Evaluation of Treatment with Cognitive Therapy and a Patient-Centered Approach in Patients with Chronic Musculoskeletal Pain and Psychiatric Co-Morbidity - A Pilot Study

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Abstract

Objective: The aim was to evaluate Cognitive therapy (CT) and a patient-centered-approach in a group of patients with chronic pain and psychiatric co-morbidity in relation to pain, dysfunction, anxiety, depression, burnout and health related quality of life (HRQoL).

Design: Pilot study.

Setting: Consulting psychiatry.

Participants: 30 consecutive patients with chronic pain, who had not responded to conventional pain treatment, were recruited during a period of 21 months.

Interventions: All patients were offered treatment with cognitive therapy (CT). Twenty patients accepted treatment with CT and 13 patients, the therapy group, completed therapy. The no therapy group consisted of 7 patients who did not complete therapy and 10 patients who were only followed-up at monthly intervals.

Main Outcome Measures: Patient reported outcome measures (PROM) were administered at baseline and at follow-up after 8 - 11 months. PROM included Relationship Scales Questionnaire (RSQ) for attachment pattern, Sense of coherence (SOC), Multidimensional Pain Inventory (MPI) for pain and dysfunction, Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), Pines’scale for burnout and Short-Form 36 (SF-36). Statistical tests were conducted at a 5% significance level. Subgroup identification was accomplished by means of Multivariate data analysis (MVDA).

Results: At the individualized follow-up the patients (n = 25) reported significant improvement of Bodily Pain and Mental Health in Short-Form 36 (SF-36), life control in MPI, depression, anxiety and SOC. There was a correlation between completed treatment with CT and improvement. Explorative modellings with MVDA suggested that patients with chronic pain and fearful attachment pattern had a better outcome than patients with preoccupied attachment pattern if they were treated with CT.

Conclusion: A patient-centered approach in combination with CT was beneficial for patients with chronic pain and psychiatric co-morbidity. MVDA indicated that the outcome of treatment may differ according to individual vulnerability and severity of burnout, depression and pain interference.

Strengths and Limitations of the Study

- This study is a small hypothesis generating pilot study and the results need to be followed up with larger randomized studies.
- Patients who dropped out from therapy were followed in the no therapy group.
- The same therapist/physician (BP) treated the entire group.
- In order to compensate for many variables and a limited number of observations explorative modellings with MVDA were performed.

Keywords: Chronic Pain; Attachment Pattern; Sense of Coherence; Subgroups in Multidimensional Pain Inventory (MPI); Cognitive Therapy
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Abbreviations

AC: Adaptive Coper; act: General Activity; ad: Affective Distress; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; BP: Bodily Pain; CT: Cognitive Therapy; ch: Change; dism: Dismissing Attachment; distr: Distracting Responses; dys: Dysfunctional Fear Fearful Attachment; HRQoL: Health Related Quality of Life; id: Interpersonal Distress; lc: Life Control; MH: Mental Health; MPI: Multidimensional Pain Inventory; Pbs: Performance Based Scale; PF: Physical Function; pi: Pain Interference; pin: Pines' Burnout Measure; pre: Preoccupied Attachment; ps: Pain Severity; pu: Punishing Responses; RE: Role Emotional; RP: Role Physical; RSQ Relationship Scales Questionnaire; SF-36 Short Form-36; SF: Social Function; sec: Secure Attachment; SOC: Sense of Coherence; sol: Solicitous Responses; sup: Support; VT: Vitality

Introduction

Patients with chronic pain comprise a heterogeneity even if they have identical medical diagnoses [1]. Psychological factors have been described to have an important role in chronic pain [2,3]. The Gate control theory supports the view of pain as a perception where the quality and intensity are influenced by the unique past history of the individual, by the meaning he or she gives to the pain-producing situation and by his or her state of mind at the moment [3]. The perception of the meaning of the chronic pain, the ability to control pain and worries about the future are examples of important factors associated with physical and mental functioning and treatment outcome [4]. Traumatic onset of chronic pain may be associated with greater perceived severity of pain and fear of injury [5]. Therefore chronic pain management must go beyond attempts to relieve pain and needs to include treatment of psychological co-morbidity and assessment of such factors as depression, abuse, psychosocial stress and defective coping skills [6]. The stress of coping with chronic pain may result in an activation of pre morbid personality characteristics such as an insecure attachment pattern and a weak Sense of Coherence (SOC) with possible exacerbation of depression and anxiety [6,7].

According to Bowlby's Attachment theory [8], an early attachment pattern between the child and its mother may play an important role in adult life activated in the face of danger and affecting the view of self and others [9]. Furthermore, the Attachment theory may allow for identification of subgroups of patients with chronic pain [10]. According to Antonovsky, SOC is also founded in childhood in relations with parents and family [11]. The three components of the concept of SOC are: comprehensibility, manageability and meaningfulness. Individuals with a strong SOC are likely to perceive stressors as predictable and explicable and they have confidence in their ability to overcome stressors. In contrast to a view of disease focused on pathology a salutogenic model focuses on the patient’s experience of illness as well as her or his total situation of life.

As yet, no treatment has proven to permanently relieve chronic pain [1]. Therefore the patients suffering from chronic pain need to have strategies and skills to function better in daily life [12]. Malterud and Hunskaar [13] describe a need for a patient-centered approach where the patient's total situation is taken into account in the treatment of chronic pain. With such an approach the clinician has to pursue the medical agenda as well as the patient's agenda [14]. It has been reported that a cognitive behavioural approach is helpful for patients to gain a sense of control of their pain and to cope with fear and frustration [15]. Here the technique applied seems to be of less importance. Rather the approach should be tailored to each patient's needs [16]. There may be challenges to adopt a more patient-centered approach in the treatment of patients with chronic pain and psychiatric co-morbidity attending both to symptoms of chronic pain and psychosocial vulnerability.

Aim of the Study

The aim of the present study was to evaluate CT and a patient-centered approach in a group of patients with psychiatric co-morbidity in relation to pain, dysfunction, anxiety, depression, burnout and health related quality of life (HRQoL).

Materials and Methods

Patients

Patients with chronic non-malignant musculoskeletal pain who were referred for psychiatric assessment in a small town in the western part of Sweden were consecutively invited. These patients had not benefited from conventional pain treatment. The inclusion period was from October 2005 to June 2007 [17].

Interventions and assessment: The patients were offered treatment with cognitive therapy (CT) with sessions every second week. In addition a bio-psychosocial treatment approach was applied where the patient's total situation was taken into account with a focus on empowerment as described by Malterud and Hunskaar [13]. This patient-centered approach also implied a cognitive approach with a collaboration between the patient and the physician on equal terms. In the cognitive therapy (CT) there was a focus on the patients' experiences and life stories. The physician/therapist listens attentively and confirming in order to legitimate the patient's feelings and
thoughts about his or her illness [18]. Equally important was the investigation of the patient’s fears and grieving caused by the loss of health and what the psychological, social and physical consequences were. By means of Socratic questions the patient was guided to discover new perspectives and to restructure his/her thoughts [19]. The therapy sessions also involved mindfulness training to learn to let go of stress and negative thoughts by focusing on breathing in the present moment [18]. Those who completed therapy, in total 13 patients, were interviewed about their experiences at the end of the therapy and the results has been reported in a previous study [18]. All patients were offered therapy but patients who did not commence therapy either had lack of motivation or had difficulties to participate in the sessions regularly.

Patient reported outcomes

The questionnaires, valid and reliable, (described below) were administered at baseline and after the treatment with CT was ended, on average after 11 months (range 7 - 18 months), depending on the length of the therapy. Questionnaires were also given to the patients who were not treated with CT at baseline and at follow-up on average after 11 months. In a few cases the questionnaires were mailed by post after a telephone contact at follow-up.

Relationship scales questionnaire

The Relationship Scales Questionnaire (RSQ) is a self-assessment instrument developed by Griffin and Bartholomew [20] for the assessment of attachment patterns according to Bowlby’s Attachment theory. A four category model is obtained from either a positive or negative view of self and others, resulting in one secure and three insecure attachment patterns: dismissing, fearful and preoccupied. The RSQ consists of 17 statements where participants rate each statement on a seven point scale ranging from 1 - 7. Scores are then averaged across the five statements for secure, five for dismissive, four for fearful and four for preoccupied attachment styles. The RSQ yields scores of all subscales of attachment. Participants can then be described as having varying degrees of each attachment style. The subscales have shown moderate consistency with Cnnbachi’s alpha coefficients for scores ranging from 0.45 for preoccupied and 0.65 for secure to 0.7 for dismissing and 0.76 for fearful [21]. The RSQ has also shown convergent and discriminant validity for these dimensions and a high test-retest reliability over an 8-months period [20].

Sense of coherence

The Sense of Coherence (SOC) used in this study contains 29 items. The concept of SOC was developed by Antonovsky to describe health promoting resources. The three components of this concept are: comprehensibility, manageability and meaningfulness [11,22]. High scores indicate a strong SOC.

Multidimensional pain inventory

The Multidimensional Pain Inventory (MPI) [23,24] is developed to assess chronic pain from a cognitive behavioural perspective [25]. The MPI (version 2) used in this study is a 61 item self-report questionnaire. The answers of the three parts of the questionnaire are grouped into 13 scales. A subgroup classification on the basis of significant differences of responses to 9 of the scales of the MPI (Pain severity, Pain interference, Affective distress, Support, Distracting responses, Solicitous responses, Punishing responses, General activity and Life control) is possible to obtain by means of cluster analysis in a specific computer program [26]. These profiles or subgroups are labelled: Adaptive Coper (AC), Anomalous (ANOM), Interpersonally Distressed (ID), Hybrid and Dysfunctional (Dys). The raw scores are hereby transformed into a 0-100 scale. The subgroups are characterized by different levels of Pain intensity and Pain interference, affective distress and reactions of significant others. AC reports less pain severity and pain interference, lower levels of affective distress and higher activity levels compared with the subgroups ID, Hybrid and Dys.

Beck anxiety inventory

The Beck Anxiety Inventory (BAI) is a 21-item self-report inventory for measuring the severity of anxiety during the past week in a psychiatric population using a four-point scale ranging from 0 (no symptoms present) to 3 (severe symptoms) [27]. The standard cut-offs are as follow: 0 - 7 indicates minimal anxiety, 8 - 15 indicates mild anxiety, 16 - 25 indicates moderate anxiety and 26 - 63 indicates severe anxiety. The BAI is widely used in examining factors underlying chronic pain [28].

Beck depression inventory

The Beck Depression Inventory (BDI) [29] is a 21-item self-report inventory using a four-point scale ranging from 0 (no symptoms present) to 3 (severe symptoms). The test-retest correlation varies between 0.48 - 0.86 according to the natural development of the depressive symptoms [30,31]. The BDI-1A was used in this study. The standard cut-offs are as follow: 0-9 indicates minimal depression, 10 - 18 indicates mild depression, 19 - 29 indicates moderate depression and 30-63 indicates severe depression.

Pines’ burnout measure

The Pines’ Burnout Measure is a 21-item scale. The scale includes items corresponding to the three components of burnout: physical exhaustion, mental exhaustion and emotional exhaustion. Of the 21 items, 17 are negative and four are positive. The score is determined as the mean response to all items with positive items reversed. The cut-off value for burnout is $> 4.0$ [32,33]. It is a context free burnout instrument correlating with emotional burnout in the Maslach burnout inventory and also correlated with psychical and somatic ill health.

Health related quality of life

Health Related Quality of Life (HRoL) was assessed using the Short-Form 36 (SF-36). The SF-36 is a generic questionnaire assessing physical and mental health, where 100 stands for the best health rating [34-36]. The 36 items in the questionnaire are grouped into eight subscale scores: Physical functioning (PF), Role limitations caused by physical problems (RP), Bodily pain (BP), General Health (GH), Energy/vitality (VT), Social functioning (SF), Role limitations caused by emotional problems (RE) and Mental health (MH) [37].

Statistics

For comparison within the group over time the Wilcoxon Sign Rank test was used in SPSS 12.0.1. All statistical tests were two-tailed and conducted at a 5% significance level.

In a next step multivariate data analysis (MVDA) was chosen. Here (PCA) [38] and Two Way Orthogonal Partial Least Squares Analysis (O2PLS) [39] were performed as an explorative method in order to confirm the results and to discover possible correlations and patterns of variables in the patient group. MVDA is a factor method used to uncover the latent structures or dimensions. A set of relevant data variables are analyzed together, for interpretation based on the yielded correlation, translated to variables and reducing “noise”, i.e. uncorrelated data. Further description of MVDA is found in supplementary information.

Ethical approval

This study was carried out in accordance with the Declaration of Helsinki. The ethics committee at University of Gothenburg approved the study (032-06). After receiving written information about the study, all participants gave their written informed consent to participate in the study. The study is registered in a national register (VGR D nr. 18571 http://www.fou.nu/is/vgr/project/16571).

Results

Characteristics of patient

Thirty consecutive patients, 24 females and 6 males were included from October 2005 to June 2007 [18]. The average age in the group was 41 years and 97% had psychiatric co-morbidity [18]. A total of 40% of the patients suffered from fibromyalgia. Other recorded pain diagnoses were chronic widespread pain (20%), chronic regional pain (10%), whiplash trauma (20%) and lumbago (10%) [18]. The most common psychiatric diagnoses according to DSM-IV were anxiety disorders, mixed states of anxiety and depression and maladaptive stress reaction. Twenty of the 30 patients accepted treatment with CT and 13 patients, the therapy group, completed therapy [18] (Figure 1). The no therapy group consisted of 7 patients who did not complete therapy and 10 patients who were only followed-up at monthly intervals. All patients in the therapy group and 12 patients in the no therapy group answered the questionnaires at follow-up. Five patients could not be reached or did not answer the questionnaires on request (Figure 1). The drop outs (n = 5) were due to hospitalization due to psychiatric illness and problems with compliance and alcohol abuse. Three patients in the therapy group did not fill out SF-36 at baseline for administrative reasons. In the whole group 28 patients were on full-time sick leave at baseline versus 26 patients at follow-up (Table 1).

<table>
<thead>
<tr>
<th>Sick-listed</th>
<th>Chronic pain Therapy</th>
<th>Chronic pain no Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-up</td>
</tr>
<tr>
<td>100%</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>75%</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>50%</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 1: Number of patients with chronic pain and psychiatric co-morbidity sick-listed or at work at baseline and after follow-up (7 - 13 months after start of therapy).

Patient reported outcomes

There was no significant difference in attachment pattern at follow-up. A predominance of dismissing attachment pattern was seen both at baseline and follow-up (Table 2). Totally 60% of the patients with chronic pain in psychiatry had traumatic experiences in childhood and, or as adults [18]. At baseline the mean value of SOC was 107. At follow-up the entire group reported a significantly improved, but still subnormal SOC, 112, \( p = 0.01 \) (Table 2).

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n = 30) Mean (SD) Range</th>
<th>Follow-up (n = 23 - 25) Mean (SD) Range</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOC</td>
<td>106.9 (28.3) 63. - 163.0</td>
<td>111.7 (25.8) 67.0 - 180.0</td>
<td>0.01</td>
</tr>
<tr>
<td>Burnout Measure</td>
<td>4.7 (1.0) 2.86 - 6.52</td>
<td>4.3 (0.9) 2.76 - 5.90</td>
<td>0.1</td>
</tr>
<tr>
<td>Attachment Fearful</td>
<td>4.1 (0.9) 1.0 - 6.75</td>
<td>4.1 (1.3) 1.25 - 6.25</td>
<td>0.67</td>
</tr>
<tr>
<td>Attachment Dismissing</td>
<td>4.9 (1.1) 2.4 - 7.0</td>
<td>4.6 (1.0) 2.4 - 6.0</td>
<td>0.75</td>
</tr>
<tr>
<td>Attachment Secure</td>
<td>3.8 (0.9) 2.2 - 5.6</td>
<td>3.5 (0.7) 1.8 - 4.8</td>
<td>0.31</td>
</tr>
<tr>
<td>Attachment Preoccupied</td>
<td>3.8 (1.0) 1.75 - 6.25</td>
<td>3.9 (1.2) 2.25 - 7.0</td>
<td>0.15</td>
</tr>
<tr>
<td>BAI</td>
<td>25.6(12.1) 7 - 51</td>
<td>22.2(11.1) 5 - 41</td>
<td>0.02</td>
</tr>
<tr>
<td>BDI</td>
<td>24.8(9.9) 9 - 47</td>
<td>20.2 (9.4) 8 - 44</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Table 2: Patients with chronic pain and psychiatric co-morbidity. SOC (Sense of Coherence), Pines’ Burnout Measure, RSQ (Relationship Scales Questionnaire), BAI (Beck Anxiety Inventory) and BDI (Beck Depression Inventory), results at baseline and at follow-up.

There were no significant changes in items of the MPI in the patient group with one exception, a significant improvement of life control (\( p = 0.04 \)) (Table 3).
A subgroup classification on the basis of significant differences of responses to 9 of the scales of the MPI was possible to obtain by means of cluster analysis in a specific computer program [26]. A predominance of Dys and ID subgroups of the MPI was seen both at baseline and at follow-up (Figure 2).

Table 3: Patients with chronic pain and psychiatric co-morbidity. MPI (Multidimensional Pain Inventory), results at baseline and at follow-up.

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n = 30) Mean (SD)</th>
<th>Follow-up (n = 24) Mean (SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain Severity</strong></td>
<td>71.7 (17.4) 44.0 - 100.0</td>
<td>67.3 (20.0) 17.0 - 100.0</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>Pain Interference</strong></td>
<td>72.3 (15.4) 49.0 - 100.0</td>
<td>69.5 (17.2) 42.0 - 100.0</td>
<td>0.62</td>
</tr>
<tr>
<td><strong>Life Control</strong></td>
<td>37.4 (15.2) 0.0 - 62.0</td>
<td>41.8 (15.4) 0.0 - 67.0</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>Affective Distress</strong></td>
<td>62.2 (14.9) 30.0 - 100.0</td>
<td>61.4 (17.8) 30.0 - 100.0</td>
<td>0.81</td>
</tr>
<tr>
<td><strong>General Activity</strong></td>
<td>51.7 (8.6) 34.0 - 68.0</td>
<td>53.8 (7.0) 42.0 - 74.0</td>
<td>0.34</td>
</tr>
<tr>
<td><strong>Dysfunction</strong></td>
<td>62.6 (11.1) 43.0 - 89.0</td>
<td>59.5 (13.2) 36.0 - 92.0</td>
<td>0.24</td>
</tr>
<tr>
<td><strong>Interpersonal Distress</strong></td>
<td>41.4 (12.1) 23.0 - 67.0</td>
<td>40.0 (12.9) 19.0 - 65.0</td>
<td>0.76</td>
</tr>
</tbody>
</table>

At baseline the mean value for anxiety assessed with BAI was 25.6. Depression assessed with BDI had a mean value of 24.8 (Table 2), which implies a moderate level of anxiety and depression. At follow-up, the whole group reported significantly lower scores of anxiety, 22.2 (p = 0.02) and depression 20.2 (p = 0.002). The distribution of patients according to minimal- mild, moderate and severe anxiety and depression at baseline and follow-up is shown in a histogram in supplementary information (Figure S1A-S1B). At baseline 40% of the patients had severe anxiety versus 28% at follow-up. The corresponding values for depression was 34.5% versus 20%. The patient group as a whole also scored above the cut-off value 4.0 on the Pines’ Burnout Measure both at baseline (4.68) and at follow-up (4.34) (Table 1). A significant improvement in Mental health (p = 0.01) and Bodily pain (p = 0.03) was reported at follow-up assessed with SF-36 (Table 4). However, compared to corresponding age and gender-matched normative populations these results were significantly impaired both baseline and at follow-up [17].
### Table 4: Patients with chronic pain and psychiatric co-morbidity. Health related quality of life according to Short-Form 36 (SF-36), results at baseline and at follow-up.

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n = 27) Mean (SD) Range</th>
<th>Follow-up (n = 25) Mean (SD) Range</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Function</td>
<td>45.1 (22.9) 15 - 85</td>
<td>52.3 (26.46) 20 - 100</td>
<td>0.21</td>
</tr>
<tr>
<td>Role Physical</td>
<td>8.3 (20.80) 0 - 75</td>
<td>22.0 (33.32) 0 - 100</td>
<td>0.06</td>
</tr>
<tr>
<td>Bodily Pain</td>
<td>19.6 (15.24) 0 - 41</td>
<td>29.4 (26.36) 0 - 100</td>
<td>0.03</td>
</tr>
<tr>
<td>General Health</td>
<td>30.6 (14.57) 0 - 60</td>
<td>35.1 (15.43) 10 - 77</td>
<td>0.41</td>
</tr>
<tr>
<td>Vitality</td>
<td>17.6 (15.89) 0 - 55</td>
<td>28.0 (19.31) 0 - 65</td>
<td>0.12</td>
</tr>
<tr>
<td>Social Function</td>
<td>35.2 (23.27) 0 - 87.5</td>
<td>44.5 (28.66) 0 - 100</td>
<td>0.23</td>
</tr>
<tr>
<td>Role Emotional</td>
<td>38.3 (44.05) 0 - 100</td>
<td>47.3 (47.06) 0 - 100</td>
<td>0.15</td>
</tr>
<tr>
<td>Mental Health</td>
<td>42.7 (21.94) 4 - 80</td>
<td>54.1 (19 - 70) 8 - 92</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**Figure S 1A:** Patients with chronic pain and psychiatric co-morbidity. Anxiety assessed with BAI at baseline and at follow-up. BAI < 16= minimal-mild anxiety, 16 - 25= moderate anxiety and >25= severe anxiety.

**Figure S 1B:** Patients with chronic pain and psychiatric co-morbidity. Depression assessed at baseline and at follow-up. BDI < 19= Minimal-mild depression, 19 - 29= Moderate depression and > 29 = Severe depression.
In summary the results of the patient reported outcomes and the assessment of traumatic experiences [18] indicated that there were signs of increased vulnerability in terms of insecure attachment pattern, a subnormal SOC, a dominance of Dysfunctional and Interpersonal distressed subgroups of the MPI and a low HRQoL. However, there was a significant improvement in anxiety, depression, SOC and in Mental health and Bodily pain in SF-36.

In order to further investigate possible differences in vulnerability and outcome of treatment analyses with PCA and O2PLS were performed.

Correlations and subgroups assessed with PCA and O2PLS

Initial modelling by PCA indicated that three principal components explained 47% of the variation of the data, (R^2_X = 0.47) with a cross validated prediction, Q^2_X = 0.21 (Figure S2A-S2C). In component 1 higher values in SOC, secure attachment pattern and HRQoL assessed with SF-36 at baseline and at follow-up were inversely correlated with items in MPI, fearful attachment pattern, anxiety, depression and burnout at baseline and at follow-up (Figure 3). Patterns and clusters of subgroups can be seen in loading and score plots combining two components p1 and p2 (Figure S2D).

![Figure 3: PCA component1, loadings, patients with chronic pain and psychiatric co-morbidity SF-36 (SF1, SF2,V2, PF2, BP1, BP2, MH1, MH2, GH1, GH2, RP2), Sense of Coherence (SOC1, SOC2) and secure attachment (sec1) correlated inversely with anxiety (BAI1, BAI2), depression (BDI1, BDI2) and MPI: Dysfunction (dys1, dys2), Pain severity (ps1, ps2) and Affective distress (ad1, ad2). 1=baseline. 2=follow-up.](image)

![Figure S 2A: PCA, patients with chronic pain and psychiatric co-morbidity. Three principal components explained 47% of the variation of the data, (R^2_X = 0.47) with a cross validated prediction, Q^2_X = 0.21.](image)
Figure S 2B: PCA principal component 2, patients with chronic pain and psychiatric co-morbidity. Interpersonal distress (id1, id2) was inversely correlated with responses from significant others (sup, sol, distr), dysfunction (dys), Pain severity (ps) and pain interference (pi) in MPI, SOC and secure attachment (sec) at baseline and at follow-up. 1=baseline, 2= follow-up.

Figure S 2C: PCA principal component 3, patients with chronic pain and psychiatric co-morbidity. Therapy (ther), preoccupied attachment (pre), support (sup), Pb, trauma, burnout (pin) were inversely correlated with Interpersonal distress (id), Role emotional (RE), SOC and Dysfunction (dys). 1= Baseline; 2= Follow-up.

Figure S 2D: PCA, patients with chronic pain and psychiatric co-morbidity. Score plot (A) coloured according to subgroups in MPI and loading plot (B) component 1 and 2. blue= AC, green=ID, yellow=Hybrid, red= Dys.
To further interpret the correlation patterns provided by the PCA, significant variables were chosen from the PCA in component 1-3 (Figure 3, Figures S2B-S2C) to be used as response variables in a multiple regression by means of O2PLS. The X matrix in this model included the remaining variables from the PCA and change variables to identify any additional correlation structures between the nominated Y and X variables. A vulnerability model with three predictive components and two orthogonal components was obtained with a cumulative explained variance $R^2_Y = 0.67$ and a prediction, $Q^2_Y = 0.42$ (Figure S3A). The Y variables had a good explained variance and prediction using the present study material indicating a high correlation between the X and Y variables.

![Figure S 3A: O2PLS (vulnerability model). Patients with chronic pain and psychiatric co-morbidity. The model comprised three predictive and two orthogonal components. The explained variance $R^2_Y$ was 0.67 with a prediction $Q^2_Y$ of 0.42. The response variables: secure (sec1), preoccupied (pre1) and fearful (fear1) attachment, therapy (ther), Social function (SF1), Bodily pain (BP1), Pain severity (ps1), dysfunction (dys1), interpersonal distressed (id1), burnout (pin1) and SOC1.](image)

In the loading histogram of the first predictive component $pq1$ (Figure 4A) a cluster was identified with resemblance of an AC subgroup of the MPI inversely correlated with a Dys subgroup. Both subgroups showed little change at follow-up. The secure attachment pattern correlated with the AC subgroup and the fearful pattern with the Dysfunctional subgroup.

![Figure 4A: O2PLS, Component 1 (Vulnerability model). Patients with chronic pain and psychiatric co-morbidity. Low scores in SF-36 (SF1, SF2, MH1, MH2, BP1, Vt1, Vt2, GH1), secure attachment (sec1), SOC1, SOC2 and life control (lc1, lc2) in MPI were correlated with high scores in fearful attachment (fear1, fear2), burnout (pin1, pin2), high scores in MPI for dysfunction (dys1), affective distress (ad2), pain severity (ps1) and pain interference (pi1) and high scores in depression (BDI1, BDI2) and anxiety (BAI1, BAI2).](image)
In the loading histogram of the second predictive component pq2 (Figure 4B) a second cluster was identified representing an ID subgroup of the MPI inversely correlated with a Dys subgroup with higher support from significant others and higher values of secure attachment and MH in SF-36. The ID subgroup correlated with therapy and positive change in HRQoL at follow-up while the Dys subgroup had a good HRQoL and support from significant others but low change at follow-up. Patterns and clusters can be seen in loading and score plots (Figure S4A-S4B). In the loading histogram of the third predictive component pq3 of the vulnerability model (Figure 4C) preoccupied attachment pattern correlated with therapy, responses from significant others in MPI, trauma, burnout, anxiety and depression at baseline and at follow-up and was inversely correlated with ID and Dys in MPI, SOC and RE in SF-36.

**Figure 4B:** O2PLS, Component 2 (Vulnerability model). Patients with chronic pain and psychiatric co-morbidity. High scores in Interpersonal distress (id1, id2) were correlated with high scores in SF-36 (PF1, PF2, BP1, BP2, GH2) activity (act1, act2) in MPI, higher mean age, therapy and positive change in SF-36. There was an inverse correlation with supporting, solicitous and distracting reactions from significant others (sup1, sup2, sol1, sol2, distr1,distr2), Pain severity (ps1, ps2). Pain interference (pi1, pi2), Dysfunction (dys1,dys2) in MPI and secure attachment (sec1). 1 = baseline. 2 = follow-up.

**Figure 4C:** O2PLS, Component 3 (Vulnerability model). Patients with chronic pain and psychiatric co-morbidity. Preoccupied attachment (pre1, pre2) was correlated with therapy (ther), trauma, support from significant others (dist1, dist2, sup1, sup2, sol1, sol2), high scores in depression (BDI1, BDI2), anxiety (BAI2), burnout (pin1, pin2). There was an inverse correlation with Interpersonal distress (id1, id2), Dysfunction (dys1), SOC1, SOC2, Role emotional (RE1, RE2). 1 = baseline. 2 = follow-up.
In order to explore change at follow-up and possible effects of the CT in the therapy group the variable therapy and significant change variables were chosen from change variables in the orthogonal component of the previous O2PLS, model (Figure S3B) to be used as response variables. Hereby a change model with three predictive and two orthogonal components was obtained according to cross validation. The cumulative explained variance $R^2_Y$ was 0.80 and the prediction was estimated to, $Q^2_Y= 0.42$ (Figure S4A). In figure S5A the response variables are illustrated according to explained variance and prediction. All response variables had a reasonably high impact on the model. One exception was the low prediction of the variable therapy ($Q^2_Y = 0.13$), while the explained variance was high ($R^2_Y=0.86$) A possible explanation to the large discrepancy between $R^2_Y$ and $Q^2_Y$ might be the small number of patients in the therapy group.

Figure S 3B: O2PLS (vulnerability model) orthogonal component, patients with chronic pain and psychiatric co-morbidity. Change in SF-36: Physical function (chPF), Role Physical (chRP), Social Function (chSF), Vitality (chVt) were inversely correlated with change in MPI: dysfunction (chdys), pain severity (chps), pain interference (chpi), and burnout (chpin). 1=baseline. 2= follow-up.

Figure S 4A: O2PLS (change model), patients with chronic pain and psychiatric co-morbidity. Three predictive and two orthogonal components were obtained according to cross validation. The cumulative explained variance $R^2_Y$ was 0.80 and the prediction $Q^2_Y$ was 0.42.
A loading histogram of the first predictive component (pq1) of the change model (Figure 5B) showed that undertaking therapy coincided with a positive change in Role physical, Bodily pain, Social function, Vitality in SF-36 and a negative change in Dysfunction, Pain severity in MPI. The exact correlation values are shown in figure S 4B. Patients in therapy who improved at follow-up also correlated at baseline with high values in fearful attachment but low values in preoccupied attachment. Patients in the no therapy group correlated with high values in preoccupied attachment and increased pain and dysfunction at follow-up.

**Figure 5A**: O2PLS (change model), patients with chronic pain and psychiatric co-morbidity, response variables: change Vitality (chVt), change Role Physical (chRP), change Pain severity (chps), change Mental Health (chMH), change Bodily Pain (chBP), change Social Function (chSF), change Dysfunction (chdys) and therapy, are illustrated according to explained variance and prediction.

**Figure 5B**: O2PLS, component 1 (change model), patients with chronic pain and psychiatric co-morbidity. Therapy (ther) was correlated with a positive change in Role physical (chRP), Bodily pain (chBP), Social function (chSF), Vitality (chVt), and a negative change in Dysfunction (chdys), Pain severity (chps), fearful attachment (chfear) and burnout (chpin). (1 = therapy, 0 = no therapy).

**Figure S 4B**: O2PLS (change model). Correlations component 1, patients with chronic pain and psychiatric co-morbidity. Therapy correlated 0.31 with the other loadings in the model. 1=baseline. 2=follow-up.

Significant variations in the orthogonal component po (Figure 5C) comprised structured data that do not correlate to the Y-matrix structure which was obtained in the first predictive component of the change model, i.e. no correlation to any of the O2PLS nominated Y-vectors. Using the present study material, the orthogonal component modelled patients with significantly higher values for Pain severity, Affective distress and Dysfunction in MPI, anxiety, depression, burnout and fearful attachment at baseline and follow-up or patients with significantly higher values of adaptive coping, secure attachment and HRQoL at baseline and at follow-up. Hence the most resilient and vulnerable patients could be found in this cluster.

Figure 5C: O2PLS orthogonal component (Change model), patients with chronic pain and psychiatric co-morbidity (significant variables not correlated with change). Patients with higher values for affective distress (ad1, ad2), anxiety (BAI1, BAI2), depression (BDI1, BDI2) and burnout (pin1, pin2), fearful attachment (fear1, fear2) and pain severity (ps1, ps2) at baseline and follow-up also had lower values for Mental Health (MH1, MH2), Social Function (SF1, SF2), Life control (lc1, lc2), Vitality (Vt1, Vt2) and secure attachment (sec1). 1=baseline. 2=follow-up.

Figure 6: O2PLS (Change model), loading plot (pq1/pq2), patients with chronic pain and psychiatric co-morbidity. The loadings of all variables are illustrated in a loading plot. Response variables are colored blue. Therapy correlated with positive change in Mental Health (chMH), Vitality (chVt), Social function (chSF) and Role physical (chRP). 1=baseline. 2= follow-up.
In figure 6 the loadings of all variables are illustrated in a loading plot where pq1 was combined with pq2. The variable therapy (i.e. patients who completed CT) was correlated with positive change in SF-36 and was inversely correlated with dysfunction, pain interference, pain severity and affective distress in MPI at follow-up.

Discussion

Patients with chronic pain and psychiatric co-morbidity in the present study improved after treatment regarding HRQoL, SOC, depression, anxiety, pain and dysfunction. The improvement correlated with completed treatment with CT. However, those patients with the highest values of pain and pain associated symptoms, anxiety, depression, burnout and fearful and preoccupied attachment did not improve at follow-up and also had a low HRQoL both at baseline and at follow-up according to the orthogonal component of the change model in O2PLS (Figure 5C). Similar results were found in a randomized study of 156 patients with chronic temporomandibular pain by Turner, et al. [40]. Their results indicated that cognitive behavioural therapy (CBT) could result in a positive change in self efficacy and pain control with less anxiety and fear of harm which was meaningful for the outcome of treatment. However, patients with higher levels of depression, somatization and perceived stress at baseline had higher levels of activity interference at follow-up after one year. This is also in line with the results from a larger study of a cohort of patients with chronic pain referred to a multidisciplinary pain center at an university hospital in Sweden [41]. Here multivariate analyses confirmed that common symptoms as pain intensity, depression and anxiety could be used to identify subgroups of patients with chronic pain. Patients with the highest values of pain intensity, depression and anxiety were those who had the greatest impairment of health and function in daily life. However, 60% of the patients in the whole cohort in that study had normal values of depression and anxiety, while in the present study only 35% had minimal or mild depression and 23% had mild anxiety at baseline (Figure S1A-S1B).

The number of patients in this study was small (n = 30). For practical reasons it was not possible to include more patients. The dropout rate from the therapy was 7 out of 20 (Figure 1). On the other hand these patients were followed up in the no therapy group. The therapist/physician (BP) treated the entire group. Patients who primary accepted treatment with CT were those who were motivated to participate but not all had enough motivation and strength to carry on. Both the dropout from therapy and the missing answers from five patients who dropped out at follow-up (n = 5) did not diverge from the group mean values at baseline.

In order to compensate for many variables and a limited number of observations multivariate data analyses were performed, by which it was possible to better separate and validate solid data from random variation and to handle missing data and outliers. Hereby it was possible to distinguish separate subgroups with different outcomes. The results of this pilot study need to be followed up with larger randomized studies. However, the obtained model indicated clinically relevant patterns.

Clinical implications

The primary goal of the therapy was to improve the patient’s wellbeing. The results of this study have indicated that patients treated with the CT reported higher values of HRQoL assessed with SF-36 but also in SOC at follow-up. Vulnerability factors such as an insecure attachment pattern, a low SOC and dysfunctional coping have interfered with the outcome of treatment in the present study and may at least to some extent explain the drop out of 7 patients out of 20 from the therapy [44,46,47]. Subgrouping in MPI and assessment of SOC and attachment pattern in combination with a patient centered approach may facilitate the choice of treatment and might also predict the outcome. The problem of drop out and lack of compliance is a common occurrence in most rehabilitation programs [48,49] and therefore a more individualized treatment is warranted [1]. A patient centered, cognitive approach has hereby proven to be of value [13,18]. Patients with a high level of burnout symptoms often have difficulties following a rehabilitation program where active participation is anticipated. In the present study high scores of the Pines’ burnout measure were correlated with poor outcome (Figure 5C).

Conclusion

An individual patient-centered treatment in combination with CT was found to be beneficial in this group of patients with chronic pain and psychiatric co-morbidity. Explorative modellings in MVDA indicated that the outcome of treatment may differ according to individual vulnerability and severity of burnout, depression and pain interference. The analyses have also entailed a new hypothesis that patients with chronic pain and a preoccupied attachment pattern might have a poor outcome while patients with fearful attachment had an improved prognosis if they were treated with cognitive therapy.

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Authors Contributions

BP was responsible for treatment and collected all data in the clinical setting. The authors BP, CM, PA, AJS contributed to the conception and design of the work and interpretation of data. JG has as an expert of MVDA together with BP performed these analyses in SIMCA-P + v13.0. All authors have agreed to the submission.

Competing Interests

There are no competing interests for any of the authors.

Data Sharing Statement

All data is presented in the manuscript and in supplemental information.

Bibliography


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