin zu untermauern.

4.2 Zusammenfassung Studie II:

Schemer, L., Vlaeyen, J.W.S., Dörr, J.M., Nater, U.M., Rief, W., & Glombiewski, J.A. (submitted). Treatment processes during exposure and cognitive-behavioral therapy for chronic back pain: A single-case study. Manuscript submitted for publication in *Pain*.

Herleitung und Relevanz der Fragestellung: Vor dem Hintergrund des FA-Modells stellen schmerzbezogene Ängste und damit einhergehendes Vermeidungsverhalten den zentralen Wirkmechanismus bei der Entstehung und Aufrechterhaltung chronischer Rückenschmerzen dar (Vlaeyen & Linton, 2000; Vlaeyen & Linton, 2012). Hierbei wird angenommen, dass Schmerzen und negative Erwartungen über die physiologische Angstreaktion zusätzlich verstärkt werden (Norton & Asmundson, 2003). Zur Behandlung dieser spezifischen Patientengruppe wurde die Wirksamkeit der Expositionstherapie (Leeuw et al., 2008; Linton et al., 2008; Woods & Asmundson, 2008) und der kognitiver Verhaltenstherapie (Henschke et al., 2011; Williams et al., 2012) in zahlreichen randomisiert kontrollierten Therapiestudien belegt. Bisher ist allerdings relativ wenig über den Einfluss isolierter Therapieelemente oder Therapieeffekte im Hinblick auf die physiologische Angstreaktion bekannt.

Ziel der Studie: Ziel dieser Studie war es daher, den Einfluss einzelner Therapieelemente der Expositionstherapie bzw. der kognitiven Verhaltenstherapie auf therapeutische Veränderungsprozesse in einem Einzelfalldesign zu evaluieren. Zusätzlich sollten erstmalig Therapieeffekte auf biologische Stressmarker exploriert werden, um somit empiriegeleitete Hypothesen für zukünftige Forschung zu generieren.

Methode: Einzelne Therapieelemente beider psychotherapeutischer Verfahren wurden in einem Einzelfalldesign mit multiplen Baselines untersucht. Es wurden n=12 hochängstliche chronische Rückenschmerzpatientinnen und Rückenschmerzpatienten in der Analyse berücksichtigt. Vor der Randomisierung auf die Therapiebedingungen wurden zunächst Patientenpaare gebildet, welche im Hinblick auf Geschlecht, Alter und schmerzbedingte Einschränkung ähnlich waren. Dieses Vorgehen stellte eine gewisse Vergleichbarkeit der beiden Therapiebedingungen sicher. Die Patientinnen und Patienten erhielten insgesamt 10 Therapiesitzungen reine Expositionstherapie oder 10 Therapiesitzungen kognitive Verhaltenstherapie. Die Behandlungstreue wurde anhand von Videomaterial von einem unabhängigen Beobachter eingeschätzt. Der Einsatz von täglichen Prozessmessungen (1-3 Wochen vor der Therapie, während der Therapie, 2 Wochen vor dem 6-Monats-Follow-up) ermöglichte die kontinuierliche Erfassung potentieller Therapieprozesse. Hierzu wurde ein Itempool aus besonders reliablen Fragebogenitems validierter Messinstrumente zusammengestellt. Die Itemformulierungen wurden leicht modifiziert, so dass sie sich auf verhaltensnahe und konkrete Aussagen über den jeweiligen Tag bezogen. Zusätzlich gab es drei intensive Hauptmessungen (Therapieanfang, Therapieende, 6-Monats-

Follow-up). Outcomemaße wurden nach internationalen Empfehlungen ausgewählt. Schmerzbezogene Angst wurde zusätzlich anhand von Selbstbeurteilungsinstrumenten und psychophysiologischen Kennwerten (Kortisol, Alpha-Amylase) im Rahmen eines Verhaltenstests erfasst. Für die statistische Auswertung wurden die beiden Therapiebedingungen in einzelne Therapiephasen eingeteilt (EXP: I. Psychoedukation, II. Exposition, III. Follow-up; KVT: I. Psychoedukation, II. behaviorale Elemente, III. kognitive Elemente; IV. Follow-up). Diese wurden mithilfe von Randomisierungstests mit dem eigenen Antwortverhalten vor Beginn der Therapie verglichen. Der generelle Therapieerfolg wurde anhand von klinischen Signifikanzwerten eingeordnet. Veränderungen bezüglich biologischer Stressmarker wurden visuell inspiziert.

Wichtige Ergebnisse: Im Rahmen der Expositionstherapie traten Veränderungsprozesse vor allem während der individuellen Expositionssitzungen auf. Diese Prozesse beinhalteten signifikante Veränderungen im Hinblick auf Schmerzwahrnehmung, Schädlichkeitseinschätzungen persönlich relevanter Aktivitäten, schmerzbezogene Selbstwirksamkeit, Schmerzakzeptanz und Körpervertrauen. Diese Veränderungsprozesse erschienen jedoch nicht zeitlich stabil. Es konnten allerdings zeitverzögerte Veränderungsprozesse im Hinblick auf die selbstberichtete Konfrontation mit angstbesetzten Bewegungen festgestellt werden. Im Rahmen der kognitiven Verhaltenstherapie gab es keinerlei Hinweise auf spezifische Veränderungsprozesse während der einzelnen Therapiemodule. Es konnten allerdings zeitverzögerte Veränderungsprozesse im Hinblick auf die Einschränkung bei der Ausführung persönlich relevanter Aktivitäten sowie deren Schädlichkeitserwartung gefunden werden. Die Ergebnisse der Hauptuntersuchungen sind vergleichbar mit großangelegten Therapiestudien. Auf den biologischen Stressmarkern konnten zum Therapieanfang keine spezifischen Veränderungsmuster im Rahmen des Verhaltenstests festgestellt werden. Allerdings zeigten sich in der Expositionsgruppe vergleichsweise niedrigere Kortisolwerte während eines Verhaltenstests unmittelbar nach Therapieende.

Diskussion: Während insbesondere die individuellen Expositionserfahrungen im Therapieverlauf eine Reihe von unmittelbaren Veränderungsprozessen bewirken, scheinen Elemente der kognitiven Verhaltenstherapie weniger spezifisch und eher zeitverzögert zu wirken. Deswegen empfehlen wir Expositionen in die Behandlung hochängstlicher Rückenschmerzpatientinnen und Rückenschmerzpatienten zu integrieren. Einzelfalldesigns sollten innerhalb der Psychotherapieforschung zukünftig vermehrt genutzt werden, um den direkten Einfluss besonders wirkungsvoller Therapieelemente abzubilden. Beispielsweise könnten nicht nur Veränderungen in Bezug auf eine Symptomreduktion und einen Kompetenzaufbau, sondern auch Auswirkungen auf den Motivationsaufbau von Interesse sein. Allerdings können hierbei zeitverzögerte Veränderungsprozesse nur eingeschränkt interpretiert werden. Vielmehr erscheint die Erforschung von Therapieeffekten auf biologische Stressmarker ein vielversprechender Untersuchungsgegenstand für zukünftige Forschung zu sein.

4.3 Zusammenfassung Studie III:

Schemer, L., Körfer, K., & Glombiewski, J.A. (submitted). Performing exposures to pain, but how? Testing therapeutic instructions in an experimental design. Manuscript submitted for publication in *The Journal of Pain*.

Herleitung und Relevanz der Fragestellung: Das Therapiemanual von Expositionstherapie zur Behandlung von hochängstlichen Rückenschmerzpatientinnen und Rückenschmerzpatienten schlägt zwei verschiedene therapeutische Instruktionen bei der Durchführung von Expositionsübungen vor (Vlaeyen et al., 2012). Bei der ersten therapeutischen Instruktion soll der Angstverlauf im Laufe der Exposition kontinuierlich erfasst werden, bis es zu einem bedeutsamen Angstabfall kommt. Dieses Vorgehen ist auf theoretische Annahmen des Habituationsmodells zurückzuführen (Foa & Kozak, 1986; Rauch & Foa, 2006). Nach Annahmen dieses Modells zeichnet sich erfolgreiches Lernen durch ein spezifisches Veränderungsmuster der psychophysiologischen Angstreaktion aus. Bei der zweiten therapeutischen Instruktion sollen konkrete Befürchtungen gezielt formuliert und anschließend im Rahmen von Expositionsübungen getestet werden. Dieses Vorgehen ist auf theoretische Annahmen des Inhibitionsmodells zurückzuführen (Craske et al., 2012, 2014). Nach Annahmen dieses Modells zeichnet sich erfolgreiches Lernen durch eine maximale Erwartungsverletzung aus. Weiterhin wird im Unterschied zu dem Habituationsmodell eine anhaltende psychophysiologische Aktivierung als förderlich für Lernprozesse angesehen.

Ziel der Studie: Ziel dieser Studie war es daher, beide therapeutischen Instruktionen während Expositionssitzungen gegenüberzustellen. Gleichzeitig sollten dadurch indirekt Rückschlüsse über zugrundeliegende Wirkmechanismen ermöglicht werden.

Methode: Beide therapeutischen Instruktionen wurden in einem 3x2 experimentellen Design mit dem Zwischengruppenfaktor Instruktion (EG1: Habituation, EG2: Erwartungsverletzung; KG: Zeitungsartikel) und dem Innersubjektfaktor Zeit (Prä-Post) gegenübergestellt. In die Analyse wurden n=112 gesunde Studentinnen einbezogen. Die Probandinnen wurden randomisiert zu einer der drei experimentellen Bedingungen zugeordnet. Als abhängige Variablen wurden sowohl schmerzbezogene Kennwerte (z.B. Schmerztoleranz, kognitive Bewältigung) als auch psychophysiologische Kennwerte (Hautleitwert, Herzrate) erhoben. Eine Woche vor der experimentellen Untersuchung füllten Probandinnen einige Fragebögen zu ihrem üblichen Umgang mit Schmerzen aus. Dadurch konnte die Vergleichbarkeit der Gruppen sichergestellt werden. Um typische schmerzbezogene Befürchtungen bei den Probandinnen zu induzieren, wurden sie zu Beginn des Experiments über vermeintliche Nebenwirkungen der experimentellen Apparatur aufgeklärt. Nach vermeintlicher Messung ihrer Hautdicke wurden sie zudem vom Versuchsleiter fälschlicherweise als Risikogruppe eingestuft. Die Induktion von Hitze während der Expositi-

onsübungen erfolgte durch eine Thermode (Thermal Sensory Analyser; TSA II). Der erste Durchlauf diente der Erhebung eines Baselinewertes. Hierbei wurden Probandinnen instruiert den Hitzereiz so lange wie möglich auszuhalten. Instruktionen der jeweiligen experimentellen Bedingung wurden standardisiert über Lautsprecher dargeboten. Anschließend hatten die Probandinnen die Gelegenheit, die jeweilige therapeutische Strategie in drei Übungsdurchgängen zu üben. Zwischen diesen Durchgängen wurden Ratings zum individuellen Angstlevel bzw. konkreten Befürchtungen abgegeben. Der letzte Durchlauf diente als finale Erhebungsphase. Hierbei wurden die Probandinnen abermals instruiert den Hitzereiz so lange wie möglich auszuhalten. Effekte der therapeutischen Instruktionen auf die schmerzbezogenen bzw. psychophysiologischen Kennwerte wurden mittels multivariaten Kovarianzanalysen ausgewertet. Abschließend wurden psychophysiologische Veränderungen als Mediatoren für den Therapieerfolg getestet.

Wichtige Ergebnisse: Die Ergebnisse bestätigten einen multivariaten Effekt der therapeutischen Instruktionen auf die schmerzbezogenen Kennwerte. Beide therapeutische Instruktionen hatten im Vergleich zu der Kontrollgruppe einen signifikanten Effekt auf die kognitive Bewältigung im Umgang mit dem induzierten Hitzereiz. Nur die Erwartungsverletzungsinstruktion führte zu einem signifikanten Anstieg in der Schmerztoleranz. Weiterhin konnte ein multivariater Effekt der therapeutischen Instruktion auf die psychophysiologischen Kennwerte bestätigt werden. Nur in der Erwartungsverletzungsgruppe zeigte sich ein spezifisches psychophysiologisches Aktivierungsmuster. Dieses Aktivierungsmuster war durch einen anfänglichen Anstieg mit einem anschließenden Abfall des Hautleitwertes während der drei Übungsdurchläufe charakterisiert. Entgegen den Annahmen des Habituationsmodells zeigte sich kein mediierender Effekt der psychophysiologischen Kennwerte auf Veränderungen in kognitiver Bewältigung oder Schmerztoleranz.

Diskussion: Unsere Ergebnisse liefern erste Hinweise auf die Überlegenheit des Testens konkreter Befürchtungen im Vergleich zu dem Fokus auf einen Angstabfall während Expositionsübungen bei schmerzbezogenen Ängsten. Unseres Wissens handelt es sich um die erste Studie, welche unterschiedliche therapeutische Instruktionen während Expositionsübungen bei schmerzbezogenen Ängsten evaluiert. Psychophysiologische Veränderungen lassen sich besser durch Annahmen des Inhibitionsmodells als durch Annahmen des Habituationsmodells erklären. Auch wenn die Untersuchung einer studentischen Stichprobe häufig einen wichtigen ersten Schritt zur Untersuchung neuer Forschungsparadigmen darstellt, sollte zukünftige Forschung versuchen unsere Ergebnisse in einer klinischen Stichprobe zu replizieren. Hierbei erscheint eine Übertragung in die klinische Praxis besonders vielversprechend, da dysfunktionale Kognitionen im Kontext von schmerzbezogenen Ängsten im Unterschied zu Angsterkrankungen häufig einen dominanten Stellenwert einnehmen.

5. Zusammenfassende Diskussion und Ausblick

5.1 Hauptergebnisse der Dissertation

In der vorliegenden Dissertation ist es gelungen unterschiedliche Forschungsdesigns und Methoden zu nutzen, um relevante Therapieprozesse und Wirkmechanismen der Expositionstherapie bzw. der kognitiven Verhaltenstherapie bei der Behandlung von hochängstlichen chronischen Rückenschmerzpatientinnen und Rückenschmerzpatienten zu untersuchen. Hierbei bezog sich der Untersuchungsgegenstand auf Therapieeffekte innerhalb einer spezifischen Patientengruppe, welche vor dem Hintergrund des FA-Modells entweder durch klar formulierte Einschlusskriterien oder durch eine experimentelle Manipulation definiert wurde.

Im Rahmen einer randomisiert kontrollierten Therapiestudie wurden zunächst therapiespezifische und gemeinsame Therapieprozesse beider Therapieansätze auf Grundlage wöchentlicher Prozessmessungen untersucht (Studie I). Entgegen der Hypothesen konnten keine Hinweise auf therapiespezifische Therapieprozesse gefunden werden. Der aktuelle Forschungsstand konnte allerdings um relevante gemeinsame Therapieprozesse erweitert werden. Eine Reduktion von Angstvermeidungsüberzeugungen verbesserte die schmerzbedingte Einschränkung sowohl während der Expositionstherapie als auch während der kognitiven Verhaltenstherapie. Zudem wurden weitere für den Therapieerfolg relevante Therapieprozesse exploriert. Veränderungen in Bezug auf Entspannung, Ablenkung, Konfrontation, Aktivitätsniveau und Selbstwirksamkeit waren ebenfalls signifikante Prädiktoren für den Therapieerfolg beider Behandlungsansätze.

Im Rahmen einer anschließenden Einzelfallstudie sollte der Einfluss einzelner Therapieelemente beider Therapieansätze auf Grundlage täglicher Prozessmessungen evaluiert und Effekte auf biologische Kennwerte exploriert werden (Studie II). Während der Expositionstherapie führten vor allem die individuellen Expositionserfahrungen zu einer Reihe von unmittelbaren Veränderungsprozessen. Beispielsweise veränderte sich die Schmerzwahrnehmung, Schädlichkeitseinschätzung, Selbstwirksamkeit, Schmerzakzeptanz und das Körpervertrauen. Diese Veränderungen erschienen allerdings zeitlich nicht stabil, mit Ausnahme von zeitverzögerten Veränderungsprozessen im Hinblick auf die selbstberichtete Konfrontation. Während der kognitiven Verhaltenstherapie konnten keine besonders wirksamen Therapieelemente identifiziert werden. Vielmehr schien das Gesamtpaket einzelner Interventionen zeitverzögerte Veränderungsprozesse im Hinblick auf die Einschränkung und Schädlichkeitserwartungen zu bewirken. Zum Therapieanfang konnte kein spezifisches Veränderungsmuster auf den biologischen Stressmarkern während eines Verhaltenstests festgestellt werden. Unmittelbar zum Therapieende zeigten sich allerdings in der Expositionsgruppe vergleichsweise niedrigere Kortisolwerte während desselben Verhaltenstests. Dieses Ergebnis könnte auf eine relative Verbesserung bezüglich schmerzbezogener Ängste hinweisen.

Im Rahmen eines Experiments sollten therapeutische Instruktionen gemäß des Habituationsmodells bzw. gemäß des Inhibitionsmodells während der Durchführung von Expositionen gegenübergestellt werden. Zusätzlich sollten dadurch möglicherweise Rückschlüsse über zugrundeliegende Wirkmechanismen ermöglicht werden (Studie III). Beide therapeutische Instruktionen hatten einen Einfluss auf die kognitive Schmerzbewältigung. Allerdings bewirkte nur die Instruktion gemäß des Inhibitionsmodells einen Anstieg in der Schmerztoleranz. Zudem führte nur die Instruktion gemäß des Inhibitionsmodells zu einem spezifischen psychophysiologischen Aktivierungsmuster, welches sich durch einen signifikant erhöhten anfänglichen Anstieg mit einem anschließenden Abfall des Hautleitwertes während der Expositionssitzungen auszeichnete. Dieses psychophysiologische Aktivierungsmuster lässt sich besser durch Annahmen des Inhibitionsmodells als durch Annahmen des Habituationsmodells erklären.

5.2 Methodische Überlegungen und Implikationen für zukünftige Forschung

Im Einklang mit bisherigen Forschungsergebnissen (Akerblom et al., 2015; Arch, Wolitzky-Taylor, Eifert, & Craske, 2012; Leeuw et al., 2008; Linton et al., 2008; Smeets et al., 2006) weisen die Ergebnisse der ersten Studie auf gemeinsame, therapieübergreifende Effekte hin. Hierbei konnte das gruppenbasierte Design der ersten Studie lediglich die Frage beantworten, welche selbstberichteten Therapieprozesse auf Seiten der Patientinnen und Patienten einen Einfluss auf das Therapieergebnis haben. Unsere Ergebnisse tragen somit zu einem besseren Verständnis wirkungsvoller Gemeinsamkeiten zwischen unterschiedlichen Therapieansätzen bei, anstatt deren konzeptuellen Unterschiedlichkeiten zu betonen (Arch, Craske, & Angeles, 2008). Aufgrund dieser teilweise therapieunspezifischen Wirkweise bleibt allerdings offen, durch welche spezifischen Therapieelemente oder durch welches spezifische Therapeutenverhalten diese Therapieprozesse beeinflusst werden können. Aufgabe zukünftiger Forschung bleibt es also zu untersuchen, inwiefern sich der Einfluss einzelner Therapieprozesse gezielt manipulieren lässt (Kazdin, 2009).

Auf den ersten Blick erscheinen die Ergebnisse des Einzelfalldesigns zu den Ergebnissen der ersten Studie teilweise widersprüchlich. In Einklang mit Forschungsergebnissen bisheriger Einzelfallstudien (Boersma et al., 2004; de Jong et al., 2005; Vlaeyen et al., 2001) schienen Expositionserfahrungen spezifische Therapieprozesse zu bewirken. Folglich scheint die Integration dieses spezifischen Therapieelements in den Behandlungsverlauf anderen Interventionen durchaus überlegen. Ein Grund für diese widersprüchlichen Befunde könnte die Wahl des Forschungsdesigns sein. Beispielsweise sind Fragebögen in Gruppendesigns so konzipiert, dass sie die gemeinsame Varianz zwischen Personen ausdrücken (Morley, Linton, & Vlaeyen, 2015). Sie versuchen unterschiedliches Antwortverhalten zwischen Personen zu erfassen, in dem sie einheitliche

Itemformulierungen für eine repräsentative Mehrheit finden. Möglicherweise sind diese Messinstrumente dadurch allerdings nur bedingt sensitiv für spezifische Therapieeffekte. Durch tägliche Messung im Rahmen von Einzelfalldesigns werden im Gegensatz dazu Veränderungsprozesse verhaltensnaher und teilweise individualisierter abgefragt. Weiterhin erscheinen tägliche Messungen weniger anfällig für eine Verfälschung durch Erinnerungseffekte oder sozial erwünschtes Antwortverhalten. Einzelfalldesigns sollten deshalb innerhalb der Psychotherapieforschung zukünftig vermehrt genutzt werden, um der Frage nachzugehen, welche spezifischen Therapieelemente Veränderungsprozesse wirkungsvoll anstoßen können. Nach dem Stufenmodell der Verhaltensänderung während des Psychotherapieverlaufs (Norcross, Krebs, & Prochaska, 2011) könnten nicht nur Veränderungen in Bezug auf eine Symptomreduktion und einen Kompetenzaufbau, sondern auch Auswirkungen auf den Motivationsaufbau für Verhaltensänderungen von Interesse sein. Gleichzeitig zeigen die Ergebnisse der zweiten Studie eine wichtige Einschränkung von Einzelfallanalysen. Da zeitkontingente Veränderungen im Rahmen von Einzelfalldesigns normalerweise kausal interpretiert werden (Morley et al., 2015), lassen sich zeitverzögerte Veränderungsprozesse nur eingeschränkt deuten. Weiterhin zeigen die Ergebnisse der zweiten Studie sehr deutlich, dass viele angestoßene Veränderungsprozesse zeitlich nicht stabil waren. Eine Herausforderung für zukünftige Forschung wird es daher sein, Therapieelemente im Hinblick auf deren Nachhaltigkeit zu untersuchen. Zu diesem Zweck könnten unter anderem innovative Ideen in Bezug auf die Maximierung von Expositionseffekten für allgemeine Angsterkrankungen und Phobien auf schmerzbezogene Ängste übertragen werden (Pittig, Berg, & Vervliet, 2015).

Weiterhin wurde im Rahmen der zweiten Studie der bisher unbeachtete Einfluss von Psychotherapie auf biologische Stressmarker untersucht. Hierbei liefern unsere Ergebnisse erste Hinweise darauf, dass Expositionstherapie alle Facetten der schmerzbezogenen Angst verändert. Zwar stützen sich unsere Ergebnisse aufgrund der kleinen Stichprobe bisher nur auf die visuelle Inspektion der Daten, allerdings konnten darauf aufbauend empiriegeleitete Hypothesen für zukünftige Forschung generiert werden. Im Bereich chronischer Schmerzen scheint die Untersuchung solcher Effekte besonders relevant, da eine zusätzliche Verstärkung von Schmerzen über die einhergehende physiologische Angstreaktion angenommen wird (Norton & Asmundson, 2003).

Im Rahmen der dritten Studie wurde die therapeutische Instruktion systematisch manipuliert, um deren direkten Einfluss auf Therapieprozesse zu erfassen. Dieses Vorgehen erlaubte es einerseits isolierte therapeutische Instruktionen innerhalb des Expositionsmanuals für hochängstliche Rückenschmerzpatientinnen und Rückenschmerzpatienten in einer kleinschrittigen Betrachtungsweise zu evaluieren. Durch den Einbezug psychophysiologischer Maße war es andererseits möglich Annahmen konkurrierender Modelle zu Wirkmechanismen von Expositionsthe-

rapie unter kontrollierten Bedingungen zu prüfen. In Einklang mit früheren Forschungsergebnissen (Baker et al., 2010; Culver et al., 2012; Kircanski et al., 2012) belegen unsere Ergebnisse eher Annahmen des Inhibitionsmodells als Annahmen des Habituationsmodells. Bei der Interpretation unserer Ergebnisse sind allerdings einige Einschränkungen vor allem im Hinblick auf deren ökologische Validität zu beachten. Zum Beispiel ist fraglich, inwieweit sich das Erleben der dargebotenen Hitzereize auf das Erleben chronischer Schmerzen übertragen lässt. Zwar wurden die Probandinnen dazu instruiert, den Schmerzreiz so lange wie möglich auszuhalten. Aus ethischen Gründen hatten sie trotzdem die Möglichkeit den Schmerzreiz jederzeit zu unterbrechen. Weiterhin bleibt offen, inwieweit sich die Motivation während eines Experiments auf die Motivation innerhalb eines Therapieverlaufs übertragen lässt. Üblicherweise werden therapeutische Interventionen aus einem individualisierten Störungsmodell abgeleitet, um die Motivation der Patientinnen und Patienten zu stärken. Da im Rahmen der dritten Studie zudem ein neues Paradigma verwendet wurde, stützte sich die Untersuchung zunächst auf Effekte innerhalb einer studentischen Stichprobe. Aufgabe zukünftiger Forschung wird es folglich sein, unsere Ergebnisse in einer klinischen Stichprobe zu untersuchen. Eine Übertragung in die klinische Praxis erscheint hierbei besonders vielversprechend, da dysfunktionale Kognitionen bei schmerzbezogenen Ängsten im Vergleich zu Angsterkrankungen häufig einen dominanten Stellenwert einnehmen (Vlaeyen et al., 2007). Weiterhin sollte zukünftige Forschung die langfristige Verbesserung von Therapieeffekten durch wirkungsvolle therapeutische Instruktionen untersuchen. Nach Annahmen des Inhibitionsmodells können Instruktionen, welche auf eine maximale Erwartungsverletzung während Expositionssitzungen abzielen, zusätzlich klinische Rückfallphänomene (z.B. Spontaneous Recovery, Context Renewal, Reinstatement) minimieren (Craske et al., 2014). Zukünftige Forschung muss diese Annahmen allerdings noch im Bereich schmerzbezogener Ängste untersuchen.

5.3 Implikationen für die klinische Praxis

Ausgehend von der vorliegenden Arbeit lassen sich mehrere Implikationen für die Behandlung hochängstlicher Rückenschmerzpatientinnen und Rückenschmerzpatienten ableiten. Ergebnisse der ersten Studie sprechen für übergreifende Therapieprozesse. Folglich sollten relevante Therapieprozesse im Behandlungsverlauf gefördert werden, um Therapieeffekte zu verbessern. Ergebnisse der zweiten Studie zeigen, dass im Behandlungsverlauf vor allem individuelle Expositionserfahrungen eine Reihe positiver Veränderungen bewirken können. Folglich sollten Expositionssitzungen in die Behandlung von hochängstlichen Rückenschmerzpatientinnen und Rückenschmerzpatienten integriert werden. Das Testen konkreter Befürchtungen als therapeutische Instruktion während Expositionen erwies sich in der dritten Studie wirkungsvoller als die

Fokussierung auf den Angstabfall. Folglich sollten Expositionsübungen in der klinischen Praxis insbesondere auf eine Veränderung in der kognitiven Bewertung fokussieren, anstelle auf eine Veränderung in der physiologischen Angstreaktion. Beispielsweise könnten Patientinnen und Patienten dazu angeleitet werden, konkrete Befürchtungen zu formulieren (z.B. „Wenn ich einen Wasserkasten hebe, schadet das meinem Rücken."), welche anschließend im Rahmen einer Expositionsübung getestet werden können.

5.4 Fazit

Im Rahmen einer randomisiert kontrollierten Therapiestudie konnten Belege für gemeinsame Therapieprozesse während einer Expositionstherapie und einer kognitiven Verhaltenstherapie bei der Behandlung hochängstlicher Rückenschmerzpatientinnen und Rückenschmerzpatienten gefunden werden. Im Rahmen einer Einzelfallstudie konnte die Durchführung von Exposition als besonders wirkungsvolles Therapieelement identifiziert werden, um zahlreiche Veränderungsprozesse anzustoßen. Interventionen der kognitiven Verhaltenstherapie scheinen hingegen eher unspezifisch und zeitverzögert zu wirken. Weiterhin wurden Ansätze für empiriegeleitete Hypothesen bezüglich Therapieeffekten auf biologische Stressmarker generiert. Im Rahmen einer experimentellen Untersuchung konnten erste Hinweise bezüglich der Maximierung von Expositionseffekten durch eine therapeutische Instruktion zur Überprüfung konkreter Befürchtungen gefunden werden. Hierbei werden psychophysiologische Aktivierungsmuster während Expositionsübungen besser durch Annahmen des Inhibitionsmodells als durch Annahmen des Habituationsmodells erklärt.

Insgesamt zeichnet sich die vorliegende Arbeit besonders durch den Einsatz verschiedener Methoden und Forschungsdesigns aus. Dadurch wurden vielseitige Blickwinkel auf Therapieprozesse und Wirkmechanismen der Expositionstherapie und der kognitiven Verhaltenstherapie bei chronischen Rückenschmerzen ermöglicht. Innerhalb der Psychotherapieforschung sollten zukünftig vermehrt verschiedenartige Forschungsdesigns genutzt werden, um Therapieprozesse und Wirkmechanismen psychologischer Schmerztherapie umfassender verstehen zu können.

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APPENDIX

Appendix A: Studie I

Schemer, L., Schröder, A., Ørnbøl, E., & Glombiewski, J.A. (submitted). Exposure and cognitive-behavioral therapy for chronic lower back pain: treatment processes. Manuscript submitted for publication in *Journal of Consulting and Clinical Psychology*.

Appendix B: Studie II

Schemer, L., Vlaeyen, J.W.S., Dörr, J.M., Nater, U.M., Rief, W., & Glombiewski, J.A. (submitted). Treatment processes during exposure and cognitive-behavioral therapy for chronic back pain: A single-case study. Manuscript submitted for publication in *Pain*.

Appendix C: Studie III

Schemer, L., Körfer, K., & Glombiewski, J.A. (submitted). Performing exposures to pain, but how? Testing therapeutic instructions in an experimental design. Manuscript submitted for publication in *The Journal of Pain*.

Appendix D: Tabellarischer Lebenslauf

Appendix E: Eidesstattliche Erklärung

Appendix A: Studie I

Schemer, L., Schröder, A., Ørnbøl, E., & Glombiewski, J.A. (submitted). Exposure and cognitive-behavioral therapy for chronic lower back pain: treatment processes. Manuscript submitted for publication in *Journal of Consulting and Clinical Psychology*.

Abstract

To improve treatment outcomes it is essential to understand the processes involved in therapeutic change. The aim of this study was to investigate the processes involved in treatment of individuals with chronic lower back pain (CLBP) and high fear-avoidance. Graded in vivo exposure (Exposure), a specific treatment, and cognitive-behavioral therapy (CBT), a general treatment, were compared. The study uses data from a three-arm randomized controlled trial. The sample comprised 61 CLBP patients (pain duration >3 months; sufficient level of fear-avoidance). Weekly measurements of session-by-session processes were taken for a maximum of 14 weeks. The primary outcome, functional disability, was assessed at pre-treatment, post-treatment and six-month follow-up. First, two-level models were used to test for treatment-related similarities and differences in the changes in session-by-session measures (i.e. common and unique treatment processes respectively). Contrary to our expectations we found no evidence of unique treatment processes. The results indicate that Exposure and CBT share some common treatment processes. Specifically, patients reported a reduction in fear-avoidance beliefs and improvements in their ability to relax, to distract themselves, to manage their pain, to confront feared movements, to be active and to enjoy things despite their pain. Second, we analyzed treatment processes as predictors of treatment outcome. Changes in fear-avoidance beliefs, relaxation, distraction, confrontation, activity and pain-related self-efficacy were related to disability reduction. These treatment processes appear to be relevant to treatment success, but it remains unclear whether they need to be targeted directly or can be supported indirectly.

Introduction

Chronic lower back pain (CLBP) is a major health problem throughout the world (Hoy et al., 2012). Cognitive-behavioral therapy (CBT) is one of the recommended psychological treatments for CLBP (Henschke et al., 2010). The goal of CBT is to provide patients with strategies for coping with pain in order to help them manage their pain and to reduce functional disability (Turk, Swanson, & Tunks, 2008). CBT manuals usually recommend combining various cognitive (e.g.

attention shifting), respondent (e.g. relaxation) and behavioral (e.g. activity pacing) interventions to ensure that the treatment is suitable for a large number of patients (Henschke et al., 2010). However, empirical evidence indicates CBT has only small to moderate effects on pain and pain-related outcomes (Henschke et al., 2010; Williams, Eccleston, & Morley, 2012). The potential benefits of tailored treatments for specific subgroups have been discussed (Bailey, Carleton, Vlaeyen, & Asmundson, 2010; Vlaeyen & Morley, 2005).

The fear-avoidance model is a comprehensive theoretical model of the influence of fear and avoidance on the development and maintenance of chronic pain (Vlaeyen & Linton, 2000, 2012). This model was the basis of Graded In Vivo Exposure, a treatment that focuses on changing fear-avoidance in people with chronic pain (Vlaeyen, Morley, Linton, Boersma, & de Jong, 2012). Similar to the treatment of phobia and anxiety, patients are confronted with fear stimuli. In the context of chronic pain, feared stimuli are movements related to pain or potential injuries of the back. The efficacy of Exposure has been investigated, initially in single-case studies and later in randomized controlled trials (RCTs). Usually Exposure was compared to graded activity, which is a standard procedure for reducing avoidance behaviors in many CBT protocols. Although the results of the single-case studies (Boersma et al., 2004; de Jong et al., 2005; Vlaeyen, de Jong, Geilen, Heuts, & van Breukelen, 2001; Vlaeyen, de Jong, Geilen, Heuts, & van Breukelen, 2002) were promising, the RCTs (Leeuw et al., 2008; Linton et al., 2008; Woods & Asmundson, 2008) produced somewhat mixed results, indicating that Exposure was only superior with respect to problem-specific outcomes such as perception of the harmfulness of activities (Leeuw et al., 2008) and fear-avoidance beliefs (Woods & Asmundson, 2008).

One way of maximizing treatment impact is to identify the critical treatment processes. Understanding treatment processes is important as a means of a) identifying processes that are common to several types of treatment, b) developing more systematic strategies for triggering critical processes, c) facilitating the translation of critical processes from research to practice and d) increasing knowledge of what constitutes optimal conditions for treatment processes (Kazdin, 2009). Few studies have investigated treatment processes in the context of CLBP. One study found that the impact of Exposure on functional disability and pain-related main complaints was influenced by the extent to which treatment decreased the frequency of catastrophization thoughts and the perceived harmfulness of activities (Leeuw et al., 2008). In the case of CBT there is evidence that treatment outcome is influenced by the extent to which CBT produces changes in pain catastrophizing, self-efficacy, pain related-anxiety, life control, affective distress, social support and even pain acceptance (Akerblom, Perrin, Fischer, & McCracken, 2015; Burns, Glenn, Bruehl, Harden, & Lofland, 2003; Smeets, Vlaeyen, Kester, & Knottnerus, 2006; Spinhoven et al., 2004). It has been suggested, however, that further research into the processes under-

lying positive treatment outcomes is needed (Ehde, Dillworth, & Turner, 2014; Kazdin, 2009).

The aim of this study was to investigate the processes occurring during the treatment of individuals with CLBP and high fear-avoidance. This was done using session-by-session data from a RCT comparing Exposure and CBT. Thus we compared the change processes involved in general (CBT) and specific (Exposure) treatments. We formulated the following hypotheses: a) Changes in fear-avoidance beliefs are specific to the processes involved in Exposure. b) Changes in physical activity are common to the processes involved in Exposure and CBT. We also planned to explore other processes occurring during both treatments in order to provide new insight into processes relevant to management of chronic pain.

Method

Study Design

This study uses data from a three-arm RCT (Clinical Trials NCT01484418). The aim of this RCT was to compare the results of using long and a short Exposure treatments (Exposure-long = 15 sessions, Exposure-short = 10 sessions) or CBT (15 sessions) to treat CLBP. Detailed descriptions of the treatment methods can be found in the study protocol (Riecke, Holzapfel, Rief, & Glombiewski, 2013). In this study we were not interested in dose effects so the Exposure-long and Exposure-short groups were combined and we assumed that they would involve identical processes. Several outcomes were assessed at pre-treatment (Pre), mid-treatment (Mid), post-treatment (Post), and six-month follow-up (6MFU) and we also carried out a maximum of 14 weekly assessments during treatment. The study was conducted in a university-based clinic in Marburg (Psychotherapieambulanz der Philipps Universität Marburg, PAM), Germany.

Participants

Patients were recruited via advertisements in local newspapers, doctors' surgeries and from the waiting list of an outpatient clinic. The inclusion criteria were CLBP (for > three months), high fear-avoidance and above-threshold disability. Fear avoidance was assessed using the Tampa Scale of Kinesiophobia (TSK; Rusu, Kreddig, Hallner, Hülsebusch, & Hasenbring, 2014) and Phoda Series of Daily Activities (Phoda; Leeuw, Goossens, van Breukelen, Boersma, & Vlaeyen, 2007) and the criterion for inclusion was TSK > 35 or harm ratings on > 13/50 Phoda activities, including 8 > 80). Disability was assessed using the Quebec Back Pain Disability Scale, QBPDS; Kopec et al., 1995; Riecke, Holzapfel, Rief, Lachnit, & Glombiewski, 2016) and the inclusion cri-

terion was QBPDS > 15. The exclusion criteria were back surgeries during the last six months or planned surgeries, "red flags" (e.g. fever, incontinence) (Royal College of General Practitioners, 1999), inability to read or write German, pregnancy, alcohol addiction, psychotic disorders and ongoing psychological treatment. Physical and psychological comorbidities (e.g. diabetes or depression) were not causes for exclusion as long as the patient was able to attend weekly therapy sessions.

After a careful screening 104 participants were declared eligible to participate. Several patients were excluded or dropped out over the course of treatment for a variety of reasons: logistical and other problems (n = 10), not meeting the criteria (n = 10), avoidance of exposures (n = 6), prevailing psychological comorbidity (n = 6) and having the subjective impression that they were not benefitting from the treatment (n = 5). As we were interested in comparing the relationship between process and outcome measures for the two Exposure conditions and the CBT condition we conducted a per-protocol analysis and only included participants who completed the entire course of treatment (n = 67); we also excluded patients with large amounts of missing process data (> 50%) (n = 6) from the analysis. Thus the final sample consisted of 61 patients (Exposure n = 37; CBT n = 24). A summary of the baseline characteristics of the sample is presented in Table 1.

[Insert Table 1 around here]

Randomization and Ethical Concerns

A blinded research assistant randomized participants to the three treatment conditions. The randomization procedure was based on a predetermined, computer-generated randomization schedule and participants were, pre-stratified according to their degree of pain catastrophizing (Pain Catastrophizing Scale, PCS; Meyer, Sprott, & Frances, 2008; Sullivan, Bishop, & Pivik, 1995) and disability (Pain Disability Index, PDI; Dillmann, Nilges, Saile, & Gerbershagen, 1994; Tait, Chibnall, & Krause, 1990). We used a randomized block design with a block size of nine to ensure that core patient characteristics were evenly distributed across strata. Neither patients nor therapists were blinded to the treatment condition as this is not feasible in psychotherapy research and for ethical concerns.

The ethics committee of the German Association of Psychology (DGPS) approved the study (WR 052010_1). Before the study started all patients received detailed information about the interventions and assessments. Participants were ensured that they could withdraw at any time without consequence. All participants gave written, informed consent to enrolment.

Intervention and Therapists

The main goal of both interventions was to reduce functional disability. The interventions were based on detailed treatment manuals. Patients received weekly 50-minute individual sessions. They were given a personalized workbook containing their therapy material together with some background information. At the start of treatment all patients were given a biopsychosocial account of their chronic pain. Patients were encouraged to formulate feasible goals for re-engaging in activities they used to do.

The treatments were delivered by two advanced clinical psychology doctoral students. Since Exposure is a relatively new treatment for CLBP the authors of the original Exposure therapy manual delivered two training workshops to the therapists carrying out the treatment and their supervisors and also provided supervision. In addition, experienced psychologists supervised all courses of treatment. Treatment fidelity was evaluated by two independent postgraduate students who viewed video-recorded sessions. It was marginally below the 70% criterion for good protocol adherence (CBT: 69.7%; Exposure: 66.5%).

Graded In Vivo Exposure

Graded in vivo Exposure is intended to reduce functional disability by acting on the processes maintaining the influence of fear-avoidance. Patients were given a comprehensive rationale for the therapy, applying the fear-avoidance model to their situation. A personalized circular model was used to illustrate the role of pain, pain cognitions and avoidance behavior. Subsequently, a personal fear hierarchy was developed for each patient using Phoda (Leeuw et al., 2007). Patients were asked to rate how harmful they thought various daily activities (shown in photographs) would be to their back. Patients were encouraged to confront these feared activities gradually, in therapist-guided exposure sessions. The purpose of doing this was to reduce patients' fear of movements they associated with pain or potential spinal injury and to challenge their pain-related catastrophic beliefs. Two forms of Exposure were offered, Exposure-long (15 sessions; 10 exposures) and Exposure-short (10 sessions; 5 exposures).

Cognitive-Behavioral Therapy

The main goal of CBT was to reduce pain-related disability by helping patients developing an adaptive approach to coping with chronic pain. Patients were introduced to various strategies for coping with pain. For example, patients were encouraged to approach re-engagement in

activities by dividing an activity they used to do into smaller steps so as to avoid placing excessive demand on their body, followed by a lengthy recovery period. They were taught to use progressive muscle relaxation as a way of coping with pain. Patients were also taught attention shifting to change their perception of pain. The links of pain-related cognitions, feelings and behavior was illustrated. Any maladaptive cognitions were challenged in order to interrupt pain-maintaining circuits. In two individualized sessions patients were given the opportunity to discuss personally relevant topics, such as work-related problems, with the emphasis on a practical, problem-solving approach. The CBT treatment consisted of 15 individual sessions.

[Insert Figure 1 around here]

Outcome Measures

Primary Outcome Measures

Outcome measures were chosen following the IMMPACT (= Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials) recommendations (Dworkin et al., 2005). Several primary outcomes were measured at the four main assessments. Primary outcomes were also assessed alongside the weekly process measures in order to monitor the course of changes more closely. Pain-related disability was measured using two questionnaires.

The PDI (Dillmann et al., 1994; Tait et al., 1990) provides a global measure of disability. It consists of 7 items describing essential life activities (e.g. family life, work, and leisure time) and respondents use an 11-point scale to indicate the extent to which their pain impairs their participation in each. Higher scores indicate greater disability (0 = no impairment, 70 = complete impairment).

The QBPDS (Kopec et al., 1995; Riecke et al., 2016) consists of 20 items describing daily activities (e.g. driving a car, climbing stairs, and putting on socks) and respondents used a five-point scale to indicate how difficult each activity is for them. Higher scores indicate greater disability (0 = no disability, 100 = highest disability). The QBPDS provides a more behavior-specific measure of disability than the PDI.

Patients also assessed the intensity of their pain using an 11-point numeric rating scale (NRS-P) (0 = no pain, 10 = pain at its worst) and pain quality was measured on an 11-point scale taken from the German Pain Questionnaire (Deutscher Schmerzfragebogen, DSF; Nagel, Gerbershagen, Lindena, & Pfingsten, 2002) (0 = unbearable, 10 = bearable).

We also assessed several secondary outcomes emotional distress, fear-avoidance, pain catastrophizing and medical costs but these are outside the scope of this study, which concentrates specifically on changes in process measures.

Weekly Process Measures

Between therapy sessions patients filled out two additional questionnaires measuring fear-avoidance and physical activity. The TSK (Rusu et al., 2014) measures fear-avoidance beliefs and concerns about re-injury using 17 items to which responses are given using a four-point scale. Higher scores indicate greater kinesiophobia (17 = no fear; 68 = high fear).

The International Physical Activity Questionnaire (IPAQ; Craig et al., 2003) was used to assess five domains of physical activity work-related physical activity, transport-related physical activity, domestic and gardening (yard) activities, leisure-time physical activity and sitting-related inactivity over the previous week. We decided to consider only changes in leisure-time physical activity as a substantial proportion of patients were not involved in any kind of work during treatment (see Table 1) and both psychological treatments were intended to change patients' behavior during their free time. We calculated a continuous Metabolic Equivalent Task (MET) score for every participant by weighting each type of activity according to its energy requirements as specified in the IPAQ scoring protocol (www.ipaq.ki.se). MET scores can be classified as follows, MET < 600: low level of physical activity; 600 < MET < 3000: moderate level of physical activity; MET > 3000: high level of physical activity.

To allow us to explore other potential treatment processes patients were also asked to keep a weekly diary in which they indicated the extent to which they agreed with eleven statements using an 11-point scale (0 = totally agree, 10 = totally disagree). The statements were based on elements from the manuals for the two therapies. For example, the item "I dared to execute movements although I was afraid they would harm my back" was intended to capture one of the processes underlying Exposure whereas the item "I managed to distract myself when I was in pain" was intended to capture one of the processes underlying CBT. Some items, such as "Overall, I managed to handle my pain", were included to capture unspecific changes that we thought might be common to both treatments. Table 3 provides an overview of the weekly diary.

[Insert Table 2 around here]

Statistical Analysis

The statistical analyses were conducted with the Stata 12 package. First, we used multiple imputation techniques to deal with missing data. Second, we used two-level models to identify common and unique treatment processes. Third, we calculated individual slopes representing the linear development of treatment processes. Fourth, we tested these individual slopes as predictors of treatment outcome.

Treatment of Missing Data

To reduce the number of missing values in the session-by-session data (29.5%) we summarized data from therapy sessions with similar content (e.g. progressive muscle relaxation I + II) as mean values (see Table 2.). In clinical trials it is generally recommended that sophisticated approaches are used to deal with missing data (Kistin, 2014) so we used multiple imputation to replace the remaining missing data (17.6%) after collapsing sessions. This method produces multiple estimates of missing data using data augmentation, a method based on multivariate normal regression techniques. We specified 50 iterations (Graham, Olchowski, & Gilreath, 2007). Process variables were imputed separately for each group. The predictors of missing values were age, gender, the same process variable at other points in time and pre-treatment values of several primary outcomes (pain intensity; pain quality; PDI score; QBPDS score; TSK score; IPAQ score). Missing values were not imputed per design (Exposure-short condition).

Detection of Common and Unique Treatment Processes

Potential treatment processes were tested with the help of two-level models (random level = individual; fixed level = time, group). This statistical method is especially recommended for repeated measurement designs as a way of accounting for the repeated interrogation of the same individuals. To detect common treatment processes (processes that followed a similar course in both treatments) we used a two-level model with two categorical explanatory variables, “Session” and “Group”. To detect unique processes (processes that followed a different course in the two treatments conditions) we used a second two-level model with three explanatory variables: “Session” was entered as categorical variable as development over time was not expected to be linear, “Group” was added as a categorical variable and “Session x Group” was entered as an interactive predictor. The level of statistical significance was set at $p < .001$ (Bonferroni adjustment for multiple tests).

Estimates for Linear Development of Treatment Processes

We carried out further analysis of processes for which "Session" or "Session x Group" were significant predictors in the first and second two-way models respectively. To summarize the session-by-session data points as a single statistical value we calculated a third two-level model including only the predictor "Session". This time "Session" was treated as a continuous variable. Thus the second model postulated linear development over time. This procedure allowed us to obtain estimates of the process measures for each individual. Random effects (i.e. unstructured variance/covariance structure) of changes in the process measures were extracted for each participant and then added to the fixed effect. These slopes represent the direction and steepness of changes in the process measures for each study participant. Other studies (Arch, Wolitzky-Taylor, Eifert, & Craske, 2012; Niles et al., 2014) have used this statistical approach to deal with multivariate longitudinal data.

Treatment Processes as Predictors of Outcome

Individual slopes were also tested as predictors in a regression model including the predictor "Process measure" (i.e. individual slope of change in treatment process) and the covariates "Treatment group" and "Outcome-Pre". The regression model is displayed in Fig. 2.

[Insert Figure 2 around here]

Results

Common Treatment Processes

The first two-way model provided evidence of temporal changes in the outcome measures QBPDS and PDI and the process measures TSK, relaxation, distraction, self-efficacy, activity, confrontation, and enjoyment ("Session": $p < .001$). These variables were examined in more detail in subsequent statistical analyses. There was no evidence of temporal changes in the outcome measures pain intensity (last week), pain intensity (now), pain quality or in the process measures IPAQ, positive thoughts, acceptance, avoidance, daily life and coping ("Session": $p > .001$). These variables were not examined further.

Unique Treatment Processes

The second two-way model provided no statistical evidence of treatment-specific temporal changes in any of the process measures ("Session x Group": p > .001). The time course of all variables is displayed in Figures 3 and 4.

[Insert Figure 3 & 4 around here]

Treatment Processes as Predictors of Outcome

Process measures that changed over time were subsequently summarized into a single slope for each participant. The average values of these slopes for the two therapy conditions are displayed in Table 3.

[Insert Table 3 around here]

Individual slopes were then tested as predictors of treatment outcome in a regression model. A decrease in TSK reduced global disability (Post: b = -.36 [-.16; -.56]; 6MFU: b = -.41 [-.18; -.64]) and specific disability (Post: b = -.26 [-.06; -.46]; 6MFU: b = -.31 [-.10; -.51]). An increase in relaxation reduced global disability (Post: b = -.60 [-.78; -.42]; 6MFU: b = -.44 [-.67; -.20]) and specific disability (Post: b = -.52 [-.71; -.32]; 6MFU: b = -.39 [-.61; -.18]). An increase in distraction reduced global disability (Post: b = -3.30 [-4.62; -1.98]; 6MFU: b = -2.49 [-4.10; -.89]) and specific disability (Post: b = -2.87 [-4.26; -1.47]; 6MFU: b = -1.84 [-3.38; -.30]). An increase in confrontation reduced global disability (Post: b =-.53 [-.74; -.33]; 6MFU: b = -.47 [-.73; -.22]) and specific disability (Post: b = -.40 [-.61; -.18]; 6MFU: b = -.37 [-.60; -.13]). An increase in self-efficacy reduced global and specific disability at the post-treatment assessment, but not the follow-up assessment (Post: b = -2.41 [-3.58; -1.24] and Post: b = -1.88 [-3.07; -.69] respectively). Similarly, an increase in activity only reduced global and specific disability at post-treatment (Post: b = -.33 [-.55; -.11] and Post: b = -.24 [-.47; -.02] respectively). Changes in enjoyment had no effect on either measure of disability at post-treatment or follow-up.

[Insert Table 4 around here]

Discussion

Summary of Main Findings

This study investigated the processes occurring during Exposure and CBT that produced changes in outcomes in individuals treated for CLBP and high levels of fear-avoidance. Our results indicate that Exposure and CBT share common treatment processes. Over the course of both treatments patients reported reductions in fear-avoidance beliefs and increases in their ability to relax, to distract themselves, to influence their pain, to confront feared movements, to be active and to enjoy things despite their pain. Contrary to our hypotheses, we found no evidence that either treatment produced changes in physical activity as measured by the IPAQ. The processes predicted a reduction in disability were changes in fear-avoidance beliefs, relaxation, distraction, confrontation, activity and pain-related self-efficacy.

Changes in Fear-Avoidance Beliefs

In line with previous research our results underline that cognitive changes influence treatment outcome. A study of a four-week multidisciplinary treatment for various forms of musculoskeletal chronic pain that included CBT found that reductions in pain catastrophizing (i.e. PCS score; Sullivan et al., 1995; sample item: "I keep thinking about how badly I want the pain to stop") at an early stage in treatment were associated with late-treatment reductions in pain interference and pain severity (Burns et al., 2003). Similarly, there is evidence that reduction in pain catastrophizing (as measured using the Pain Cognition List, PCL; van Breukelen & Vlaeyen, 2005; sample item: "My thoughts are always concentrated on the pain") mediates the effect of CBT interventions on positive treatment outcomes for CLBP patients (Smeets et al., 2006; Spinhoven et al., 2004). Interestingly, this mediation effect was also found in one comparison group that only received active physical treatment (Smeets et al., 2006). In fear-avoidant CLBP patients reductions in pain catastrophizing (as measured by PCS score) and the perceived harmfulness of daily activities (as measured with Phoda; Leeuw et al., 2007) were shown to mediate the effect of Exposure on disability and main complaints (Leeuw et al., 2008). Together these results suggest that cognitive changes seem to underlie the effectiveness of various psychological and physical treatments.

Our results also highlight the importance of changes in fear-avoidance beliefs (as measured by the TSK; Rusu et al., 2014; sample item: ''I am afraid that I might injure myself if I exercise"). Although only the Exposure therapy explicitly targeted fear-avoidance beliefs both groups showed changes in these beliefs during the course of treatment. This finding contradicts our

previous assumption of specific treatment processes. However, the CBT treatment did involve two sessions devoted to patients' personal dysfunctional cognitions and since we limited our sample to individuals with strong fear-avoidance beliefs it seems likely that their dysfunctional cognitions were related to common fear-avoidance beliefs or could be generalized in this way. It is also possible that the weekly interrogation of participants influenced their fear-avoidance beliefs. An early meta-analysis of psychotherapy outcome research (Smith & Glass, 1977) concluded that the studies that used the most transparent indicators demonstrated the greatest therapeutic gain. This finding might reflect a general effect of reactivity to questionnaires, which could have influenced our results.

However other research comparing other competing therapeutic approaches has produced somewhat mixed results with regard to therapy-specific treatment processes. For example, a study of a mixed sample of anxiety disorder patients found that changes in anxiety-related beliefs – which were specifically targeted in the CBT condition were related to the effects of both CBT and an Acceptance and Commitment Therapy (ACT) condition including exposure (Arch et al., 2012). Conversely changes in cognitive defusion specifically targeted in the ACT treatment were related to both CBT and ACT. According to Arch and Craske (2008) comparison of competing psychological therapies risks overemphasizing the differences between them. The main objective of empirical research should, instead, be to identify the elements of treatment that are most efficient and effective at producing long-lasting improvements. Our results indicate that changing patients' fear-avoidance beliefs has a positive influence on treatment outcome, but not whether such beliefs need to be explicitly targeted if change is to occur.

Changes in Physical Activity

Contrary to our hypotheses patients' physical activity levels as measured by the IPAQ did not increase. This self-report instrument requires respondents to indicate minutes of leisure activities (e.g. "time spent with moderate physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis"). Some participants reported that they had difficulty providing the required information for various reasons, for example because they had trouble remembering exact minutes or because they felt unable to distinguish between vigorous or moderate activity and some listed the same activity in several categories. In contrast to our findings, a case study of six individuals with CLBP found that Exposure did produce meaningful changes in physical activity, which was assessed using ambulant activity monitors (de Jong et al., 2005). It is possible, therefore that the IPAQ did not capture behavioral changes effectively. This notion is corroborated by the fact that we found changes in a single-item measure of activi-

ty ("I was active despite the pain") over the course of therapy. Future studies should use behavioral measures to index potential changes in physical activity. It is particularly important to do this given the physical benefits of behavioral change in CLBP patients.

Exploration of Further Treatment Processes

Our results also provide further information about processes that are common to Exposure and CBT. In both treatments increases in relaxation, distraction, confrontation, activity and pain-related self-efficacy were associated with reduced disability. These results corroborate other studies of the processes involved in multidisciplinary, CBT-based pain programs which found that perceived personal pain control (Spinhoven et al., 2004) and reductions in pain helplessness (Burns et al., 2003) were related to positive treatment outcome. Interestingly, changes in self-efficacy have also been shown to mediate the improvements in pain-related disability that are produced by stretching and yoga classes (Sherman, Wellman, Cook, Cherkin, & Ceballos, 2013). Our results add to previous research by showing that changes in self-efficacy appear equally important to Exposure therapy.

Moreover, increased ability to relax was associated with a better therapy outcome. A longitudinal analysis of the mechanisms underlying the development of pain-related disability found that psychological distress accounted for approximately 30% of the variance in the relationship between initial pain and later disability in patients with sub-acute lower back pain (Hall et al., 2011). Conversely it appears likely that increasing patients' ability to relax reduces their functional disability. In our study the CBT group was actively trained in progressive muscle relaxation whereas the Exposure group did not learn a specific relaxation technique.

The ability to distract oneself from pain was also associated with a better treatment outcome. A study that investigated the short-term effects of various strategies for coping with experimentally induced thermal pain found that distraction instructions led to lower pain intensity than acceptance instructions (Kohl, Rief, & Glombiewski, 2014). In our study distraction was only explicitly taught as a strategy for coping with pain in the CBT condition.

Our findings are in line with the core assumptions of the fear-avoidance model, which predicts that excessive avoidance behavior is followed by disuse, depression and disability, whereas confronting one's fear of movements leads to recovery (Crombez, Eccleston, van Damme, Vlaeyen, & Karoly, 2012; Vlaeyen & Linton, 2000). Our results indicate that an increase in activity and confronting one's fear are both associated with disability reduction. Thus the present results provide further evidence that several common processes underlie the effectiveness of CBT and Ex-

posure. It remains unclear, however, whether such processes need to be targeted specifically or whether they can be promoted indirectly.

Methodological Strengths and Limitations

This study investigated treatment processes using session-by-session data. This allowed us to identify measures that changed during the course of treatment and predicted treatment outcome. We categorized process and outcome measures based on theoretical considerations and time of measurement, but visual inspection of the data revealed that changes in what we had labeled process and outcome measures happened in parallel rather than sequentially. The next step will be to determine whether the isolated manipulation of process variables leads to better outcomes or whether they are simply correlates of treatment effects (Kazdin, 2009). Second, we used a pre-stratified, computer-generated randomization schedule to assign patients to groups, but this did not result in gender-balanced groups. To give us a relatively broad overview of other treatment processes without overburdening the participants, we asked them to keep a diary incorporating a list of one-item measures of putative treatment processes. The decision to ask patients to compose their own diary entries may have cost us the opportunity to use more reliable instruments. Because our findings relating to behavioral change are based solely on participants' self-reports they must be treated with caution. In future they should be replicated using established questionnaires or behavioral indices. Third, we used data from a three-arm RCT that was designed to investigate dose effects. This meant that there were two Exposure conditions that differed in length but not approach and so we pooled these data for the purposes of the analyses reported here. However, all the participants knew about the existence of all the other groups and so motivational confounders must be considered. Due to the high number of missing values on the weekly assessments we conducted a per-protocol analysis. Forth, we only included CLBP patients with strong fear-avoidance beliefs. Future studies should investigate the same treatment processes in other subgroups (e.g. according to endurance model (Hasenbring & Verbunt, 2010)) to explore necessary conditions for treatment processes depending on specific patient characteristics.

Conclusions

Our results indicate that Exposure and CBT involve similar processes of change. Specifically, changes in fear-avoidance beliefs, relaxation, distraction, activity, confrontation, and pain-related self-efficacy appear to predict with disability reduction. Clinicians should promote these processes in order to increase treatment impact. Further research is needed to determine whether these processes need to be directly targeted or if they can also be supported indirectly.

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Conflict of Interest

The authors declare that they have no competing interests.

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Tables and Figures

Table 1. Baseline variables for study participants (n = 61)

Variables	CBT (n = 24)	EXP (n = 37)
Age	51.7 ± 9.4	52.3 ± 8.7
Gender (% female)	66.7%	37.8%
Education		
low	12.5%	29.7%
middle	45.8%	35.2%
high	41.7%	35.2%
Work status		
(self-)employed	54.2%	51.4%
unemployed	8.3%	13.5%
houseman/-woman	4.2%	2.7%
retirement pension	8.3%	16.2%
disability pension	20.8%	16.2%
Pain history		
Previous back surgeries	29.2%	32.4%
Duration of pain (in years)	15.1 ± 10.3	15.2 ± 10.0
Pain intensity (NRS-P)	5.4 ± 1.6	5.6 ± 1.9
Pain quality (DSF)	4.7 ± 2.3	4.8 ± 2.6
QBPDS	43.4 ± 16.1	44.8 ± 16.6
PDI	33.1 ± 10.4	32.9 ± 11.0

Note. Values presented as means (± standard deviation) or percentage. Abbreviations: CBT, Cognitive Behavioral Therapy; EXP Exposure Therapy; QBPDS, Quebec Back Pain Disability Scale; PDI, Pain Disability Index.

Table 2. Items of the weekly diary

	Item formulation
Relaxation	*I was able to relax.*
Distraction	*I managed to distract myself when I was in pain.*
Positive thoughts	*Positive thoughts helped me to cope better with the pain.*
Self-efficacy	*I was able to influence my pain.*
Activity	*I was active despite the pain.*
Acceptance	*I was able to accept my pain.*
Confrontation	*I dared to execute movements although I was afraid they would harm my back.*
Avoidance	*I canceled activities because I was in pain.*
Daily life	*Despite the pain, I was able to execute my daily business.*
Enjoyment	*I was able to enjoy things despite the pain.*
Coping	*Overall, I managed to handle my pain.*

Table 3. Individual slopes of relevant treatment processes

	CBT (N = 24)	**EXP (N = 37)**
TSK	-.45 [-.66; -.24]	-.45 [-.65; -.26]
Relaxation	.23 [.16; .30]	.27 [.22; .32]
Distraction	.28 [.22; .34]	.28 [.22; .33]
Self-efficacy	.29 [.23; .35]	.26 [.19; .32]
Activity	.22 [.19; .24]	.24 [.23; .25]
Confrontation	.33 [.27; .39]	.40 [.35; .43]
Enjoyment	.29 [.22; .34]	.23 [.18; .27]

Note. Average individual slopes with the two therapy conditions EXP and CBT presented as means with confidence interval (95%).

Table 4. Individual slopes as predictors for treatment outcome

	Global disability	**Specific disability**
	b [CI]	**b [CI]**
TSK		
POST:	**-.36 [-.16; -.56]**	**-.26 [-.06; -.46]**
FU:	**-.41 [-.18; -.64]**	**-.31 [-.10; -.51]**
Relaxation		
POST:	**-.60 [-.78; -.42]**	**-.52 [-.71; -.32]**
FU:	**-.44 [-.67; -.20]**	**-.39 [-.61; -.18]**
Distraction		
POST:	**-3.30 [-4.62; -1.98]**	**-2.87 [-4.26; -1.47]**
FU:	**-2.49 [-4.10; -.89]**	**-1.84 [-3.38; -.30]**
Self-efficacy		
POST:	**-2.41 [-3.58; -1.24]**	**-1.88 [-3.07; -.69]**
FU:	-1.36 [-2.74; .02]	-.95 [-2.22; .31]
Activity		
POST:	**-.33 [-.55; -.11]**	**-.24 [-.47; -.02]**
FU:	-.12 [-.38; .13]	.06 [-.30; .18]
Confrontation		
POST:	**-.53 [-.74; -.33]**	**-.40 [-.61; -.18]**
FU:	**-.47 [-.73; -.22]**	**-.37 [-.60; -.13]**
Enjoyment		
POST:	-.18 [-.40; .05]	-.13 [-.34; .08]
FU:	-.04 [-.29; .21]	-.02 [-.22; .21]

Note. Individual slopes with confidence interval (95%) as predictors for global disability (measured by Pain Disability Index, PDI) and specific disability (measured by Quebec Back Pain Disability Scale, QBPDS). Abbreviations: TSK, Tampa Scale of Kinesiophobia (inverted); POST, disability at post-treatment; FU, disability at 6 months follow-up, all values were z-standardized.

Session	EXP-long	EXP-short	CBT
1	Anamnesis	Anamnesis	Anamnesis
2	Psycho-education	Psycho-education	Psycho-education
3	Fear Avoidance Model	Fear Avoidance Model	Goal setting
4	Fear hierarchy	Fear hierarchy	Behavior analysis
5	Exposure 1	Exposure 1	Graded activity I
6	Exposure 2	Exposure 2	Graded activity II
7	Exposure 3	Exposure 3	Health behavior
8	Exposure 4	Exposure 4	Progressive relaxation I
9	Exposure 5	Exposure 5	Progressive relaxation II
10	Exposure 6	Completion	Attention shifting
11	Exposure 7		Identification of automatic thoughts and core beliefs
12	Exposure 8		Reconstruction of dysfunctional thoughts and beliefs
13	Exposure 9		Individual session I
14	Exposure 10		Individual session II
15	Completion		Completion

Figure 1. Overview treatment sessions in Exposure Therapy, EXP and Cognitive Behavioral Therapy, CBT; treatment sessions which were combined to reduce missing values are marked in the same box.

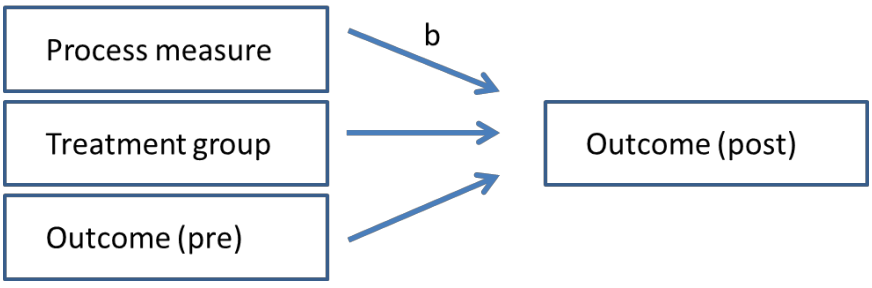

Figure 2. Regression model with treatment processes as predictor for treatment outcome. Predictor = process measure (i.e. individual slope for change in treatment process); covariates = treatment group, outcome (pre).

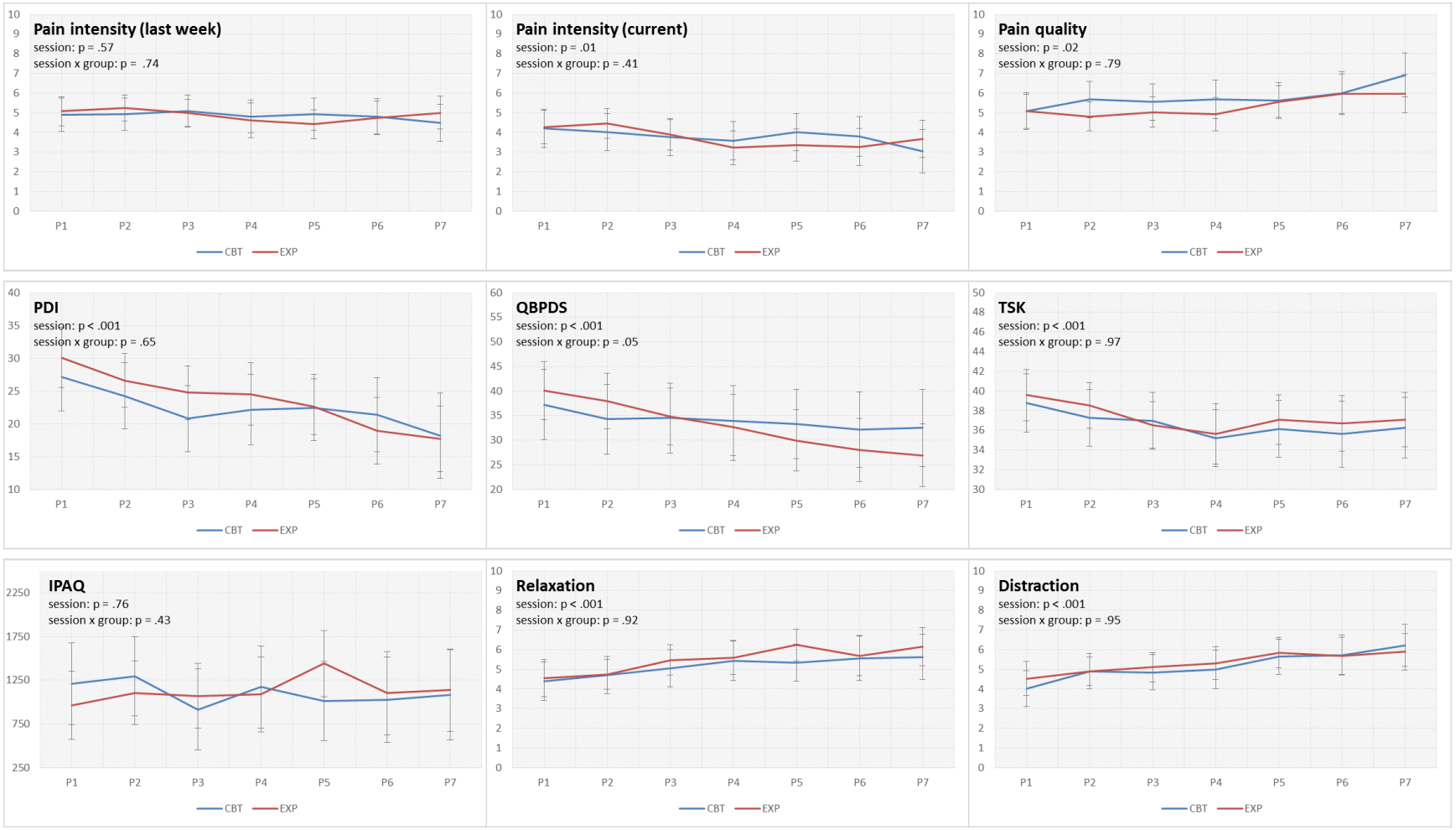

Figure 3. Two-level models of changes in outcome and process measures. X-axis = therapy sessions of similar content (e.g. graded activity I+II); p-values = level statistical significance for the predictor "Session" of the first two-way model and the predictor "Session x Group" of the second two-way model (Wald x^2 test); PDI, Pain Disability Scale; QBPDS, Quebec Back Pain Disability Scale.

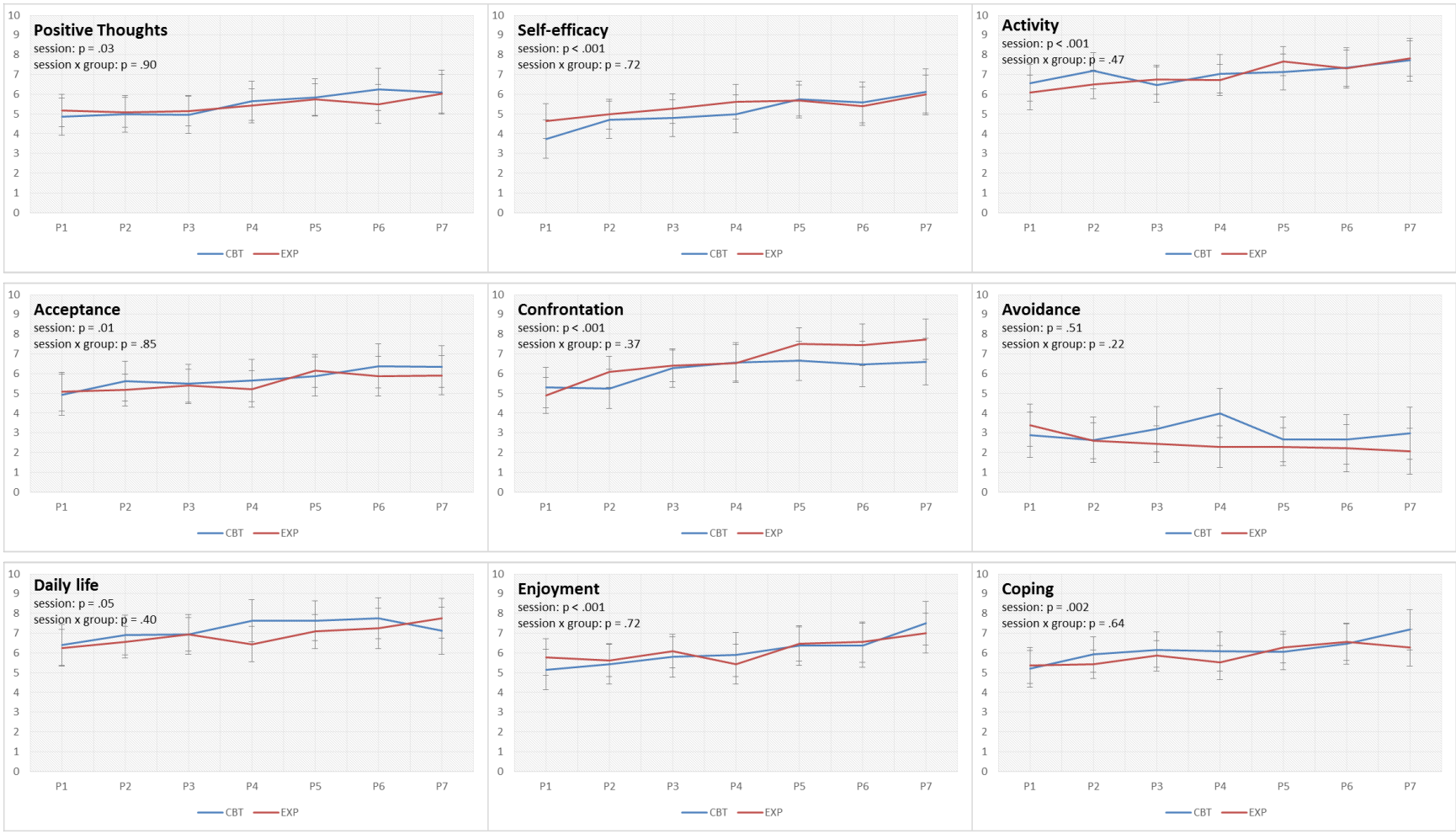

Figure 4. Two-level models of changes in process measures. X-axis = therapy sessions of similar content (e.g. graded activity I+II); p-values = level statistical significance for the predictor "Session" of the first two-way model and the predictor "Session x Group" of the second two-way model (Wald x^2 test).

Appendix B: Studie II

Schemer, L., Vlaeyen, J.W.S., Dörr, J.M., Nater, U.M., Rief, W., & Glombiewski, J.A. (submitted). Treatment processes during exposure and cognitive-behavioral therapy for chronic back pain: A single-case study. Manuscript submitted for publication in *Pain*.

Abstract

Several psychological approaches exist for treating individuals with chronic low back pain (CLBP) and high levels of fear-avoidance. While there is evidence for their overall effectiveness, little is known about the particular influence of isolated elements within these multicomponent treatment approaches. This study aimed at evaluating the effect of treatment elements during graded in vivo exposure (EXP) and cognitive-behavioral therapy (CBT) in a single-case design. Twelve participants (pain > 6 months; high levels of fear-avoidance) were randomly assigned to the respective treatment condition. They underwent intensive assessments including psychobiological measures at pre-treatment, post-treatment, and 6-months follow-up. Moreover, they provided daily ratings on several measures during a baseline (1–3 weeks), treatment (approx. 5 weeks), and 6-months follow-up phase (2 weeks). Within the EXP approach, our results suggest that change only occurred during exposure sessions. Specifically, there were changes in pain perception, perceived harmfulness of personally relevant activities, self-efficacy, acceptance, and body confidence. Although these differences disappeared in the follow-up phase, there were delayed improvements in the self-reported exposition. Within the CBT treatment approach, there were only delayed improvements in the difficulty in performing personally relevant activities and their expected harmfulness.

In addition, this study explored treatment effects on biological stress markers. While there was no evidence for a clear-cut biological stress response, the overall cortisol level was higher in the CBT than in the EXP group during post-assessment. This effect is not attributable to inter-individual differences or time of day and, therefore, appears a promising object of future investigations.

Introduction

The fear-avoidance model provides a comprehensive theoretical model of psychological influences in the development of chronic pain [10,67]. Its central concepts are pain-related fear and avoidance as key elements in the development and maintenance of chronic pain. Pain-related

fear is assumed to be accompanied by a psychophysiological stress response when confronted with feared situations (similar to phobia-like fear) [49]. This reaction pattern might, in turn, contribute to pain perpetuation through repeated activation and dysregulation of the autonomic nervous system and the hypothalamic pituitary adrenal axis [61].

Several approaches exist for treating individuals with chronic low back pain (CLBP) and high levels of fear-avoidance [1]; graded in vivo exposure (EXP) is directly based on the above-described model [69]. Patients are encouraged to adapt their individual situation to the fear-avoidance model and create an individualized fear hierarchy. Subsequently, patients are motivated for individually tailored exposure sessions. Essentially, this therapy approach aims to change idiosyncratic harm beliefs towards specific movements. Therefore, EXP represents a specific treatment approach for a particular group of patients. Cognitive-behavioral therapy (CBT) protocols usually combine various techniques such as cognitive and behavioral interventions [18,39]. These interventions aim to provide patients with various pain coping strategies to reduce functional disability. Compared to EXP therapy, however, these interventions oftentimes are not specifically tailored [1]. For example, they might discuss strategies to reengage in former activities by modifying contingencies between pain behaviors and their direct consequences (e.g. graded activity). However, they usually do not explicitly target the maintaining factor of fear-avoidance to the same degree. Therefore, CBT represents a general-treatment approach.

Several randomized control trials confirmed the overall effectiveness of CBT [17,23,26] and EXP [35,37,72] therapy. These study approaches usually seek to evaluate the overall effects of complex multicomponent treatments [44]. However, it is impossible to differentiate the particular influence of isolated treatment elements. Therefore, alternatives to traditional study approaches have been discussed to further improve the field [45]. Single case designs, for example, are considered an efficient way for evaluating isolated treatment components and establishing causal effects. This procedure provides continual feedback on individual change processes *during* treatment compared to the response behavior of the same patients *prior to* treatment [50]. Subsequent conclusions on common change patterns across patients can be drawn. This offers the opportunity to generate hypotheses for future research [58].

We used a single-case experimental multiple baseline design to evaluate the effect of isolated elements on treatment processes during a specific (EXP) and general (CBT) treatment approach. To the best of our knowledge, no other study has contrasted these treatment approaches in a single-case design. Previous single-case studies evaluated the feasibility of EXP therapy (stage I according to the stage model) [4,31,64,65]. Their focus was the investigation of EXP effects on fear-avoidance as the key factor in the maintenance of chronic pain. The present study, however, intends to explore the development of additional treatment processes by evaluating isolated

effects of psycho-educational, behavioral, cognitive, and exposure elements (stage II). By doing this, we assume that especially effective treatment elements are followed by immediate changes on the respective daily measurements. Moreover, we explored effects of both treatments on biological stress markers.

Method

Study Design

A single case design with multiple baselines was employed. Twelve chronic low back pain patients with a substantial level of fear-avoidance were randomly assigned to either cognitive-behavioral therapy (CBT) or exposure therapy (EXP). All patients filled out daily assessments during a baseline period (1–3 weeks), during the entire course of the intervention (approx. 5 weeks), and during the follow-up period (2 weeks). In the EXP condition, psycho-educational and exposure elements were contrasted to the baseline period. In the CBT condition, psycho-educational, behavioral elements, and cognitive elements were contrasted to the baseline period. Moreover, participants ran through an intensive secondary assessment including psychobiological measures at pre-treatment, post-treatment, and 6-months follow-up. Figure 1 provides an overview on the study design. The protocol was registered (ClinicalTrial.gov NCT03157622) and approved by the institutional ethics committee of the psychology department at the Philipps-University.

[Insert Figure 1 around here]

Recruitment and Randomization

Potential participants were recruited via advertisements in local newspapers, doctor's offices, and from the waiting list of an outpatient clinic. Patients who suffered from long lasting chronic low back pain (> 6 months) and reported substantial fear-avoidance beliefs were considered for study participation. Cut-off values for fear-avoidance beliefs were determined based on baseline data deriving from a previous RCT [54] (cut-off values > mean – SD: PCS [42,62] > 35, PASS [38,71] > 20, QBPDS [32,55] > 30, PDI [15,63] > 20 and Phoda [34] harm ratings of 13 activities > 50, including 8 > 80). Exclusion criteria were back surgeries during the previous six months or planned surgeries, inability to read or write German, pregnancy, alcohol addiction, psychotic disorders, and current psychological treatment. Figure 2 provides an overview on the flow of study participants.

[Insert Figure 2 around here]

Before participation, patients were provided with detailed information about the study procedure. All participants gave written consent before study enrollment. Moreover, participants were informed about their opportunity to decline their study participation at any time without consequences. Three blinded research assistants conducted the allocation of patients to the respective treatment condition with sealed envelopes. Neither patients nor therapists were blinded for the treatment condition due to the lack of feasibility within psychotherapy research as well as for ethical concerns.

Participants

Twelve patients were included in the final data analysis. To ensure their comparability, these patients were combined to six matching pairs in regard to their gender, age (+/- 15 years), and level of disability (+/- 15 PDI [15,63], +/- 15 QBPDS [32,55]). This proceeding minimized possible systematic influences on treatment processes in the two treatment conditions. Their background characteristics are summarized in Table 1.

[Insert Table 1 around here]

Intervention and Therapists

Patients received ten individual sessions of 50 minutes of either CBT or EXP therapy. Both treatments aim to restore functioning and decrease pain-related disability. They were based on detailed treatment manuals. Figure 3 provides an overview on the treatment session of both conditions. Patients were offered a personalized workbook for the respective treatment condition, which provided them with coherent therapy material and comprehensive background information. Sessions were held twice a week over a 5-week period in a university-based clinic in Marburg (Psychotherapieambulanz der Philipps-Universität Marburg, PAM), Germany. Two advanced clinical psychology doctoral students delivered the treatment. When possible, both patients of a matching pair were assigned to the same therapist. Due to organizational difficulties, this was only possible in 4 out of 6 matching pairs. The treatment process of each patient was supervised by an experienced psychologist. The supervision mainly reflected on the therapist-patient-interaction through the analysis of video-recorded sessions.

Graded *In Vivo* Exposure

The EXP protocol consisted of two phases. a) During the psycho-educational sessions, patients were given information about a biopsychosocial understanding of their chronic pain with the help of video material. They were given a careful explanation of the fear-avoidance model. Patients were encouraged to adopt the model to their individual situation. Factors for the maintenance of chronic pain (such as catastrophic pain belief and pain-related fear) were discussed. In particular, negative consequences of avoidance behavior were highlighted. In preparation for the exposure session, patients developed an individual fear hierarchy using the Photo Series of Daily Activities [34]. b) During the subsequent exposure sessions, patients were encouraged to test their fear-avoidance beliefs during behavioral experiments and to reduce avoidance behaviors during individually tailored exposure exercises.

Cognitive-Behavioral Therapy

The CBT protocol can be divided into three phases. a) During the psycho-educational sessions, patients were equally given information about a biopsychosocial understanding of their chronic pain with the help of video material. Moreover, patients were encouraged to formulate feasible treatment goals for re-engagement in former activities. b) During the behavioral sessions, patients were introduced to the principle of graded activity as a strategy to re-engage in former activities by dividing these activities into smaller steps. Predetermined resting periods were thereby offered as a form to prevent patients from phases of excessive demands followed by long terms of recovery. Thus, graded activity intends to shape healthy behaviors (e.g. gardening) by modifying contingencies between pain behaviors and their direct consequences. In contrast the exposure-based approach intends to reduce fear-avoidance towards specific movements (e.g. bending forward for lifting a water crate). Progressive muscle relaxation was introduced as a further technique to improve the pain experience. c) During the cognitive sessions, the strategy of attention shifting was presented to change the perception of pain. Maladaptive pain-related cognitions were identified and challenged by restructuring techniques in two subsequent therapy sessions.

[Insert Figure 3 around here]

Treatment Fidelity

Treatment fidelity was evaluated on the bases of video recordings using the method of assessing treatment delivery (MATD) [36]. For each session of the respective treatment condition, five

items of "essential and unique" treatment elements were generated on the basis of the treatment manual (e.g. EXP, session 4: "An individualized fear hierarchy is established"; CBT, session 4: "Behavioral rules according the principle of graded activity are explained"). Additional five items of "essential and not-specific" (e.g. "The therapist reacts with empathy towards reported pain experience"), and five items of "prohibited" (e.g. "Therapist reinforces a biomedical understanding of pain") treatment elements were formulated. A scoring form listed items in a randomized order. Each item was rated on a dichotomous rating scale (0 = did not occur; 1 = did occur). It also included a question to predict the session number. Since we were interested in the evaluation of isolated treatment components, the adherence to the specified chronological order of treatment elements was especially relevant. Therefore, we considered the fidelity of treatment session a stricter approach than the fidelity of treatment condition.

A graduate student was trained as a rater by two practice video ratings. Prior to his work, this student had access to the treatment manuals and workbook material. The rater had no previous involvement in the study. He was not blinded for treatment condition, but for session number. Out of 120 treatment sessions performed, 93 sessions were recorded (77.5%). For the ratings, 52 videos had a sufficient sound quality (43.4%). We drew a random sample of 10 video recordings for each treatment condition to be rated for actual treatment delivery.

Primary Assessments

Several iPod touch® evening measures were administered on a daily basis during a baseline period (7–26 measure points), during the entire course of the intervention (23–44 measure points) as well as during the follow-up period (11–30 measure points). Each patient was provided with coherent item definitions of the primary daily assessments in order to enhance a comparable interpretation of items among participants. An additional description about the utilization of the device prevented possible technical difficulties. An alarm clock reminded patients to complete the assessments every evening at an individually set point in time. To enhance their adherence, patients were individually greeted before their daily examination. If desired, patients had the opportunity to load their personal music on the provided iPod device or use its additional features during their study participation.

Pain Symptoms

Patients were asked about their symptoms on a daily basis. They had to quantify their current pain intensity (0 = no pain, 10 = worst pain), their average pain intensity during the day (0 = no

pain, 10 = worst pain), as well as their pain perception (0 = bearable, 10 = unbearable) on an 11-point scale. To assess their individual level of disability, patients were requested to nominate one personally relevant activity for each day (e.g. sitting, walking, or lifting). Subsequently, patients were requested to rate their difficulty in performing this activity (0 = no problem, 10 = impossible), its expected harmfulness *before* engaging in the activity (0 = not harmful, 10 = very harmful), and its perceived harmfulness *after* engaging in the activity (0 = not harmful, 10 = very harmful).

Treatment Processes

Patients were asked about potential treatment processes every day. For the operationalization of each treatment process, three items with high internal consistencies were selected from standardized measures. Item formulations were adopted to statements about the present day and to the specific application for back pain. Patients were requested to rate these statements on an 11-point scale (0 = total disagreement, 10 = total agreement). Items of related treatment processes were subsequently summarized by calculating mean values (0 = minimal index, 10 = maximal index). To keep the attention during the repeated daily examination, items were presented in a randomized order. One item of each item group was inverted in order to prevent answering tendencies. Table 2 provides an overview of the daily assessments of potential treatment processes.

[Insert Table 2 around here]

Secondary Assessments

There were three intensive secondary assessments at pre-treatment, post-treatment, and 6-months follow-up. Outcomes were considered following IMMPACT (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials) recommendations [16]. Patients completed the self-rating questionnaires at home. The rest of the assessments were conducted by three especially trained graduate students.

Level of Fear-Avoidance

Two self-rating questionnaires were used to quantify the individual level of fear-avoidance. The pain anxiety symptom scale (PASS) [38,71] assesses four components of pain-related anxiety, namely, cognitive anxiety, pain-related fear, escape and avoidance, and physiological anxiety, of 20 items on a 5-point scale (0 = never, 4 = always). A higher index indicates a higher degree of

pain-related anxiety (0 = minimal index; 100 = maximal index). The pain catastrophizing scale (PCS) [42,62] measures factors of pain catastrophizing thoughts, namely rumination, magnification, and helplessness, of 13 items on a 5-point scale (0 = not at all, 4 = all the time). A higher index indicates higher levels catastrophizing (0 = minimal index; 52 = maximal index). Moreover, patients were requested to rate the perceived harmfulness of 40 daily activities on a harmfulness thermometer (0 = not harmful at all, 100 = extremely harmful) using the short version of the Photo Series of Daily Activities (Phoda) [34]. A mean score was calculated to summarize ratings of the presented activities. A higher index indicates a higher perception of harmfulness (0 = minimal index; 100 = maximal index). Avoidance behavior was quantified using the behavioral avoidance test (BAT-back) [27]. In this test, patients first observed the investigator performing three isolated sequences of movements (bending forward, lifting a water crate, and rotating). Then, they had to repeatedly lift the water crate themselves (no more than ten times). A maximum of 10 performances of these isolated sequences of movements were evaluated by the investigator on a 3-point scale (0 = like model; 1 = safety behavior; 2 = avoidance). A higher index indicates higher avoidance behavior (0 = minimal index; 60 = maximal index).

Pain Intensity

Pain intensity was assessed by the brief pain inventory (BPI, items 12-15) [8,53]. This scale differentiates between current pain intensity as well as highest, lowest, and average pain intensity during the last week on an 11-point numeric rating scale (0 = no pain, 10 = pain at its worst). A higher index indicates greater levels of pain (0 = minimal index, 10 = maximal index).

Physical Functioning

Physical functioning was measured by two questionnaires. The pain disability index (PDI) [15,63] asks patients to indicate their level of impairment of 7 items on an 11-point scale (0 = no impairment, 10 = complete impairment) to participate in essential life activities (e.g. family life, work, and leisure time). Thus, it measures disability on a global level. A higher index indicates greater levels of disability (0 = minimal index, 70 = maximal index). The Quebec back pain disability scale (QBPDS) [32,55] asks patients to indicate their difficulty in pursuing daily activities (e.g. driving a car, climbing stairs, and putting on socks) of 20 items on a 5-point scale (0 = no effort, 5 = not able to). Thus, it measures disability on a more specific behavior-based level. A higher index indicates greater levels of disability (0 = minimal index, 100 = maximal index).

Emotional Functioning

Emotional functioning was evaluated by the hospital anxiety and depression scale (HADS) [24,73]. Patients have to answer 7 items concerning their level of depression and 7 items concerning their level of anxiety on a 4-point scale. A higher index point to higher levels of depression and anxiety (0–7 = normal, 8–10 = borderline abnormal, 11–21 = abnormal).

Participant Ratings of Satisfaction with Treatment

The treatment motivation was quantified by four statements concerning the individual devotion to the treatment on an 11-point scale (0 = totally disagree, 10 = totally agree) at the pre-treatment assessment. A higher index indicates a higher level of treatment motivation (0 = minimal index, 40 = maximal index). The treatment satisfaction was measured by 10 statements concerning the evaluation of the therapy on an 11-point scale (0 = strongly disagree, 10 = absolutely agree) at the post-treatment and 6-months follow up assessment. A higher index indicates a higher level of treatment satisfaction (0 = minimal index, 100 = maximal index).

Physiological Assessments

Salivary Cortisol and Alpha-Amylase

We incorporated two additional physiological markers to assess the participants' biological stress reaction to fear-eliciting stimuli during the BAT-back. Saliva samples of each participant were obtained using the SaliCap® (IBL, Hamburg, Germany) system in order to extract salivary cortisol (a marker of HPA axis activity) as well as salivary alpha-amylase (a marker for ANS activity). Saliva collection took place during the behavioral test (BAT-back) at the pre-treatment, post-treatment and follow-up assessments. Samples were taken 8 times: (1) -30 min, (2) -15 min and (3) immediately prior to the observation phase, (4) between the observation and execution phase, (5) immediately after the execution phase, as well as (6) +10 min, (7) +25 min, (8) +40 min delayed. The procedure for saliva collection is described in Figure 4. For the analysis of cortisol, a commercially available enzyme-linked immunoassay (IBL, Hamburg, Germany) was used. Alpha-amylase was analyzed using a kinetic colorimetric test and reagents obtained from Roche's quantitative enzyme. Mean inter-assay variance was 10.14% for salivary cortisol analyses, 7.03% for salivary alpha-amylase analyses. Mean intra-assay variance was 8.55% for salivary cortisol analyses, 4.67% for salivary alpha-amylase analyses.

[Insert Figure 4 around here]

Hair Cortisol

Small hair strands were taken scalp-near from the posterior vertex region of the participants at each time point. The first 3 cm were analyzed, which represents a time frame of about 3 months. Hair wash and cortisol extraction procedures based on a previous laboratory protocol [59] with minor modifications. In brief, hair samples were washed twice for 3 min using 3 mL isopropanol. For cortisol extraction, 10±.5 mg whole, finely cut hair was incubated in 1.8 mL methanol for 18 h at room temperature. After incubation, 1.6 mL was transferred to another glass vial. Then, 1.6 mL of the supernatant was evaporated at 50 °C until samples were completely dried. Finally, the samples were resuspended with 150 µL HPLC gradient grade water (Fisher Scientific) and vortexed for 20 sec. For cortisol determination, 50 µL was used for analysis using commercially available cortisol luminescence immunoassay (LIA; IBL, Hamburg, Germany). Inter- and intra-assay coefficients of variation were below 10% for all assays. The analyses were carried out at our local laboratory (Clinical Biopsychology, University of Marburg). There is evidence that hair cortisol validly reflects long-term cortisol secretion as compared with saliva and urine samples, as well as indirectly in conditions that are known to present with hyper- or hypocortisolism. Test-restest associations in different time frames were found to be rather high (between .68 and .79) [61].

Statistical Analysis

Statistical Analysis of Treatment Fidelity

Protocol adherence was computed by dividing the average number of observed required treatment elements (“essential and unique”; “essential and not specific”) by the maximum possible number of these elements. The occurrence of at least 70% of essential treatment elements was considered as sufficient treatment adherence [36]. Treatment contamination was computed by dividing the number of observed forbidden treatment elements (“prohibited”) by the maximum possible number of these elements. The occurrence of maximally 10% of prohibited treatment elements was defined as sufficient low treatment contamination [36]. Session differentiation was determined by calculation of the percentage of adequate treatment categorization. The session differentiation of more than 90% was considered appropriate [36].

Statistical Analysis of Primary Assessments

The statistical analyses of the daily iPod measures were conducted with the R package. We conducted the analyses in two steps. First, data was analyzed on an individual level. Data of the daily

measures were tested for significant differences between baseline and intervention phase for each patient by the single-case randomization test (SCRT) [6,25]. The advantage of this test is that it requires no assumption about the data distribution. Instead, the test utilizes the randomization distribution of the collected data. We were especially interested in the effect of isolated treatment elements on potential treatment processes. Therefore, we divided the EXP condition into the following two phases: psycho-education (session: 1-4) and exposure (session 5-10). For the CBT condition, we had a closer look at the following three phases: psycho-education (session: 1-3), behavioral elements (session: 4-6), and cognitive elements (session: 7-9). Moreover, we combined the variety of CBT-specific techniques (session: 4-10) for the indirect contrast with the EXP condition. For each comparison, the null hypothesis (= no mean difference between baseline vs. respective treatment phase) was tested against the one-tailed alternative hypothesis (= significant decrease of pain symptoms during the respective intervention phase; = significant increase of treatment processes during the respective intervention phase). Second, previously obtained results were summarized into a general p-value across study participants by the single-case meta-analysis (SCMA). The program offers the combination of p-values by an additive approach using Edgington's formula. The summary of individual p-values was done separately for both treatment groups.

Statistical Analysis of Secondary Assessments

The statistical analyses of the main assessments were conducted with the SPSS package. The calculation of the reliable change index (RCI) as well as clinically significant change (CSC) [30] helped to evaluate pre-post as well as pre-follow-up changes despite the limited number of data. The RCI indicates whether the observed treatment effect exceeded possible random changes due to measurement error. The index equals pre-post and pre-follow-up changes divided by the standard error of difference. To obtain estimates for the standard error of difference, we used indices of the retest reliability or, if this information was not available, indices of internal consistency given by previous literature. We tested treatment effects in a one-tailed directional manner ($RCI \geq 1.65$, $p \leq .05$). The CSC does not only assess the statistical reliability of treatment effects but also evaluates their practical importance. To evaluate the clinical importance, we used normative cut off scores established by previous research on clinically meaningful change scores (*criterion n*). If this information was not available, we used established criteria [29]. These criteria are defined as follows: (a) the post-treatment score is outside the range of the dysfunctional population, that is, extending 2 SD units beyond the mean of a clinical sample (*criterion a*); (b) the post-treatment score is within the range of a functional population, that is, including 2 SD units within the mean of a non-clinical sample (*criterion b*); (c) the post-treatment

score is statistically more likely to belong to the non-clinical than to the clinical population (*criterion c*). If distributional data were available for a non-clinical sample, we used *criterion c*. If this information was not available, we used *criterion a*. Details of the reliability and clinically significant change data are shown in Table 3.

[Insert Table 3 around here]

Statistical Analysis of the Physiological Assessments

Cortisol and alpha-amylase values were analyzed on a descriptive basis as well as using visual inspection techniques [28]. We calculated the difference between baseline (pre-BAT-back) and +25 min value for cortisol (Δcort) as well as the difference from baseline (pre-BAT-back) to post-BAT-back value in alpha-amylase (Δaa) to account for the time point of expected peak in the respective parameters in commonly applied stress tests [43,47]. Furthermore, we calculated the slope of both parameters throughout the entire assessments. Hair cortisol was also analyzed using visual inspection and descriptive values.

Results

Results of Treatment Fidelity

For the treatment fidelity, 83% (SD = 9.49) of the required elements occurred during the respective treatment sessions in the EXP group. Similarly, 86% (SD = 6.99) of the required elements occurred during the respective treatment sessions in the CBT group. Thus, the preset criterion of good protocol adherence was met in both groups. For the treatment contamination, no prohibited elements occurred either in the EXP group or in the CBT group. Thus, there was no treatment contamination in either group. For session differentiation, 100% of the sessions in the EXP group and in the CBT group were correctly allocated. Therefore, sessions in both treatment groups could be sufficiently differentiated.

Results of Primary Assessments

First, data of the daily assessments were examined on an individual level. An individual p-score for each treatment phase on the various daily measures was calculated. Second, previously obtained results were summarized across study participants. For the EXP condition, changes in pain perception, perceived harmfulness of personally relevant activities, pain-related self-efficacy, pain acceptance, as well as body confidence reached the level of significance ($p \leq .05$) during exposure sessions (5-9) but not during other educational sessions (1-4). During the fol-

low-up phase only changes in exposition reached the level of significance ($p \leq .05$). For the CBT condition, there were no significant common change patterns across patients for either comparison during the course of therapy. However, there were significant changes ($p \leq .05$) in the difficulty in performing a personally relevant activity and its expected harmfulness *before* engaging in this activity compared to the baseline. Meta-analytic results are presented in Table 4.

[Insert Table 4 around here]

Results of Secondary Assessments

Results for the Level of Fear-Avoidance

In the EXP condition, there were clinically relevant symptom reductions for pain-related anxiety (PASS: Post = 3; FU = 3), pain catastrophizing thoughts (PCS: Post = 2; FU = 1), perception concerning the harmfulness of daily activities (PHODA: Post = 1; FU = 1), and avoidance behavior (BAT-back: Post = 2; FU = 1). In the CBT condition, there were clinically relevant symptom reductions for pain-related anxiety (PASS: Post = 1; FU = 1), pain catastrophizing thoughts (PCS: Post = 1; FU = 1), and avoidance behavior (BAT-back: Post = 1).

Results for Pain Intensity

In the EXP condition, some patients reported clinically relevant symptom reductions with regard to their highest level of pain intensity (Post = 2; FU = 1) and their average pain intensity (Post = 2). In the CBT condition, some patients reported clinically relevant symptom reductions with regard to their average pain intensity (Post = 2; FU = 1) and current level of pain intensity (Post = 1; FU = 3).

Results for Physical Functioning

Only in the EXP condition, some patients reported clinically relevant reductions in their level of global disability (Post = 2; FU = 1) and specific disability (Post = 2; FU = 3).

Results for Emotional Functioning

In the EXP condition, some patients reported reliable reductions in their depressive (Post = 2) and anxiety symptoms (Post = 2; FU = 1). In the CBT condition, some patients reported reliable reductions in their depressive (FU = 1) and anxiety symptoms (FU = 1).

Results for Satisfaction with Treatment

The average treatment motivation in the EXP (pre: M = 33.5, SD = 2.4) as well as CBT (pre: M = 34.5, SD = 3.6) condition was equally high before the treatment. Similarly, patients in the EXP (post: M = 86.2, SD = 9.4) and CBT (post: M = 90.7, SD = 6.2) condition reported a similar high treatment satisfaction at the end of treatment.

[Insert Table 5 & 6 around here]

Results for the Physiological Assessments

There was no pattern of increase in cortisol or alpha-amylase from baseline (pre-BAT-back) to the expected peak time points because the BAT-back could be detected (for descriptives, see Tables 5 and 6). The delta as well as slope values rather suggest a decrease or no difference in cortisol and alpha-amylase values during the assessments in both groups. (Only one person showed an increase in cortisol level between baseline and expected peak that would be considered a stress response (Δcort = 2.01) [43], and only at the follow-up assessment.) Visual inspection of the data suggests a decrease in cortisol and a slightly u-shaped curve for alpha-amylase during the assessment periods (see Figure 4). Notably, the overall cortisol level was apparently higher in the CBT than in the EXP group during post-assessment. This effect is not attributable to inter-individual differences (when compared with pre-assessment and follow-up) as well as time of day (which did not differ between groups).

Concerning hair cortisol, increases as well as decreases can be found from pre-treatment to post-treatment in both groups. Visual inspection suggests that the level of hair cortisol approaches the pre-treatment value at follow-up in every person that provided hair samples at all three time points.

[Insert Figure 5 & 6 around here]

Discussion

Summary of the Main Findings

With this study, we were able to analyze detailed psychological and biological processes during a specific (EXP) and general (CBT) treatment of individuals with CLBP and high levels of fear-avoidance using a single-case design. Within the specific (EXP) treatment approach, our results suggest that therapeutic change mainly occurred during exposure but not during previous educational sessions. These changes incorporated modifications in pain perception, perceived harmfulness of personally relevant activities, self-efficacy, pain acceptance, and body confidence. Alt-

hough these differences disappeared in the follow-up phase, there were delayed improvements in self-reported exposition. Within the general (CBT) treatment approach, we could not find any statistical evidence pinpointing to isolated, especially powerful therapy elements. However, our results indicate delayed improvements in the difficulty in performing personally relevant activities and their expected harmfulness during the follow-up phase.

Treatment Processes during EXP Therapy

In line with results from previous single-case studies [31,64–66], change processes mainly occurred during exposure sessions. For example, fear of movement/(re)injury, pain catastrophizing, and pain-related fear only changed during the exposure period but not during the graded activity period. In our study, exposure experience did not only change perceived impairment and harmfulness of personally relevant activities, but also increased self-efficacy, pain acceptance, and body confidence. Craske and colleagues argue that the purpose of exposures is not to reduce fear but rather to tolerate it [9]. While fear is the obvious problem in anxiety disorder, pain is the obvious problem in chronic pain [70]. Therefore, the experience during exposure sessions might have enabled patients to better tolerate and, hence, accept their pain. At the same time, they could adopt a feeling of control and body confidence. This finding fits well with results from general EXP research. For example, changes in self-efficacy significantly influenced treatment outcome among individuals with social anxiety disorder [22] and panic disorder [19]. Thus, our study confirms the importance of exposure experience within psychological treatment of CLBP and adds knowledge about further relevant change processes.

Our results revealed no particular effect of the first educational sessions. In another study protocol the educational sessions were held with a physician [31]. Interestingly, this intervention already initiated relevant change processes, which were further amplified during the following exposure sessions. Therefore, our educational intervention mainly based on video material might not have been strong enough. It is possible that our educational sessions mainly motivated patients for the later exposure sessions. For example, Norcorss, Krebs, and Prochaska highlight the importance of tailoring interventions to the individual stage of change [48]. Accordingly, interventions for patients in the *contemplation stage* need to increase awareness and motivation for change. Instead, interventions for patients in the *action phase* need to focus on the minimization of passivity, anxiety, and avoidance. Our daily measures, however, did not cover motivational aspects. Future studies should include motivational aspects to facilitate a multidimensional understanding about relevant treatment processes.

Treatment Processes during CBT Therapy

There was no indication of particularly powerful therapy elements during CBT. This seems especially surprising considering the comparative richness of applied interventions. The strength of this widespread approach is its feasible application to a large population. However, several authors highlight the importance to match treatments to patients' characteristics [39,45,68]. Therefore, the lack of specificity might explain our non-significant results. This interpretation would further strengthen the argument made for tailored interventions. However, some methodological decisions must be considered. To standardize the treatment procedure, each session was based on detailed manuals and the chronological order was predetermined. It is possible that effects of previous treatment elements were carried over to the next treatment phases. This might impede finding any specific interventional effects. Therefore, future studies randomizing the order of treatment elements are needed to allow valid interpretations of our current results.

Delay and Maintenance of Treatment Processes

Interestingly, both CBT and EXP appeared to have initiated changes that only evolved during the follow-up phase. While EXP elicited later changes in exposition, CBT facilitated changes in the difficulty in performing personally relevant activities and their expected harmfulness. It is possible that only after the end of therapy, patients were able to practice and transfer new coping strategies to their everyday life. This might be an important restriction of our previous assumption of time contingent changes. Other previously relevant changes during the EXP phase, however, disappeared during the follow-up phase. This raises the question of how to sustain therapeutic change. For general exposure-based treatments, two kinds of possible strategies are discussed [52]: procedural (implemented during exposure sessions) and flanking techniques (implemented before and after exposure sessions). There is some initial evidence for positive effects of strategies such as mental reinstatement [46] and the usage of retrieval cues [11] for other forms of anxiety related disorders. Future research needs to investigate these strategies in the context of chronic pain.

Alignment of the Main Assessments

The percentages of patients with clinically significant changes ranged from 16.7% to 66.7% in the EXP condition and from 16.7% to 50% in the CBT condition depending on the outcome and time of measurement. For some measures, no patient experienced any clinically significant improvements. Our results are similar to findings of other studies. In a more representative study

on the clinical effectiveness of a multidisciplinary treatment (N=833), the percentage of clinically significant improvements was 13% for the average pain intensity (compared to 0%–33.3% in the present study) and 14–19% for depressive and anxiety symptoms (compared to 0%–33.3% in present study) (64). Other studies found clinically significant improvements for functional disability ranging from 34%–58% (compared to 16.7%–50% in the EXP condition) [35,57]. Surprisingly, we found no clinically relevant effect of CBT on functional disability in our study. Further empirical validation of treatment elements might increase treatment impact by identifying especially powerful components.

We were the first to investigate the cortisol and alpha-amylase response to back pain-related movements in a group of CLBP patients scoring high on fear-avoidance. We did not find clear-cut biological stress responses either in cortisol (reflecting HPA axis activity) or in alpha-amylase (reflecting ANS activity). This finding is in line with two studies showing a lack of fear or stress responses to back pain-related movements in patients scoring high on fear-avoidance using fMRI [2] or investigating the startle response [33]. Thus, patient's knowledge (beliefs and attitudes) about back pain-related movements might be a more important factor in the fear-avoidance model than phobia-like fear resulting in a stress response. In one of our own studies, we found an increase in skin conductance as well as interbeat interval and muscle tension in the lower back when CLBP patients were confronted with pictures of back pain-related movements and the prospect of carrying out these movements [21]. The difference in our findings may suggest that while increases occur in specific back pain-related ANS measures, a general stress response pattern cannot be detected. The negative slope of cortisol during the assessments reflects the normal decline of cortisol during the day [7].

The fact that participants in the EXP group showed lower cortisol levels during the post-treatment assessment than the CBT group could be associated with their stronger improvement in anxiety symptoms. However, this effect has to be interpreted with caution in light of the small sample size. Of note, changes in hair cortisol levels occurred, and they seemingly went back to pre-treatment levels at follow-up. More research is needed on the effect of treatments on hair cortisol levels and potential moderating factors that contribute to changes in the cortisol concentration.

Strength and Limitations of Study Results

Methodical strengths of this study include employment of multiple baselines, matching of patients prior to randomization, implementation of treatments based on detailed manuals, verification of treatment fidelity based on video recordings, inclusion of various levels of measurement,

and continuation of daily assessments during the follow-up phase. Besides these strengths, there are also some limitations. First, a general criticism of single-case studies is the lack of generalization. In contrast to the traditional group-based research, single-case designs look at individual treatment effects before accumulating results of similar patients [3]. Subsequent studies are needed to ensure the general validity of our results. By doing this, a randomization of treatment elements might be a stricter evaluation approach. Second, the conduction of daily assessments in an outpatient setting came along with various other sources of errors (e.g. large amount of missing data, technical difficulties). Third, the treatment was delivered by two therapists. Matching pairs were allocated to the same therapist to control for cofounding effects. Due to organizational difficulties, this was not possible for two of six pairs.

Conclusion

While exposure experience appears to initiate immediate positive change processes, cognitive-behavioral interventions seem to build their effect only later in time. Thus, we recommend integrating exposure elements during the treatment of individuals with CLBP and high levels of fear-avoidance. Single-case designs offer the opportunity to investigate particular change processes of isolated treatment elements. However, they have their limits in describing delayed change processes. Moreover, treatment effects on biological stress markers appear to complement psychobehavioral evaluations in future investigations of chronic pain treatments.

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Conflict of Interest

The authors declare that they have no competing interests.

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Tables and Figures

Table 1. Baseline characteristics of matching partners (n=12)

No.	Cond.	Gender	Age	Work status	Pain description
1	EXP	female	58	disability pension	*"Problems with back for 15 years. Operation on the lower back did not reduce the symptoms. Is not able to work anymore."*
	CBT	female	56	employed	*"Low back pain for 20 years. Is afraid of losing control over her life due to back pain."*
2	EXP	male	57	employed	*"Low back pain for 20 years after herniated disc. Feels guilty not to be able to play with his son."*
	CBT	male	51	sick leave	*"Pain problems from early adulthood. Interprets pain as warning signals for severe body damage."*
3	EXP	female	58	employed	*"Low back pain for 15 years after bicycle accident. Pain attacks at her work as school counselor."*
	CBT	female	67	pension	*"Pain in lower back for 10 years after falling down stairs. Pain causes problems with sitting and pursuing household activities."*
4	EXP	male	58	disability pension	*"Low back pain for 26 years. Cannot work anymore. Reports severe sleeping deprivation."*
	CBT	male	62	disability pension	*"Pain in lower back for 3 years. Two hip replacement surgeries lead to pain in his lower back. Not able to drive long distances."*
5	EXP	female	41	sick leave	*"Unexplained back pain for 2 years. Suffers not to be capable of engaging in former leisure activities (e.g. basketball)."*
	CBT	female	55	employed	*"Back pain for 5 years. Several herniated discs in upper and lower pain. Was on sick leave for more than a year. Afraid of long sitting periods during work."*
6	EXP	male	58	unemployed	*"Back pain for 19 years. Fear to end in a wheelchair. Several surgeries did not change pain severity."*
	CBT	male	58	employed	*"Back pain for 5 years after herniated disc in lower back. Especially struggling with depressive side effects."*

Table 2. Overview of daily process measures

Treatment process	Questionnaire	Example item
Self-efficacy	FESV [20] – Experience of Competence	*"When I had back pain today, I still had the feeling to be in control."*
Positive thoughts	FESV [20] – Cognitive Restructuring	*"When I had back pain today, I told myself that I can better handle it than before."*
Acceptance	CPAQ [49]	*"My life is going well, even though I have chronic back pain."*
Exposition	PASS [38,74] - Escape/Avoidance	*"Today, I continued activities even though I felt the upcoming back pain."*
Cognitive anxiety	PASS [38,74] – Cognitive Anxiety	*"When I hurt today, I did not constantly think about the back pain."*
Catastrophizing	PCS [42,62] - Rumination	*"Today, there was a moment when I stopped thinking about the back pain."*
Body confidence	FKKS, FbeK [14,60]- Uncertainty/Concern about Body Processes	*"Today, I could confide in my body."*

Table 3. Reliability and clinically significant change data

	Rel. type	Rel. coef-ficient	RCI	CSC cri-terion	CSC cut point	Scale range	Reference
Fear-avoidance							
PASS	α	0.91	14.3	*n*	34	0-100	[5,38]
PCS	r	0.8	9.7	*c*	9.7	0-52	[12,42,56]
Phoda	r	0.9	14.1	*a*	14.1	0-100	[34]
BAT Back	α	0.95	8.6	*c*	8.6	0-60	[27]
Pain symptoms (BPI)							
highest	r	0.96	0.8	*n*	30%	0-10	[50,53]
lowest	r	0.78	2.8	*n*	30%	0-10	[50,53]
average	r	0.86	1.7	*n*	30%	0-10	[50,53]
current	r	0.93	1.4	*n*	30%	0-10	[50,53]
Physical functioning							
PDI	α	0,88	9.7	*c*	24.2	0-70	[15,41,63]
QBPDS	α	0,94	10.3	*n*	30%	0-100	[13,50,55]
Emotional functioning							
HADS-D	α	0.83	3.6	*n*	8	0-21	[24]
HADS-A	α	0.85	3.7	*n*	8	0-21	[24]

Note. Rel. type: r, retest reliability, α, internal consistency. RCI, value of reliable change index. CSC criterion, criterion type according to n, normative, c, Jacobson criterion c, a, Jacobson criterion a. CSC cut point, scale point used to determine a clinically significant change.

Table 4. Meta-analytical results of patients in the exposure (EXP) and cognitive behavioral therapy (CBT) condition

	EXP condition			**CBT condition**				
	Psycho-edu. (1-4)	Exposure (5-10)	FU	Psycho-edu. (1-3)	Behav. elements (4-6)	Cog. elements (7-10)	Combi-nation (4-10)	FU
Symptoms								
Pain intensity	.24	.24	.70	.35	.49	.34	.55	.06
(now)	.33	.06	.44	.07	.09	.34	.41	.05
Pain intensity (av)	.13	**≤.05**	.22	.14	.43	.09	.47	.05
Pain perception	.06	.07	.24	.62	.23	.23	.31	**≤.05**
Disability	.19	.06	.07	.32	.47	.74	.60	**≤.05**
Expectation	.06	**≤.05**	.15	.73	.50	.18	.43	.17
Harmfulness								
Treatment process								
Self-efficacy	.75	**≤.05**	.26	.63	.23	.35	.12	.34
Positive thoughts	.90	.43	.17	.40	.57	.14	.22	.50
Acceptance	.86	**≤.05**	.15	.59	.66	.15	.88	.55
Exposition	.70	.24	**≤.05**	.75	.73	.71	.23	.99
Cognitive anxiety	.86	.08	.26	.74	.48	.15	.76	.16
Catastrophizing	.86	.09	.51	.53	.56	.42	.33	.07
Body confidence	.84	**≤.05**	.15	.80	.74	.31	.47	.46

Note. Individual p-values were combined by Single-Case-Meta-Analysis (SCMA) using the Edgington's additive approach.

Table 5. Number (percent) of participants in the exposure (EXP) condition with reliable and/or clinically significant change

	Pre M (SD)	Post M (SD)	RCI (%)	CSC (%)	FU M (SD)	RCI (%)	CSC (%)
Fear-avoidance							
PASS							
PCS	53.2 (6.2)	32.7 (14.1)	1 (16.7)	3 (66.7)	30.3 (17)	1 (16.7)	3 (66.7)
Phoda	22.8 (7.1)	16.3 (7.3)	-	2 (33.3)	19.5 (8.4)	-	1 (16.7)
BAT Back	50.7 (8.1)	41.6 (23.4)	1 (16.7)	1 (16.7)	45.5 (23.4)	1 (16.7)	1 (16.7)
	26.7 (9.2)	24.5 (8.6)	-	2 (33.3)	32.7 (11.5)	1 (16.7)	1 (16.7)
Pain (BPI)							
highest	7.3 (2)	7.3 (2.3)	-	2 (33.3)	5 (2.2)	2 (16.7)	1 (16.7)
lowest	3 (1.7)	2.5 (1.5)	-	-	7.2 (1.6)	-	-
average	5.2 (1.2)	4.8 (1.9)	1 (16.7)	2 (33.3)	3.3 (2.4)	-	-
current	4.3 (1.9)	4.8 (2)	-	-	5.3 (1.6)	-	-
Physical functioning							
PDI	30 (7.3)	27.5 (13.3)	-	2 (33.3)	32 (12.2)	-	1 (16.7)
QBPDS	47.5 (8.6)	37.3 (11.9)	-	2 (33.3)	36.5 (10.4)	-	3 (50)
Emotional functioning							
HADS-D	11.5 (3.9)	7.2 (3.1)	-	2 (33.3)	9 (2.5)	1 (16.7)	-
HADS-A	10.3 (3.4)	6.5 (4)	-	2 (33.3)	8.5 (3.7)	-	1 (16.7)
Cortisol							
Δcort	-1.0 (0.5)	-0.4 (0.5)	-	-	-0.3 (1.3)	-	-
Slope	-0.03(0.01)	-0.02(0.02)	-	-	-0.01(0.02)	-	-
Alpha-amylase							
Δaa	-24.6(58.4)	-17.6(64.9)	-	-	-5.8(42.7)	-	-
slope	-0.5 (0.7)	0.3 (0.5)	-	-	-0.2 (0.6)	-	-
Hair cortisol	12.3 (14.0) n=5	13.5 (5.2) n=4	-	-	15.4 (15.7) n=3	-	-

Table 6. Number (percent) of participants in the cognitive behavioral therapy (CBT) condition with reliable and/or clinically significant change

	Pre M (SD)	Post M (SD)	RCI (%)	CSC (%)	FU M (SD)	RCI (%)	CSC (%)
Fear-avoidance							
PASS							
PCS	47.5 (17.7)	41.8 (17.3)	-	1 (16.7)	41 (22.6)	-	1 (16.7)
Phoda	30.5 (8.1)	24.5 (8.6)	-	1 (16.7)	26 (12.9)	-	1 (16.7)
BAT Back	51.6 (4)	52 (7.7)	-	-	48.2 (9.5)	1 (16.7)	-
	23 (4)	29.3 (14.5)	-	1 (16.7)	27.7 (6.9)	-	-
Pain (BPI)							
highest	7.7 (1.5)	8 (1.4)	1 (16.7)	-	3.8 (2.3)	2 (33.3)	-
lowest	2.3 (2.1)	2.5 (2.3)	-	-	8.2 (1.2)	-	-
average	5.5 (1.4)	4.8 (1.6)	-	2 (33.3)	1.8 (1.9)	-	1 (16.7)
current	4.7 (2.1)	3.5 (1.9)	1 (16.7)	1 (16.7)	4.7 (1.4)	-	3 (50)
Physical functioning							
PDI	32.7 (13.3)	30.3 (9.2)	1 (16.7)	-	31.5 (12.9)	1 (16.7)	-
QBPDS	49.3 (12.6)	47.3 (10.7)	2 (33.3)	-	51 (8.7)	1 (16.7)	-
Emotional functioning							
HADS-D	11.5 (2.6)	9.3 (3.3)	2 (33.3)	-	8.8 (3.6)	2 (33.3)	1 (16.7)
HADS-A	10.3 (4.8)	10.2 (4.8)	-	-	8.5 (5.8)	-	1 (16.7)
Cortisol							
Δcort	-0.1 (0.3)	-1.8 (1.4)	-	-	-0.4 (0.8)	-	-
Slope	-0.01(0.02)	-0.03(0.02)	-	-	-0.02(0.01)	-	-
Alpha-amylase							
Δaa	-21.5(35.9)	-7.7 (17.8)	-	-	-15.1(27.1)	-	-
slope	0.7 (1.2)	-0.2 (0.6)	-	-	-0.7 (2.1)	-	-
Hair cortisol	4.2 (1.4) n=5	4.6 (4.1) n=4	-	-	10.2 (8.7) n=3	-	-

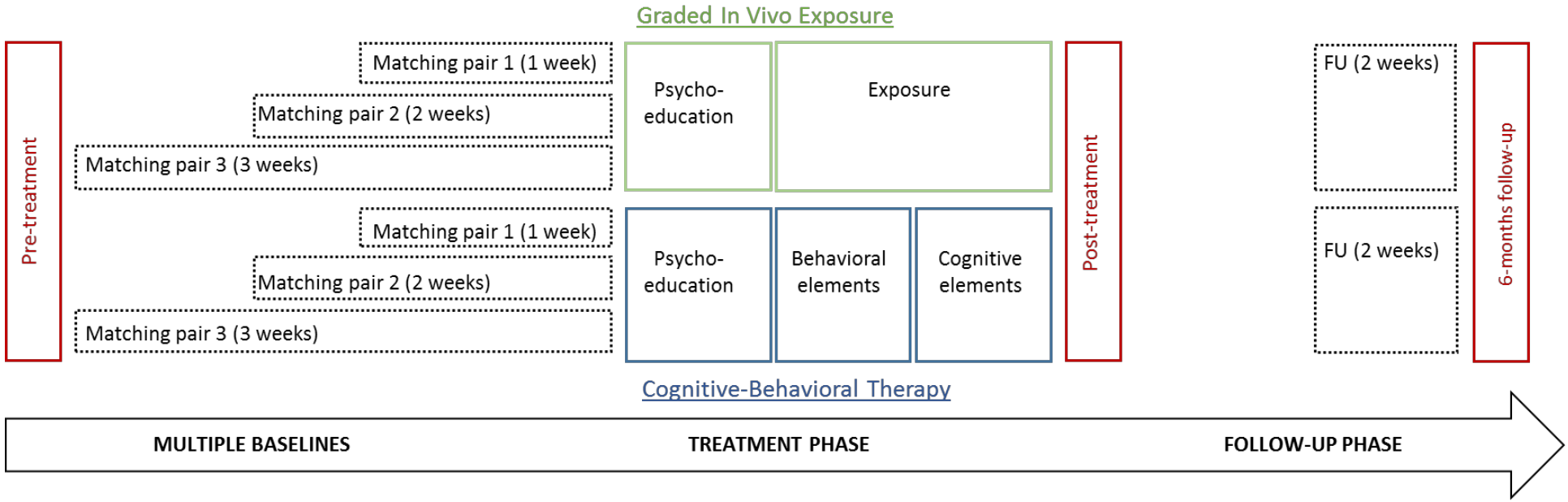

Figure 1. Single-case experimental multiple baseline design.

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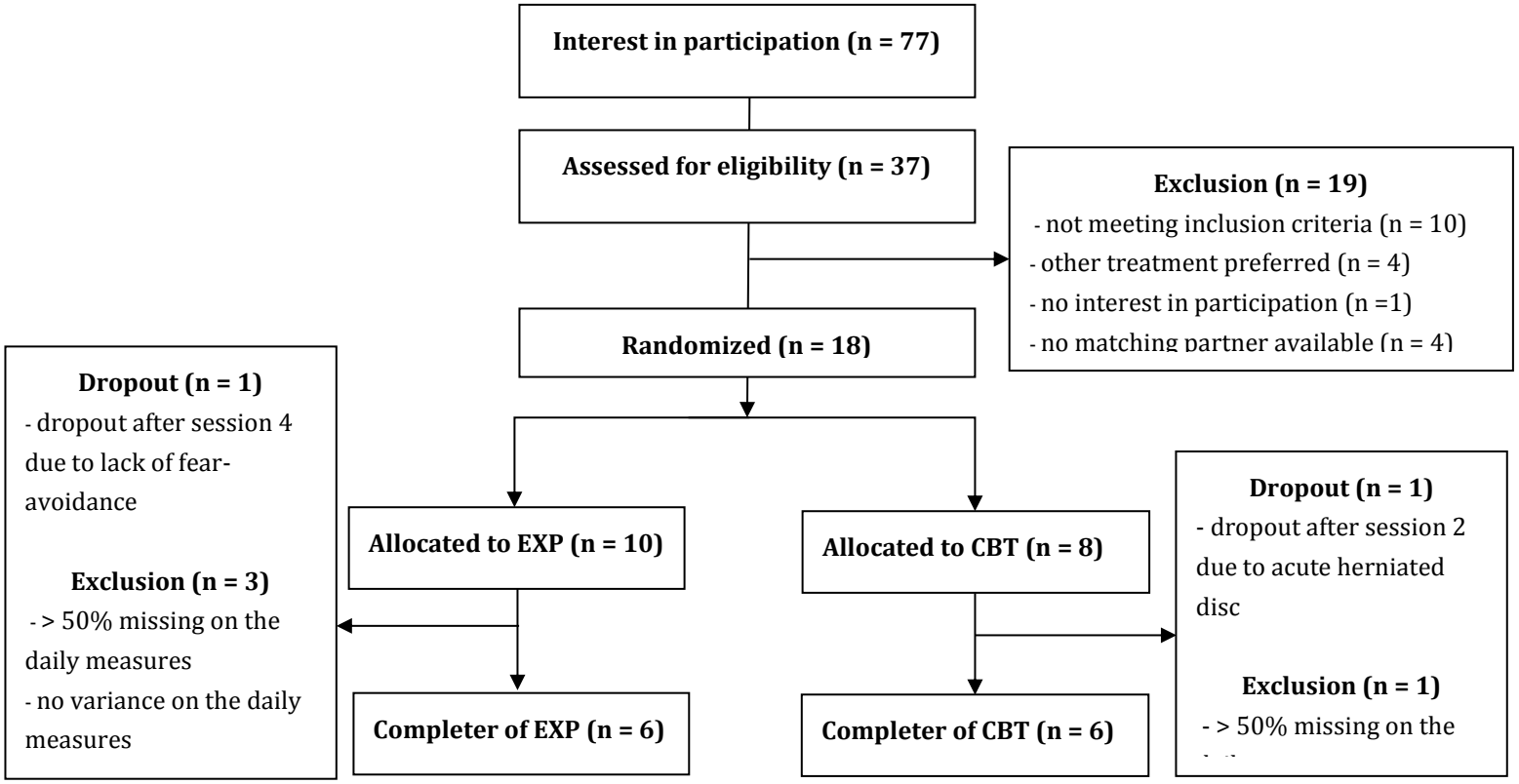

Figure 2. Flow chart of study inclusion procedure.

Session	EXP	CBT
	I. Psycho-education	**I. Psycho-education**
1	Anamnesis	Anamnesis
2	Biopsychosocial model	Biopsychosocial model
3	Fear avoidance model	Goal setting
4	Fear hierarchy	---
	II. Exposures	**II. Behavioral elements**
4	---	Graded activity I
5	Exposure 1	Progressive relaxation
6	Exposure 2	Graded activity II
		III. Cognitive elements
7	Exposure 3	Attention shifting
8	Exposure 4	Identification and reconstruction
9	Exposure 5	of dysfunctional thoughts
10	Completion	Completion

Figure 3. Overview on treatment sessions.

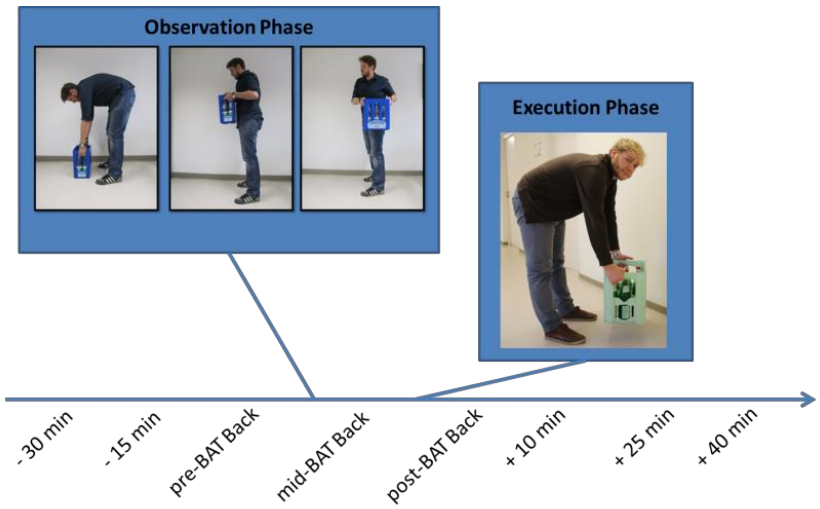

Figure 4. Collection of salvia samples during the Behavioral Avoidance Test (BAT Back) at pre-treatment, post-treatment, and 6-months follow-up. Study participants first observed the investigator performing three isolated sequences of movements (bending forward, lifting a water crate, and rotating). Then, participants were instructed to repeatedly lift the water crate themselves (no more than ten times).

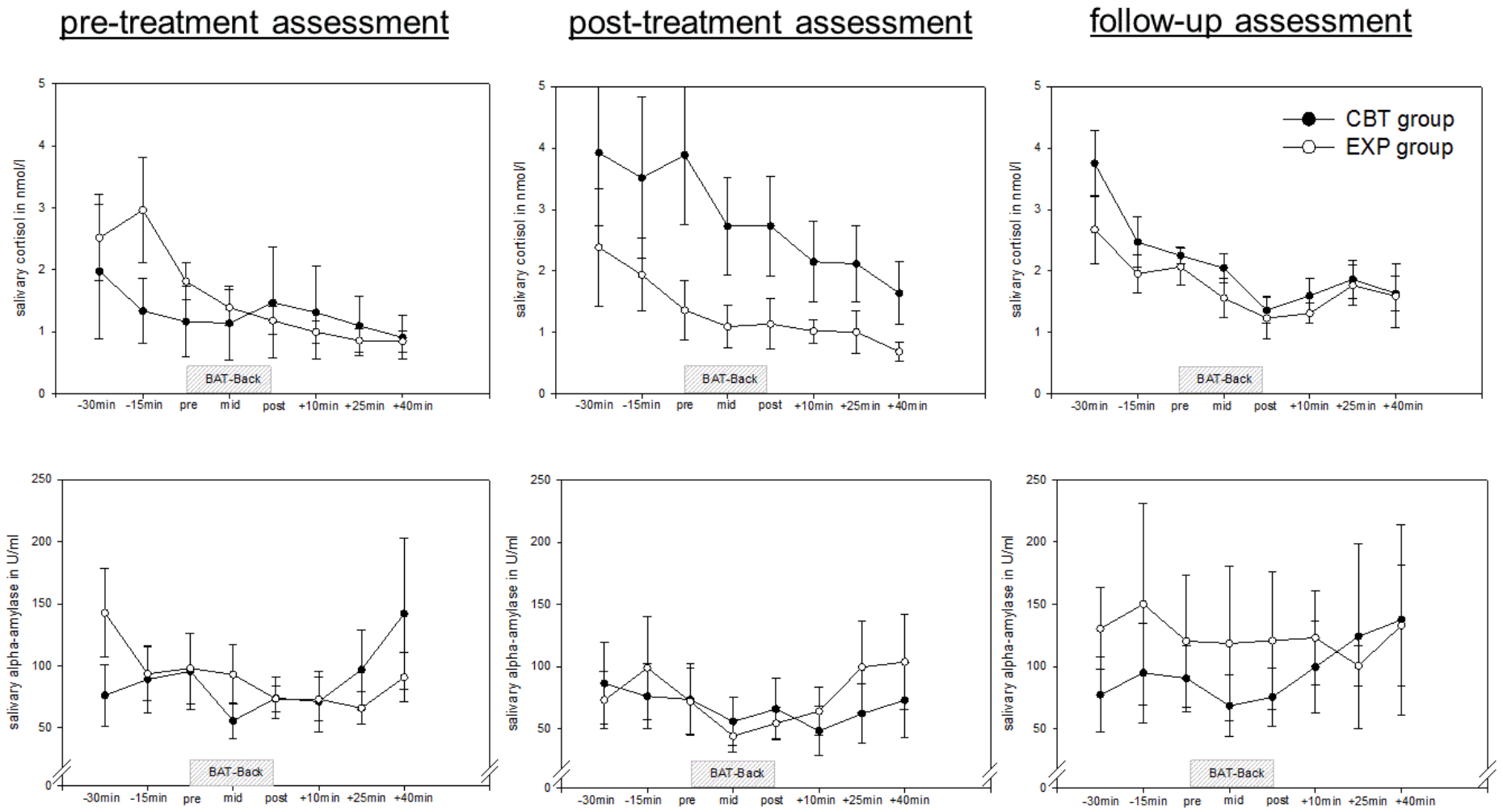

Figure 5. Mean values and standard errors of salivary cortisol (reflecting HPA axis activity; top 3 graphs) and salivary alpha-amylase (reflecting ANS activity; bottom 3 graphs) of the participants in the cognitive behavioral therapy (CBT) condition and in the exposure (EXP) condition during the Behavioral Avoidance Test (BAT) at pre-treatment, post-treatment and 6-months follow-up.

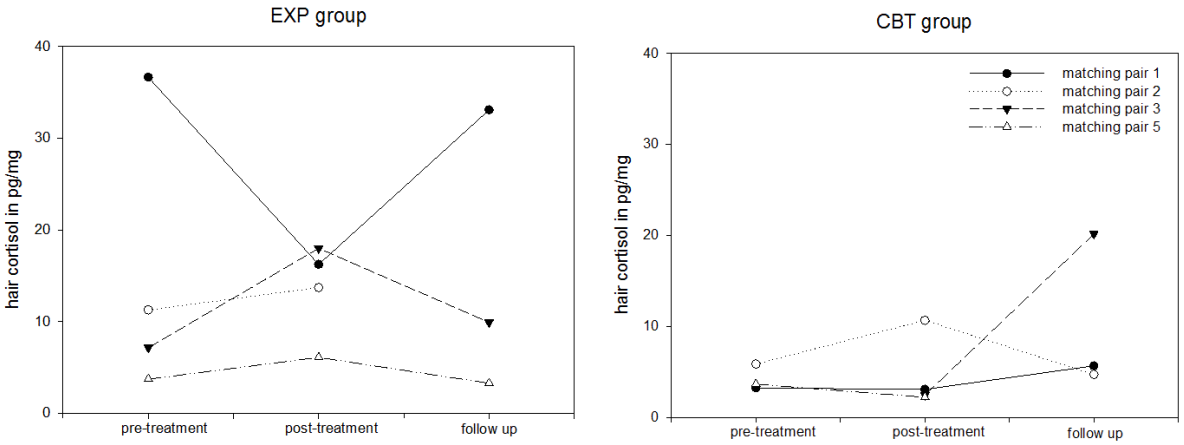

Figure 6. Hair cortisol levels of matching pairs 1, 2, 3, and 5 in the cognitive behavioral therapy (CBT) condition and in the exposure (EXP) condition at pre-treatment, post-treatment and 6-months follow-up.

Appendix C: Studie III

Schemer, L., Körfer, K., & Glombiewski, J.A. (submitted). Performing exposures to pain, but how? Testing therapeutic instructions in an experimental design. Manuscript submitted for publication in *The Journal of Pain*.

Abstract

Exposure therapy is an effective treatment for individuals with chronic pain and high levels of fear-avoidance. However, competing theories exist regarding underlying mechanisms. The habituation model suggests that therapists should focus on fear reduction. The inhibitory learning approach suggests that therapists should maximally violate negative expectancies. The goal of this study was to generate recommendations for clinical exposure techniques by comparing both therapeutic strategies in a mixed 3x2 experimental design with the between-group factor instruction (habituation, expectation violation, control) and the within-group factor time (pretest, posttest). Nociceptive thermal pain was induced to female students (N=112). Both instructions improved cognitive pain coping. Only the expectation violation instruction increased pain tolerance. Similarly, only the expectation violation instructions lead to specific psychophysiological changes, characterized by a significantly higher initial increase and subsequent decrease in the skin conductance level throughout three exposure practice trials. In contrast to predictions of the habituation model, these psychophysiological changes did not mediate exposure effects. Our results highlight the potential of testing concrete expectancies during exposures instead of focusing on the reduction of fear. Future research needs to translate our findings into clinical practice.

Introduction

Exposure therapy is an effective treatment for individuals with chronic pain and high levels of fear and avoidance[2]. During treatment, patients are guided to formulate an individualized fear-avoidance model including pain, pain cognitions, and avoidance. This circular model serves as a basis for explaining the therapeutic rational. By means of the Photo Series of Daily Actives, patients develop an individual fear hierarchy. Based on the fear hierarchy, activities and movements are selected for the subsequent exposure sessions. The exposure treatment manual recommends two therapeutic strategies during the exposure sessions[44]: (a) in vivo exposure sessions target at changing the emotional response, during which emotional response is monitored (e.g. distress on a scale from 0 to 10) until distress significantly declines; and (b) behavioral ex-

periments aim to violate expectations (e.g. "If I lift a water crate, my spine will be damaged") during which perceived probability of the predicted harm is monitored throughout the behavioral experiment. Although the effectiveness of exposure therapy for chronic pain is well supported[27,28,46], isolated components of the manual have not been evaluated.

Both therapeutic strategies are justified by competing theories regarding mechanisms of change of general exposure-based interventions. The habituation model[15,38] proposes that changes in psychophysiological activation are necessary for successful learning. Initial fear activation (IFA), characterized by increased physiological arousal and self-reported fear, provides an opportunity for corrective learning through integration of incompatible information. Within-session habituation (WSH) describes fear reduction during prolonged exposure to feared stimuli. Between-session habituation (BSH) describes the decline in peak magnitude of fear across exposure sessions. The habituation model suggests that therapists should focus on fear reduction during exposure sessions to enhance treatment effects. In contrast, the inhibitory learning model[9,10] suggests that exposure experiences establish a new CS-no US association, which competes with the original CS-US association. Neuroimaging research[32] suggests that this occurs as the prefrontal cortex exerts inhibitory control over the neurobiological fear system. Moreover, sustained fear, rather than fear reduction, is thought to facilitate new learning. This theory suggests that to improve exposure efficacy, therapists should design exposures to maximally violate patients' negative expectancies.

Previous studies have investigated the assumptions of both models. In contrast to the predictions of the habituation model, neither IFA nor WSH affected outcomes among students scoring high on agoraphobia[3]. While BSH influenced post-treatment outcome, this effect disappeared at 2-week follow-up. Similarly, sustained fear and emotional variability throughout the exposures, rather than habituation, facilitated reduction of fear among individuals fearful of public speaking[11]. In one experiment[22], spider-fearful individuals were instructed to verbally express their emotional response together with worst possible outcome (e.g. "I feel anxious that the disgusting tarantula will jump on me") during exposure to a spider. Consistent with the inhibitory learning model, this instruction was associated with reduced skin conductance level (SCL) at 1-week follow-up compared to the other groups (appraisal, distraction, exposure alone). Thus, empirical results seem to support the predictions of the inhibitory learning model rather than the habituation model. However, no study has yet compared these models in the context of pain-related fear.

The goal of this study was to generate recommendations for clinical exposure techniques by experimentally comparing both therapeutic strategies. Consistent with the assumptions from

the inhibitory learning theory, we expected the focus on negative expectancies to lead to greater improvements compared to the focus on fear reduction.

Method

Participants

An a priori power analysis was performed with G*Power 3.1.2. using expected effect-size of .3, alpha criterion of .05, test power of .90, 3 experimental groups, 2 repeated measures, and expected correlation of .5 among repeated measurements. The power analysis indicated that a sample of 111 participants was needed to detect effects. We expected an effect size of .3 because treatment effects of psychological interventions usually range from d = .2 - .5.[33].

Participants were students at the Philipps-University Marburg recruited through announcements and e-mails. Students received either course credit or monetary reimbursement for their participation. Exclusion criteria were male gender, chronic and acute pain conditions, Raynaud's disease, high blood pressure, neuropathy, coronary diseases, diabetes, current alcohol, drug use, or pain medication (last 24 hours), as well as insufficient knowledge of German language. We excluded male participants for several reasons. First, there is evidence that men and women differ in their pain sensitivity[14]; thus, the inclusion of both genders could have added confounding variables to our experiment and thereby reduced internal validity. In addition, several authors have recommended the study of female participants due to the higher prevalence of pain conditions among women[18]. Since we had three different experimenters (2 = female, 1 = male), we aimed to reduce cross-gender interactions by including only female participants[21].

One hundred eighty-five participants completed the online questionnaires. One hundred thirty-nine participants completed the experiment and were randomized to one of three experimental conditions following a predetermined and computer-generated schedule. It was ensured that the three experimenters conducted a proportionally equal number of trials in each group. In analyses of pain-related measures, seven participants were identified as univariate and/or multivariate outliers (see Data Preparation) and were excluded from subsequent analyses (N=112). For analyses of physiological data, eight additional participants were excluded due to missing values (>10%) and/or extreme values (N=104) (see Data Preparation). Participants' ages ranged from 18 to 38 years (mean = 23.36, SD = 4.0). Participants' courses of study included 26 different disciplines, such as psychology (13.4%), medicine (9.8%), and biology (8.0%).

The study procedure was approved by the institutional ethics committee of the psychology department at the Philipps-University and was registered at ClinicalTrials.gov (NCT03146832). All participants gave written informed consent to participate and were informed that they could withdraw from the experiment without any consequences. They were blinded for their experi-

mental condition. At the end of the experiment, participants were debriefed, the purpose of the initial threat manipulation was explained, and participants had the opportunity to ask questions about the experiment.

Study Design and Procedure

A mixed between-within design was employed. The between-group factor was the instruction condition (habituation, expectation violation, control). The within-group factor was time point (pretest, posttest). The study procedure was as follows: a) One week prior to the experiment, participants filled out an online survey. Several self-report questionnaires were used to assess possible factors that can impact pain experience and to ensure comparability of experimental groups. b) The experiment took place in at the department of clinical psychology and psychotherapy at the Philipps-University Marburg. The entire experiment was conducted on the same day. The threat manipulation was performed by asking participants to sign a sheet that falsely informed them about potential negative side effects of the experimental heat stimuli. The threat value of these side effects was further increased by providing participants with false feedback on the thickness of their skin. c) Pain was operationalized using heat induced by a thermode. In the pretest trial, the initial experience with the heat stimulus was used to establish a baseline value of pain tolerance for each participant. d) Participants were randomized to one of the three instruction conditions, including the two different coping strategies and the control instructions. In the following three practice trials, they were asked to practice the strategy to which they had been randomized. Subsequently, they rated the credibility of the instructions they had been given. e) In the final posttest trial, participants were instructed to use the strategy they had learned to endure the heat stimulus as long as possible. Finally, participants completed some final assessments.

Online Survey

Participants answered the following six self-report questionnaires at home one week prior to the experiment. This procedure allowed us to control for possible group differences in pain processing prior to our experimental manipulation. The Pain Sensitivity Questionnaire (PSQ)[40] measured the experience of pain during potentially painful situations. Respondents rate 17 daily life situations (e.g. “Imagine you grazed your knee falling off your bicycle”) for pain intensity on an 11-point scale (0= not at all painful, 10 = most severe pain imaginable). Higher mean scores indicate higher pain sensitivity. The Pain Vigilance and Attention Questionnaire (PVAQ)[29] assessed attention processes during the sensation of pain. Respondents rate 16 items (e.g. “I pay

close attention to my pain") for frequency on a 6-point scale (0 = never, 5 = always). Higher sum scores (range 0 – 80) indicate higher tendency to focus attention on pain. The Pain Catastrophizing Scale (PCS)[31,42] assessed pain catastrophizing thoughts. Respondents rate 13 items (e.g. "I worry all the time about whether the pain will end") for frequency on a 5-point scale (0 = not at all, 4 = all the time). Higher sum scores (range 0 – 52) indicate higher levels of catastrophizing. The Pain Anxiety Symptom Scale (PASS)[30,45] assessed pain-related anxiety. Respondents rate 20 items (e.g. "I worry when I am in pain") for frequency on a 5-point scale (0 = never, 4 = always). Higher sum scores (range 0 – 100) indicate higher pain-related anxiety. The Questionnaire for the Assessment of Pain Processing (Fragebogen zur Erfassung der Schmerzverarbeitung, FESV)[17] measured cognitive as well as behavioral pain coping strategies. Respondents rate 24 items (e.g. "When I am in pain, I know several possible ways to handle it") on a 6-point scale (1 = not at all true, 6 = completely true). Higher sum scores (range 24 – 144) indicate stronger pain coping strategies. The Beck Depression Inventory (BDI-FS)[4,23] was used to screen for depressive symptoms. This measure includes 7 multiple choice questions in which respondents choose the item that best describes their emotional state, on a 4-point scale (e.g. 0 = "I do not feel sad."; 3 = "I am so sad and unhappy that I can't stand it."). Higher sum scores (range 0 – 21) indicate higher levels of depression.

Manipulation of Threat

Exposure therapy is a tailored treatment approach for patients with elevated fear of negative health-related consequences. For an analogue, we needed to create a context in which fear of negative health-related outcomes was especially relevant to our study participants. For this purpose, we first conducted a pilot study (N = 18) to compared two threat manipulations inspired by previous studies[12,20]. In the first condition (threat of an uncertain situation), the experimenter pretended that the thermode device did not work properly (accompanied by odd noises from the device). In the second condition (threat of bodily harm), participants were falsely informed about possible negative side effects of the experimental heat stimulus. It was explained that, for insurance purposes, participants needed to sign a list of occasional short-term side effects (e.g. skin redness, allergic reactions) and rare short-term side effects (e.g. skin burns, loss of consciousness). In both conditions, most participants later rated the given information as considerably (threat of an uncertain situation: 44.4%; threat of bodily harm: 66.7%) or substantially (threat of an uncertain situation: 55.6%; threat of bodily harm: 22.2%) credible. However, a substantial percentage of participants in the first condition (threat of uncertain situation) did not anticipate negative consequences to themselves (55.5%). In contrast, the majority in the second condition (threat of bodily harm) indicated some concerns about experiencing negative side

effects themselves (66.7%). Thus, we chose the second, more explicit threat manipulation over the more ambiguous threat manipulation.

We altered the manipulation in the main experiment to further increase the threat value of these side effects. The experimenter explained that the ethics committee required measurement of the thickness of the skin prior to study participation in order to minimize the occurrence of possible side effects for people at risk. The experimenter used a forehead thermometer ("Hylogy Infrarot Stirnthermometer") to measure skin temperature (in Fahrenheit) on each arm, at the location where the thermode was later applied. The experimenter falsely explained that this was an indicator for skin thickness. The experimenter commented on the measurement by stating, "Your skin thickness is right on the edge of higher risk. However, since you are already here, I suggest we continue with the study anyhow. Just tell me if you experience any trouble."

Threat Manipulation Check

As a manipulation check, participants were asked to rate three items on a 4-point scale (0 = not at all; 3 = highly) at the end of the experiment. These items asked about the credibility of the information sheet on potential negative side- effects, the credibility of the measurement of the skin thickness, and the participant's level of concern about the occurrence of these side effects.

Stimulus Material

Heat stimuli between 32°C and 52°C were delivered to the forearm via a 3 x 3 cm peltier-based thermode (TSA II: Thermal Sensory Anaylzer, Medoc Ltd, Israel) for the experimental induction of pain. Heat stimuli were applied in three trials (pretest, practice, posttest). In the pretest and posttest trials, the thermode was applied to the dominant arm. The thermal stimulus started at 32°C and rose with a slope of .5°C per second. Participants were instructed to tolerate the heat stimulus as long as possible. When the maximum temperature was reached, participants could stop the stimulus by telling the experimenter. The software then automatically returned the thermode to the baseline temperature of 32°C. Trial durations ranged from 25 to 42 seconds per trail. The practice trial consisted of three short trials. The thermode was applied to the non-dominant arm to avoid changes in sensitivity to heat stimuli. The thermal stimulus again started at 32°C but rose with a slope of 1°C per second to the individual's maximum pain tolerance point from the pretest. The thermode stayed at that temperature without the possibility of ending the stimulus for one second. Participants were asked to practice the pain-coping strategy for which they had received instructions during the three practice trials.

Instructional Sets

The instructions were presented via loudspeakers. Both experimental instructions[1] as well as the control instructions[24] have been used in previous studies. All instructions were approximately the same length (~ 400 words). The experimental conditions (habituation, expectation violation) followed a similar structure: the instructions started with a definition of exposure therapy. This definition introduced exposure therapy as a form of treatment approach for overcoming anxiety problems. It was explained that for this purpose people gradually confront feared situations. Next, the respective therapy rationale was explained and illustrated using the example of fear of giving a blood sample. Finally, participants were provided with concrete instructions about how to practice this new strategy. In between the three practice trials, participants answered questions designed to prompt them to focus on the respective strategy. The instructions can be found in the Supplementary Materials A.1-3.

Habituation

The habituation instructions focused on changes in the fear response during exposure sessions. It was explained that level of anxiety gradually decreases, or habituates, each time someone faces a feared situation. For example, the fear of an individual who is afraid of giving a blood sample will gradually decrease during repeated exposures at a blood donation center. Participants were then instructed to observe their own level of fear during the three practice trials with the thermode. The experimenter asked participants to indicate their level of distress on an 11-point scale (0= neutral, 10 = very high) between and after the three practice trials. After the practice trials, participants were instructed to consider the course of their level of physical responses during the test trials.

Expectation Violation

The expectation violation instructions focused on the violation of negative expectancies during exposure sessions. It was explained that exposure exercises help individuals to test their predictions about negative outcomes through their own exposure experiences. For example, someone afraid of giving blood samples can learn via exposures at a blood donation center that the loss of blood does not cause any dangerous health-related consequences. The experimenter encouraged participants to formulate concrete concerns regarding the practice trials with the thermode. Before the practice trails, participants were asked to indicate the likelihood of their concerns occurring on an 11-point scale (0= not likely, 10 = very likely). After the practice trials, they were

instructed to evaluate their concerns via standardized questions (e.g. “Did what you were most worried about occur?”; “How do you know?”; “What did you learn?”). Participants were encouraged to consider their experiences during the test trial with the thermode when answering these questions.

Control Group

Participants in the control group were not provided with information about exposure therapy. Instead, they listened to a newspaper article describing the daily work in a botanical garden. The experimenter then asked participants to describe the most interesting aspect of the article. Before the practice trials, participants were asked to rate is the likelihood that they would seek further information about botanical gardens on an 11-point scale (0= not likely, 10 = very likely). After the practice trials, participants were asked some further questions about the newspaper article (e.g. “Did you find the newspaper article interesting?”; “Why?”; “Did your likelihood of reading more about botanical gardens change?”). Participants had to give this rating to ensure the comparability with the two experimental groups. However, they were not instructed to engage in any cognitive exercise during the heat stimulation. Accordingly, the control condition was not meant to distract them and, therefore, did not serve as a distraction instruction. The control instructions did not provide participants with any coping strategies for pain.

Adherence to Instructions and Credibility Ratings

Participants in the two experimental conditions (habituation, expectation violation) were asked to complete the Credibility Expectancy Questionnaire (CEQ)[13]. The two subscale of this questionnaire measure treatment expectancy and rationale credibility. Item formulations were adapted to the experimental instructions. Participants had to rate 3 items measuring cognitively-based credibility (e.g. “How confident would you be in recommending this strategy to a friend in a similar situation?”) as well as 3 items measuring affectively-based expectancy (e.g. “How much do you feel that this strategy will help you to cope with the pain stimulus?”). The questionnaire used two different scales, a 9-point scale (1 = not at all; 9 = very much) as well as a percentage rating scale (0% = not at all; 100% = very much), which was transformed to a common 9-point scale. Higher sum scores (range 3 – 27) indicate higher credibility and/or more positive treatment expectancies. At the end of the experiment, participants were asked to indicate the percentage of time they adhered to the instructions provided (0% = not at all; 100% = all the time). They were also asked to indicate whether they found the instructions to be helpful on a dichotomous scale (yes/no).

Outcome Measures

Pain Symptoms

We defined pain tolerance as a primary outcome, which was determined by the temperature at which the participant stopped the heat stimulus at the pre- and posttest. Additionally, participants were asked to rate pain intensity on an 11-point scale (0 = no pain; 10 = worst imaginable pain). They were also asked to describe the pain quality on an 11-point scale (0 = bearable; 10 = unbearable).

Cognitive Pain Coping

After the posttest, participants were asked to complete three questionnaires (the PCS[31,42], PASS[30,45], and FESV[17]) as additional secondary measures of cognitive pain coping. The instructions for the questionnaires were adapted to the experimental setting. Participants were asked to answer all questions in reference to the posttest trial with the thermode. For this purpose, the escape/avoidance subscale of the PASS needed to be adapted. For example, the item "as soon as pain comes on, I take medication to reduce it" was changed to "As soon as pain comes on, I try to somehow reduce it." For the FESV, we only used the subscale for cognitive pain-coping, since the subscale for behavioral pain-coping (e.g. "When I am in pain, I watch TV or videos") was not relevant to the experimental setting. The scale type of the three questionnaires was transformed to a unified 5-point scale (0 = not at all; 4 = always).

Psychophysiological Measurement

We assessed psychophysiological indicators as further secondary outcome in order to examine components of the habituation model. IFA was defined as the initial peak in the psychophysiological response during the first practice trial. WSH was defined as the average change in the psychophysiological response during each of the three practice trails. BSH was defined as the overall change in the peak magnitude of the psychophysiological response from the first to the last practice trail. Psychophysiological signals were recorded using a 10-channel equipped encoder (FlexComp Infiniti; Thought Technology, Montreal, Canada). We used two indicators for the psychophysiological assessment. Interbeat-Interval (IBI), an indicator of heart rate (HR), was measured by continuously recording blood-volume pulse by a photoplethysmograph (SA90309M BVP-/HR) on the tip of the non-dominant thumb. The following formula was used to transform IBI into HR: HR = 60 x 1000/IBI[8]. HR deceleration is considered to indicate attentional

processing towards negative affective states[6,7]. Skin conductance level (SCL), representing the level of moisture exuded by the eccrine sweat glad, was recorded continuously using finger-cuff sensors (SA9309M Skin Conductance Flex/Pro; Input range 0 - 30 µs) placed on the non-dominant index- and middle-finger[16]. As HR is influenced by various other factors in addition to autonomic fear-based arousal, SCL is regarded as a more sensitive and reliable indicator of arousal[5,26].

Data Analyses

Data Preparation

Analyses were conducted using the Statistical Package for Social Sciences (SPSS, Windows v.22: SPSS Inc, Chicago, IL). Prior to the main analyses, the data were checked for univariate (z-score in excess of +/- 3.29) and multivariate outliers (Mahalanobis-Distance: χ^2 (9) = 27.877, p < .001). Seven participants were excluded from subsequent analyses due to either extreme values and/or an unusual response pattern. To ensure the comparability of the three experimental groups, we compared baseline characteristics across experimental conditions using multivariate analyses of variance (MANOVA). The experimental conditions were compared using a series of multivariate and univariate analyses of variance (MANOVA, ANOVA) for continuous variables and chi-square analyses for categorical variables. The manipulation check for the credibility ratings was evaluated using an independent samples t-test. Distress ratings (in the habituation condition) and expectations ratings (in the expectation violation condition) were analyzed by comparing means in the first and last practice trial using a dependent samples t-test. Moreover, change scores were correlated with the outcome measures.

For the preparation of the physiological data, recordings were checked for mistakes and oversights. Both SCL and HR signals were resampled at 32 Hz per seconds. Artifacts in the physiological signal were rejected, and value averages and maximum values were calculated using a custom LabVIEW program. Artifacts were defined as outliers deviating more than 2.5 standard deviations from the trial's mean. Eight participants were excluded from further analyses of psychophysiological data due to either missing values (>10%) and/or extreme values. To achieve comparability, exposure trials were split into tertiles of 8-second segments[3]. Only the first and last 8-second segments of each trial were of interest for calculating IFA and WSH. Indices of IFA, WSH, and BSH were calculated for SCL and HR. IFA was operationalized as peak in the first 8 seconds of the first practice trial. WSH was operationalized as the difference between the means during the first 8 seconds and the last 8 seconds of each trial, averaged across the three practice

trials. BSH was operationalized as the difference between the peaks from the first to the last practice trial.

Main Analyses

Data analyses were performed in several sequential steps. First, we performed a multivariate analysis of covariance (MANCOVA) to assess differential effects of instruction condition on the outcome measures (N=112). The assumptions for this test (normal distribution, homogeneity of covariance matrices) were sufficiently fulfilled. For the main analyses, instruction condition was entered as an independent variable, pretest data was entered as covariates, and posttest data was entered as dependent variables. We also controlled for the information gathered via the threat manipulation check. Since we investigated exposure as a tailored treatment approach, we assumed that instructions would be more powerful when the threat manipulation was more successful. Subsequent univariate analyses of covariance (ANCOVA) and post hoc pairwise analyses were performed to identify the nature of differences between the three experimental conditions (Bonferroni adjustment for multiple testing). In addition, we calculated effect sizes (Cohen's d).

Second, differential effects of instruction on psychophysiological measures were assessed using separate MANCOVAs for IFA, WSH, and BSH (N=104). IFA, WSH, and BSH were tested in separate MANCOVAs because they are assumed to be distinct psychophysiological processes according to the habituation model. Instruction condition was entered as an independent variable. Physiological baseline scores, relevant pretest scores, and the threat manipulation check were entered as covariates. The two physiological measures (HR & SCL) were entered as dependent variables. Subsequently, we performed univariate analyses of covariance (ANCOVA) and post hoc pairwise analyses (Bonferroni adjusted for multiple testing). Only outcome measures (first MANCOVA) and physiological indices (second MANCOVA) that significantly differed across instruction conditions were included in the subsequent mediation analysis.

Third, the SPSS PROCESS Macro[37] was used to investigate the mediating effect of the physiological indices. As we were interested in the pairwise comparisons between the two instruction conditions (rather than the comparison between the effect of each condition and the overall effect), each pairwise comparison was probed in a single mediation model. Group was entered as the predictor and physiological indices were entered as mediators. Mediation analyses were conducted separately for each of the previously significant outcome measures. The indirect paths were estimated on basis of the collected data, and bootstrapping was used to check for

statistical significance. The standard error and a 95 %-confidence interval for indirect effects were estimated based on 5000 bootstraps taken from the original data[36].

Results

Baseline Characteristics

Means and standard deviations for the baseline questionnaires by instruction condition are shown in Table 1. Multivariate analyses indicated no significant differences among conditions on baseline questionnaire scores (Wilks' $\lambda = .53$, $F [14,206] = 1.556$, $p = .094$). Univariate ANOVAS revealed no significant differences among instruction conditions for depressive symptoms, pain sensitivity, pain vigilance, pain catastrophizing, and pain processing. For pain anxiety, however, there were significant differences among instruction conditions ($F [2,109] = 3.090$, $p = .05$). Post hoc pairwise analyses indicated that the expectation violation group had higher pain anxiety scores compared to the habituation group, although this comparison was only significant at the trend level ($p = .095$). The participants in the control condition had also higher pain anxiety scores compared to participants in the habituation condition, although this comparison did not reach significance ($p= .11$). To account for these preexisting differences, pain anxiety was entered as a covariate in subsequent analyses.

[Insert Table 1 around here]

Experimental Conditions

The average room temperature was about 20.8°, and did not differ across experimental groups ($F [2,109] = .853$, $p = .429$). The experimenters conducted a proportionally equal number of trials in each group ($\chi^2 (6) = 2.204$, $p = .9$). Thus, we concluded that the experimental conditions were equal across the three groups.

Threat-Manipulation Check

The majority of participants rated the information about possible negative side effects as either highly (38.4%) or substantially (52.7%) credible. Similarly, most participants rated the measurement of their skin thickness as either highly (43.8%) or substantially (36.6%) credible. The majority of participants indicated either considerable (29.5%) or some (59.8%) concerns that they might personally experience negative side effects. There was no significant difference

among experimental groups on any of these manipulation check measures (Wilks' λ = .939, F [6,214] = 1.144, p = .341). Thus, the threat manipulation appeared to be equally successful across experimental groups.

Adherence to Instructions and Credibility Check

Participants indicated that they had adhered to the instructions 70.13% (+/- 20.03%) of the time during trials with the thermode. Adherence did not differ across groups (t [74] = -.742, p = .46). In the expectation violation condition, there was a significant decrease in expectation ratings from the first to the last practice trial (t [37] = 10.692, p < .001). The expectation ratings for 92.1% of the participants decreased throughout the three practice trials. 78.8% reported to have a decrease in expectation ≥ 3 on an 11-point scale. Three participants (7.9%) indicated no change in their expectation. In the habituation condition, there was a significant decrease in the level of distress from the first to the last practice trial (t [37] = 2.094, p < .05). The level of distress decreased for 50% of the participants throughout the three practice trials. However, 26.3% of the participants reported no changes and 23.7% reported an increase in their level of distress. Neither change in expectation ratings nor change in distress ratings were significantly correlated with any outcome measure.

[Insert Figure 1 around here]

The two sets of instructions were rated as equally credible (t (74) = -.478, p = .634). Participants had higher treatment expectancy of the expectation violation instructions (M = 16.76, SD = 4.69) compared to the habituation instructions (M = 14.58, SD = 5.51), but this difference was not statistically significant (t (74) = -1.86, p = .067). After the experiment, more participants rated the expectation violation instructions as useful compared to the habituation instructions (87.8% vs. 71.1%), but the difference was not statistically significant (χ^2 (1) = 2.85, p = .091).

Results for Outcome Measures

There was a significant multivariate effect of instruction condition on the outcome measures (Wilks' λ = .785, F [12,190] = 1.991, p < .05, partial Eta^2 = .112), with significant group differences on pain tolerance (F [2,100] = 4.162, p < .05, partial Eta^2 = .077) and cognitive pain coping (F [2,100] = 6.543, p < .01, partial Eta^2 = .116). Post hoc pairwise analyses indicated that the expectation violation instructions were significantly more effective than the control instructions at increasing pain tolerance (p < .05, Cohen's d = .724), while the difference between the habituation condition and the control condition did not reach the level of significance (p = .288). How-

ever, the expectation violation condition did not significantly differ from the habituation condition with respect to pain tolerance ($p = .691$) (see Figure 1). The expectation violation instructions ($p < .01$, Cohen's $d = .873$) and the habituation instructions ($p < .05$, Cohen's $d = .606$) were both significantly more effective than the control instructions at increasing cognitive pain coping. Again, the expectation violation instructions did not significantly differ from the habituation instructions with respect to cognitive pain coping ($p = 1.0$) (see Figure 1).

Results for Physiological Measures

Multivariate analyses of IFA indicated a significant effect for instruction condition (Wilks' $\lambda = .898$, $F [4, 188] = 2.591$, $p < .05$, partial $Eta^2 = .052$), with a significant group difference in SCL ($F [2, 95] = 4.362$; $p < .05$, partial $Eta^2 = .084$). Post-hoc pairwise comparisons revealed a significant difference between the expectation violation and habituation groups ($p < .05$, Cohen's $d = .517$), as well as between the expectation violation group and the control group ($p < .05$, Cohen's $d = .555$), with a higher IFA in the expectation violation condition in each case. However, there was no significant difference between the habituation group and the control group ($p = .88$) (see Figure 1). No significant group differences were found for IFA measured by HR ($F [2, 95] = .484$, $p = .681$). Multivariate analyses of WSH indicated no significant effect of instruction condition (Wilks' $\lambda = .023$, $F [4, 188] = .55$, $p = .699$, partial $Eta^2 = .012$). Multivariate analyses of BSH indicated a significant effect for instruction condition (Wilks' $\lambda = .886$, $F [4, 188] = 2.923$, $p < .05$, partial $Eta^2 = .059$), with a significant group difference in SCL ($F [2, 95] = 5.773$, $p < .01$, partial $Eta^2 = .108$). Post-hoc pairwise comparisons revealed a significant difference between the expectation violation and habituation groups ($p < .01$, Cohen's $d = .685$), as well as between the expectation violation group and the control group ($p < .01$, Cohen's $d = .539$), with greater BSH in the expectation violation condition. However, no significant difference was found between the habituation group and the control group ($p = .674$) (see Figure 1). No significant differences between groups were found for BSH measured by HR ($F [2, 95] = .268$, $p = .765$).

[Insert Figure 1 around here]

Mediation Model

Analyses of SCL indicated a significant positive direct effect of the expectation violation instructions on IFA ($b = 2.63$, $SE = 1.18$, $p < .05$) and BSH ($b = .558$, $SE = .2647$, $p = < .05$) relative to the control instructions. However, we did not find indirect effects on cognitive pain coping through either IFA ($b = .003$, BCa CI [-.068, .493] or BSH ($b = -.129$, BCa CI [-.506, .086]. Similarly, we

found no indirect effects of instruction condition on pain tolerance either through IFA (b = .116, BCa CI [-.161, 5179] or BSH (b = .005, BCa CI [-.267, .422]. Nonetheless, the expectation violation instructions, relative to the control instructions, positively predicted cognitive pain coping (b = .557, SE = .164, p < .01), and there was a trend toward a similar predictive effect for pain tolerance (b = .571, SE = .312, p < .1). These positive direct effects are also reflected in significant total effects of instruction condition on cognitive pain coping (b = .535, SE = .164, p < .01) and pain tolerance (b = .735, SE = .31, p < .05). Thus, it appears that there was a distinct pattern of physiological activation in the expectation violation group. However, our results do not support the mediating effect of physiological changes on the outcome measures. All regression coefficients of interest are shown graphically in the Supplementary Materials A.4 Mediation Model.

Discussion

Summary of Main Findings

We compared two therapeutic strategies (habituation vs. expectation violation) as well as a control instruction during exposure to nociceptive thermal pain. Both therapeutic instructions improved cognitive pain coping, while only the expectation violation instruction increased pain tolerance. Similarly, the expectation violation instructions, but not the habituation instructions, led to changes in psychophysiological activation relative to the control group. This activation was characterized by a significantly higher increase in initial skin conductance level (SCL) and a subsequent decrease in SCL response across the three practice trials. However, this psychophysiological pattern was unrelated to changes in pain tolerance and cognitive pain coping. Overall, our results highlight the potential utility of testing specific negative expectancies rather than focusing on reduction of fear during exposure to pain-related fear.

Evaluation of Therapeutic Strategies

As hypothesized, only the expectation violation instructions led to an increase in pain tolerance compared to the control instruction. Both exposure instructions improved cognitive pain coping. Thus, our results provide experimental evidence for the general effectiveness of exposure therapy in the context of pain-related fear. In line with previous research, exposure experiences seem to affect cognitive pain coping not only by reducing fear-avoidance beliefs[28,46], perceived harmfulness of activities[27], and pain catastrophizing[27,28,46], but also by improving cognitive pain coping strategies. It remains unclear whether these cognitive changes are mechanisms of exposure therapy or whether they are simple correlates. Nevertheless, our results support the assumption that exposure experiences mainly alter cognitions - regardless of whether the therapeutic strat-

egy focuses on emotional or cognitive response[19]. The pronounced emphasis on cognitive change in the expectation violation instructions might explain the superiority of these instructions in improving cognitive pain coping, as well as the improvement in pain tolerance only in the expectation violation group. Thus, our results, in line with previous studies [22,41], highlight the benefit of focusing on cognitive change during exposure therapy. However, it should be noted that the length of the practice trials was standardized to ensure comparability among groups. Thus, participants in the habituation condition did not remain in the situation until their fear declined, as recommended by the habituation model[38]. This becomes especially evident looking at the distress ratings throughout the practice trials with only 50% of the participants reporting a decrease in their level of distress. As it is possible there was insufficient time for habituation to occur, our results must be interpreted with caution.

Conclusions on Mechanisms of Change

The expectation violation group showed a distinct psychophysiological response pattern, with significantly higher IFA measured by SCL compared to participants in the other groups. Moreover, participants in this group showed greater BSH in SCL. In other words, participants in the expectation violation group showed the greatest decrease in physiological arousal over the course of the trials. At first glance, these results seem to be in line with the habituation model, but several predictions of the model were not supported. Neither psychophysiological index supported the occurrence of WSH, thought to be an essential precursor for BSH. In line with previous studies[3,11,25], neither IFA nor BSH was significantly related to outcome measures. It is possible that the physiological changes could be better explained by cognitive inhibition of the neurobiological fear system. As predicted by the inhibitory learning model[10], this inhibitory response might be enhanced when cognitions were explicitly targeted during exposure sessions. However, this explanation remains purely hypothetical. On the other hand, change in expectation ratings throughout the practice trials were not correlated to outcome measures. This finding contradicts predictions of the inhibitory learning model.

While general arousal, indexed by SCL, declined across exposure trials, negative appraisal, indexed by HR, did not. This could be interpreted as a decrease in general arousal, with little change in negative affect. Thus, the nociceptive stimulus was still aversive (e.g. pain still hurts; indicated by HR) but it appeared to become less threatening (indicated by SCL). These results might support the emphasis on fear tolerance rather than fear reduction in the inhibitory learning model[9].

Strengths of the Study

While previous studies have investigated these exposure strategies in other fear-related conditions (e.g. social, agoraphobic, and specific fears), this study is the first to do so in the context of pain-related fear. Strengths of the study include use of a highly standardized thermal pain induction procedure, assessment of preexisting group differences in pain experience and/or pain coping, use of a threat manipulation that was tested in a pilot study and assessed via a manipulation check, use of an instructional set validated in a previous study, assessment of adherence to and credibility of instructions, and inclusion of a control group. We included various levels of measurement to operationalize pain symptoms (e.g. pain tolerance), cognitive pain coping (e.g. FESV, PCS), and psychophysiological responses (e.g. skin conductance). The present results highlight the potential of investigating isolated therapeutic strategies within standardized experimental situations for the refinement of clinical techniques.

Limitations

Results of this study may not fully generalize from acute to chronic pain. Pain was operationalized using short-term heat stimuli, and although participants were instructed to endure these stimuli as long as possible, they had the option to stop. As chronic pain may be experienced as uncontrollable, it is possible that different coping processes may be involved. Moreover, the isolation of a therapeutic strategy in an experimental situation may not reflect the motivational aspects of a therapeutic context: study participants had no obvious benefit from enduring the experimental pain, while individuals with chronic pain often experience functional limitations, and may experience an increased sense of control over their lives as they confront feared situations. As these motivational aspects are usually discussed during the course of exposure therapy, the present results may be only partially generalizable to clinical practice. Another limitation is the use of a university student sample. Although the percentage of psychology students (13.4%) was relatively low, the sample is still restricted in terms of age, level of education, and prior pain experience. Thus, generalizability to the population of individuals suffering from chronic pain is unclear. However, the investigation of healthy participants represents an important initial step in understanding patterns of change. Additionally, while we followed experimental guidelines in including only female participants, this may limit our results to gender-specific effects. Finally, both male and female experimenters conducted the study trials. Although the experimenters conducted a proportionally equal number of trials in each group, we could not fully eliminate the potential influence of cross-gender interactions.

Clinical Implications

The present results support the effectiveness of exposure-based interventions for coping with pain-related fear in acute pain, and highlight the usefulness of maximizing expectation violation experiences instead of focusing on fear reduction. Although this study included healthy participants, we believe that the results can be translated to the management of chronic pain for two reasons. First, individuals with chronic pain and pain-related fear are often convinced that their avoidance serves a protective function, in contrast with individuals with other types of phobias, who are typically aware that their fear and avoidance are somewhat excessive[43]. Formulating concrete expectations allows pain patients to directly test the likelihood of their worst imagined outcome, which may result in change in unhelpful beliefs. Thus, a focus on cognitions in exposure therapy may be of particular importance in the context of pain-related fear. Second, as acute pain transitions to chronic pain, patients must reevaluate the meaning of pain in order to maintain their functioning[34]. While acute pain previously served as a warning signal, chronic pain is not a useful warning signal. Thus, a focus on cognitions might facilitate this relearning process.

Implications for Future Research

Future studies should replicate this experiment in a chronic pain sample to test whether expectation violation experiences can also optimize exposure effects in this population. Other procedural techniques (i.e., techniques implemented during exposures) and flanking techniques (i.e., techniques implemented before and after exposure sessions) from general exposure-based interventions should also be evaluated for efficacy in the management of chronic pain[35]. Further studies should also examine the long-term effectiveness of these expectation violation experiences. This is of special importance since the inhibitory learning model to exposure is designed to minimize retention of the original excitatory association (e.g. spontaneous recovery, context renewal, reinstatement, and rapid acquisition)[10]. Moreover, some expectation violation situations appear to fail to modify expectations due to immunization and/or assimilation processes[39]. For example, a patient with chronic back pain might not generalize from expectation violation experiences, but instead might reframe the exposure situation (e.g. “This time my back was not damaged, but it might mean that next time I will have less luck.”). Clarifying these expectation-maintaining mechanisms could help to improve exposure-based interventions in the context of chronic pain.

Conclusions

This study provides experimental evidence for the effectiveness of exposure-based interventions among individuals confronting acute thermal pain. Instructions addressing expectation violations appeared to produce the greatest effects. Therefore, we recommend therapist to design pain exposures according to the inhibitory learning model in order to test specific negative expectations.

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Conflict of Interest

The authors declare that they have no competing interests.

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Tables and Figures

Table 1. Baseline characteristics from online survey

	Habituation (n = 38)	**Expectation violation** (n = 38)	**Control** (n = 36)	F-value*
BDI, mean (SD)	2.3 (2.1)	1.9 (2.1)	2.2 (2.1)	.473
PSQ, mean (SD)	3.5 (1.0)	3.1 (1.1)	3.5 (1.2)	1.871
PVAQ, mean (SD)	37.7 (10.2)	33.7 (8.7)	37.1 (7.8)	2.156
PCS, mean (SD)	19.0 (8.2)	14.9 (6.8)	16.7 (8.4)	2.577
PASS, mean (SD)	31.3 (13.7)	24.7 (11.3)	31.2 (14.4)	3.09
FESV (cog) , mean (SD)	48.0 (11.0)	47.9 (7.8)	45.0 (7.6)	1.322
FESV (bev) , mean (SD)	33.9 (8.5)	38.1 (9.6)	35.9 (9.0)	1.976

** All F-values are non-significant (p > .05) expect for the PASS (p = .05); SD = standard deviation*

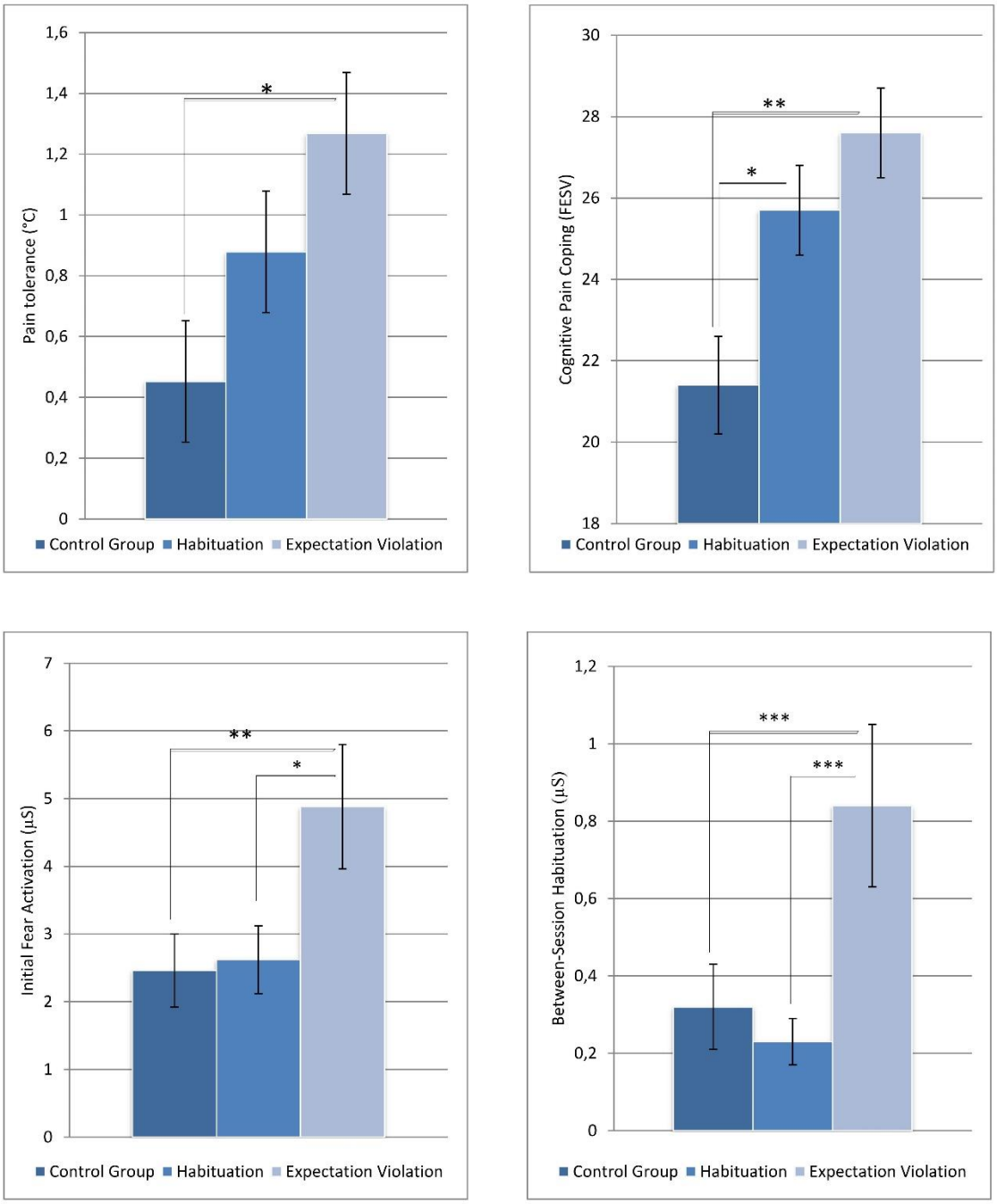

Figure 1. Means and standard errors for pre-post difference in pain tolerance, cognitive pain coping (assessed at posttest via adapted subscale of FESV), initial fear activation, and between-session habituation (assessed via skin conductance level (SCL)). Significant group differences are indicated as follows: * = $p < .05$. ** = $p < .01$.

Supplementary Materials

A.1 Definition of Exposure

What is exposure? **-** Exposure therapy is an approach for overcoming anxiety problems in which people gradually confront feared situations (e.g. places, objects, thoughts, or memories). Purposely facing feared situations is called 'exposure'. For example, if you fear *giving a blood sample*[1] you might *specifically practice this at a blood donation center.* People do exposure exercises during therapy sessions and on their own between sessions.

A.2 Habituation Rationale

And how does exposure work? **-** Exposure exercises aim to reduce or eliminate your anxiety and fear. Here's how it works. After doing repeated exposures, your anxiety and fear will habituate - that is, they will gradually decrease each time you face what you fear. By the end of treatment, the situations that currently trigger your anxiety should trigger little anxiety. For example, let's say you fear *giving a blood sample*. At first, when you expose yourself to *giving a blood sample at a blood donation center*, you may feel anxious and scared. But after *donating your blood* again and again, you will start to get used to this experience, or habituate, and your anxiety will gradually decrease. As a result, you will likely feel much less anxious in *other medical* situations *which require giving a blood sample*.

A.3 Expectation Violation Rationale

And how does exposure work? **-** Exposure exercises can help you learn, through your own direct experience, whether feared situations are as dangerous or bad as you believe. Exposure exercises allow you to put your anxious thoughts to the test so you can find out whether the negative outcomes you predict actually occur. If the negative outcomes do occur, you can see whether they are as bad as you expect. For example, if you fear *giving a blood sample*, you can practice *it at a blood donation center* in order to learn how likely it is that the *loss of blood causes dangerous consequences to your health*, and whether the *medical service* reacts *to your potential circulation problems* as negatively as you expect. By conducting exposure exercises to test your negative predictions, you can learn that feared situations are not as dangerous or bad as you once believed them to be.

[1] *changes marked in italics*

A.4 Mediation Model

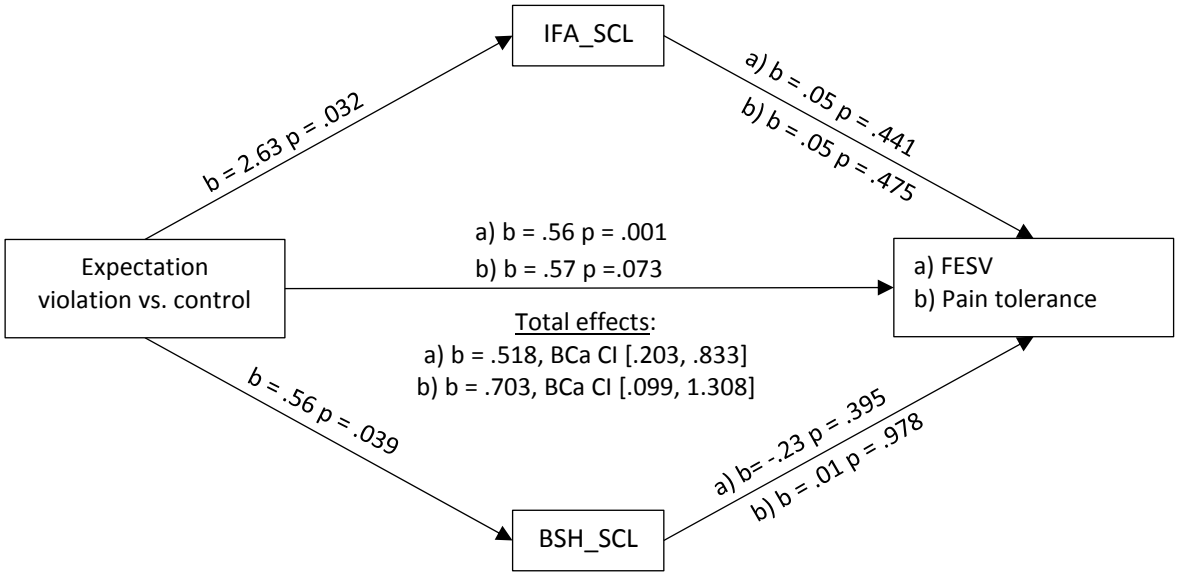

Figure 3. Regression results for the mediated impact of therapeutic instruction on a) cognitive pain coping and b) pain tolerance through (1) initial fear activation and (2) between-session habituation in skin conductance level.

N = 66. Unstandardized coefficients are reported. All results are controlled for their pre-test scores, baseline mean of SCL, and credibility of deception. Significance levels were calculated by PROCESS Macro. Significance levels for the conditional indirect effects through 95%, 90%, 99% bootstrapped confidence intervals are given in parentheses. IFA_SCL = Initial fear activation in skin conductance level. BSH_SCL = Between-session habituation in skin conductance level. FESV = cognitive pain coping.

Appendix D: Tabellarischer Lebenslauf

(Der Lebenslauf ist nicht Teil der Veröffentlichung.)

Appendix E: Eidesstattliche Erklärung

Hiermit versichere ich meine Dissertation "Therapieprozesse und Wirkmechanismen psychologischer Schmerztherapie" selbst und ohne fremde Hilfe verfasst zu haben. Ich habe keine anderen als die angegebenen Quellen und Hilfsmittel genutzt. Alle vollständig oder sinngemäß übernommenen Zitate sind als solche gekennzeichnet. Die Dissertation wurde weder in der vorliegenden noch in einer ähnlichen Form bei einer anderen in- oder ausländischen Hochschule anlässlich eines Promotionsgesuchs oder zu anderen Prüfungszwecken eingereicht.

Marburg an der Lahn, November 2017

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